MJFAS MALAYSIAN JOURNAL OF FUNDAMENTAL AND APPLIED SCIENCES
PRINT ISSN: 2289-5981 | ONLINE ISSN: 2289-599X

RESEARCH ARTICLE

Comparison of choroidal thickness between amblyopic and non-amblyopic eyes

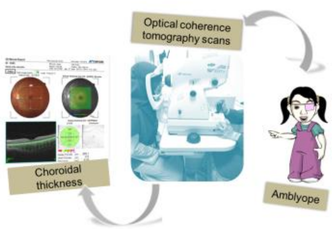
Elly Liyana Zainodin, Ai-Hong Chen*

Optometry and Vision Science Research Center (iROViS), Faculty of Health Sciences, Universiti Teknologi MARA Selangor, 42300 Puncak Alam, Malaysia.

* *Corresponding author: aihong0707@yahoo.com*

Article history
Received 20 Mac 2018
Revised 5 April 2018
Accepted 8 May 2018
Published Online 3 September 2018

Graphical abstract



Abstract

Our study examined the choroidal thickness profile of children with myopic anisometropic amblyopia and compared the thickness with the fellow eyes. The choroidal thickness was measured with the enhanced depth imaging with spectral-domain optical coherence tomography. Manual segmentations of the choroid were performed on a 25-raster horizontal scan. The choroidal thickness measurements of the 9 subfields defined by the Early Treatment Diabetic Retinopathy Study (ETDRS) were evaluated. The mean spherical equivalent of the amblyopic eyes was -10.80 ± 0.41 D and the fellow eyes was -4.40 ± 2.05 D. The mean best corrected visual acuity of the amblyopic eyes and the fellow eyes were 0.94 ± 0.27 and 0.14 ± 0.05 logMAR respectively. The amblyopic eyes have longer axial length (26.46 ± 0.44 mm) compared to the fellow eyes (23.59 ± 1.18 mm). The average subfoveal choroidal thickness was 124.30 ± 40.71 µm in the amblyopic eyes and 246.80 ± 58.63 µm in the fellow eyes. The horizontal and vertical distribution pattern of choroidal thickness in amblyopic eyes was different from the fellow eyes. In amblyopic eye the choroidal thickness reduced from the temporal region to the nasal region. The fellow eyes had thickest choroid at the subfoveal area, followed by the temporal region and nasal region. In conclusion, the choroid was thinner in the amblyopic eyes than that of the fellow eyes at all regions.

Keywords: Myopic anisometropic amblyopia, choroidal thickness, children, optical coherence tomography

INTRODUCTION

Amblyopia is a condition characterized by unilateral or bilateral reduced visual acuity even with optimum refractive correction and in absence of other pathological diseases (Rouse, 2004). Depending on the etiology, amblyopia is classified into strabismus, form deprivation and anisometropia. It is ascertained that amblyopia occurs as a result of morphological changes to the lateral geniculate nucleus and the visual cortex during infancy and early childhood (Campos, 1995; Moss, 2005). A number of studies have investigated the retinal nerve fibre layer thickness (Wu *et al.*, 2013; Yen *et al.*, 2004) and retinal thickness (Pang *et al.*, 2015) in the eyes of amblyopia. However, there has been dispute between those studies regarding involvement of the retina in amblyopia.

Recent studies suggest that the choroid may play a role in the regulation of refractive state and maybe involved in the emmetropization process. Choroid is one of the most vascularized pigmented structures of the eye that lies between the retina and sclera. It is mainly responsible to deliver nutrition and oxygen to the retina and drains aqueous humor from the anterior chamber through the uveoscleral pathway (Ruiz-Moreno *et al.*, 2013). Evidence from animal studies showed that the choroid modulates its thickness as a result of the axial length changes during emmetropization process (Hung *et al.*, 2000; Troilo *et al.*, 2000). In marmosets (Troilo *et al.*, 2000) and macaque monkeys (Hung *et al.*, 2000), myopic defocus and hyperopic defocus were compensated with choroidal thickening and choroidal thinning respectively. The existing bodies of research on the ability of the choroid to modulate its thickness in the eyes of these animal models raised the possibility if the same phenomenon occurs in humans.

The anatomy of the choroid has been studied extensively in the normal eyes of human (Agawa *et al.*, 2011; Chhablani *et al.*, 2014; Coşkun E1 *et al.*, 2014; Ding *et al.*, 2011; Ruiz-Moreno *et al.*, 2013). In normal eyes, the choroid was reportedly reduced in thickness with increased degree of myopia (Jin *et al.*, 2016). However, only a limited number of studies have examined choroidal thickness in adults and children with amblyopia (Aygit et al., 2015; Kantarci et al., 2015; Nishi, Ueda, Hasegawa, Miyata, & Ogata, 2014; Tenlik et al., 2014). The non-invasive optical coherence tomography with enhanced depth imaging technique allows high resolution visualization of the choroid in those studies (Aygit et al., 2015; Kantarci et al., 2015; Mori, Sugano, Maruko, & Sekiryu, 2014; Nishi et al., 2014; Tenlik et al., 2014; Xu et al., 2014). Those studies which predominantly determined choroidal thickness in strabismus and hyperopic anisometropic amblyopia found thicker choroid in the amblyopic eyes compared with the fellow eyes or controls.

However, research to date has not yet determined the choroidal thickness in children with myopic anisometropic amblyopia. Our study aimed to determine the anatomical profile of the choroid in myopic anisometropic amblyopia using the spectral domain optical coherence tomography (SD-OCT) with enhanced depth imaging

(EDI) technique. In addition to elucidate whether the anatomy of the choroid in the amblyopic eye was different from the fellow eye.

EXPERIMENTAL

The choroidal profile of the amblyope was examined and compared with the fellow non-amblyopic eyes in a cross-sectional study design. Measurements of choroidal thickness were made within 6 mm macular area using spectral-domain optical coherence tomography, supplemented with enhanced depth imaging technique. Reduced choroidal thickness presented in the eyes with amblyopia by the ETDRS topography map would indicate different choroidal profile of the amblyope from the normal.

Choroidal thickness was measured in five myopic anisometropic amblyopes who were recruited from Hospital Selayang. All subjects were follow-up patients diagnosed with anisomyopic amblyopia in the hospital. Ethics approval was obtained from the UiTM research ethics committee and the Medical Research & Ethics Committee (MREC) in accordance to the ICH Good Clinical Practice Guidelines and the Declaration of Helsinki. Written informed consent was obtained from the child's parent or legal guardian before the participation.

Choroidal imaging and segmentation

The images of the choroid of the anisomyopic eyes were obtained by Heidelberg Spectralis Optical Coherence Tomography (Heidelberg Engineering, Heidelberg, Germany) using enhanced depth imaging (EDI-OCT) technique. In order to avoid diurnal variations of the choroidal thickness measurement, all examinations were performed between 12:00 to 15:00. The method of obtaining EDI OCT images has been reported previously (Spaide *et al.*, 2008). The OCT scans were performed on the amblyopic eye and fellow eye of the amblyopes. A 25 raster horizontal scan protocol using enhanced depth imaging (EDI) was employed for each image scans. In order to get the best image of the choroid, the images were averaged for 100 scans using the automatic averaging feature. The axial length was measured with a non-contact biometer (IOL Master; Carl Zeiss Meditec).

A topographic retinal map analysis based on the ETDRS (Early Treatment Diabetic Retinopathy Study) grid was selected to display the numeric average of the choroid thickness measurements. The map divided the macula into 3 concentric circles, that regard to the 1 mm central area, the parafoveal 3 mm inner circle and the perifoveal 6 mm outer circle. The 3 mm and 6 mm circles were further divided into four subfields which are nasal, temporal, superior and inferior to the fovea. The choroidal thickness values that appeared in the described subfields were produced from manual segmentations of the outer border of the hyperreflective line corresponding to the retinal pigmented epithelium (RPE), and the chorioscleral border. Manual segmentations of the RPE and the chorioscleral border of each image were performed by 2 examiners independently using the built-in Heidelberg Eye Explorer software (version 1.5.12.0; Heidelberg Engineering). The manual segmentation of the choroid was performed by moving the line on internal limiting membrane layer to the RPE, and the line on Bruch membrane to the chorioscleral border for each 25 horizontal scan. Complete segmentation of the 25 horizontal scans automatically altered the retinal thickness displayed on the ETDRS grid to choroidal thickness. The average of all points within the 1 mm central circle represented the subfoveal choroidal thickness.

RESULTS AND DISCUSSION

The mean best corrected visual acuity of the amblyopic eyes and the fellow eyes were 0.94 (± 0.27) and 0.14 (± 0.05) logMAR respectively. The mean spherical equivalent of the amblyopic eyes was -10.80 (± 0.41) D, which was more myopic than the fellow eyes (-4.40 ± 2.05 D). The amblyopic eyes had longer axial length (26.46 ± 0.44 mm) compared to the fellow eyes (23.59 ± 1.18 mm). The subfoveal choroid of the amblyopic eyes was much thinner (124.30 µm) compared with the fellow eyes (246.80 µm). In the amblyopic eyes, the choroid was thinnest in the nasal region followed by thesubfoveal, inferior, superior and temporal region for the 3 mm and 6 mm diameter macular areas (Fig. 1). The choroidal thickness for each of the macular subfield within the 3 mm diameter parafoveal region in the amblyopic eyes was 122.00 (± 39.23) µm in the nasal, 138.20 (± 53.64) µm in the inferior, 141.90 (± 54.01) µm in the superior, and 144.70 (± 52.66) µm in the temporal. For the 6 mm perifoveal region, the choroidal thickness of the amblyopic eyes was 93.75 (± 33.04) µm in the nasal subfield, 136.60 (± 63.59) µm in the inferior subfield, 145.30 (± 47.09) µm in the superior subfield and 148.50 (± 49.46) µm in the temporal subfield. The choroidal thickness for the nasal, temporal, inferior and superior 3 mm parafoveal subfields in the fellow eyes was 203.10 (± 38.40) µm, 245.20 (± 53.55) µm, 218.40 (± 48.18) µm and 250.10 (± 59.27) µm respectively. For the 6 mm perifoveal region, the choroidal thickness of the fellow eyes was 146.40 (± 25.61) µm in the nasal subfield, 231.50 (± 51.86) µm in the temporal subfield, 191.70 (± 36.80) µm in the inferior subfield and 243.20 (± 38.92) µm in the superior subfield.

Overall, the choroid was thinner in the amblyopic eyes at all parafoveal and perifoveal macular subfields than the fellow non-amblyopic eyes. The horizontal and vertical distribution of the choroid in the amblyopic eyes was different from the fellow eyes. The choroid reduced in thickness horizontally from the temporal quadrant to the nasal quadrant in the amblyopic eyes. However, the choroid was the thickest in the fellow non-amblyopic eyes at the subfoveal area followed by the temporal region and the nasal region. The vertical choroidal profile in the amblyopic eyes was also different from the fellow eyes. In the amblyopic eyes, the choroid was thinnest at the subfoveal area but thicker at the superior and inferior subfields for the 3 mm parafoveal and 6 mm perifoveal regions. For the fellow eyes, the choroid was thinner at the inferior 3 mm and 6 mm diameter subfields than the superior regions.

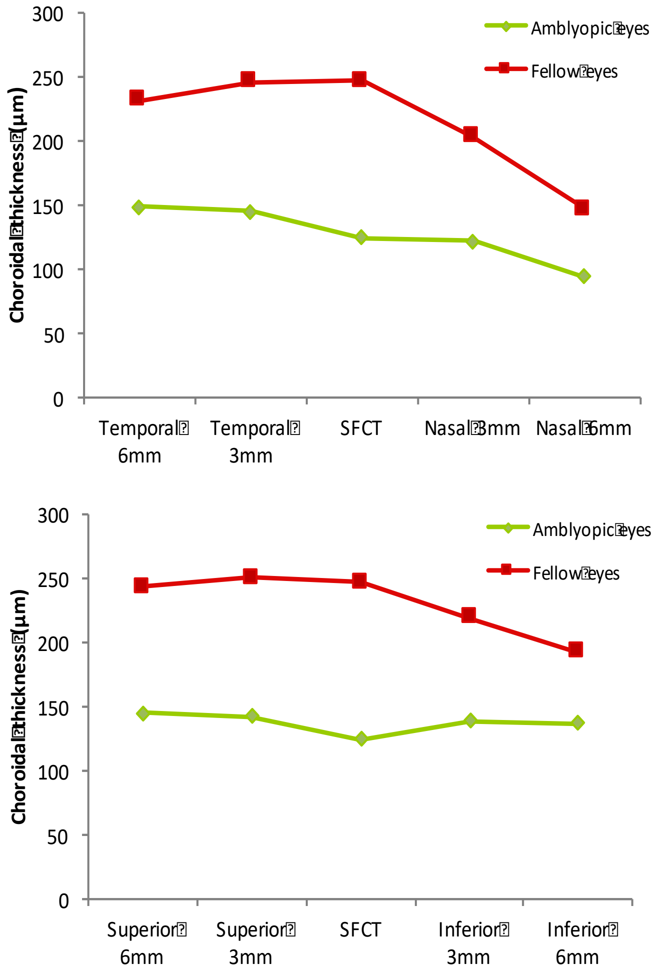


Fig. 1 The average choroidal thickness profile of the amblyopic eyes and fellow eyes in horizontal (A) and vertical (B) meridians.

Our findings suggested that the choroidal thickness profile of the amblyopic eyes was different from the non-amblyopic eyes. The amblyopic eyes were found to have thinner choroid in all regions of the macular subfields compared with the fellow eyes. Our findings seemed to be consistent with what have been postulated earlier in animal studies. In a study on young monkeys, choroidal thickness was reported to change rapidly to compensate changes in the effective refractive state (Hung *et al*., 2000). The choroid thickened in response to imposed myopic defocus, but thinned in response to imposed hyperopic defocus in order to adjust the position of the retina to maintain clear vision. Following several lines of evidence from other animal studies, it was postulated that other than nourishing the retina, the choroid was also involved in the regulation of the refractive state in the early life of the humans (Hung *et al*., 2000; Troilo *et al*., 2000; Wildsoet & Wallman, 1995). If the same mechanism occurred in human eyes, a myopic defocus would be expected to cause the choroid to thicken as in the animal eyes. Choroidal thickness of children with hyperopic anisometropic amblyopia was found to be thicker in the amblyopic eyes than that of the fellow eyes and controls using optical coherence tomography (Nishi *et al.*, 2014). In that study they hypothesized that in young children, hyperopic defocus caused choroidal thinning in the fellow eyes and control eyes but the choroidal compensation did not occur in amblyopic eye hence the choroid was found thicker. Our findings of thinner choroid in the amblyopic eyes than the fellow eyes might suggest that the choroid was unable to compensate the myopic defocus in anisomyopic amblyopic eye. Our amblyopic eyes data displayed a horizontal distribution pattern of a choroid that was thickest at the temporal region, followed by the subfoveal, and nasal region where it was thinnest. The choroid in the fellow eyes on the other hand was thickest in the subfoveal area, followed by the temporal and nasal region. The choroidal profile of the fellow eyes were in agreement with those obtained previously from normal children's eyes (Flores-Moreno *et al.*, 2013; Ruiz-Medrano *et al*., 2014). The choroid was reported to be thickest at the subfoveal area, followed by the temporal region and was thinnest at the nasal region (Chui, Zhong, and Burns, 2011). They believed that the choroid was thinner nasally due to the adjacent location to the optic nerve head where the choroid was most susceptible to chorioretinal stretching during axial elongation in myopia development (Chui *et al.*, 2011). Thinner choroid was reported in all regions of 7 to 10 year-old myopic children compared to emmetropic and hyperopic children (Jin *et al*., 2016). The interocular difference in choroidal thickness between the amblyopic eyes and the fellow eyes in our study might be related to the degree of myopia and the axial length. A difference that most apparent at perifoveal 6 mm subfield, a region closest to the optic nerve head.

Previous studies on the choroidal thickness profile in anisometropic hyperopic amblyopia (Mori *et al*., 2014; Nishi *et al.*, 2014; Tenlik et al., 2014) reported different thickness profile of the choroid in their amblyopes compared with ours. The choroid of their amblyopic eyes showed different profile, namely that the choroid was thickest in the subfoveal region, followed by the temporal region and the thinnest at the nasal. Taken together previous research findings on the hyperopic anisometropic amblyopia and the results of the present study, choroidal thickness profile seemed to vary with the types of refractive amblyopia. Although our findings revealed the choroidal thinning in the myopic anisometropic amblyopia, it remained inconclusive whether the choroid of the amblyopic eye thinned in relation to the fellow eye because it failed to alter its thickness in the presence of amblyopia or as a result of higher degree of myopia progression during the eye development. A future study might benefit from a larger sample size of the amblyope, direct comparison with a control group with age-match and refractive-match with the amblyope, prospective longitudinal follow up study design. The information would be useful to establish our understanding of the potential role of the choroid during early eye development.

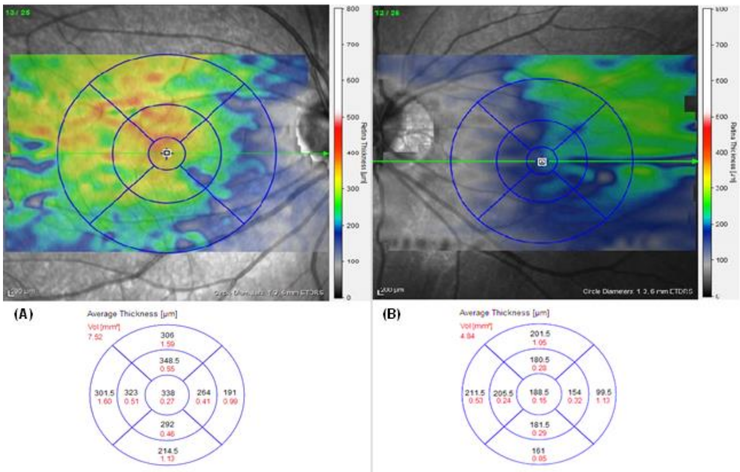


Fig. 2 : Choroidal thickness map of a representative anisomyopic amblyope. (A) Fellow eye of the amblyope. (B) Amblyopic eye. Average thickness values are presented in the Early Treatment Diabetic Retinopathy Study (ETDRS) map.

CONCLUSION

As the conclusion of the choroidal thickness study of children with myopic anisometropic amblyopia, the amblyopic eyes were found to have thinner choroid compared with the fellow eyes at all macular subfields. The choroidal thickness profile of the amblyopic eyes was also different from the fellow eyes.

ACKNOWLEDGEMENT

Financial support under the Research Acculturation Grant Scheme, Ministry of Higher Education (Project Code: (600-RMI/RAGS 5/3) (69/2014). Special thanks to Hospital Selayang for collaboration in term of supporting staff and facilities sharing such as the Spectral Domain OCT and IOL master. Thanks to Fitri Helyani and Norilani in assisting subject recruitment.

REFERENCES

Agawa, T., Miura, M., Ikuno, Y., Makita, S., Fabritius, T., Iwasaki, T., … Yasuno, Y. (2011). Choroidal thickness measurement in healthy Japanese subjects by three-dimensional high-penetration optical coherence tomography. *Graefe's Archive for Clinical and Experimental Ophthalmology*, 249, 1485-1492.

Aygit, E. D., Yilmaz, I., Ozkaya, A., Alkin, Z., Gokyigit, B., Yazici, A. T., & Demirok, A. (2015). Choroidal thickness of children's eyes with anisometropic and strabismic amblyopia. *Journal of American Association for Pediatric Ophthalmology and Strabismus {JAAPOS}*, 19(3), 237–241.

Campos, E. (1995). MAJOR REVIEW Amblyopia, *40*(1).

Chhablani, J., Rao, P. S., Venkata, A., Rao, H. L., Rao, B. S. K., Kumar, U., … Pappuru, R. R. (2014). Choroidal thickness profile in healthy Indian subjects. *Indian Journal of Ophthalmology*, 62(11), 1060–1063.

Chui, T. Y. P., Zhong, Z., Burns, S. A. (2011). The relationship between peripapillary crescent and axial length: Implications for differential eye growth. *Vision Research*, 51(19), 2132–2138.

Coşkun E1, Okumuş S, Gürler B, Yuyuspayi R, Oren B, Kaydu E, Cömez A, E. I. (2014). Choroidal thickness in healthy Turkish subjects. *Turkish Journal of Medical Sciences*, 44(1), 56–61.

Ding, X., Li, J., Zeng, J., Ma, W., Liu, R., Li, T., … Tang, S. (2011). Choroidal thickness in healthy Chinese subjects. *Investigative Ophthalmology and Visual Science, 52*(13), 9555–9560.

Flores-Moreno, I., Lugo, F., Duker, J. S., Ruiz-Moreno, J. M. (2013). The relationship between axial length and choroidal thickness in eyes with high myopia. *American Journal of Ophthalmology*, 155(2), 314–319.e1.

Hung, L.-F., Wallman, J., Smith, E. L. (2000). Vision-dependent changes in the choroidal thickness of macaque monkeys. *Investigative Ophthalmology & Visual Science*, 41(6), 1259–1269. Retrieved from http://www.iovs.org/content/41/6/1259.abstract

Jin, P., Zou, H., Zhu, J., Xu, X., Jin, J., Chang, T. C., … He, X. (2016). Choroidal and retinal thickness in children with different refractive status measured by swept-source optical coherence tomography. *American*

Journal of Ophthalmology, 168, 164–176.

Kantarci, F. A., Tatar, M. G., Uslu, H., Colak, H. N., Yildirim, A., Goker, H., … Gurler, B. (2015). Choroidal and peripapillary retinal nerve fiber layer thickness in adults with anisometropic amblyopia. *European Journal of Ophthalmology*, 25(5), 437-442.

Mori, T., Sugano, Y., Maruko, I., Sekiryu, T. (2014). Subfoveal Choroidal thickness and axial length in preschool children with hyperopic anisometropic amblyopia. *Current Eye Research*, (August), 1–8.

Moss, M. H. (2005). Amblyopia. *Pediatrics for Parents*, 22(3), 10.

Nishi, T., Ueda, T., Hasegawa, T., Miyata, K., Ogata, N. (2014). Choroidal thickness in children with hyperopic anisometropic amblyopia. The British Journal of Ophthalmology, 98(2), 228–232.

Pang, Y., Frantz, K. A., Block, S., Goodfellow, G. W., Allison, C. (2015). Effect of Amblyopia treatment on macular thickness in eyes with myopic anisometropic amblyopia. I*nvestigative Ophthalmology & Visual Science,* 56, 2677–2683.

Rouse, M. (2004). *Care of the Patient With Amblyopia*. American Optometric Association. Retrieved from https://www.aoa.org/documents/optometrists/CPG-4.pdf

Ruiz-Medrano, J., Flores-Moreno, I., Peña-García, P., Montero, J. A., Duker, J. S., Ruiz-Moreno, J. M. (2014). Macular Choroidal thickness profile in a healthy population measured by swept-source optical coherence tomographySS-OCT and CT in a healthy population. *Investigative Ophthalmology & Visual Science,* 55*(*6), 3532–3542.

Ruiz-Moreno, J. M., Flores-Moreno, I., Lugo, F., Ruiz-Medrano, J., Montero, J. A., Akiba, M. (2013). Macular Choroidal thickness in normal pediatric population measured by swept-source optical coherence tomographySS-OCT and choroidal thickness in pediatric population. *Investigative Ophthalmology & Visual Science*, 54*(1)*, 353–359.

Spaide, R. F., Koizumi, H., Pozonni, M. C. (2008). Enhanced Depth imaging spectral-domain optical coherence tomography. *American Journal of Ophthalmology*, 146(4), 496–500.

T Tenlik, A., Güler, E., Kulak, A. E., Totan, Y., Dervişoğulları, M. S., & Gürağaç, F. B. (2014). Evaluation of choroidal thickness in amblyopia using enhanced depth imaging optical coherence tomography. C*urrent Eye Research*, (August), 1–5.

Troilo, D., Nickla, D. L., Wildsoet, C. F. (2000). Choroidal Thickness changes during altered eye growth and refractive state in a primate. *Investigative Ophthalmology & Visual Science*, 41(6), 1249–1258.

Wildsoet, C., & Wallman, J. (1995). Choroidal and scleral mechanisms of compensation for spectacle lenses in chicks. *Vision Research*, 35(9), 1175–1194.

Wu, S.-Q., Zhu, L.-W., Xu, Q.-B., Xu, J.-L., & Zhang, Y. (2013). Macular and peripapillary retinal nerve fiber layer thickness in children with hyperopic anisometropic amblyopia. *International Journal of Ophthalmology*, 6(1), 85–89.

Xu, J., Zheng, J., Yu, S., Sun, Z., Zheng, W., Qu, P., … Yu, X. (2014). Macular choroidal thickness in unilateral amblyopic children. *Investigative Ophthalmology & Visual Science,* 55, 7361-7368.

Yen, M.-Y., Cheng, C.-Y., & Wang, A.-G. (2004). Retinal Nerve Fiber Layer Thickness in Unilateral Amblyopia. *Investigative Ophthalmology & Visual Science*, 45(7), 2224–2230.