RESEARCH ARTICLE

Evaluation of the Macular Thickness by Optical Coherence Tomography in Amblyopia

Suat Altındağ[1], Muhammed Şahin[2]

ABSTRACT

Objective: To measure and compare macular thicknesses (MT) in patients that have amblyopia and control group eyes with optical coherence tomography (OCT) and to define OCT as an early diagnosis tool.

Methods: 27 patients having amblyopia associated strabismus classified as group 1, 18 patients having amblyopia associated anisometropia classified as group 2 and 45 healthy volunteers classified as group 3 were enrolled into the study. All participants were underwent into the full ophthalmological examination and were measured MT by OCT.

Results: There was a statistical significance between control group and group 1 in central MT (p=0.01). But there was no significant differences between areas as we divided the macular thicknesses other quadrants. When we compare group 2 and group 3 there was thinner statistical significance in temporal quadrants (p=0.04). There was no significant difference between the other quadrants and central MT (p<0.05). There was significant difference between group 1 and group 2 in central MT (p=0.03). No significant difference was found between group 1 and group 2 in other quadrants (p<0.05).

Conclusion: Changes in macular thicknesses in strabismic amblyopia measured by OCT shows that structural changes can develop in amblyopia. OCT gives hope as early diagnosis tool with the non-invasive feature in vivo. *J Clin Exp Invest 2016; 7 (2): 178-183*

Key words: Amblyopia, macular thickness, optical coherence tomography

Ambliyopi Olgularında Makula Kalınlığının Optik Koherens Tomografi ile Değerlendirilmesi

ÖZET

Amaç: Bir gözü ambliyop olan hastaların makula kalınlığını (MK), makuladaki yapısal değişiklikleri, sağlıklı kontrol grubu gözlerinin makula parametreleriyle optik koherens tomografi (OKT) yoluyla değerlendirmektir.

Yöntemler: Şaşılığa bağlı ambliyopisi olan 27 göz grup 1, anizometropiye bağlı ambliyopisi olan 18 göz grup 2 ve ambliyopisi olmayan 45 göz ise grup 3 olarak sınıflandırıldı ve kendi aralarında karşılaştırıldı. Tüm olgularda tam bir oftalmolojik muayeneye ek olarak OKT ile MK analizi yapıldı.

Bulgular: Grup 1 ile grup 3 karşılaştırıldığında santral MK, istatistiksel anlamlı olarak grup 1'de daha kalın bulundu (p=0,01). Diğer makula kadranları arasında ise istatiksel olarak anlamlı bir fark bulunmadı. (p<0,05). Grup 2 ile grup 3 karşılaştırıldığında temporal kadran MK'da, istatistiksel anlamlı olarak grup 2'de daha ince bulundu (p=0,04). Diğer makula kadranları arasında ise istatiksel olarak anlamlı bir fark bulunmadı. (p<0,05). Grup 1 ile grup 2 karşılaştırıldığında grup 1 santral MK, istatistiksel anlamlı olarak daha kalın bulundu (p=0,03). Diğer makula kadranları arasında ise istatiksel olarak anlamlı bir fark bulunmadı. (p<0,05).

Sonuç: Ambliyopide saptanan makula kalınlığındaki değişiklikler, makula da yapısal değişikliklerin olabileceğini göstermektedir. İn vivo, non-invaziv bir görüntüleme yöntemi olan OKT ambliyopi olgularında erken tanı aracı olarak umut vaad edebilir.

Anahtar kelimeler: Ambliyopi, makuler kalınlık, optik koherens tomografi

[1] Dr. Münif İslamoğlu Devlet Hastanesi, Göz Kliniği, Kastamonu, Türkiye
[2] Dicle Üniversitesi Tıp Fakültesi Göz Hastalıkları Anabilim Dalı, Diyarbakır, 21280, Türkiye
Correspondence: Muhammed Şahin,
Dicle Üniversitesi Tıp Fakültesi Göz Hastalıkları AD, Diyarbakır Türkiye   Email: drmuhammedsahin@gmail.com

INTRODUCTION

Amblyopia is characterized by a reduction in visual acuity in one or both eyes during visual development due to visual deprivation or abnormal binocular inter-action, with no identifiable organic cause [1,2]. Al-though it is defined as a difference of two or more rows between the two eyes in the Snellen chart, the severity of amblyopia varies from not being able to read a few characters on the 10/10 row to having visual acuity at the level of hand motions. The condition is usually unilateral but may also be bilateral. Various studies have determined the prevalence of amblyopia as 2-5% [3-5]. In Turkey, Çaça et al. found a prevalence of 2.6% among pediatric patients [6]. Amblyopia is the most common sensory abnormality seen with strabis-mus and is the most common cause of low vision in pediatric patients. Amblyopia is classified into three subtypes: strabismic, anisometropic and deprivational [7]. Children are most susceptible to amblyopia at 2-3 years of age, and susceptibility gradually decreases until age 6-7, when visual development is complete and the retinocortical pathways and visual centers are resistant to abnormal visual input [8].

Diagnosis and treatment in the early stages is crit-ical in order to enable binocular vision and prevent the progression of amblyopia. Autopsy studies of patients with strabismus have revealed that the cells of the lat-eral geniculate nucleus (LGN) are smaller and fewer in number in these patients [9]. In animal studies it has been demonstrated that blurred vision and strabismus in early visual development may case structural and functional damage to the LGN and striate cortex [10]. Although the primary manifestations of strabismus and amblyopia are changes in the visual cortex, it is also possible to detect changes in the retina secondary to strabismus and amblyopia by quantitatively evalu-ating macular thickness (MT) with optical coherence tomography (OCT).

OCT was first introduced by Fujimoto of the Massachusetts Institute of Technology and the first ru-dimentary OCT devices came into use in ophthalmol-ogy [11]. OCT is a noninvasive and noncontact meth-od that allows high-resolution cross-sectional imaging of tissues. The aim of this study was to assess retinal structural changes and evaluate the utility of OCT as an early diagnostic tool in amblyopia by comparing MT in amblyopic eyes with eyes of healthy control subjects.

METHODS

The study included 45 patients with amblyopia who were examined in the Strabismus Unit of the Dicle University School of Medicine Department of Oph-thalmology between August 2012 and May 2014. The study was conducted in accordance with the statutes of the Declaration of Helsinki and participants signed informed consent forms.

A detailed medical history was obtained from all study participants. Patients were asked about age, gen-der and systemic diseases. Corrected visual acuity was assessed using the Snellen chart, intraocular pressure was measured with pneumotonometer, and slit-lamp examination of the anterior segment was performed. All patients were assessed for strabismus using alter-nating cover tests. Near and distance angles of devia-tion were measured in patients with strabismus using the prism cover test. Refractive errors were assessed with autorefractometer and skiascope 30 minutes af-ter 3 instillations of 1% tropicamide drops (Tropamid, Bilim, Turkey) at 10 minute intervals. Corrected visu-al acuity was measured after correcting for refractive errors. Fundoscopy was performed using a +90 D non-contact lens to examine the fundus for pathology. Cri-teria used for a diagnosis of amblyopia were complete or near complete vision in one eye, a difference in best corrected visual acuity between the two eyes of two or more Snellen rows, and the absence of signs of organic pathology in the eye with low vision. Exclusion criteria included presence of nystagmus; intraocular pressure over 21 mmHg as measured by pneumatic tonometry; presence of corneal or lens opacity which would im-pair vision and prevent imaging; abnormal appearance of the optic nerve head, macular or vascular structures; presence of peripapillary choroidal atrophy; spherical or cylindrical refractive error greater than ± 5.0 D in both eyes; and presence of eccentric fixation. Patients with spherical or cylindrical refractive error over ± 1.0 D were not included in the study group. Differences of 2 D in spherical equivalent and over 1 D in refraction were accepted as anisometropia.

According to these criteria, the study participants were analyzed in three groups: group 1 included 27 eyes of patients with strabismic amblyopia, group 2 comprised 18 eyes of patients with anisometropic amblyopia, and group 3 included 45 eyes of control patients.

OCT Measurements

MT was measured with a Spectralis® OCT instrument (Heidelberg Engineering, Heidelberg, Germany) while the pupils were still dilated from the instillation of 1% tropicamide for refraction measurements. A 6 mm ETDRS ring with 9 regions was used when assessing macular thickness (Figure 1). The macular map was divided into 9 regions: 3 concentric rings of 1, 3 and 6 mm diameter for the fovea, inner macula and outer macula, with the outer concentric rings divided into 4 quadrants each. In the current study, the fovea, inner inferior, inner nasal, inner superior and inner temporal regions were taken as the macula. All measurements were performed by the same experienced technician (SA).

Statistical Analysis

SPSS version 18.0 (Statistical Package for the Social Sciences, IBM, USA) was used for all statistical analyses. Categorical variables were expressed as number and percentage, numerical variables as mean and standard deviation. The chi-square test was used in comparisons of categorical values. In comparisons of numerical values within groups, one-way ANOVA was used for data with normal distribution and the Kruskal-Wallis test was used for data with non-normal distribution. The chi-square and Mann-Whitney U tests were used in comparisons between groups. The level of significance was accepted as 0.05 for all analyses.

RESULTS

Demographic Characteristics

The mean ages of the study groups were 11.9±6.3 (range, 4-28) years for the 27 patients with strabismic amblyopia, 11.3±3.5 (range, 6-18) years for the 18 patients with anisometropic amblyopia, and 11.4±5.2 (range, 4-28) years for the 45 control subjects. There were no significant differences in age or gender between the groups (p>0.05). The patients' demographic characteristics are shown in Table 1.

Table 1. Patients' demographic characteristics according to three groups

	Group 1	Group 2	Group 3
Age (years)	11.9 ± 6.3	11.3 ± 3.5	11.4 ± 5.2
Gender (male)	14 (52%)	10 (55%)	24 (53%)
Gender (female)	13 (48%)	8 (44%)	21 (46%)

Macular Thickness

Central MT and 3 mm inner MT values for each group are shown in Table 2.

Central MT was significantly greater in group 1 than in group 3 (p=0.01). No other significant differences in MT were found between groups 1 and 3 in the other regions (p>0.05).

MT in the inner temporal region was significantly thinner in group 2 than in group 3 (p=0.04). There were no other significant differences in MT between groups 2 and 3 (p>0.05).

Group 2 showed significantly lower central MT values than group 1 (p=0.03). No statistical differences in MT were observed between groups 1 and 2 in the superior, inferior, nasal or temporal macular regions (p>0.05).

Table 2. Central macular thickness and 3 mm inner macular thickness values for each group

|		n	Macular Thickness (Mean±SD) (μm)	p value (I-III)	p value (II-III)
Central	Group 1 (I)	27	303 ± 42	0.01	
	Group 2 (II)	18	278 ± 28		
	Control (III)	45	268 ± 30		
Inferior (3 mm)	Group 1 (I)	27	340 ± 24		
	Group 2 (II)	18	336 ± 13		
	Control (III)	45	335 ± 22		
Superior (3 mm)	Group 1 (I)	27	341 ± 21		
	Group 2 (II)	18	336 ± 22		
	Control (III)	45	345 ± 18		
Temporal (3 mm)	Group 1 (I)	27	325 ± 27		
	Group 2 (II)	18	317 ± 15		0.04
	Control (III)	45	328 ± 17		
Nasal (3 mm)	Group 1 (I)	27	340 ± 33		
	Group 2 (II)	18	336 ± 19	0.20	
	Control (III)	45	345 ± 18		

MT: macula thickness, SD: Standard deviation

Visual Acuity

Visual acuity was significantly lower in groups 1 and 2 compared to the control group (p=0.001), but the difference between group 1 and group 2 was not significant (p=0.8). Evaluation of the visual acuity of each group is shown in Table 3.

Tablo 3. Evaluation of the visual acuity of each group

		Number of cases	Visual acuity (Mean±SD)	p value (Group 1-Controls)	p value (Group 2-Controls)
Visual acuity (Snellen)	Group 1	27	0.37 ± 0.21	0.001	
	Group 2	18	0.41 ± 0.23		0.001
	Control	45	0.93 ± 0.19		

SD: Standard deviation
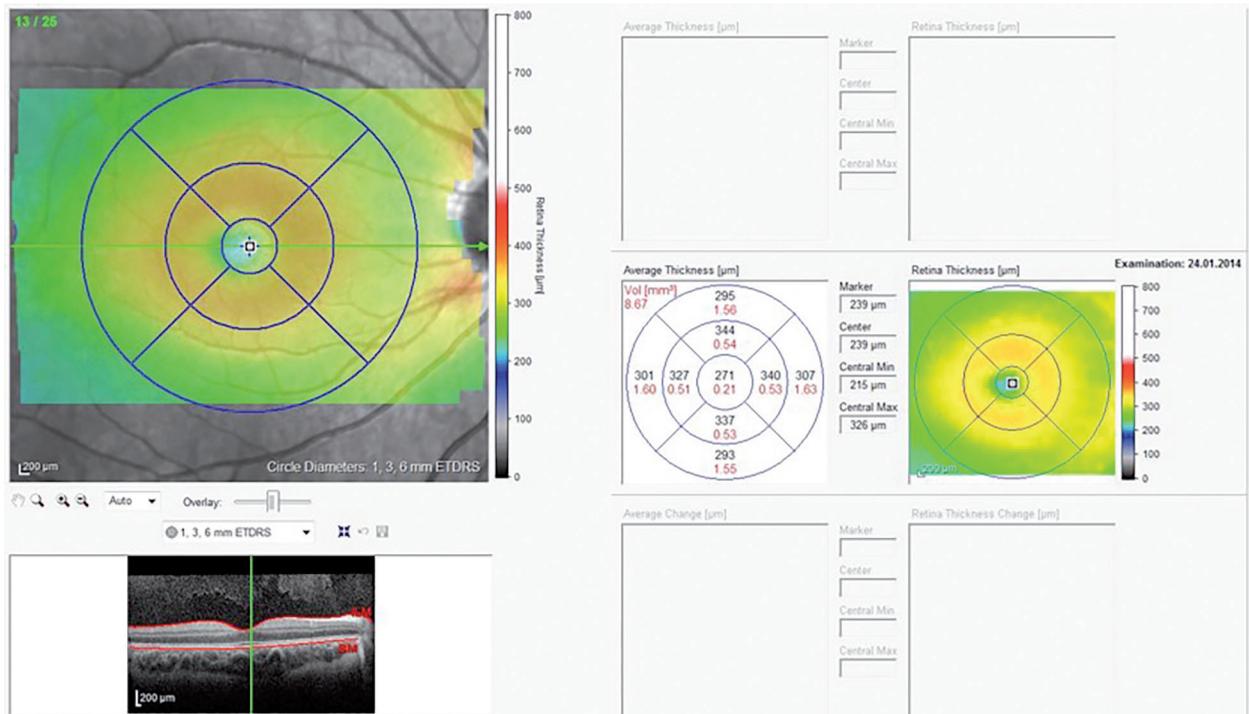
Figure 1. Macular thickness analysis with spectral OCT (A 6 mm ETDRS ring with 9 regions was used when assessing macular thickness)

DISCUSSION

Amblyopia is characterized by a reduction in visual acuity in one or both eyes despite no apparent organic pathology [12]. Although no structural abnormalities can be detected in amblyopia, it has been shown that anatomic and functional changes in the visual cortex and LGN may occur due to visual deprivation [7]. The visual pathway begins in the photoreceptor layer and ends in the visual cortex. Therefore, amblyopia may affect the visual pathway at various levels and bring about certain anatomic alterations in the retina [10]. However, the changes in the retina are controversial. Many studies have attempted to explain the relationship between strabismus and amblyopia and the LGN [10,13]. Hubel et al. [14] investigated projections from the LGN to the visual cortex in monkeys with covered eyes and found that the cortical pathways narrowed, while the cortical pathways from the healthy eyes widened. It has been demonstrated that blurred vision and strabismus in early visual development may cause structural and functional damage to the LGN and striate cortex [9,10,15,16].

OCT is a noninvasive, noncontact method for in vivo visualization of retinal structures. In the present study, we utilized OCT to detect changes in the retinas of patients with amblyopia. Central MT of patients with strabismic amblyopia was significantly greater than that of patients with anisometropia and control subjects. Furthermore, patients with anisometropic amblyopia had higher MT values in the 3 mm inner temporal region (in ETDRS ring) compared to control subjects. Many studies in the literature report results

consistent with our own, while many others have contradictory findings [17-23].

In a study by Huynh et al. [20] with a large case series, amblyopic eyes showed greater MT than normal eyes, though the difference was not statistically significant. Dickmann et al. [24] found thicker maculas in eyes with strabismic amblyopia but detected no difference in anisometropic amblyopia. Altıntaş et al. [17] and Repka et al. [25] reported no statistically significant differences in MT in strabismic amblyopia. Yoon et al. [18] found no difference in MT between the amblyopic and normal eyes of patients with unilateral anisometropic amblyopia, but reported the retinal nerve fiber layer (RNFL) was thicker in the amblyopic eyes. Ayyıldız and Çallı [26], on the other hand, detected a significant difference in MTs measured by spectral domain OCT in pediatric patients with unilateral anisometropic amblyopia. In a study of anisohypermetropic and strabismic amblyopia patients, Erşan et al. [27] found that macular parameters were thicker in amblyopic eyes compared to their fellow eyes. Sefiyurdakul et al. [28] did not detect a significant difference in RNFL thickness between eyes with strabismic or anisohypermetropic amblyopia and normal eyes, but found greater central MT in anisohypermetropic amblyopic eyes. Although Ulaş et al. [29] found differences in some RNFL segments between the amblyopic and normal eyes of patients with unilateral anisometropic amblyopia, they reported that MT values were comparable.

In a study using spectral domain OCT, no significant difference in MT could be detected between the amblyopic and healthy eyes of patients with strabismic amblyopia [22]. In another study, All-Haddad et al. [23] compared strabismic and anisometropic amblyopia patients with a healthy control group; they found a significantly greater MT in the amblyopic eyes of the anisometropic amblyopia group, but the difference was nonsignificant in the strabismic amblyopia and non-amblyopic anisometropia groups.

In the current study, no significant difference in MT was detected in the superior, inferior and nasal regions in eyes with strabismic amblyopia, but central MT was thicker than that of the control group. It has been theorized that the increased MT in amblyopic eyes may be related to incomplete development, particularly inhibition of the formation of the foveal depression. However, we found that inner temporal MT values were significantly lower in anisometropic amblyopia patients than in control subjects. This may

be explained by the theory that the loss of different neural cells may occur depending on the etiology of the subtype of amblyopia.

In this study, we observed increased thickness in certain parameters of the MT measurements of amblyopic eyes on OCT. Despite the studies demonstrating damage to the higher visual pathways like the LGN and visual cortex in amblyopia, our findings of increased macular thickness also suggests the presence of structural changes in the retina. Progressive macular thickening in OCT measurements taken at different times may be a indicator of amblyopia development. Although there is a need for histological studies demonstrating the presence of retinal damage in amblyopia, we believe the in vivo, noninvasive imaging method OCT is a promising tool for the early diagnosis of amblyopia.

In conclusion, our findings of markedly thicker macular parameters in patients with strabismic amblyopia compared to the control group suggests that although amblyopia primarily affects the visual cortex, it is also a process that leads to secondary changes at the retinal level. However, prospective studies with larger case series and more advanced instruments measuring a wider variety of parameters are needed.

REFERENCES

1. Von Noorden GK. Amblyopia: a multidisciplinary approach. Proctor lecture. Invest. Ophthalmol Vis Sci. 1985;26:1704-16.

2. Wright KW. Visual Development and Amblyopia. In: MD KWW, MD PHS, editors. Pediatr. Ophthalmol. Strabismus [Internet]. Springer New York; 2003 [cited 2016 Feb 23]. p. 157-71. Available from: http://link.springer.com/chapter/10.1007/978-0-387-21753-6_10.

3. Eibschitz-Tsimhoni M, Friedman T, Naor J, et al. Early screening for amblyogenic risk factors lowers the prevalence and severity of amblyopia. J Am Assoc Pediatr Ophthalmol Strabismus. 2000;4:194-9.

4. Friedman DS, Repka MX, Katz J, et al. Prevalence of amblyopia and strabismus in white and African American children aged 6 through 71 months the Baltimore Pediatric Eye Disease Study. Ophthalmology. 2009;116:2128-34.e1-2.

5. Groenewoud JH, Tjiam AM, Lantau VK, et al. Rotterdam AMblyopia screening effectiveness study: detection and causes of amblyopia in a large birth cohort. Invest Ophthalmol Vis Sci. 2010;51:3476-84.

6. Caca I, Cingu AK, Sahin A, et al. Amblyopia and refractive errors among school-aged children with low socioeconomic status in southeastern Turkey. J. Pediatr. Ophthalmol. Strabismus. 2013;50:37-43.

7. Von Noorden GK. Classification of amblyopia. Am J Ophthalmol. 1967;63:238-44.

8. Von Noorden GK. New clinical aspects of stimulus deprivation amblyopia. Am J Ophthalmol. 1981;92:416-21.

9. Von Noorden GK, Crawford ML. The lateral geniculate nucleus in human strabismic amblyopia. Invest Ophthalmol Vis Sci. 1992;33:2729-32.

10. Von Noorden GK, Middleditch PR. Histology of the monkey lateral geniculate nucleus after unilateral lid closure and experimental strabismus: further observations. Invest Ophthalmol. 1975;14:674-83.

11. Huang D, Swanson EA, Lin CP, et al. Optical coherence tomography. Science. 1991;254:1178-81.

12. Campos E. Amblyopia. Surv Ophthalmol. 1995;40:23-39.

13. Von Noorden GK, Crawford ML. Form deprivation without light deprivation produces the visual deprivation syndrome in Macaca mulatta. Brain Res. 1977;129:37-44.

14. Hubel DH, Wiesel TN, LeVay S. Functional architecture of area 17 in normal and monocularly deprived macaque monkeys. Cold Spring Harb Symp. Quant. Biol. 1976;40:581-9.

15. Von Noorden GK, Crawford ML, Levacy RA. The lateral geniculate nucleus in human anisometropic amblyopia. Invest. Ophthalmol. Vis Sci. 1983;24:788-90.

16. Von Noorden GK, Crawford ML. The effects of total unilateral occlusion vs. lid suture on the visual system of infant monkeys. Invest. Ophthalmol. Vis Sci. 1981;21:142-6.

17. Altintas O, Yüksel N, Ozkan B, Caglar Y. Thickness of the retinal nerve fiber layer, macular thickness, and macular volume in patients with strabismic amblyopia. J Pediatr Ophthalmol Strabismus. 2005;42:216-21.

18. Yoon SW, Park WH, Baek S-H, Kong SM. Thicknesses of macular retinal layer and peripapillary retinal nerve fiber layer in patients with hyperopic anisometropic amblyopia. Korean J Ophthalmol KJO. 2005;19:62-7.

19. Pang Y, Goodfellow GW, Allison C, et al. A prospective study of macular thickness in amblyopic children with unilateral high myopia. Invest. Ophthalmol. Vis Sci. 2011;52:2444-2449.

20. Huynh SC, Samarawickrama C, Wang XY, et al. Macular and nerve fiber layer thickness in amblyopia: the Sydney Childhood Eye Study. Ophthalmology. 2009;116:1604-9.

21. Soyugelen G, Onursever N, Bostancı Ceran B, Can İ. Evaluation of macular thickness and retinal nerve fiber layer by optical coherence tomography in cases with strabismic and anisometropic amblyopia. Turk J Ophthalmol. 2011;41:1-9.

22. Walker RA, Rubab S, Voll ARL, et al. Macular and peripapillary retinal nerve fibre layer thickness in adults with amblyopia. Can. J. Ophthalmol. J Can Ophtalmol. 2011;46:425-7.

23. Al-Haddad CE, Mollayess GMEL, Cherfan CG, et al. Retinal nerve fibre layer and macular thickness in amblyopia as measured by spectral-domain optical coherence tomography. Br J Ophthalmol. 2011;95:1696-9.

24. Dickmann A, Petroni S, Salerni A, et al. Unilateral amblyopia: An optical coherence tomography study. Pediatr. Ophthalmol. Strabismus. 2009;13:148-50.

25. Repka MX, Kraker RT, Tamkins SM, et al. Retinal nerve fiber layer thickness in amblyopic eyes. Am J Ophthalmol. 2009;148:143-7.

26. Ayyıldız T, Çallı Ü. Comparison between amblyopic and non-amblyopic of the same patient's eye in terms of macula and retinal nerve fiber layer thickness with the help of spectral optical coherens tomography. Yeni Tıp Derg. 2015;32:148-52.

27. Erşan İ, Oltulu R, Zengin N, Pekel H. The Evaluation of Macula in patients with unilateral anisometropic and strabismic amblyopia using optical coherence tomography. Turk Klin J. Ophthalmol. 2013;22:71-3.

28. Sefi-yurdakul N, Coşar A, Koç F. Strabismik ve anizohipermetropik ambliyopi olgularında retina sinir lifi tabakası ve makula kalınlığı. Turk Klin J Ophthalmol. 2014;23:201-4.

29. Ulaş F, Kaymaz A, Doğan Ü, et al. Evaluation of retinal nerve fiber layer thickness and macular thickness measurements using optical coherence tomography in patients with unilateral anisometropic amblyopia. Turk Klin J Ophthalmol. 2012;21:220-6.