

CHOROIDAL THICKNESS AND CENTRAL MACULAR THICKNESS MEASUREMENTS WITH CIRRUS HD-OCT IN HEALTHY INDIVIDUALS IN THE TURKISH POPULATION

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SUMMARY

Aim: This research was conducted to determine the normal values of choroidal thickness in healthy individuals and to evaluate the relationship between this thickness and age, gender, refraction, axial length and average macular thickness using OCT.

Material and Method: In the study, the right eyes of 400 healthy individuals (234 women, 166 men) between the ages of 4 and 70 years, who applied to the Department of Ophthalmology outpatient clinic for examination, were evaluated.

Results: Macular thickness, macular volume, and foveal thickness were found to be $249.12 \pm 21.32 \mu\text{m}$, $9.98 \pm 0.5 \mu\text{m}^3$ and $280 \pm 13.45 \mu\text{m}$, respectively. According to linear regression analysis, a negative correlation was detected between age and subfoveal choroidal thickness ($p < 0.05$). It was determined that foveal thickness, retinal volume and average retinal thickness were higher in men, and foveal thickness increased with age ($p < 0.05$).

Conclusion: As a result of the research, it was determined that age is an important factor affecting choroidal thickness. It is thought that, in future, improving in vivo imaging of the choroid and measuring choroidal thickness using OCT will facilitate understanding of the pathophysiological basis of many ophthalmological diseases.

Key words: Cirrus HD-OCT, choroidal thickness, central macular thickness, age

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INTRODUCTION

The choroidal layer, extending from the ora serrata to the optic nerve head, is a vascularized and pigmented structure that carries oxygen and metabolites from the outer segment of the retina and the prelaminar region of the optic nerve [1]. The choroidal layer absorbs excess light due to the melanocytes contained in the retinal pigment epithelium and acts as a cooler by absorbing the heat generated in many physiological events.

A structurally and functionally intact choroidal tissue is vital for retinal functions. Abnormal choroidal blood flow can cause photoreceptor dysfunction and death

in the retina [2]. Studies have reported that the choroidal layer plays important roles in the pathophysiology of many diseases, such as central serous retinopathy, age-related macular degeneration, pachychoroid disease, pathological myopia, and Vogt-Koyanagi Harada [3–6]. Therefore, a clear and accurate definition of the changes in this layer is extremely important in the correct evaluation of many posterior segment diseases. However, since the structures in the choroidal tissue are not arranged in layers in a certain order as in the retina and do not have different reflection properties as in the retina, it has for a long time not been possible to evaluate them in detail like the retina. In addition, it is very

difficult to obtain full-thickness images and therefore there are many difficulties in obtaining information from the cross-sectional anatomy of the choroid [7]. Until recent years, a method that provides detailed information about the actual choroidal thickness and morphology, which allows obtaining in-vivo cross-sectional images about the anatomy of the retinal pigment epithelium and choroidal layer by detecting choroidal vascular abnormalities and changes in blood flow, has not been developed. In previous years, indocyanine green angiography, Laser Doppler flowmetry and B-scan ultrasonography were used to evaluate cross-sectional images of the choroid [8]. However, the expected benefit could not be achieved, because the resolution of the images obtained was not at the desired level, different sections could not be obtained after each evaluation, and their poor repeatability [9]. Currently, the Optical Coherence Tomography (OCT) technique, a non-invasive and non-contact method that provides high resolution in cross-sectional imaging of tissues and plays an important role in the diagnosis and follow-up of many macular diseases, optic nerve diseases and glaucoma, has been developed. OCT is a non-invasive retinal imaging method that enables reliable, fast, reproducible and objective examinations [10]. With OCT, retina, optic nerve head, peripapillary retinal nerve fiber layer (RNFL) and ganglion cell complex (GHC) thicknesses can be evaluated both quantitatively and qualitatively, and are used in the diagnosis and follow-up of many neuro-ophthalmological diseases [11]. The literature review revealed that choroidal thickness varies according to ethnicity, but it was determined that there are very limited studies on this subject. In addition, very few studies have been found investigating choroidal thickness, central macular thickness and axial length depending on age among populations [8–11]. In this regard, this study aims to determine choroidal thickness values with Cirrus HD-OCT in healthy individuals between the ages of 4 – 70 years in the Turkish population, to evaluate the relationship of these measurements with age, gender, refraction and axial length (AL), and also to evaluate the relationship between macular thickness and choroidal thickness.

MATERIAL AND METHOD

Research Location

This research was conducted on the right eyes of 400 healthy individuals, (234 females and 166 males), randomly selected, aged 4–70 years, who applied to the Ophthalmology Polyclinic of xxxx University Faculty of Medicine between July 2013 and February 2014 (Protocol No: 2013/-09).

Research Design

Patients were divided into 6 age groups: 4–20 years, 20–30 years, 30–40 years, 40–50 years, 50–60 years and 60–70 years. After a complete ophthalmological exami-

nation, including fundus examination, axial length measurements [average of 3 measurements were taken] were made on the right eyes of each individual with Nidek AL-Scan optical biometry [Nidek CO, LTD.] All measurements were repeated 3 times at different times by the same researcher. Finally, the average of 3 measurements for all parameters was taken. In children aged 4–18 years, 3 drops of 1% cyclopentolate were instilled into the eye at 5-minute intervals and cycloplegic refraction was measured 20–35 minutes later, while in adults aged 19–70 years, non-cycloplegic refraction was measured with a TopCon KR-8800 autorefractometer. Choroidal thickness and macular thickness (macular 512x128 A-scan) were measured with Cirrus HD-OCT (Carl Zeiss Meditec, Dublin, CA, USA). The average macular volume and thickness and central foveal thickness were measured by macular scanning performed with OCT. With choroid scanning, central choroidal thickness, 100 µm nasal, 300 µm nasal, 100 µm temporal and 300 µm temporal choroidal thickness from the fovea were measured manually by the same person and on the same day.

In summary, the following measurements were made in the research:

Axial length (AL), Spherical equivalent (SE) subfoveal choroidal thickness (SFCC), 1 mm temporal choroidal thickness (TA), 1 mm nasal choroidal thickness (N1), 3 mm temporal choroidal thickness (T3), 3 mm nasal choroidal thickness (N3), foveal thickness (FT), retinal volume (RV), mean retinal thickness (MRT).

Inclusion Criteria

- Best corrected visual acuity 1.0 according to Snellen chart,
- Absence of ocular pathology other than refractive error,
- Spherical equivalent in the range of +6 -6 diopters [D],
- Cup/disc ratio < 0.5,
- Cup/disc asymmetry ratio between both eyes < 0.2,
- Absence of any systemic pathology that may or may not affect vascular structures.

Exclusion criteria

- High refractive errors [spherical equivalent > +6 D, astigmatism > 3 D],
- Presence of strabismus and amblyopia,
- Retinal-optic disc anomalies and systemic disease.

Ethics Committee

Approval from the local Ethics Committee was obtained. The Informed Consent form was read and signed by the adult individuals and the child patients themselves or their parents.

Statistical analysis

All measurements were repeated three times at different times by the same researcher. Measurements with good centralization, no artifacts, and signal quality of 8 or above were considered valid. Data analysis

was done with SPSS 21.0 for Windows (SPSS Inc., Chicago, IL, USA). Descriptive statistics were shown as mean, standard deviation, median, minimum, maximum for continuous variables, and nominal variables were shown as number of patients and (%). Whether there was a statistically significant relationship between macular/choroidal measurements and age, axial length, spherical equivalent and gender was investigated using Pearson's correlation test and simple linear regression analysis. Choroidal thicknesses, foveal thicknesses and volumes according to gender were investigated by independent t- test. The paired t- test was used to determine the difference between subfoveal, nasal 1 mm, nasal 3 mm, temporal 1 mm, temporal 3 mm choroidal thicknesses. One-way ANOVA analysis was used to determine the difference in choroidal thickness between decades. Results for $p < 0.05$ were considered statistically significant.

RESULTS

Of the 400 healthy individuals included in this study, 234 were female (58.1%) and 166 were male [41.2%]; The average age was determined as 28.85 ± 17.05 mm. AL, foveal thickness, retinal volume and mean retinal thickness were found to be higher in men than in women ($p < 0.05$). Table 1 presents no statistically significant difference found between men and women in terms of subfoveal choroidal thickness, temporal 1 mm choroidal thickness, nasal 1 mm choroidal thickness, temporal 3 mm choroidal thickness, and nasal 3 mm choroidal thickness ($p > 0.05$). (Table 1).

It was determined that the spherical equivalent showed a statistically significant difference between decades. There was a shift towards hyperopia from the 2nd decade to the 6th decade, and there was a decrease in the

AL value. It was also reported that there was an increase in foveal thickness with age ($p < 0.05$).

A statistically significant difference was detected in terms of choroidal thickness between decades. When all thickness values are considered, the highest choroidal thickness values were seen in the 1st decade (SFCC 394.87 ± 8.12 , T1 395.50 ± 8.80 , N1 395.13 ± 8.20 , T3 391.06 ± 7.07 , N3 390.63 ± 6.82) and the lowest choroidal thickness values were in the 2nd decade (SFCC 313.18 ± 4.30 , T1 302.43 ± 4.90 , N1 306.51 ± 4.57 , T3 310.79 ± 4.75 , N3 315.08 ± 4.50). Table 2 presents that the choroidal thickness was observed to decrease from the 3rd decade to the 6th decade (Table 2).

According to linear regression analysis, a negative correlation was detected between age and subfoveal choroidal thickness ($r: -0.385$, $p < 0.05$).

DISCUSSION

OCT gives a quantitative and qualitative estimate of static choroidal structure, rather than full choroidal blood flow. Interpretation of age-related choroidal changes is based on the assumption of changes in choroidal thickness secondary to hemodynamic alteration at the microstructural level. Imaging the choroid and measuring its thickness can be done by using SD-OCT, an increased depth imaging technique, and averaging multiple B-scan signals at the same position. Our research was conducted to evaluate age-related changes in the choroidal layer with OCT in order to assist in the treatment of neurophthalmological diseases.

Spaide et al., who measured choroidal thickness with OCT for the first time, found the average subfoveal choroidal thickness to be $318 \mu\text{m}$ in the right eye and $335 \mu\text{m}$ in the left eye [12]. In subsequent studies, it was reported that the average subfoveal choroidal

Table 1. Variation of research parameters between genders

| Parameters | Total | Female | Male | P |
|------------|--------------------|-------------------|-------------------|------|
| Age | 37.85 ± 17.05 | 36.66 ± 1.06 | 39.33 ± 1.15 | .227 |
| SE | -0.4 ± 1.39 | -0.55 ± 0.12 | -0.64 ± 0.13 | .982 |
| AL | 23.49 ± 1.03 | 23.48 ± 0.07 | 24.07 ± 0.08 | .00 |
| FT | 249.12 ± 21.32 | 247.78 ± 1.60 | 258.26 ± 1.86 | .00 |
| RV | 9.8 ± 0.5 | 9.91 ± 0.04 | 10.11 ± 0.04 | .006 |
| RK | 280 ± 13.45 | 278.04 ± 1.04 | 283.67 ± 1.23 | .004 |
| SFCC | 349.45 ± 56.32 | 332.11 ± 3.84 | 332.17 ± 5.06 | .824 |
| T1 | 333 ± 51.81 | 331.32 ± 3.90 | 335.57 ± 5.26 | .643 |
| N1 | 335.11 ± 49.96 | 33.86 ± 3.78 | 336.80 ± 4.95 | .922 |
| T3 | 340.56 ± 51.07 | 339.23 ± 3.95 | 343.84 ± 5.13 | .670 |
| N3 | 341.21 ± 46.92 | 339.69 ± 3.76 | 344.39 ± 4.48 | .541 |

Tests: independent t test and paired t test, $P < 0.05$

AL – Axial length, SE – Spherical equivalent, SFCC – subfoveal choroidal thickness, T1 – 1 mm temporal choroidal thickness, N1 – 1 mm nasal choroidal thickness, T3 – 3 mm temporal choroidal thickness, N3 – 3 mm nasal choroidal thickness, FT – foveal thickness, RV – retinal volume, ORK – mean retinal thickness

thickness varied between 270.82–332 μm [13–16]. In studies conducted on the Turkish population, it has been stated that this value varies between 287.66–326.00 μm [17–19]. The average subfoveal choroidal thickness was found to be 349.45 μm in all groups in our study. It was determined that our results were compatible with the literature, but were higher than other studies conducted in the Turkish population. There are many studies stating that the differences in the results of the studies are due to the different software used, differences in the light source of OCT, ethnic differences, age, refractive error and axial length differences in the patient profile. We consider it an advantage that our study was conducted with a large number of patients who were completely healthy, within a wide age range, and whose refractive error range was kept narrow. Previous studies conducted in the Turkish population did not include such a wide age range and number of patients. Previous studies conducted in Turkish society were conducted in the age range of 20–80 ($n = 100\text{--}250$) and the average AL varied between 23.41–26.78 [11,17,18].

A topographic change in choroidal thickness occurs. It is usually maximum at the fovea or just above/temporal to the fovea. The thick choroid serves as a metabolic sink for the highly active foveal area [20]. According to our research findings, the choroid is thicker in the subfoveal region than in the nasal and temporal regions. While Wakatsuki et al. stated that the choroid is thickest in the subfoveal area and that the thickness decreases towards the nasal region [21], Bhayana et al. reported that the choroidal thickness in the subfoveal region is higher than the choroidal thickness in both the temporal and nasal regions, and that the choroidal thickness in the nasal region is higher in the temporal and subfoveal regions. They reported that it was thinner than the cho-

roidal thickness in the region [20]. These results show us that regional measurement of choroidal thickness is another useful value for monitoring changes in choroidal thickness.

In this study, in line with the literature, it was determined that age was the parameter that had the most impact on SFCC, and that there was a decrease in choroidal thickness with increasing age, especially after the 3rd decade. Studies have shown that SFCC decreases by 1.2–3.5 μm every year, and this decrease is much more evident after the age of 60 [22–24]. In addition, in our research, the thickest choroidal layer measurement was determined in the 1st decade and the thinnest choroidal layer measurement was determined in the 2nd decade. A decrease in choroidal thickness values is observed starting from the 3rd decade. We think that this difference is due to the predominance of hyperopic refraction error in the first decade and myopic refraction error in the second decade.

Refraction error is one of the most effective parameters on choroidal thickness. As the axial length increases, it causes myopia, and as it decreases, it causes hyperopia. Ikuno et al. stated that the choroidal thickness in high-degree myopes is three times thinner than in normal eyes, and that the choroidal thickness decreases by 9.3 μm for every 1 diopter decrease in refractive error [25]. Shin et al. also found that there is a correlation between refractive error and choroidal thickness (13.6 μm thinning in choroidal thickness for each diopter) [15]. In our study, although we evaluated all age groups, we could not detect a statistically significant relationship between refractive error and SFCC. We think that the reason for this is that the refractive error range of the eyes we included in the study was kept narrow [$-4\text{ D} - +4\text{ D}$]. The fact that the lens thickness decreases relatively in eyes with long axial length, and that the lens thickness increases in eyes with short axial length, and that the lens grows throughout

Table 2. Changes in research parameters according to decades

| | 1. decade | 2. decade | 3. decade | 4. decade | 5. decade | 6. decade | P |
|--------------------------|-------------------|-------------------|-------------------|-------------------|-------------------|--------------------|------|
| Age | 10.30 \pm 0.44 | 24.66 \pm 0.34 | 34.53 \pm 0.35 | 44.20 \pm 0.39 | 53.60 \pm 0.53 | 64.62 \pm 0.34 | .000 |
| Gender (female %) | 34.75 | 18 | 17.5 | 16.5 | 9 | 4.25 | .457 |
| SE | -0.13 \pm 0.10 | -1.32 \pm 0.17 | -0.90 \pm 0.16 | -0.45 \pm 0.14 | 0.31 \pm 0.17 | 1.50 \pm 0.31 | .000 |
| AL | 23.09 \pm 0.97 | 23.97 \pm 0.12 | 23.75 \pm 0.11 | 23.56 \pm 0.09 | 23.57 \pm 0.14 | 23.22 \pm 0.15 | .000 |
| FT | 242.35 \pm 1.80 | 249.72 \pm 2.48 | 253.15 \pm 2.74 | 253.43 \pm 2.42 | 253.65 \pm 2.89 | 253.87 \pm 6.33 | .000 |
| RV | 9.93 \pm 0.04 | 9.96 \pm 0.07 | 10.08 \pm 0.05 | 9.97 \pm 0.07 | 10.07 \pm 0.07 | 9.87 \pm 0.15 | .246 |
| MRT | 278.27 \pm 1.33 | 280.11 \pm 1.67 | 282.32 \pm 1.60 | 279.76 \pm 1.69 | 282.51 \pm 1.80 | 276.31 \pm 4.17 | .226 |
| SFCC | 394.87 \pm 8.12 | 313.18 \pm 4.30 | 341.01 \pm 0.66 | 338.29 \pm 6.03 | 320.08 \pm 7.69 | 319.11 \pm 8.12 | .000 |
| T1 | 395.50 \pm 8.80 | 302.43 \pm 4.90 | 346.47 \pm 6.07 | 342.00 \pm 6.30 | 323.77 \pm 7.94 | 322.29 \pm 8.80 | .000 |
| N1 | 395.13 \pm 8.20 | 306.51 \pm 4.57 | 344.80 \pm 5.70 | 343.58 \pm 5.91 | 328.86 \pm 8.39 | 326.18 \pm 9.38 | .000 |
| T3 | 391.06 \pm 7.07 | 310.79 \pm 4.75 | 356.20 \pm 5.46 | 351.53 \pm 6.93 | 333.53 \pm 7.92 | 326.94 \pm 10.17 | .000 |
| N3 | 390.63 \pm 6.82 | 315.08 \pm 4.50 | 355.40 \pm 5.55 | 349.23 \pm 5.73 | 331.81 \pm 6.98 | 335.76 \pm 10.81 | .000 |

Test: Oneway ANOVA, $P < 0.05$

AL – Axial length, SE – Spherical equivalent, SFCC – subfoveal choroidal thickness, T1 – 1 mm temporal choroidal thickness, N1 – 1 mm nasal choroidal thickness, T3 – 3 mm temporal choroidal thickness, N3 – 3 mm nasal choroidal thickness, FT – foveal thickness, RV – retinal volume, MRT – mean retinal thickness

life, was also shown in our study, and it was thought that this situation may be one of the emmetropization mechanisms developed by the eye itself.

Gender-related differences in axial length and intraocular pressure have been reported in previous studies [26,27]. In addition, gender-related changes in retinal thickness have been reported in studies conducted with OCT [28,29]. These structural and physiological differences between males and females have been attributed to hormonal effects, or the wider eyes of men [16,30]. It is thought that gender and hormonal exposure may affect choroidal blood flow, due to estrogen receptors found in the human choroid [26,28]. In studies including Chinese, Japanese, Iranian, British, white and black American populations, no significant difference in choroidal thickness was detected between males and females [28-30]. In our study, a statistically significant difference was observed between males and females in terms of AU, foveal thickness, retinal volume and average retinal thickness, and AU was found to be higher in males.

As a result, it seems that the parameter that affects choroidal thickness the most is age. Researchers have just begun to study choroidal thickness, and more information is needed to understand choroidal abnormalities. The pathophysiology behind choroidal changes should be additionally investigated with a flow-based study, rather than purely structural evaluation. Scan-derived OCT and OCT angiography, a recent addition to choroidal imaging tools, may provide new information about choroidal changes in hypertensive individuals in future larger prospective comparative studies. In addition, there is no consensus on whether the area showing high scattering behind the choroidal vessels is exactly the choriocleral area. Scanning the scleral surface using polarized-sensitive 1- μ m swept-source OCT may provide more accurate results [77]. In the future, improving in vivo imaging of the choroid and measuring choroidal thickness using OCT will facilitate the differential diagnosis of many ophthalmological diseases.

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