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The Effect of Age on Subfoveal Choroidal Thickness in Healthy Subjects

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ABSTRACT

To assess the normative values of subfoveal choroidal thickness (SFCT) in healthy Turkish subjects using spectral-domain optical coherence tomography (SD-OCT, Spectralis®, Heidelberg Engineering, Germany) and its relationship with age and gender.

One hundred sixty-nine emmetropic healthy subjects (84 men; 49.7%, 85 women 50.3%) underwent a detailed ophthalmological examination. The subjects were divided into 5 groups according to age; Group 1 (n = 42): 18-29 years, group 2 (n = 34): 30-39 years, group 3 (n = 33): 40-49 years, group 4 (n = 34): 50-59 years, group 5 (n = 26): 60 years and older.

There were statistically significant differences in mean SFCT values among different age groups ($p < 0.05$). Mean SFCT was highest in subjects under 30 years (364.87 ± 71.24 μm) and lowest in subjects over 60 years (261.25 ± 52.39 μm). There was a statistically significant negative correlation between age and SFCT values ($r = -0.52$, $p < 0.001$). Slope of change in SFCT over time in the subjects was -2.59 μm per year. When all subjects were evaluated, the mean SFCT value was 322.73 ± 64.00 μm in men and 310.47 ± 60.11 μm in women ($p = 0.34$). Except group 4, SFCT did not differ between men and women.

SFCT decreases with aging and sex does not seem to alter the measurements. Our normative data according to age groups and gender might be used to demonstrate SFCT changes in various retinal and choroidal diseases in Turkish population.

Keywords: Age, gender, healthy subjects, optical coherence tomography, subfoveal choroidal thickness

Introduction

Choroid is one of the most highly vascularized tissues of the body, located between retina and sclera (1). Oxygen and nutrient supply of the outer retinal segments, including photoreceptors, are provided from the choroid (2). Structural or functional disorders of the choroid may affect the retinal and the visual functions (1-2). Optical coherence tomography (OCT) is a fast, non-invasive and non-contact measurement device that provides high resolution and cross-sectional images of the retina using light waves (3). It is widely used in the diagnosis and follow-up of several retinal and optic nerve disorders such as age-related macular degeneration, macular edema, and glaucoma (4). The OCT device provides many measurements, such as retinal nerve fiber layer (RNFL) thickness, optic nerve head parameters (cupping, neuroretinal rim) or macular retinal thickness (5). Choroid, which has a dynamic structure, has been evaluated in-vivo with the enhanced depth imaging (EDI) method that has been recently used for clinical purposes. Choroid plays a key role in the pathophysiology of chorioretinal disorders, such as central serous chorioretinopathy, age-related macular degeneration, and Vogt-Koyanagi-Harada disease and in the literature, there are many studies on choroidal thickness measurements in health and diseases (6-10). Many factors have been shown to affect choroidal thickness, such as axial length, refractive error, amblyopia, puberty, pregnancy, thyroid disease and drug use (11-16).

The aim of the present study is to establish a normative database for subfoveal choroid thickness (SFCT) measurements in healthy Turkish subjects using spectral-domain OCT (SD-OCT, Spectralis®, Heidelberg Engineering, Heidelberg, Germany) and evaluate its relationship with age and gender.

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Materials and Methods

The local ethics committee approval was obtained. Written informed consent was obtained from all subjects and the principles of the Helsinki Declaration were followed throughout the study. In this cross-sectional study, healthy volunteers who had no ocular disease other than minor refractive errors (>-1.00 D or <+1.00 D) were included. Those with systemic diseases such as diabetes mellitus and hypertension and those with a history of drug, cigarette, and alcohol use that may affect the retina and the choroidal thickness were excluded. The subjects with a history of ocular surgery, refractive spheric error >1.00 D, anisometropia, astigmatism above 1.50 D, those with poor OCT scans that obscure the evaluation of the choroidal borders were also excluded.

All patients were examined between 9:00 am and 10:00 am to exclude diurnal variation. Choroidal imaging was performed as a single horizontal line scan passing through the fovea in the EDI mode of the OCT device (Spectralis®, Heidelberg Engineering, Heidelberg, Germany). During the measurement, the OCT scans were carried out from the same section through the eye-tracking program, and the number of repetitive scanning was set to 100. Choroidal thickness was measured manually as the distance between the outer border of the hyper-reflective retinal pigment epithelium and the choroid/sclera junction from the subfoveal region using the program of the device (Figure 1). Multiple OCT scans were obtained by a technician. Those with poor image quality were excluded and the best one was used included in the study. The SFCT measurement was done by the same investigator.

Spectralis® OCT usually takes 6x6 mm square sections centered on the fovea. In images taken in EDI mode, the device head is brought closer to the eye, and the reverse image that is normally not reflected on the screen is reflected on the screen. In this way, the deep choroidal parts approach the zero-delay line and thus the inverted image provides more information for the choroidal structures than the normal flat image. The system has a dual laser scanner system that simultaneously provides cross-section and reference scanning. From the reference points determined from the image obtained by cross-sectional scanning; fundus fluorescein angiography, indocyanine green angiography, infrared image, fundus autofluorescence or red-free images can be created. SD-OCT that is performing 40,000 A-scans per second is integrated into the system. While the resolution level is 14 μm in transverse sections, this value is 7 μm in axial sections. Thanks to five different imaging modes obtained by reference scanning, it is possible to determine different anatomical features with different wavelengths. At the same time, a more detailed choroidal image is obtained by taking multiple scans from the same area using eye tracking system and improving signal-to-noise ratio.

The subjects were divided into 5 groups according to their age ranges; group 1 (n = 42), 18-29 years; group 2 (n = 34), 30-39 years; group 3 (n = 33), 40-49 years; group 4 (n = 34): 50-59 age; group 5 (n = 26), 60 years and older. The obtained data were coded and transferred to the computer program.

Statistical Analysis: Descriptive statistics for the studied variables were presented as Mean and Standard Deviation Normality assumption of the variables was tested with Kolmogov-Smirnov test. In order to compare independent and dependent groups independent t test and Paired t tests were performed for the normally distributed variables. In addition, one-way ANOVA test was used to determine the differences in choroidal thickness between the groups. If there was statistical significance, Duncan, a post hoc test, was used for pairwise group comparisons. Pearson correlation test was used to analyze the relationship between choroidal thickness and age. Statistical significance level was considered as 5% and SPSS (ver: 18) statistical program was used for all statistical computations.

Results

One hundred and sixty-nine healthy volunteers between the ages of 18-72 years were included in the study. Eighty-four (49.7%) were men and 85 (50.3%) were women. There was no statistically significant difference in terms of gender by age groups (p = 0.96). The mean ages of men and women were 41.09 ± 14.16 and 41.78 ± 14.89 years, respectively (p=0.26). The demographic characteristics of the participants of the study are given in Table 1.

Mean SFCT values in the right and left eyes were 314.34 ± 71.37 μm and 319.82 ± 76.03 μm, respectively (p= 0.14). There were statistically significant differences in mean SFCT values among different age groups (range 138-537 μm) (p <0.001) (Table 2). Mean SFCT was highest in subjects under 30 years (364.87 ± 71.24 μm) and lowest in subjects over 60 years (261.25 ± 52.39 μm). In each decade over the age of 18,

Table 1. Demographic Characteristics of The Groups

Groups	Case (n)	Age range (years)	Men		Women	
			n (%)	Age (year ± SD)	n (%)	Age (year ± SD)
1	42	18-29	21 (50)	23.14 ± 3.52	21 (50)	23.14 ± 3.54
2	34	30-39	17 (50)	34.12 ± 2.93	17 (50)	34.12 ± 3.05
3	33	40-49	16 (48.5)	44.38 ± 3.1	17 (51.5)	44.59 ± 2.49
4	34	50-59	18 (52.9)	54.44 ± 3.08	16 (47.1)	53.5 ± 2.92
5	26	60-73	12 (46.2)	64.42 ± 3.72	14 (53.8)	63.71 ± 3.18
Overall	169	18-72	84 (49.7)	41.09 ± 14.16	85 (50.3)	41.78 ± 14.89

SD: Standard Deviation

Table 2. The Comparison of the Mean Subfoveal Choroidal Thickness Between Groups

		Mean	Std. Dev.	SE	Min.	Max.	p #
SFCTright	1	361,74a	67,25	10,38	217,00	537,00	0,001
	2	331,24b	77,00	13,20	193,00	468,00	
	3	309,85c	60,05	10,45	189,00	430,00	
	4	278,88c	51,29	8,80	179,00	382,00	
	5	266,50c	49,56	9,72	138,00	354,00	
	Total	314,15	71,20	5,48	138,00	537,00	
SFCT left	1	368,00a	75,71	11,68	200,00	516,00	0,001
	2	341,38ab	75,53	12,95	182,00	465,00	
	3	318,06b	67,01	11,67	172,00	434,00	
	4	285,06c	49,52	8,49	200,00	385,00	
	5	256,00c	55,55	10,90	153,00	351,00	
	Total	318,98	76,58	5,89	153,00	516,00	
p value (For group 1: right vs left) = 0,402 (Paired t test)							
p value (For group 2: right vs left) = 0,144 (Paired t test)							
p value (For group 3: right vs left) = 0,341 (Paired t test)							
p value (For group 4: right vs left) = 0,358 (Paired t test)							
p value (For group 5: right vs left) = 0,120 (Paired t test)							

a, b, c, d ↓: Different lower letters represent statistically significant differences among the groups in right and left side (Duncan test)
#: One-way ANOVA

approximately 25 μm choroidal thinning was observed. Slope of change in SFCT over time in the subjects was -2.59 μm per year. There was a statistically significant negative correlation between age and SFCT (r=-0.517, p <0.001) (Figure 2). In pairwise group comparisons, there was a statistically significant difference between groups 1 and groups 3, 4 and 5 (p <0.001 for all); between group 2 and groups 4 and 5 (p <0.001 for all); between group 3 and groups 1, 4 and 5 (p <0.001, p = 0.034, p <0.001, respectively). When all subjects were evaluated, the mean SFCT value was 322.73 ± 64.00 μm in men and 310.47 ± 60.11 μm in women (p= 0.343). Except group 4, SFCT did not differ between men and women (Table 3).

Discussion

In this study, we evaluated the effect of age and gender on SFCT in healthy subjects to establish a normative database to be used in further investigations. In the literature, the age is the most studied factor in its relationship with choroidal thickness. In an autopsy study by Ramrattan et al. (17), the mean choroidal thickness was found to be 193.5 μm in the first decade and 84 μm in the 10th decade. However, the choroidal thickness measurements in histopathological studies may not fully reflect the real values, since fixation processes, shrinkage and tissue damage and cessation of circulation after death might cause alterations in the choroidal thickness (18-19).

Table 3. Descriptive Statistics and Comparison Results For Gender

	Gender	Mean	SE	Std. Dev.	Min.	Max.	p #
SFCTright	Male	319,64	8,10	74,22	138,00	537,00	0,320
	Female	308,72	7,38	68,08	179,00	496,00	
SFCT left	Male	325,81	8,55	78,40	153,00	516,00	0,250
	Female	312,22	8,09	74,59	162,00	496,00	
p value (For men: right vs left) = 0,219 (Paired t test)							
p value (For women: right vs left) = 0,421(Paired t test)							

#: Independent samples t test

Table 4. The Mean Subfoveal Choroidal Thickness (Sfct) Of Healthy Eyes In Published Literature With Different OCT Devices

Study	Used method	n (case)	n (eyes)	Age range (years)	Mean age (years)	SFCT (µm)
Spaide et al.20	Spectralis®	17	34	19-54	33.4	right 318 left 335
Rahman et al.21	Spectralis®	50	100	30-49	38 ±5	right 332 ±90 left 332 ±91
Gök et al.22	Spectralis®	239	478	10-83	42.08 ±20.87	334.59 ±64.60
Margolis et al.23	Spectralis®	30	54	19-85	50.4	287 ±76
Noori et al.24	Spectralis®	32	-	-	65.81	248.93 ±50.92
Pongsachareonnont et al.25	DRI-OCT Triton™	144	144	18-85	41 ±13	326.0 ±86.2
Bhayana et al.26	DRI-OCT Triton Plus	119	238	19-60	28.70 ±11.28	299.10 ±131.2
Ikuno et al.28	1060 nm OCT	43	86	23-88	39.4 ±16.0	354 ± 111
Manjunath et al.29	Cirrus® HD-OCT	34	34	22-78	51.1	272 ±81
Our Study	Spectralis®	169	338	18-72	41.45 ±14.22	right 314.34 ±71.37 left 319.82 ±76.09

µm: micrometer

In our study, mean SFCT measurements taken with the EDI mode of the Spectralis® (Heidelberg Engineering) were 314.34 ± 71.37 µm in the right eye and 319.82 ± 76.03 µm in the left eye within a range of 138-537 µm. Mean SFCT values differed remarkably among different age groups ($p<0.05$), being highest in subjects under 30 years (364.87 ± 71.24 µm) and lowest in subjects over 60 years (261.25 ± 52.39 µm). The correlation between age and SFCT values was remarkable ($r=-0.52$, $p<0.001$). Slope of change in SFCT over time was -2.59 µm per year. Using the same device, Spaide et al. (20) found the mean SFCT value of the right and left eyes of 17 healthy subjects with a mean age of 33.4 years as 318 µm and 335 µm. Similarly, in the study performed by Rahman et al. (21), the mean values of SFCT were 332 ± 90 µm in the right eyes and 332 ± 91 µm in the left eyes of 50 healthy individuals with a mean age of 38 ± 5 years. The mean age of group 2 in our study was 34.12 ± 2.92 years and the mean SFCT value was 336.31 ± 75.87 µm, which was comparable to the studies of Spaide (20) and Rahman (21). In the study of Gök et al. (22) on 239 patients with same SD-OCT device, the mean age was 42.08 ± 20.87 years and the mean SFCT value was 334.59 ± 64.60 µm, which was higher than our population, although the mean ages were similar. In the study

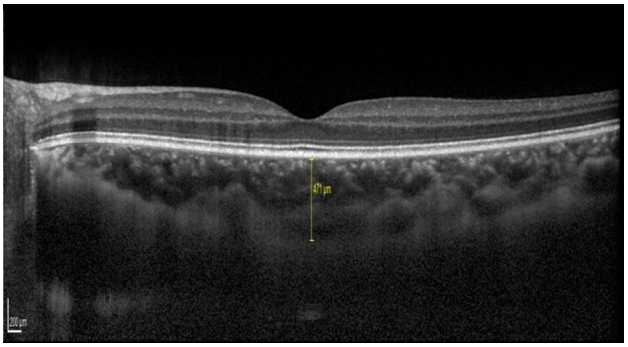

Fig. 1. Manual Measurement of SFCT in Oct Image Obtained By EDI Mode of The Spectralis® Device

of Margolis and Spaide (23), the mean SFCT value was 287 ± 76 μm in individuals with a mean age of 50.4 years, which was similar with group 4 (50-59 years). In the study of Noori et al. (24), mean SFCT was 248.93 ± 50.92 μm in healthy individuals with a mean age of 65.81 years, similar with group 5 with a mean SFCT value of 261.25 ± 52.391 μm. The details of the studies measuring SFCT via Spectralis SD-OCT in the literature were given in Table 4.

In many studies done with swept-source OCT (SS-OCT), a negative correlation has been reported between age and SFCT (25-26). In the study of Pongsachareonnont et al. (25), mean SFCT was found to be 326.0 ± 86.2 μm. Women comprised the majority (80%) of the cases. SFCT was negatively correlated with age (r2 = 0.097, p <0.001) and was found to be decreased by 1.5 μm with each year. This study is similar with our study in terms of age. In the study of Bhayana et al. (26) mean SFCT was found to be 299.10 ± 131.2 μm in a group of patients with a mean age of 28.70 ± 11.28 years (19-60 years). There was no statistically significant correlation between age and SFCT (r = -0.096, p = 0.139), while the correlation between axial length and SFCT was remarkable. In healthy eyes, Philip et al. (27) showed a high correlation between SD-OCT and SS-OCT measurements. SD-OCT measurements were higher than SS-OCT measurements. SS-OCT that uses a 1050-nm wavelength light source is superior to SD-OCT. The visualization of structures beneath the RPE is much better with SS-OCTdue to decreased sensitivity roll-off and attenuation of the OCT signal in deeper structures, particularly the choroid. In SD-OCT system, 840 nm light source does not allow deep penetration and light scattering is greater. In another study performed with a 1060 nm OCT device, age was found to be the most associated factor with choroidal thickness (28). In the study of Manjunath et al. (29), mean SFCT measured with Cirrus® HD-OCT was 272 ±81 μm in a

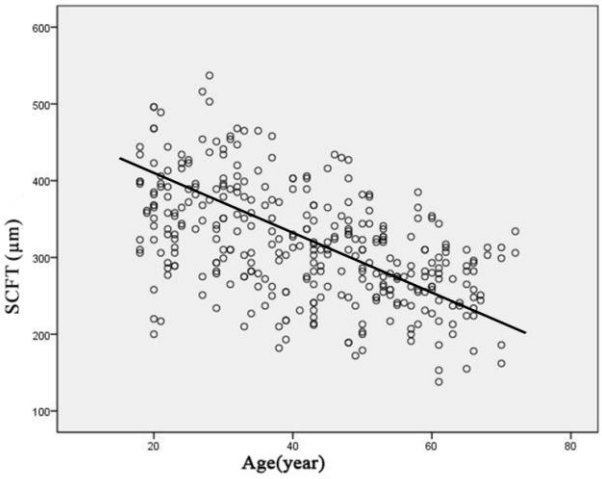

Fig. 2. Scatter/Dot Graph Showing The Subfoveal Choroidal Thickness (SFCT) Distribution By Age

study group with a mean age of 51.1 years. The authors found a negative correlation between age and SFCT. The details of the studies in the literature were given in Table 4.

In the literature, there are studies which evaluate the relationship between gender and choroid thickness (30-34). In the study of Li et al. (30) mean SFCT was 62 μm thicker in males than females. Ding et al. (31) reported higher SFCT values in males (270 μm) compared to females (254 μm) (p = 0.057). Barteselli et al. (32) found the mean central choroidal volume as 7.664 ± 2.283 mm3 in males and as 7.138 ± 2.077 mm3 in females (p <0.05), while Kim et al. (33) and Fujiwara et al. (34) did not find any difference in SFCT between men and women (p>0.05). In our study, mean SFCT did not differ statistically significant between men and women in age groups, expect group 4, in which mean SFCT was statistically significant higher in men (301.42 ± 50.21) compared to women (260.09 ± 40.66) (p<0.05).

In conclusion, SFCT decreases with aging and sex does not seem to alter SFCT measurements. Our results will provide useful data for further investigations in choroidal disorders. Our normative data according to age groups and gender might to be helpful to demonstrate SFCT changes in various retinal and choroidal diseases in Turkish population.

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