Original Article

Choroidal Thickness Profile in Normal Iranian Eyes with Different Refractive Status by Spectral-Domain Optical Coherence Tomography

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Abstract

Purpose: To investigate the choroidal thickness and its association with age, gender, spherical equivalent (SE), and axial length (AL) in a sample of Iranian population with different refractive status using spectral-domain optical coherence tomography (SD-OCT).

Methods: In a cross-sectional study, a total of 469 right eyes of 469 healthy subjects comprising 194 (41.4%) males and 275 (58.6%) females were examined. The mean age was 32.76 ± 15.77 years (range, 4-60 years). All subjects were divided into different groups according to their refractive status, age, and AL. The choroidal thickness was evaluated through enhanced-depth imaging (EDI) modality at subfoveal (Sf), 1, and 3 mm nasal (N1 and N3, respectively), temporal (T1 and T3, respectively), superior (S1 and S3, respectively), and inferior (I1 and I3, respectively) to the foveal center.

Results: In the whole population, the mean subfoveal choroidal thickness (SfChT) was 329.83 ± 70.33 μm, and the choroid was thickest at S1 (342.04 ± 71.28 μm) and thinnest at N3 (209.00 ± 66.0 μm). Our data indicated a significant difference in the mean choroidal thickness across all points in different age groups ($P < 0.0001$). For emmetropic, myopic, and hyperopic subjects, mean SfChT values were 346.64 ± 59.63, 319.66 ± 73.17, and 364.00 ± 74.54 μm, respectively. Linear regression estimated that SfChT decreased about 12.8 and 8.71 μm for every 10 years of aging and each diopter increasing in myopia, respectively. Additionally, the SfChT decreased as 13.48 μm per mm increase in AL.

Conclusions: The mean SfChT of a sample of Iranian emmetropic subjects was 346.64 ± 59.63 μm. The choroidal thickness has a decreasing trend with increasing age, and the choroid is thinner in myopes and thicker in hyperopes compared with emmetropic subjects. In the whole participants, the thickest and thinnest points were S1 and N3, respectively.

Keywords: Choroidal thickness, Enhanced-depth imaging, Iran, Optical coherence tomography

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Introduction

The choroid is a highly vascular tissue that is located between the retina and the sclera and plays an essential role in some functional activities of the visual system including nutrients and oxygen supply to the sensory and pigmentary portion of the retina, regulating retinal temperature, etc.[1]

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The advent of optical coherence tomography (OCT) technique was one of the main advancements in the area of medical instrumentation and was known as a non-invasive method for examination of the posterior segment.[2-4]

Spectral-domain OCT (SD-OCT) devices (wavelength of 840 nm) have been playing an important role in direct observation of the choroidal profile *in vivo* accompanied by high-resolution imaging which enabled us to visualize and measure the choroidal thickness all over the tissue. Prior studies have shown that the repeatability of thickness measurements by SD-OCT devices was highly correlated in evaluating retinal profile.[5,6] The specialized modality with commercially available SD-OCT devices for imaging the realtime choroidal structure referred to as enhanced-depth imaging OCT (EDI-OCT).[4] In this specialized imaging technique, the zero delay line moves more posteriorly near the sclera, hence the deeper tissues like choroid become visible in more detail.[4]

One of the most popular ideas in ophthalmology literature is the idea that the choroidal thickness might be an indicator of retinal health, and its abnormal alterations could be considered a clinical sign of detrimental pathologies to the visual system. Of these pathologies affecting the choroidal thickness, central serous chorioretinopathy,[3] age-related macular degeneration,[7] and diabetic retinopathy[8] are most known. As the choroidal thickness alteration is an effective parameter reflecting the development of the aforementioned pathologies, investigation of the choroidal thickness provides beneficial information for practitioners.

A common strategy used to study choroidal thickness is to investigate the localized topographic variations of choroidal profile,[9,10] and it might be beneficial due to different metabolic requirements of the retina in various regions in addition to anatomic and vascular properties of the choroid.[11] However, the majority of prior research has studied the subfoveal choroidal thickness (SfChT),[12-16] and few studies investigated wide areas of the choroidal structure.[17] Prior studies have shown that the choroidal thickness may vary by age,[18-21] axial length (AL),[10,22] refractive status,[23,24] and ethnicity.[25,26] Therefore, there are growing appeals for standardization of normal choroidal thickness at different age groups in each nationality.[27-32] Entezari *et al*.[33] measured for the first time normal choroidal thickness profile in Iranian adults at different horizontal locations. As far as we know, obtaining information regarding choroidal thickness in different age groups, especially children and teenagers, is essential to conceive normal development of the eye in these ages, and it is an applicable test for the detection of posterior pole diseases. To the best of our knowledge, there has been less previous evidence in Iranian subjects which include children and adult age ranges.[33]

The overall goal of this cross-sectional study was to characterize the distribution of normal choroidal thickness profile at different horizontal and vertical locations in a large sample of healthy Iranian children and adult subjects in relation to age, sex, spherical equivalent (SE), and AL using EDI-OCT. To illuminate this uncharted area, we examined populations with a wide age range from 4 to 60 years old. Also, we evaluated the relationship between the choroidal thickness with age, AL, and sex.

Methods

This cross-sectional comparative, non-interventional study of healthy Iranian subjects 4-60 years of age was conducted at Basir Ophthalmology Clinic, Tehran, Iran. The study adhered to the tenets of the World Medical Association's Declaration of Helsinki. The Ethics Committee of Mashhad University of Medical Sciences approved the design of the study. After explaining the purpose of the study, written consent was obtained from all subjects and from the parents or legal guardians of children under age 7 participating in the study. All participants were in good health as reported by themselves. Subjects were excluded if they did not fulfill the consent form to participate in this study. All examinations were performed in one session. All subjects had come for their annual ophthalmic checkup from January 2018 to July 2018. A total of 534 healthy Iranian subjects (534 eyes) were recruited in the study.

Thorough demographic information was obtained during a routine ophthalmic checkup. The subjects were included if they had no ocular disorder except refractive error less than -6.00 D of myopic SE (SE was defined as the spherical power in addition to one-half of the cylinder power) and +5.00 D of hyperopic SE without any significant astigmatism (≤1.00 D) and normal funduscopic appearance. The subjects were excluded if they had any previous ocular surgery, strabismus, amblyopia, glaucoma, retinal disorders, or abnormal optic nerve cupping. Additionally, pregnant women, smokers, diabetic, hypertensive, migraine, and renal failure patients were excluded.

Ophthalmic evaluation

A comprehensive ophthalmic examination was performed by an experienced ophthalmologist in all subjects. Only the data of the right eye of each participant was included for statistical analysis.

Unaided visual acuity (UVA) and best corrected visual acuity (BCVA) of each eye were recorded using a Snellen tumbling E-chart at a distance of 6 m. Objective refraction data was achieved first using a Topcon RM-800 auto-refractometer (Topcon Medical Systems, Inc., Oakland, NJ, USA), and for confirmation, manual objective refraction was performed by Heine β-200 retinoscope (HEINE Optotechnik, Herrsching, Germany). Afterward, subjective refraction carried out by an experienced optometrist (M.H.). AL and keratometry of the subjects were measured by a non-contact partial coherence interferometry device (IOL-master 500; Carl Zeiss Meditec AG, Jena, Germany). BCVA of all subjects considered 20/25 and better because BCVA of less than 20/25 met the cutoff for amblyopia suspect. UVA based on the decimal scale

of Snellen visual acuity chart was converted to logMAR for the statistical analysis.

All enrolled participants were classified into three categories according to their SE of refractive error on subjective refraction testing: those with +0.75 D to +5.00 D were assigned to the hyperopia category, those with +0.50 D to -0.25 D were assigned to the emmetropia category, and those with -0.50 D to -6.00 D were assigned to the myopia category. For the purpose of the analyses, each hyperopia and myopia groups were allocated into two subgroups: low hyperopia as SE lower than +2.00 D, moderate hyperopia as SE between +2.25 D to +5.00 D,[34] low myopia as SE lower than -3.00 D, and moderate myopia as SE between -3.25 D to -6.00 D.[35] Based on AL, subjects were classified as short (AL <22.5 mm), medium (22.51-25.5 mm), and long eyes (>25.51 mm).[36]

Enhanced depth imaging measurements

At the final phase of the examinations, choroidal thickness was measured with the EDI mode of an SD-OCT device (Spectralis HRA-OCT; software version 5.2.0.3; wavelength: 870 nm; Heidelberg Engineering, Heidelberg, Germany). All images were recorded by an experienced examiner and performed at 3 PM-6 PM to avoid diurnal variation in choroidal thickness. In the EDI mode, the device moves closer to the eye than the conventional imaging modality to display the choroidal tissue in more detail.[4] Following user manual guidelines of the Spectralis, prior to capturing the images, keratometry and SE of refraction of the subject were entered into the software of the OCT device to estimate optical magnification. The EDI mode of the device was selected, and the choroidal thickness was defined as the perpendicular distance between the outer limit of the Bruch's membrane/retinal pigment epithelium complex (BM/RPE complex) to the hyperreflective line of the choroidoscleral interface (CSI). As suggested by the manufacturer, the choroidal scans with quality index (QI) value more than 25 dB were included for analyses.[37] Multiple images comprising 100 average B-scans [with the function of automatic real-time (ART) eye tracking on the instrument] were recorded, and those with the best definition of CSI and centered on the fovea were selected for the analysis. For each EDI recording, a series of four lines of four 8 mm x 8 mm radial scans centered on the fovea were captured.

Additionally, using grayscale imaging modality and increasing the contrast of images, we made the boundaries clearer to facilitate the measurements. The line of BM/RPE complex was automatically identified by the software itself, whereas the hyper-reflective line of CSI was outlined manually by fitting inner-limiting membrane (ILM) line to this border [Figure 1]. The reason for manual calibration of the outer border of the choroid was owing to inaccessibility to a commercially available software to automatically identify CSI. When the outer border of the choroid was unclear, the outer boundary of the choroidal vascular area was outlined by a smooth line to separate the sclera, and the choroidal thickness would then be measured up to that limit.[38]

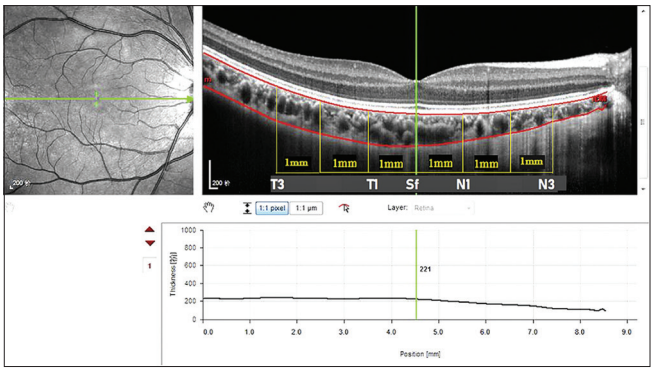

Figure 1: The thickness profile of line scan and manually calibration of the posterior border of the choroid with moving inner-limiting membrane (ILM) line to the choroidoscleral interface (CSI)

The choroidal thickness was measured manually through the scale embedded into the software at the subfoveal (Sf) point and points located at 1 and 3 mm nasally (N1 and N3), temporally (T1 and T3), superiorly (S1 and S3), and inferiorly (I1 and I3) relative to the foveal center (the deepest point in the central foveal area). All measurements were analyzed by an experienced optometrist who was masked to the ocular findings of the participants by using the Heidelberg Eye Explorer software (v. 1.9.10.0; Heidelberg Engineering Co.).

Statistical analysis

Data were analyzed with SPSS version 23 (IBM Inc., Chicago, Illinois, USA). The normality of the data was confirmed using the Kolmogorov-Smirnov test; then parametric tests were applied accordingly. The one-way analysis of variance (ANOVA) with Tukey adjustment for multiple comparisons was used to determine the mean of the variable in different groups. Regional variations in choroidal thickness were examined using a repeated measure ANOVA. The Independent Samples *t*-test was used to compare the means of parameters between the male and female groups. Pearson correlation test was employed to assess the correlation between SfChT and age, AL, and SE. Linear regression analysis was used to evaluate the independent variables of age, SE, and AL with respect to the dependent variable of SfChT as well as the independent variable of age with respect to the dependent variable of average total choroidal thickness. *P* values less than 0.05 were considered significant.

Results

Of 534 scans, 65 images were later excluded: 25 images did not have optimal quality (most of them were because of decentered scans as a result of unstable fixation in pediatric age group), 19 scans did not have a detectable limit of posterior border of the choroid (CSI), and 21 subjects were missed out due to the fact that participants left the exams for private concerns. The final analyses included 469 cases (469 eyes), 275 (58.6%) females and 194 (41.4%) males, with a mean age of 32.76 ± 15.76. Considering the age group, 45 cases (9.6%), 67 cases (14.3%), 113 cases (24.1%),

90 cases (19.2%), 70 cases (14.9%), and 84 cases (17.9%) were assigned to the age groups ≤10, 11 to 20, 21 to 30, 31 to 40, 41 to 50, and older than 50 years old, respectively. Considering SE, 152 cases (32.41%), 190 cases (40.51%), and 127 cases (27.08%) were assigned to the emmetropia, myopia, and hyperopia categories, respectively. According to the classification of subjects based on AL, 80 cases (17.1%), 373 cases (79.5%), and 16 cases (3.4%) had short, medium, and long eyes. The general demographic information of subjects is displayed in Table 1.

Choroidal thickness findings and horizontal and vertical local variations

In the total population with the mean SE of refractive error of -0.38 ± 1.84 D, the SfChT was 329.83 ± 70.33 µm (range, 120 to 553), and the local thicknesses across the choroid were 313.20 ± 70.61 and 209.00 ± 66.00 µm at N1 and N3, respectively, and 323.74 ± 70.27 and 289.23 ± 66.34 µm at T1 and T3, respectively. Also, choroidal thickness measurements at vertical locations were recorded. Choroidal thicknesses were 342.04 ± 71.28 and 314.14 ± 66.10 µm at S1 and S3, respectively, and 334.74 ± 75.31 and 297.76 ± 69.01 µm at I1 and I3, respectively. There was a statistically significant difference between different regions ($P < 0.05$). The choroid was thickest at S1 and thinnest at N3 for the total population [Figure 2].

The relationships between choroidal thickness and gender, age, spherical equivalent, and axial length

Mean SfChT was 327.38 ± 73.18 and 331.56 ± 68.31 µm for male and female subjects, respectively. There was not any statistically significant difference between genders at different locations ($P > 0.05$) except T3 point ($P = 0.02$). Choroidal thickness at T3 point in females was 14.41 µm thicker than in males (295.19 ± 66.32 vs 280.78 ± 65.62).

All subjects were classified into 6 age groups. Subjects age ≤10, 11 to 20, 21 to 30, 31 to 40, 41 to 50, and older than 50 years old were categorized as Groups 1, 2, 3, 4, 5, and 6, respectively.

One-way ANOVA showed significant differences in the mean of the choroidal thickness at different locations between all six age groups ($P < 0.0001$). Multiple comparisons using the Tukey test showed statistically significant differences in choroidal thickness at Sf and other locations between Groups 1 and 5 as well as Group 6 ($P < 0.05$), but no significant difference was observed in choroidal thickness at N1, N3, S1, S3, I1, I3, and T1 between Group 1 and other age groups ($P > 0.05$). Also, there was a significant difference in choroidal thickness at T3 between Group 1 and other age groups ($P < 0.05$). There were no statistically significant differences in choroidal thickness at different locations between Groups 2, 3, and 4 ($P > 0.05$). Figure 3 shows the choroidal thickness differences across locations between six age groups.

For emmetropic, myopic, and hyperopic subjects, mean SfChT were 346.64 ± 59.63 µm (range, 207-495 µm), 319.66 ± 73.17 µm (range, 120-499 µm), and 364.00 ± 74.54 µm (range, 172-553 µm), respectively. As shown in Table 2 and Figures 4, 5, in all three categories of refractive status, the thickest and thinnest points were S1 and N3, respectively. Increasing age was associated with significant choroidal thickness reduction in all three groups (for emmetropic, myopic, and hyperopic participants, the negative associations were r = -0.285, $P < 0.0001$; r = -0.212, $P = 0.003$; and r = -0.365, $P < 0.0001$, respectively).

Our results showed that there was no statistically significant difference between low and moderate myopia in choroidal thickness at Sf ($P = 0.396$), N1 and N3 ($P = 0.161$ and 0.583, respectively), T1 and T3 ($P = 0.727$ and 0.525, respectively), S1 and S3 ($P = 0.582$ and 0.987, respectively), as well as I1 and I3 ($P = 0.622$ and 0.801, respectively) for the total population. Also, no statistically significant difference between low and moderate hyperopia in choroidal thickness at Sf ($P = 0.231$), N1 and N3 ($P = 0.262$ and 0.118, respectively), T1 and T3 ($P = 0.529$ and 0.948, respectively), S1 and S3 ($P = 0.453$ and 0.663, respectively), as well as I1 and I3 ($P = 0.790$ and 0.502, respectively) was seen.

To compare choroidal thickness at different points, one-way ANOVA showed significant differences in choroidal thickness at Sf ($P = 0.004$), N1 and N3 ($P = 0.001$ and 0.007, respectively), and T1 and S1 ($P = 0.022$ and 0.012, respectively) as well as I1 and I3 ($P = 0.022$ and 0.007, respectively), but no

Table 1: General characteristics of all 469 subjects

Variables	Mean±SD	Range
Age (years)	32.76±15.77	4-60
SE (diopter)	−0.38±1.84	−6.00-+4.50
UVA (logMAR)	0.29±0.36	0.00-1.40
Mean K (diopter)	43.86±1.48	39.60-48.50
AL (mm)	23.46±1.04	20.14-26.80

SE: Spherical equivalent, UVA: Unaided visual acuity, Mean K: Mean keratometry, AL: Axial length, SD: Standard deviation

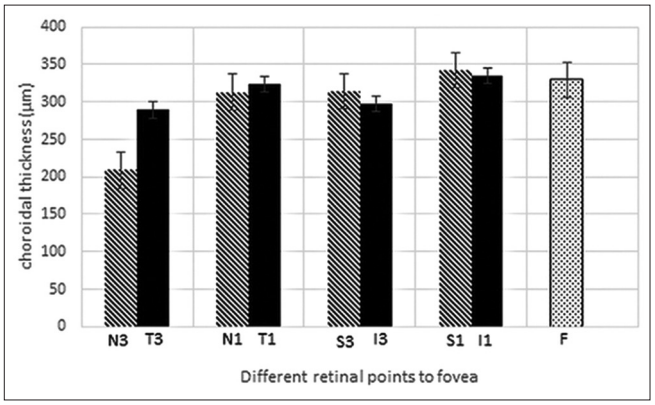

Figure 2: Comparison of horizontal and vertical choroidal thickness profiles. N3: 3 mm nasal to the fovea; S3: 3 mm superior to the fovea; N1: 1 mm nasal to the fovea; S1: 1 mm superior to the fovea; F: Fovea; T1: 1 mm temporal to the fovea; I1: 1 mm inferior to the fovea; T3: 3 mm temporal to the fovea; I3:3 mm inferior to the fovea

Table 2: Comparison of choroidal thickness based on the refractive status of the subjects

Variables	Groups	Mean differences (μm)	95% CI	*P**	*P*[k]
Sf	Emmetropia and myopia	26.98	9.20, 44.75	**0.001**	**0.001**
	Emmetropia and hyperopia	−17.36	−21.07, 41.34	**0.026**	
	Myopia and hyperopia	−44.34	−53.99, 13.45	**0.041**	
N1	Emmetropia and myopia	30.47	12.69, 48.25	**<0.0001**	**<0.0001**
	Emmetropia and hyperopia	−13.22	−20.14, 44.42	**0.009**	
	Myopia and hyperopia	−43.69	−64.42, 13.03	**<0.0001**	
N3	Emmetropia and myopia	23.82	7.10, 40.54	**0.003**	**0.004**
	Emmetropia and hyperopia	−13.63	−22.10, 34.84	**0.004**	
	Myopia and hyperopia	−37.45	−45.06, 10.16	**0.001**	
T1	Emmetropia and myopia	24.59	6.82, 42.37	**0.003**	**0.002**
	Emmetropia and hyperopia	−10.03	−25.34, 44.60	**0.045**	
	Myopia and hyperopia	−34.63	−48.34, 19.10	**0.009**	
T3	Emmetropia and myopia	18.89	2.19, 35.60	**0.022**	**<0.0001**
	Emmetropia and hyperopia	−10.11	−19.43, 50.35	**0.01**	
	Myopia and hyperopia	−29.00	−34.60, 30.60	**0.003**	
S1	Emmetropia and myopia	27.93	9.98, 45.89	**0.001**	**<0.0001**
	Emmetropia and hyperopia	−20.80	−39.37, 49.04	**0.002**	
	Myopia and hyperopia	−48.73	−67.63, 20.19	**0.006**	
S3	Emmetropia and myopia	27.48	10.97, 43.99	**<0.0001**	**<0.0001**
	Emmetropia and hyperopia	−16.72	−18.04, 54.52	**<0.0001**	
	Myopia and hyperopia	−44.20	−58.59, 26.19	**0.006**	
I1	Emmetropia and myopia	28.27	9.29, 47.25	**0.001**	**<0.0001**
	Emmetropia and hyperopia	−8.55	−9.49, 52.42	0.061	
	Myopia and hyperopia	−36.81	−46.81, 23.18	**0.006**	
I3	Emmetropia and myopia	23.64	6.36, 40.92	**0.004**	**<0.0001**
	Emmetropia and hyperopia	−10.2	−18.71, 56.89	0.054	
	Myopia and hyperopia	−33.83	−44.035, 32.37	**0.001**	

*Tukey HSD test, [k]One-way ANOVA. Bold values are significant. A $P<0.05$ was considered statistically significant. Sf: Subfoveal, N: Nasal, T: Temporal, S: Superior, I: Inferior, 1: 1 mm to the fovea, 3: 3 mm to the fovea, CI: Confidence interval, HSD: Highly significant difference, ANOVA: Analysis of variance

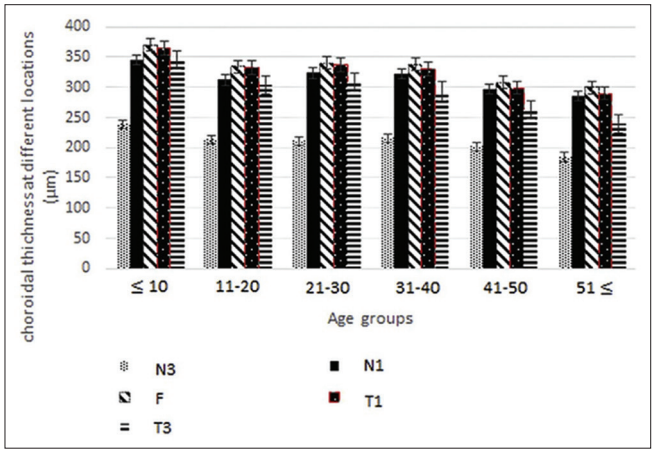

Figure 3: Choroidal thickness at different locations in different age groups

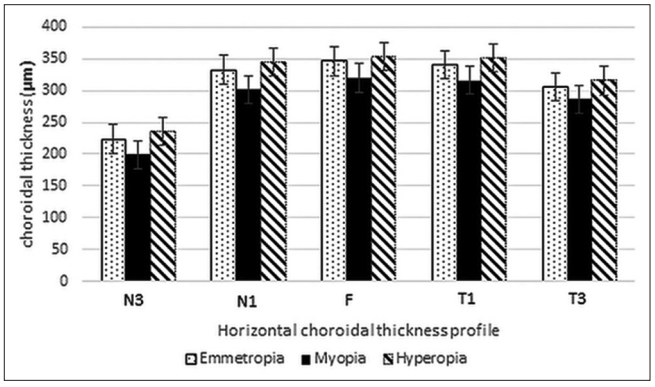

Figure 4: Comparison of choroidal thickness based on refractive error state of the subjects at horizontal locations. N3: 3 mm nasal to the fovea; N1: 1 mm nasal to the fovea; F: Fovea, T1: 1 mm temporal to the fovea; T3: 3 mm temporal to the fovea

statistically significant difference in choroidal thickness at T3 and S3 ($P = 0.090$ and 0.150, respectively) was found between subjects who had short, medium, and long eyes. Multiple comparisons using the Tukey test results are displayed in Table 3.

The association of the SfChT was positive with SE of refractive error (r = 0.147; $P = 0.001$) and negative with AL (r = -0.199; $P < 0.001$) for the total population. In addition, the association of the age and SfChT was negative (r = -0.287; $P < 0.001$) for all subjects.

Average horizontal and vertical choroidal thicknesses in emmetropic subjects were 309.59 ± 54.83 (175.2-445.60) and 343.06 ± 55.55 (213.4-477.40), respectively. For emmetropic participants, total choroidal thickness (average horizontal and vertical choroidal thickness profiles)

Table 3: Comparison of choroidal thickness at different locations based on the axial length (AL)

Variables	Groups	Mean difference (95% CI) (μm)	*P**
Sf	Short and medium eyes	18.17 (−2.01, 38.36)	0.087
	Short and long eyes	60.09 (15.23, 104.94)	**0.005**
	Medium and long eyes	41.92 (0.10, 83.73)	**0.049**
N1	Short and medium eyes	17.03 (−3.17, 37.23)	0.180
	Short and long eyes	70.26 (25.37, 115.16)	**0.001**
	Medium and long eyes	53.23 (11.38, 95.09)	**0.008**
N3	Short and medium eyes	21.32 (2.36, 40.28)	**0.023**
	Short and long eyes	46.54 (4.40, 88.68)	**0.026**
	Medium and long eyes	25.22 (−14.07, 64.51)	0.287
T1	Short and medium eyes	17.10 (−3.14, 37.33)	0.117
	Short and long eyes	48.63 (3.65, 93.60)	**0.030**
	Medium and long eyes	31.53 (−10.40, 73.45)	0.182
T3	Short and medium eyes	12.73 (−6.44, 31.89)	0.263
	Short and long eyes	36.60 (−5.99, 79.19)	0.108
	Medium and long eyes	23.87 (−15.83, 63.58)	0.335
S1	Short and medium eyes	14.14 (−6.36, 34.64)	0.237
	Short and long eyes	56.53 (10.96, 102.09)	**0.010**
	Medium and long eyes	42.39 (−0.09, 84.86)	0.051
S3	Short and medium eyes	8.25 (−10.86, 27.36)	0.568
	Short and long eyes	34.76 (−7.71, 77.24)	0.133
	Medium and long eyes	26.52 (−13.08, 66.11)	0.258
I1	Short and medium eyes	18.96 (−2.67, 40.59)	0.099
	Short and long eyes	61.80 (13.73, 109.88)	**0.007**
	Medium and long eyes	42.84 (−1.98, 87.66)	0.065
I3	Short and medium eyes	15.017 (−4.86, 34.89)	0.187
	Short and long eyes	49.71 (5.55, 93.88)	**0.023**
	Medium and long eyes	34.70 (−6.48, 75.87)	0.118

*Tukey HSD test. Bold values are significant. A $P<0.05$ was considered statistically significant. Sf: Subfoveal, N: Nasal, T: Temporal, S: Superior, I: Inferior, 1: 1 mm to the fovea, 3: 3 mm to the fovea, CI: Confidence interval, HSD: Highly significant difference

was 324.07 ± 52.78 (208.11-458.56). This average horizontal, vertical, and total choroidal thicknesses in each age group are shown in Figure 6.

Correlation analysis and linear regression models

As shown in our results, choroidal thickness at T3 decreased after 10 years old, but choroidal thickness at other locations decreased after 41 years old. Linear regression showed that SfChT decreased by about 12.8 μm every 10 years. Regression formula is SfChT = 371.84-1.28 × age.

Linear regression showed that the average total choroidal thickness decreased about 14 μm every 10 years [Figure 7]. Regression formula is the average total choroidal thickness = 351.42-1.39 × age.

Linear regression showed that SfChT decreased about 8.71 μm for each diopter increasing in myopia. Regression formula is SfChT = 337.39 + 8.71 × myopia. Also, linear regression showed that SfChT increased about 10.25 μm for each diopter increasing in hyperopia. Regression formula is: SfChT = 357.81 + 10.25 × hyperopia.

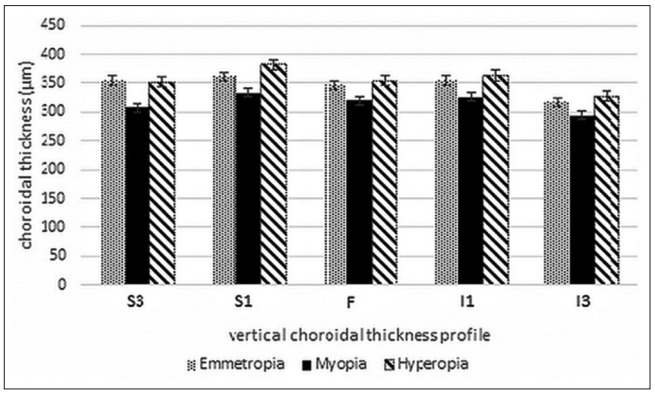

Figure 5: Comparison of choroidal thickness based on refractive error state of the subjects at vertical locations. S3: 3 mm superior to the fovea; S1: 1 mm superior to the fovea; F: Fovea; I1: 1 mm inferior to the fovea; I3: 3 mm inferior to the fovea

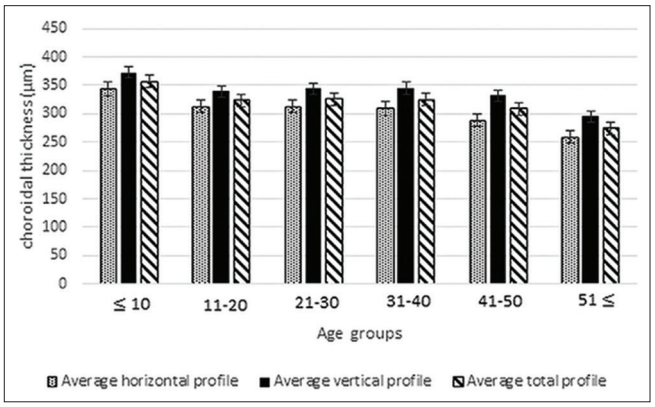

Figure 6: Average horizontal, vertical, and total choroidal thicknesses in different age groups

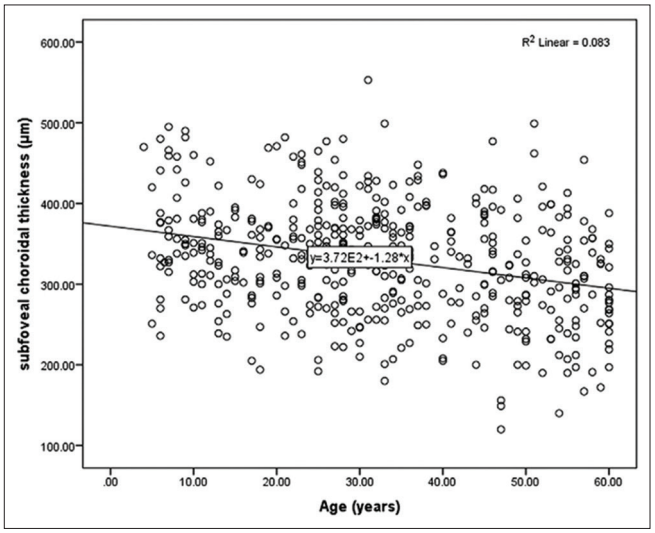

Figure 7: Association between subfoveal choroidal thickness (SfChT) and age in the total participants

Our results showed that for every 1 mm increase in AL, the SfChT decreased as 13.48 μm in the total population. The regression formula is SfChT = 645.95-13.48 × AL.

Table 4 shows the results of multiple regression analysis. Age and SE were associated with SfChT ($P < 0.0001$), but the effect of AL on SfChT thickness was approach significance level ($P = 0.06$). The multiple regression models predicted are as follows: SfChT = 548.27-1.45 × age + 5.91 × SE-7.20 × AL.

Discussion

The choroid primarily is a pigmented vascular tissue located between retina and sclera and acts as a supplier of nutrients and oxygen to the sensory retina.[39] The current cross-sectional study utilized EDI imaging mode of an SD-OCT device to record the thickness profile of the choroid at different horizontal and vertical locations. We evaluated the effect of different parameters on choroidal thickness at various locations in healthy Iranian subjects with different refractive status. Our results showed that in total participants with the mean age of 32.76 ± 15.77 (range, 4-60 years), SfChT was 329.83 ± 70.33 mm. For emmetropic subjects, mean SfChT was 346.64 ± 59.63 mm (range, 207-495 mm), and the thickest and thinnest points were S1 and N3, respectively. Our findings revealed that SfChT was negatively associated with age (r = -0.285; $P < 0.0001$) by about 20 percent. Regression analyses estimated that SfChT and total choroidal thickness in emmetropic subjects had a decreasing trend of 12.8 mm and 14 µm for every 10 years, respectively.

The effect of aging on choroidal parameters has been well documented in prior cross-sectional studies indicating that choroidal thickness undergoes changes with increasing age.

Table 4: Results of multiple regression analysis (Dependent variable: Subfoveal choroidal thickness)

Independent variable	β	Standard error	P
	548.27	88.54	**<0.0001**
Age (years)	−1.45	0.2	**<0.0001**
SE (diopter)	5.91	2.23	**0.008**
AL (mm)	−7.20	3.83	0.061

Bold values are significant. A $P<0.05$ was considered statistically significant. SE: Spherical equivalent, AL: Axial length

Consistent with previous findings,[10,20,32,40-42] our results showed that SfChT was negatively associated with age (r = -0.285; $P < 0.0001$). This trend was similar for emmetropic, myopic, and hyperopic groups. Nagasawa *et al*.[43] reported significantly thicker choroid in children compared with adults. The possible reasons for thinning of the choroid with aging might result from loss of visible vessels[44] or a phenomenon called senile choroidal sclerosis in which sheathing of the choroidal vessels happens or choroidal channels eliminate.[45] The choroidal thinning is mostly attributed to the Haller's layer.[46] Some publications, however, demonstrated that there might not be an association between age and choroidal thickness.[30,32,47-50] This discrepancy might be due to various sources such as patient selection, choroidal thickness measurement technique, inclusion criteria, and ethnicity differences. Table 5 shows the findings of SfChT in some previous studies in different ethnicities.

The average horizontal, vertical, and total (average of horizontal and vertical profiles) choroidal thicknesses in emmetropic subjects were 309.59 ± 54.83 (175.2-445.60), 343.06 ± 55.55 (213.4-477.40), and 324.07 ± 52.78 (208.11-458.56), respectively. Furthermore, the finding of the SfChT in the healthy emmetropic group of the current study (346.64 ± 59.63 µm; range between 207 and 495 µm) is comparable with previous studies utilizing SD-OCT device.[28,52,56,57] The mean SfChT finding of the present study also is consistent with the results of the novel technique of Swept-source OCT (SS-OCT) [Table 5].[10,50,54,55]

A closer look at the literature on the choroidal profile in different countries has shown that the choroidal thickness differs considerably between various ethnicities even with relatively similar age ranges.[26,30,40,43,58,59] The first study on the choroidal thickness on healthy Iranian subjects was conducted in 2018.[33] This prospective study examined 208 eyes of 104 healthy Iranian subjects (mean age of 34.6 ± 9.8 years ranged 18-57 years). The subjects considered emmetropic with the refractive error ranged between ± 1.00 D, and their BCVA was 20/20. Based on the results, the mean SfChT

Table 5: Previous reports of subfoveal choroidal thickness in different ethnicities

First author (year of publication)	Number of subjects	Mean age (year)	Ethnicity	OCT device	SfChT (µ)
Margolis (2009)[51]	54	50.4	Caucasian	Spectralis	276±76
Ikuno (2010)[10]	79	39.4	Asian/Japanese	SS-OCT	354±111
Li (2011)[52]	93	24	Caucasian	Spectralis	342±118
Fujiwara (2012)[27]	145	45.7	Asian/Japanese	Spectralis	265.5±82.4
Ruiz-Moreno (2013)[50]	43	10	Caucasian	SS-OCT	312±65.3
Wei (2013)[31]	3232	64.3	Asian/Chinese	Spectralis	253.8±88.42
Karaca (2014)[53]	110	44	Asian/Turkish	Spectralis	315.5±78.6
Ruiz-Medrano (2014)[54]	154	55.5	Caucasian	SS-OCT	301.89±80.53
Moussa (2016)[55]	71	38,65	African/Egyptian	SS-OCT	319.72±76.45
Lee (2017)[28]	89	8.25	Asian/Korean	Spectralis	302.21±66.12
Entezari (2018)[33]	104	34.6	Middle-eastern/Iranian	Spectralis	363±84
Current study	469	32.76	Middle-eastern/Iranian	Spectralis	329.83±70.33

OCT: Optical coherence tomography, SfChT: Subfoveal choroidal thickness, SS-OCT: Swept-source OCT

was 363 ± 84 μm. Moreover, the choroidal thicknesses were 292 ± 76 and 194 ± 58 μm at 1500 and 3000 μm nasal to the fovea, respectively, and 314 ± 77 and 268 ± 66 μm at 1500 and 3000 μm temporal to the fovea, respectively. The study intended to define normal choroidal thickness profile in Iranian adults at different ages and different horizontal locations of the choroid. However, it did not consider vertical locations and younger age groups. Also, the study was performed on emmetropic subjects and did not investigate myopic and hyperopic cases. As far as we know, there has been no such report on Iranian subjects which included a large sample size including children and adults. In addition, the majority of previous studies have been conducted on adults, and younger age groups and children have been neglected. The reason for this might be the lack of cooperation in the ophthalmic evaluation of children; hence most of them have been performed on few children.[40,58,60,61] Our study included an extended age range from childhood to adulthood, and the mean SfChT in the total population with the mean SE of -0.38 ± 1.84 D was 329.83 ± 70.33 μm. The choroidal thickness in healthy children was significantly thicker compared with other age groups. The SfChT finding of 346.64 ± 59.63 μm in emmetropic subjects in the current study was lower than the 363 ± 84 μm found in the study of Entezari *et al*.[33] in the Iranian population.

Based on topographic studies on the choroidal structure, the choroidal thickness differs in various locations of the posterior segment[26,59,62-65] and decreases from the fovea to the outer parts of the macula and generally has a thicker profile in superior and temporal areas and prominently thinner profile in nasal areas.[23,58,66,67] The choroidal thickness in the macular area is thinner in myopic children[40,68,69] and myopic adults[9,65,70,71] which is more remarkable at the fovea relative to the peripheral areas.[61,63,71] Our results tie well with the findings of Nagasawa *et al*.[43] and Kim *et al*.[72] wherein we found that in healthy subjects, the choroidal thickness has an asymmetric nature. Based on our findings, the choroid has a bowl-shaped appearance in linear scans of emmetropic healthy subjects, and the thickest point is S1 with the mean thickness of 361.26 ± 65.49 μm. The choroid reaches the thinnest point at N3 with the mean thickness of 223.08 ± 65.65 μm. When comparing our results to those of older studies,[51,72] it must be pointed out that the choroidal thickness dramatically decreases toward nasal areas.

The main factor affecting choroidal thickness in healthy subjects of the present study was the age of participants. The results showed that from ages 4 to 60, choroid became thinner by about 20 percent. Regression analyses estimated that in emmetropic subjects, SfChT and total choroidal thickness decreased by 12.8 μm and 14 μm for every 10 years, respectively. Results of the model defined in the present study were comparable with the findings of a study conducted by Margolis *et al*.[51] However, several studies showed different results.[10,31] For instance, Tuncer *et al*. found that SfChT decreased by 31.4 μm for every 10 years.[73] These discrepancies can be partly attributed to age and ethnicity differences.

The literature review shows that sex-related differences in structure and physiology of the posterior eye have been ascribed to size and hormonal differences between male and females.[74,75] In relation to the choroidal structure, most of the previous studies have not documented any differences in the choroidal thickness between genders.[16,27,40] However, there are some publications that reported inconsistent choroidal thickness differences between males and females.[52,76] In the current study, we found no differences between genders in the parameter of SfChT.

Other factors affecting the choroidal thickness were the AL and the SE of refractive error.[22,24,31] These two parameters mostly have a strong correlation together and as myopia increases, the AL accordingly rises. Previous reports have found that there was a positive correlation between refractive error and choroidal thickness; however, the estimates are different. For instance, the choroidal thinning for each diopter increasing in myopia were 5.3 μm,[50] 8.7 μm,[24] 15 μm,[31] 29.13 μm[10] and 50.24 μm.[73] Our results revealed 8.71 μm reduction in the choroidal thickness for each diopter increase in myopia and 10.25 μm increasing in the choroidal thickness for each diopter increase in hyperopia. Overall, in line with prior research, we found that the choroidal thickness was thinnest in myopes and thicker in hyperopes.[30,40,77,78] The choroidal thickness alterations with AL have been reported as a negative association in both pediatric and adults.[19,22,31,79] Previous research has estimated that for every millimeter increase in AL, choroid underwent thinning ranging from 25.4 μm[52] to 43.8 μm.[61] The discrepancies might be due to various instrumentation, the difference in the age group of subjects, and differences in locations relative to the center of the fovea in studies that investigated para-foveal areas. Our results verified that for every 1 mm increase in AL, the SfChT changed by 13.48 μm.

There are some limitations to the present study. The main limitation was that the choroidal thickness had been segmented and measured manually because there was no commercially available instrument to automatically specify CSI for measuring the choroidal thickness. This source of error was more pronounced in the hyperopic group in which choroidal thickness was thicker, and accordingly in some scans, the CSI was more difficult to outline. Due to the large sample of the study and multiple examinations, we were not able to administer cycloplegic refraction on subjects. Another limitation of our work was that the measurements were performed by an examiner. Despite the limitations, our data are valuable in light of the information obtained from the choroidal profile in Iranian subjects. Future studies with automated software are preferable to determine choroidal thickness objectively. Further studies with a larger sample size covering wider refractive status including high myopia are preferable to make the study more precise. Finally, cross-sectional studies are insufficient to determine the effect of aging on the choroidal thickness, and we recommend longterm longitudinal studies to determine the trend of choroidal thickness changes with aging.

To conclude, the results of the present study revealed that emmetropic healthy Iranian subjects had a mean SfChT of 346.64 ± 59.63 μm (range, 207-495 μm), and the thickest and thinnest points were S1 and N3, respectively. Our findings estimated that the SfChT in healthy Iranian subjects decreased about 12.8 and 8.71 μm for every 10 years increase in age and each diopter increasing in myopia, respectively. Comparing emmetropic subjects, the choroidal thickness was significantly thinner in participants with myopia and thicker in hyperopes. Additionally, we found the choroid in myopic, hyperopic, and emmetropic subjects was thickest 1 mm superiorly and thinnest 3 mm nasally. This finding also applies to the total population.

In summary, this paper argued that the choroidal thickness has a decreasing trend with increasing age in total population, and the choroid is thinner in myopes and thicker in hyperopes compared with emmetropic subjects.

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Conflicts of interest
There are no conflicts of interest.

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