Comparison of the Retinal and Choroidal Structures in 3 Refractive Groups

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Abstract
Objectives: This study investigated the retinal layer thickness, choroidal thickness (CT), and retinal nerve fiber layer (RNFL) parameters in 3 refractive groups.
Methods: A total of 201 eyes of 201 subjects were enrolled in this prospective and comparative study. The patients were divided into 3 groups according to refractive status: Group 1 consisted of 60 eyes of myopic subjects, Group 2 comprised 72 eyes of emmetropic subjects, and 69 eyes of hyperopic subjects were categorized as Group 3. The retinal layer thickness, CT, and RNFL parameters were measured using optical coherence tomography and compared between groups.
Results: The mean age of the patients was 22.33±10.11 years in Group 1, 21.55±8.3 years in Group 2, and 23.73±11.08 years in Group 3 (p=0.741). Group 1 consisted of 34 women and 26 men, Group 2 contained 44 women and 28 men, and Group 3 was made up of 45 women and 24 men (p=0.124). The mean spherical equivalent value was −6.16±2.01 D in Group 1, 0.13±0.5 D in Group 2, and 5.48±1.32 D in Group 3 (p<0.001). The RNFL and macular thickness values were lower in the myopic patients compared with those of the other groups (p<0.05). The CT measurement was lower in the myopic patients and higher in the hyperopic patients compared with the emmetropic patients (p<0.05).
Conclusion: The myopic patients had a lower CT and RNFL thickness measurement than the emmetropic and hyperopic patients, whereas the hyperopic patients had a higher CT than the other patient types.
Keywords: Choroidal thickness, emmetropia, hyperopia, myopia, retinal nerve fiber layer

Introduction
Spectral domain optical coherence tomography (SD-OCT) is a non-invasive method to examine the posterior segment of the eye and is important in direct observations of the retina and the choroid (1-3). Enhanced depth imaging OCT (EDI-OCT) is a specialized modality used for choroidal imaging (3). The choroid is a highly vascular tissue layer that has an essential role in various functional activities of the visual system (4). In the current literature, the choroid is considered an indicator of retinal health; abnormal alterations to the choroid have been described in retinal diseases, such as diabetic retinopathy, age-related macular degeneration, and central serous chorioretinopathy (5). In addition, the cho-
roid has been shown to play an important role in the development of refractive errors in animal models (6,7).

The objective of the present study was to investigate differences in choroidal thickness (CT), retinal layer thickness, and retinal nerve fiber layer (RNFL) parameters in 3 refractive groups.

**Methods**

**Ethical Considerations**

This prospective study was performed in the department of ophthalmology of Adıyaman University Training and Research Hospital. The study protocol was approved by the university clinical research ethics committee on September 22, 2020 (No: 2020/8-9) and conformed to the tenets of the Declaration of Helsinki. Written, informed consent was obtained from all of the participants prior to their enrollment in the study.

**Study Population**

This cross-sectional study included 201 eyes in 201 subjects who were categorized into 3 refractive groups. Group 1 comprised 60 eyes of myopic subjects, Group 2 included 72 eyes of emmetropic subjects, and 69 eyes of hyperopic subjects were categorized as Group 3. Myopia was defined as a spherical equivalent (SE) of ≤−0.75 D, hyperopia was defined as a SE of ≥+0.75 D, and emmetropia was defined as an SE between +0.50 and −0.50 D. Patients with astigmatism values between -0.50 and +0.50 were included in all of the study groups.

All of the participants underwent a total ophthalmic examination, which included evaluation of refraction, visual acuity, and intraocular pressure, as well as biomicroscopy. Patients with any ocular or systemic disease other than refractive errors were excluded.

**Measurement Procedure**

The peripapillary RNFL, central macula, and retinal layer thickness parameters were evaluated using an SD-OCT device (Spectralis; Heidelberg Engineering GmbH, Heidelberg, Germany) and Heidelberg Eye Explorer software (Heidelberg Engineering GmbH, Heidelberg, Germany). The measurements were recorded under dim lighting conditions in all cases. The peripapillary RNFL thickness was obtained from the 3.4 mm-diameter peripapillary circular area at the center of the optic disk. The macular thickness map, formed by a 25-line horizontal raster scan, was centered on the fovea. The system also measured the average thickness of the retinal layers in the macular area (Fig. 1).

The EDI capability of the OCT system was used to manually measure CT in the subfoveal region and at a distance of 1500 µm and 3000 µm, both nasally and temporally, from the foveal center (Fig. 2). To avoid diurnal variations in CT values, all of the measurements were performed between 3 pm and 6 pm. Two independent examiners, who were blinded to the study and its aims, performed all of the required measurements and the mean value was used for the analysis. Only scans that were determined to have a good signal strength, comprising a signal-to-noise ratio of ≥20 dB, were selected for evaluation.

**Statistical Analysis**

All of the statistical analyses were performed using IBM SPSS Statistics for Windows, Version 26.0 software (IBM Corp.,...
Armonk, NY, USA). Descriptive statistics were reported as the mean±SD. Categorical values were compared using a chi-squared test. The Kolmogorov-Smirnov test was used to assess the normal distribution of the variables. Independent samples were compared using a 2-sample t-test. A p value of <0.05 was considered significant.

**Results**

A total of 201 eyes of 201 participants were enrolled in this prospective, comparative study. Group 1 comprised 60 eyes of myopic subjects: 34 women and 26 men; Group 2 included 72 eyes of emmetropic subjects: 44 women and 28 men; and Group 3 consisted of 69 eyes of hyperopic subjects: 45 women and 24 men (sex distribution: p=0.124). The mean age was 22.33±10.11 years (range: 10-40 years) in Group 1, 21.55±8.3 years (range: 12-39 years) in Group 2, and 23.73±11.08 years (range: 11-39 years) in Group 3 (p=0.741). The mean SE value was −6.16±2.01 in Group 1, 0.13±0.5 in Group 2, and 5.48±1.32 in Group 3 (p<0.001). The mean AL was 24.5±1.2 mm in Group 1, 22.8±0.7 mm in Group 2, and 21.5±1.0 mm in Group 3. The AL was the greatest in the myopic group, followed by the emmetropic and hyperopic groups (all p<0.0001).

The RNFL thickness and macular thickness values were lower in the myopic patients than in the other groups. The peripapillary RNFL, central macular, and retinal layer thickness values are summarized in Table 1. The CT measurement was lower in myopic patients and higher in hyperopic patients in all of the localized measurements. The CT values of all 3 groups are shown in Table 2.

Spearman correlation analysis determined a significant positive correlation between the refractive error and measurements of the macular thickness locations: temporal-inner: p<0.001, r=0.421; superior-inner: p<0.001, r=0.451; nasal-inner: p<0.001, r=0.437; inferior-inner: p<0.001, r=0.448; nasal-outer: p<0.001, r=0.345; and inferior-outer: p<0.001, r=0.433. In addition, a positive correlation was found between the refractive error and the CT value at all locations: subfoveal CT: p<0.001, r=0.712; nasal 1500 µm CT: p<0.001, r=0.719; nasal 3000 µm CT: p<0.001, r=0.776; temporal 1500 µm CT: p<0.001, r=0.694; and temporal 3000 µm CT: p<0.001, r=0.732.

**Discussion**

The choroid is a vascular tissue layer located between the retina and the sclera that supplies oxygen and nutrients to the sensory retina (8). Assessment of the optic nerve head (ONH) is a key factor in the diagnosis of ocular diseases, such as glaucoma, optic nerve edema, and myopia (9). Several studies have shown that the ONH, RNFL thickness, and the CT peripapillary retinal thickness can vary among the healthy population (10–12). This study was an examination of the effects of refractive status on CT, retinal thickness, and RNFL thickness.

Our findings indicated that patients with myopia had a lower CT, RNFL thickness, and macular thickness compared with the emmetropic and hyperopic patients. However, the mean retinal layer thickness did not differ significantly between groups. The hyperopia patients had a greater CT compared with those in the myopic and emmetropic groups. Kaderli et al. (13) studied the correlation between hyperopia and CT and found that patients with hyperopia had a greater CT, and that this was associated with increased hyperopic errors. In a cohort study in China, patients with myopia had a lower CT compared with emmetropic patients, and patients with high myopia had the lowest CT values (14). In another study, Heirani et al. (15) examined CT and refractive
status and found that patients with myopia had a lower CT and patients with hyperopia had a greater CT. Similarly, we also found that myopic patients had a lower CT and hyperopic patients had a greater CT.

Choroidal tissue facilitates axial extension by reshaping the scleral extracellular matrix and plays an important role in emmetropization (16). This has also been demonstrated in animal models of induced myopia and hyperopia (17-18). It has been observed that choroidal thinning occurred in the early stage of myopia progression during emmetropization in childhood (19). CT may be an important marker to predict myopia and myopic progression.

Our examination of RNFL thickness between groups revealed that myopic patients had a thinner RNFL in some quadrants and a thinner retinal layer compared with those in the emmetropic and hyperopic patients. No significant difference was observed in the RNFL thickness between the emmetropic and hyperopic groups. Oner et al. (20) also studied the effects of refractive status and AL on RNFL thickness, and demonstrated that myopic eyes had a thinner RNFL than emmetropic and hyperopic eyes. In a study of children and adolescents, myopic eyes were found to have a thinner RNFL, whereas no RNFL thickness difference was seen between the emmetropic and hyperopic groups (21),

| Table 1. Demographic and clinical characteristics of the study groups |
|---------------------------------------------------------------|
| Group 1 Group 2 Group 3 p1* p2* p3*                          |
| Myopic Emmetropic Hyperopic                                  |
| Peripapillary RNFL thickness (µm)                            |
| Global            | 94.70±12.06 | 104.13±10.26 | 103.91±9.51 | 0.001 | 0.003 | 0.933 |
| Temporal          | 72.41±9.64  | 79.90±17.44  | 73.86±14.51 | 0.031 | 0.646 | 0.186 |
| Temporal superior | 128.26±24.4 | 140.5±15.1   | 126.82±17.61| 0.015 | 0.804 | 0.004 |
| Temporal inferior | 131.7±36.34 | 154.02±19.54 | 136.52±19.34| 0.002 | 0.538 | 0.001 |
| Nasal             | 65.86±17.06 | 81.52±13.43  | 85.95±18.8  | <0.001 | <0.001 | 0.296 |
| Nasal superior    | 102.83±18.31| 113.66±22.58 | 119±28      | 0.035 | 0.014 | 0.424 |
| Nasal inferior    | 100.96±22.53| 117.05±20.13 | 125.17±22.53| 0.003 | <0.001 | 0.155 |
| Central macula thickness (µm)                                |
| Central           | 252.96±17.94| 259.61±21.78 | 266.91±20.24| 0.187 | 0.011 | 0.202 |
| Temporal inner    | 312.13±21.98| 329.02±18.90 | 327±16.07   | 0.001 | 0.006 | 0.672 |
| Superior inner    | 326.43±23.19| 345.19±16.94 | 342.21±17.6 | <0.001 | 0.009 | 0.519 |
| Nasal inner       | 326.93±19.83| 341.8±18.62  | 343.26±19.75| 0.003 | 0.004 | 0.776 |
| Inferior inner    | 324.06±23.4 | 340.97±19.41 | 340.52±16.65| 0.002 | 0.006 | 0.927 |
| Temporal outer    | 277.7±10.17 | 286.72±15.01 | 279±22.99   | 0.007 | 0.783 | 0.124 |
| Superior outer    | 291.36±19.1 | 305.38±13.14 | 288.6±40.19 | 0.001 | 0.742 | 0.064 |
| Nasal outer       | 306.1±17.83 | 324.38±14.47 | 314.04±13.22| <0.001 | 0.082 | 0.008 |
| Inferior outer    | 282±17.72   | 294.77±12.55 | 293.13±16.32| 0.001 | 0.023 | 0.664 |
| Retinal layer thickness (µm)                                 |
| Nerve fiber       | 11±2.33     | 11.58±2.37   | 12.43±2.9   | 0.320 | 0.06  | 0.223 |
| Ganglion cell     | 13.76±3.99  | 14.11±4.5    | 15.21±4.6   | 0.746 | 0.226 | 0.365 |
| Inner plexiform   | 19.36±3.32  | 19.52±3.22   | 20.47±3.77  | 0.843 | 0.261 | 0.306 |
| Inner nuclear     | 17.1±7.07   | 15.8±4.04    | 21.34±6.92  | 0.355 | 0.033 | 0.001 |
| Inner retinal layers| 168.03±18.13| 172.25±21.33 | 180.3±20.96 | 0.396 | 0.027 | 0.160 |
| Outer plexiform   | 26.23±5.25  | 23.36±6.96   | 25.65±8.31  | 0.068 | 0.757 | 0.258 |
| Outer retinal layers| 84.93±3.8   | 87.38±4.31   | 86.6±4.04   | 0.018 | 0.132 | 0.490 |
| Retinal pigment epithelium                                  |
| 16.4±2.2         | 16.16±1.46  | 15.04±2.01   | 0.609 | 0.025 | 0.026 |

p1: Group 1 compared to Group 2; p2: Group 1 compared to Group 3; p3: Group 2 compared to Group 3; Bold denotes statistical significance (p<0.05); *: Independent t-test; RNFL: Retinal nerve fiber layer.
which suggests that myopia begins to affect the peripapillary RNFL thickness at an early age. This thinning may be a risk factor for the development of glaucoma, since it has been proposed that variations in the arrangement of ONH fibers make myopic eyes more susceptible to glaucomatous damage (22).

Limitations of this study include the small sample size and small variation in participant age. Additional research with a larger sample and greater range of age and sex among participants is necessary to confirm our findings.

In conclusion, the results of the present study demonstrated that myopic eyes had lower choroidal, RNFL, and retinal layer thickness measurements, and that hyperopic eyes had a higher CT value. This information may be valuable in the effort to determine markers of progression and prediction of ocular disease.

Disclosures
Ethics Committee Approval: The study protocol was approved by the university clinical research ethics committee on September 22, 2020 (No: 2020/8-9) and conformed to the tenets of the Declaration of Helsinki.

Peer-review: Externally peer-reviewed.

Conflict of Interest: None declared.

Authorship Contributions: Involved in design and conduct of the study (GAA, AHB, SSC); preparation and review of the study (EA, ASK); data collection (GAA, SSC); and statistical analysis (AHB, EA).

References
1. Huang D, Swanson EA, Lin CP, Schuman JS, Stinson WG, Chang W, et al. Optical coherence tomography. Science 1991;254:1178–81. [CrossRef]
2. Imamura Y, Fujitaya T, Margolis R, Spaide RF. Enhanced depth imaging optical coherence tomography of the choroid in central serous chorioretinopathy. Retina 2009;29:1469–73. [CrossRef]
3. Spaide RF, Koizumi H, Pozzoni MC. Enhanced depth imaging spectral-domain optical coherence tomography. Am J Ophthalmol 2008;146:496–500. [CrossRef]
4. Nickla DL, Wallman J. The multifunctional choroid. Prog Retin Eye Res 2010;29:144–68. [CrossRef]
5. Kim SW, Oh J, Kwon SS, Yoo J, Huh K. Comparison of choroidal thickness among patients with healthy eyes, early age-related maculopathy, neovascular age-related macular degeneration, central serous chorioretinopathy, and polypoidal choroidal vasculopathy. Retina 2011;31:1904–11. [CrossRef]
6. Hung LF, Wallman J, Smith EL III. Vision-dependent changes in the choroidal thickness of macaque monkeys. Invest Ophthalmol Vis Sci 2000;41:1259–69.
7. Wallman J, Wildsoet C, Xu A. Moving the retina: choroidal modulation of refractive state. Vision Res 2006;46:267–83.
8. Mrejen S, Spaide RF. Optical coherence tomography: Imaging of the choroid and beyond. Surv Ophthalmol 2013;58:387-429.
9. Jonas JB, Budde WM, Panda-Jonas S. Ophthalmoscopic evaluation of the optic nerve head. Surv Ophthalmol 1999;43,293–320. [CrossRef]
10. Hoffmann EM, Schmidtmann I, Siouli A, Schuster AK, Beutel ME, Pfeiffer N, et al. The distribution of retinal nerve fiber layer thickness and associations with age, refraction, and axial length: the Gutenberg health study. Graefes Arch Clin Exp Ophthalmol 2018;256,1685–93. [CrossRef]
11. Wei WB, Xu L, Jonas JB, Shao L, Du KF, Wang S, et al. Subfoveal choroidal thickness: the Beijing eye study. Ophthalmology 2012;119,175–80. [CrossRef]
12. Ren R, Li B, Gao F, Li L, Xu X, Wang N, et al. Central corneal thickness, lamina cribrosa and peripapillary scleral histomorphometry in non-glaucomatous Chinese eyes. Graefes Arch Clin Exp Ophthalmol 2010;248,1579–85. [CrossRef]
13. Kaderli A, Acar MA, Ünlü N, Üney GÖ, Örnek F. The correlation of hyperopia and choroidal thickness, vessel diameter and area. Int Ophthalmol 2018;38:645–53. [CrossRef]
14. Duan F, Yuan Z, Deng J, Wong YL, Yeo AC, Chen X. Choroidal thickness and associated factors among adult myopia: a baseline report from a medical university student cohort. Ophthalmic Epidemiol 2019;26:244–50. [CrossRef]
15. Heirani M, Shandiz JH, Shojaei A, Narooie-Noori F. Choroidal thickness profile in normal iranian eyes with different refractive status by spectral-domain optical coherence tomography. J Curr Ophthalmol 2020;32:58–68. [CrossRef]
16. Vincent SJ, Collins MJ, Read SA, Carney LG. Retinal and choroidal thickness in myopic anisometropia. Invest Ophthalmol Vis Sci 2013;54:2445–56. [CrossRef]
17. Hung LF, Wallman J, Smith EL 3rd. Vision-dependent changes in the choroidal thickness of macaque monkeys. Invest Ophthalmol Vis Sci 2000;41:1259–69.
18. Nickla DL, Wildsoet C, Wallman J. Compensation for spectacle lenses involves changes in proteoglycan synthesis in both the sclera and choroid. Curr Eye Res 1997;16:320–6. [CrossRef]
19. Jin P, Zou H, Zhu J, Xu X, Jin J, Chang T. Choroidal and retinal thickness in children with different refractive status measured by swept-source optical coherence tomography. American Journal of Ophthalmology 2016;168:164–76. [CrossRef]
20. Oner V, Aykut V, Tas M, Alakus MF, Iscan Y. Effect of refractive status on peripapillary retinal nerve fibre layer thickness: a study by RTVue spectral domain optical coherence tomography. Br J Ophthalmol 2013;97:75–9. [CrossRef]
21. Lee JY, Yau GSK, Woo TTY, Yick DWF, Tam VTY, Lai JSM. Retinal nerve fiber layer thickness in myopic, emmetropic, and hyperopic children. Medicine (Baltimore) 2015;94:e699. [CrossRef]
22. Ma F, Dai J, Sun X. Progress in understanding the association between high myopia and primary open-angle glaucoma. Clin Exp Ophthalmol 2014;42:190–7. [CrossRef]