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ORIGINAL PAPER

Choroidal thickness in relation to sex, age, refractive error, and axial length in healthy Turkish subjects

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Abstract The aim of this study was to investigate the association between choroidal thickness (CT) and sex, age, refractive error (RE), and axial length in healthy subjects. This is a study of 154 eyes in 154 healthy subjects. CT measurements were performed by the same experienced technician using a spectral domain optical coherence tomography device. CT was measured perpendicularly from the outer edge of the retinal pigment epithelium to the choroid–sclera boundary at the fovea and at six more points which are located at, respectively, 500 μm nasal to the fovea, 1,000 μm nasal to the fovea, and 1,500 μm nasal to the fovea, 500 μm temporal to the fovea, 1,000 μm temporal to the fovea, and 1,500 μm temporal to the fovea. The RE was measured by autorefractometry, and the axial length was measured by interferometry. Statistical analysis was performed to evaluate CT at each location, and to the correlations of CT with sex, age, RE, and axial length. The mean subfoveal CT was 265.86 ± 60.32 μm, the mean age was 49.01 ± 19.19 years, the mean RE was −0.17 ± 1.20 diopters (D), and the mean axial length was 23.39 ± 0.76 mm. CT profile indicated that the choroid was thicker at the fovea than at temporal and nasal locations. Univariable linear regression analysis showed that subfoveal CT decreased 3.14 μm for each year of age and decreased 79.33 μm for each mm of axial length ($P = 0.000$, $R^2 = 0.249$; $P = 0.000$, $R^2 = 0.487$, respectively). In a similar analysis, subfoveal CT was found to decrease by 50.24 μm/D myopia-shifted change in refraction ($P = 0.000$, $R^2 = 0.201$). The subfoveal choroid was 99.16 μm (39.22 %) thicker in men than women when adjusting for age and axial length ($P = 0.000$, $R^2 = 0.249$). CT decreases with increasing myopia, age, and axial length. Men had thicker choroid than women, and CT varies depending on location.

Keywords Age · Axial length · Choroidal thickness · Refractive error · Sex

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Introduction

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].

A recently developed technique known as enhanced depth imaging optical coherence tomography (EDI–OCT) enables in vivo cross-sectional imaging of the choroid [2].

It is little known about the role of choroidal layers behind the choriocapillaris, which appear to account for most of the variations in total choroidal thickness (CT). Hyperopia is associated with a thick choroid and myopia with a thin choroid [1, 3]. Central serous chorioretinopathy (CSC) is associated with a thicker than average choroid, while age-related macular degeneration (ARMD) is associated with a thin choroid [4, 5]. The thicker choroid reported in patients with CSC has been linked to hyperpermeability and increased hydrostatic pressure in the choroidal circulation which may be a central part of the pathogenesis of the disease [4]. Choroidal thinning due to increased axial length and age may be likely to degenerative changes observed in high myopia [3]. Gender is a risk factor in all the aforementioned conditions. CSC is more common in men than in women, while myopia and ARMD are more common in women [6–11].

Recent studies in a healthy population report a range of CT from 270 to 350 μm. A negative correlation between CT and age was previously reported [12–15]. Choroidal thinning is prominent in highly myopic eyes, and refractive error (RE) affects CT [16].

Ozdogan Erkul et al. [17] reported the association between subfoveal CT and age and RE in 72 healthy Turkish patients. However, in this study, the effects of sex and axial length of the CT were not evaluated.

In the present study, we therefore investigated the association between CT and sex, age, RE, and axial length in healthy Turkish subjects.

Subjects and methods

Subjects

One hundred fifty-four eyes of 154 healthy subjects were included in the study. The eligibility criteria for eyes were considered healthy, which were examined by funduscopy and OCT. Only one eye per subject was randomly selected for measurements. Patients were excluded if they had a history of ocular surface disorder, previous ocular surgery, or ocular injury or if they had a history of any chronic drug use including analgesics, sildenafil, decongestants, and antihistamines. High myopic and hyperopic RE greater than −6.0 or +6.0 diopters (D) were also excluded from this study. Participants who were smokers with migraine, epilepsy, arterial hypertension, pregnant, and breast-feeding women were excluded. All the participants were selected randomly. This study was conducted in accordance with the Declaration of Helsinki, and informed consent was obtained from each subject.

Measurement of RE and axial length

Objective refraction was measured using an autorefractometer (Nikon NRK 8000; Inc., Tokyo, Japan) 20 min after instillation of cyclopentolate 1 % and tropicamide 1 %. The spherical equivalent RE values were calculated as the sum of the sphere plus half the cylindrical power. Axial length was measured using interferometry (IOL-Master; Carl Zeiss Meditec, Dublin, CA). All measurements were repeated three times. The average values were used in the analysis.

Image acquisition

All subjects were imaged by the same experienced specialist (MOZ) through dilated pupils using a spectral domain (SD)-OCT device ($\lambda = 840$ nm, 27,000 A-scans/s, and 5 μm axial resolution) and 3D OCT-2000 (Topcon Corporation, Tokyo, Japan). The protocol of the enhanced choroidal mode cross-scan was performed centering on the fovea. This protocol consisted of 6-mm cross lines with 1,024 A-scans/B-scans and overlapping 4 B-scans per image, and direct B-scan observation was available. After the B-scan, scale was adjusted to 1:1, approximately doubling the size of imaging, the observer determined CT perpendicular from the outer edge of the hyperreflective retinal pigment epithelium to the inner sclera, using the caliper tools of the software. Low-quality scans (image quality under 70 according to the software of OCT device) were not included. CT measurements in horizontal sections were evaluated for using the manual segmentation method (Fig. 1). Two masked observers measured the CT. The average value of CT was used for analysis.

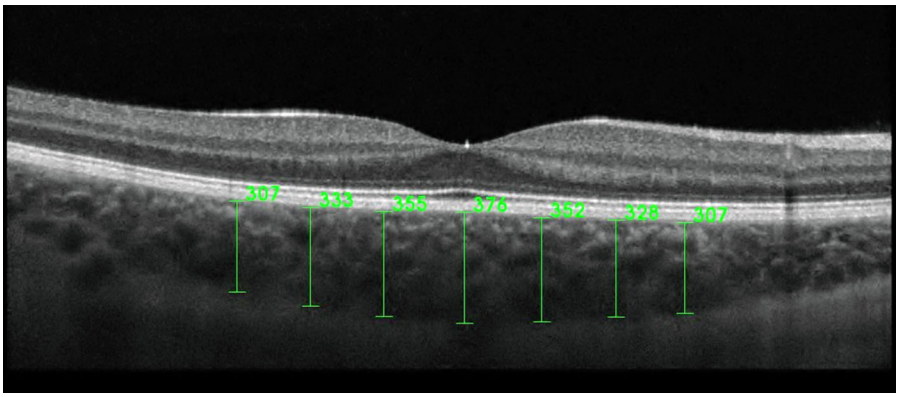

Fig. 1 The choroidal thickness was measured at 500 μm intervals up to 1,500 μm temporal and nasal to the fovea (*left* temporal, *right* nasal)

Table 1 A summary of the study population

	Total	Male	Female	*P* value
n	154 (100)	68 (44.15)	86 (55.85)	
Age (years)	49.01 ± 19.19	46.57 ± 17.92	50.94 ± 20.03	0.161
Refractive error (D)	−0.66 ± 0.89	−0.76 ± 0.85	−0.58 ± 0.92	0.215
Axial length (mm)	23.39 ± 0.76	23.35 ± 0.70	23.42 ± 0.80	0.559
Subfoveal CT (μm)	265.86 ± 60.32	282.38 ± 66.21	252.80 ± 51.99	0.002*
Overall CT (μm)	255.70 ± 56.51	268.49 ± 60.58	245.59 ± 51.18	0.012*

Data are presented as mean ± SD or *n* (%)

CT choroidal thickness

* Statistically significant

Statistical analysis

The data were analyzed using a paired *t* test to compare thickness at different points and by univariable and multiple stepwise linear regression analysis using a statistical software package (version 11.6, SPSS, Inc., Chicago, IL, USA). A *P* value of <0.05 was considered statistically significant.

Results

Data analysis included 154 eyes from 154 subjects (Table 1): sixty-eight male and 86 female having a mean age of 49.01 ± 19.19 years (range 16–87 years). The mean RE was −0.17 ± 1.20 D (range −2.75 to 2.50 D), and mean axial length was 23.39 ± 0.76 mm (range 21.40–25.90 mm).

Mean subfoveal CT was 265.86 ± 60.32 μm (range 135–404 μm), and the mean overall CT was 246.05 ± 59.12 μm (range 105–410 μm). Figure 2 shows the geographical distribution of CT. CT profile indicated that the choroid was thicker at the fovea than at temporal and nasal locations. The mean CT at each location is shown in Table 2.

The subfoveal choroid was 99.16 μm (39.22 %) thicker in men than women when adjusting for age and axial length ($P = 0.000$, $R^2 = 0.249$). Age, RE, and axial length were significantly correlated with mean subfoveal and mean overall CT with univariable linear regression analysis (Table 3). Table 4 summarizes the results of multiple linear regression analysis of subfoveal CT. Univariable linear regression analysis showed that subfoveal CT decreased 3.14 μm for each year of age (Fig. 3) and decreased 79.33 μm for each mm of axial length (Fig. 4; $P = 0.000$, $R^2 = 0.249$; $P = 0.000$, $R^2 = 0.487$, respectively). In a similar analysis, subfoveal CT was found to decrease by 50.24 μm/D myopia-shifted change in refraction ($P = 0.000$, $R^2 = 0.201$; Fig. 5).

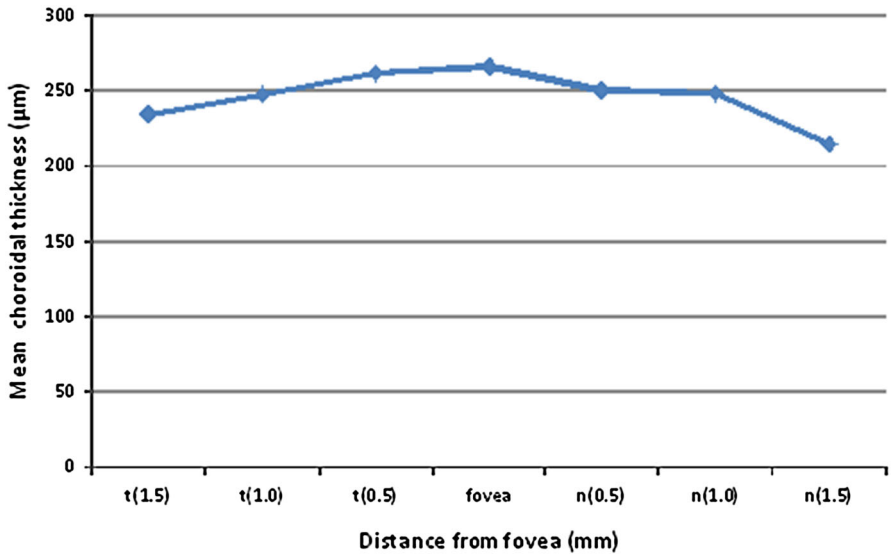

Fig. 2 Mean choroidal thickness at each of seven locations. *t* temporal, *n* nasal

Table 2 Mean choroidal thickness profile in 500 µm intervals

Location from fovea (mm)	Mean CT (µm)	Difference subfoveal CT (µm)	*P* value
Temporal (1.5)	234.34	31.52	0.000*
Temporal (1)	247.50	18.36	0.072
Temporal (0.5)	261.62	4.24	0.995
Fovea	265.86		
Nasal (0.5)	250.23	15.63	0.198
Nasal (1)	248.27	17.59	0.098
Nasal (1.5)	214.55	51.31	0.000*

CT choroidal thickness

* Statistically significant

Table 4 Multiple linear regression analysis for subfoveal choroidal thickness by age, refractive error, and axial length

Factors	Coefficients	Beta	*P* value
Constant	1,279.070		0.000*
Age (years)	−0.945	−0.301	0.000*
Refractive error (D)	12.624	0.251	0.000*
Axial length (mm)	−41.234	−0.520	0.000*

* Statistically significant, $R^2 = 0.625$

Discussion

The choroid is a highly vascular tissue, necessitating in vivo imaging to accurately determine its true structure and thickness. Until recently, information regarding CT in normal eyes was based primarily on histologic results, which do not necessarily reflect the true measurements of this dynamic tissue [18]. Based on histologic study, CT ranges from 170 to 220 µm [19].

Adequate visualization of the choroid using OCT has not been possible until recently. However, new technological development in OCT software gives the opportunity to evaluate the choroidal structure. Adequate measurement of CT using SD-OCT is possible by the introduction of the EDI technique and by averaging several B-scan signals from the same

Table 3 Univariable linear regression analysis for choroidal thickness by age, refractive error, and axial length

Factors	Subfoveal choroidal thickness			Overall choroidal thickness		
	Coefficients	R^2	*P* value	Coefficients	R^2	*P* value
Age (years)	−1.569	0.249	0.000*	−1.789	0.369	0.000*
Refractive error (D)	22.510	0.201	0.000*	19.843	0.178	0.000*
Axial length (mm)	−55.379	0.487	0.000*	−50.232	0.456	0.000*

* Statistically significant

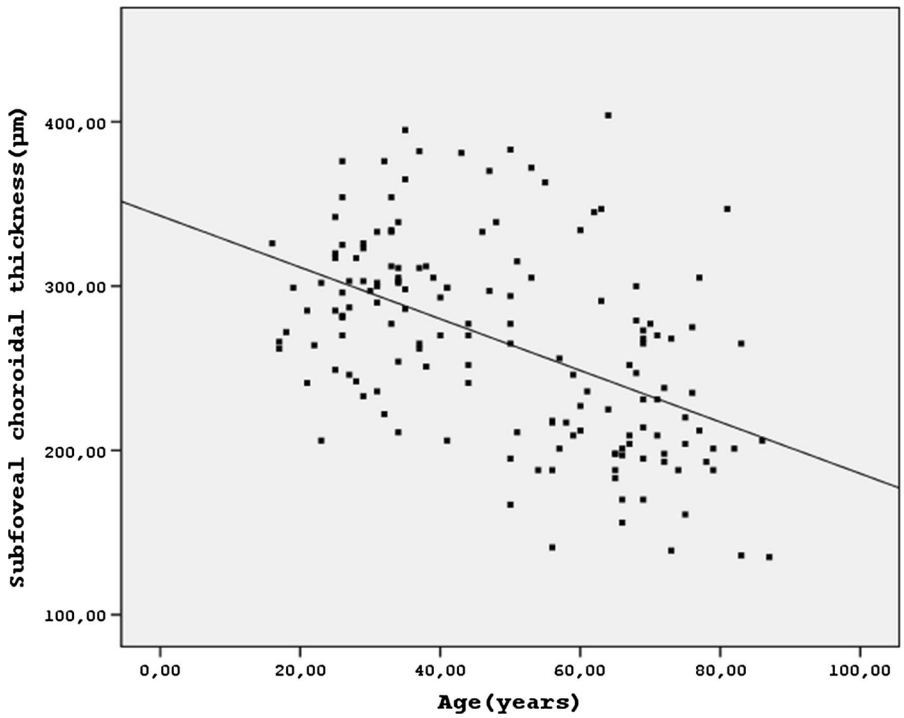

Fig. 3 Scatterplot of age and subfoveal choroidal thickness of all subjects shows a significant negative correlation in linear regression analysis ($P = 0.000$, $y = -1.569x + 342.779$, $R^2 = 0.249$)

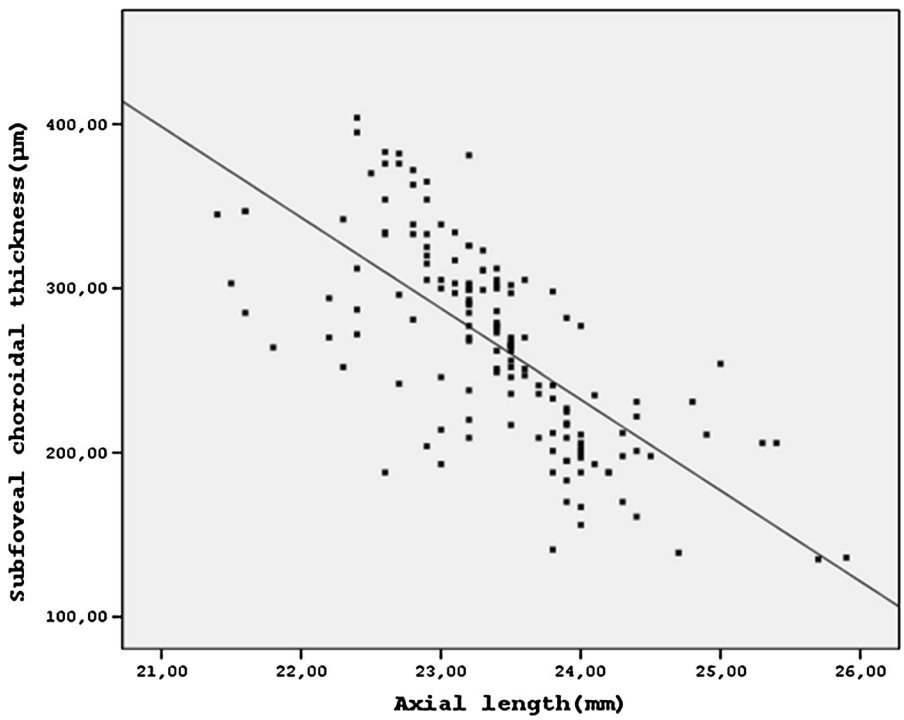

Fig. 4 Scatterplot of axial length and subfoveal choroidal thickness of all subjects shows a significant negative correlation in linear regression analysis ($P = 0.000$, $y = -55.379x + 1{,}561.454$, $R^2 = 0.487$)

position. Using a long wavelength (1,060 nm), light source is another approach to visualize the posterior choroid and sclera [2, 12–14].

In the present study, mean subfoveal CT was found to be 265.86 μm, which was thinner than reported previously. Shin et al. [20] reported mean CT of

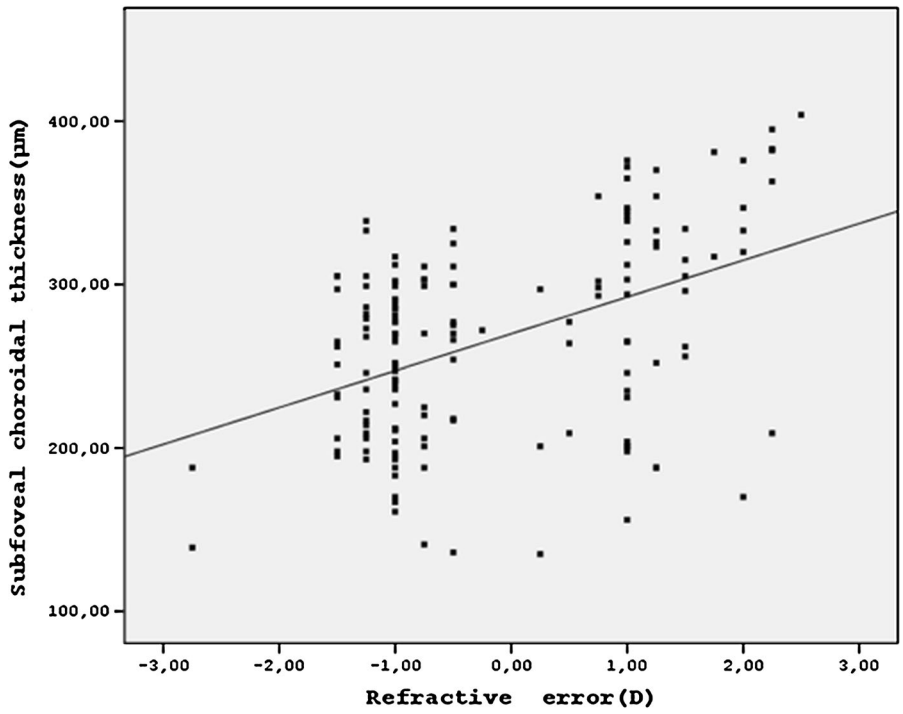

Fig. 5 Scatterplot of refractive error and subfoveal choroidal thickness of all subjects shows a significant positive correlation in linear regression analysis ($P = 0.000$, $y = 22.510x + 269.810$, $R^2 = 0.201$)

270.82 µm, Manjunath et al. [14] reported 272 µm, Margolis and Spaide [13] reported 287 µm, Ikuno et al. [12] reported 354 µm, Li et al. [21] reported 342 µm, Karaca et al. [22] (Turkish) reported 315.5 µm, and Ozdogan Erkul et al. [17] (Turkish) reported 280.23 µm. Different instruments may result in small differences for CT also b/o difference in segmentation.

Previous studies showed that the choroid was thicker at the macula than nasally or temporally probably because of high metabolic demand [12–14, 20]. Our results of CT profile indicated that the choroid was thicker at the fovea than at temporal and nasal locations. This pattern was consistent with the results of previous studies of CT in normal eyes [2, 12–14, 20].

In the present study, we found that men had a thicker (39.22 %) choroid compared with women after adjusting for axial length and age. The difference of 99.16 µm in our study was higher to the 62.2 µm (18 %) found in a previous study of the 93 healthy volunteers [21]. Difference in hormonal exposure is a likely biological explanation. One study reported estrogen receptor in human choroid, and it has been indicated that sex and hormonal status may influence choroidal blood flow [23–25]. Ulaş et al. [26] reported that CT decreased significantly in the mid-luteal phase of the menstrual cycle in young healthy women. This information highlights one of the limitations of our study. A recent study reported that smoking caused acute, significant increase in CT that returned to baseline level after 1 h [27]. Another study stated that phosphodiesterase-5 inhibitors increased CT [28]. CT measurements change according to systemic variations.

With aging, physiological functions of the choroid decrease, and histological evaluation shows decrement in the vascular density, overall luminal area, and diameter of the choriocapillary vessels [29, 30]. A previous histologic study showed that CT decreases 1.1 µm/year [29]. A recent in vivo study showed CT reduction 1.56 µm/year [13], and interestingly, we found further decrease (3.14 µm reduction) in CT for each year of age using univariable linear regression analysis. Similarly, another study reported that CT decreases 3.14 µm/year within the Turkish population [17].

In highly myopic eyes, the choroid is three times thinner than that in normal eyes, and RE has great impact on choroidal thinning in terms of regression [12, 16, 17, 31]. Previous studies showed 9.3–13.6 µm increment of subfoveal CT/D of refractive change [12, 20]. We found a correlation between subfoveal CT and RE in univariable linear regression analysis

(50.24 μm/D). Interestingly, Ozdogan Erkul et al. [17] did not find significant correlation between RE and CT within the Turkish population.

We also found that the subfoveal CT decreased by 79.33 μm/mm axial length in univariable linear regression analysis (age range 16–87 years). A previous study showed that CT decreases 58.2 μm/mm axial length (age range 19–33 years) [21]. Another study reported that CT decreases 22.4 μm/mm axial length (age range 23–88 years) [12]. Our result is higher than in previous studies.

One limitation of our study is that the distributions of age, RE, and axial length did not exactly reflect those of a normal population because the participants were a small group of subjects. It is also difficult to directly compare the present results with those of other studies due to the difference of participant profiles.

In conclusion, this study demonstrated that CT decreases with increasing myopia, age, and axial length. Men had thicker choroid than women, and CT varies depending on location. Further research will be needed to investigate various ocular factors or diseases of the posterior pole and their effects on CT.

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