## **Original Article**

# Assessment of the macula and choroid in pediatric keratoconus patients



Ihsan Yilmaz\*; Basak Saracoglu Yilmaz; Nimet Burcu Guleryuz; Irfan Perente; Abdullah Ozkaya; Muhittin Taskapili

## Abstract

Purpose: To present choroidal and macular thickness measurements in pediatric patients with keratoconus and to evaluate a possible correlation between anterior and posterior segment parameters.

Methods: 50 eyes of 50 patients and 50 eyes of 50 age-matched controls were included in this cross-sectional comparative study. The participants underwent ophthalmologic examination including; refraction, visual acuity, biomicroscopy, corneal topography and optical coherence tomography. The choroidal thickness (CT) was measured at subfoveal area and at 500 microns intervals to the nasal and temporal to the fovea up to 1500 microns.

Results: The mean age of the patients and controls were  $12.4 \pm 1.9$  and  $12.0 \pm 2.1$  years. The mean thinnest corneal pachimetry was 456  $\pm$  57  $\mu$ m, the mean central macular thickness (CMT) was 258  $\pm$  24  $\mu$ m and the mean subfoveal choroidal thickness was 342  $\pm$  30  $\mu$ m for the patients. There was no significant difference between the patients and controls in regards of CMT and CT at any measured points (p > 0.05 for all). There was no correlation between anterior segment parameters and CMT. There was no correlation between anterior segment parameters and subfoveal choroidal thickness.

Conclusions: We may conclude that keratoconus does not affect the CMT and CT of pediatric keratoconus patients, and we may propose that we do not need a correction for this group of patients when we need to evaluate the CMT and CT.

Keywords: Choroidal thickness, Keratoconus, Macular thickness, Optical cohorence tomography

© 2017 The Authors. Production and hosting by Elsevier B.V. on behalf of Saudi Ophthalmological Society, King Saud University. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/). https://doi.org/10.1016/j.sjopt.2017.10.010

### Introduction

Keratoconus is characterized by progressive corneal protrusion and thinning, leading to irregular astigmatism and impairment in visual function.<sup>1</sup> It has been shown that keratoconus progression is more frequent and faster in patients under 18 years of age, with a seven-fold higher risk of requiring corneal transplantation.<sup>2</sup>

For the diagnosis and management of anterior segment disease like keratoconus, corneal topography devices has been commonly used.<sup>3</sup> Some devices combine a rotating Scheimpflug camera with a Placido disc and allow physicians to detect even the small irregularities on the cornea.<sup>4</sup> Similarly, optical coherence tomography (OCT) devices has been commonly used for the diagnosis and management of posterior segment disease. OCT scans allow physicians to measure the thickness of the retina and choroid at various locations.<sup>5</sup>

In literature, there are some studies which present OCT measurements in patients with keratoconus.<sup>6,7</sup> Moschos et al. presented central foveal thickness of 32 patients with keratoconus and they reported that a macular dysfunction which is not visible ophthalmoscopically may coexist in some cases

Received 8 September 2015; received in revised form 5 November 2016; accepted 30 October 2017; available online 4 November 2017.

University of Health Sciences Beyoglu Eye Research and Training Hospital, Istanbul, Turkey

\* Corresponding author at: Bereketzade Cami Sokak No: 2, Beyoğlu, Istanbul, Turkey. Fax: +90 212 2450948. e-mail address: ihsanyilmaz.dr@gmail.com (I. Yilmaz).





Peer review under responsibility of Saudi Ophthalmological Society, King Saud University



Access this article online: www.saudiophthaljournal.com www.sciencedirect.com

and the low visual acuity could be due not only to the corneal abnormality, but also to the retinal dysfunction.<sup>6</sup> Cankaya et al. presented optic disc and retinal nerve fiber layer (RNFL) measurements in 46 patients with keratoconus and they reported a significance difference of optic disc parameters in keratoconic patients compared to normal subjects.<sup>7</sup> However, the choroidal thickness of pediatric patients with keratoconus has not been established yet. In this study, we aimed to present choroidal and macular thickness measurements in pediatric patients with keratoconus.

#### Methods

#### Study design

This cross-sectional observational study was performed between May 2014 and March 2015. The research followed the tenets of the Declaration of Helsinki. Written informed consent was obtained from all participants' guardians. Beyoglu Eye Training and Research Hospital Local Ethics Committee approved the study.

#### Examination

The participants underwent full ophthalmologic examination; including refraction, visual acuity, slit-lamp biomicroscopy and dilated fundoscopy. Before the pupil dilation corneal topography scan via Sirius (Schwind eye-techsolutions GmbH & Co. KG, Kleinostheim, Germany) and optical coherence tomography (OCT) scan via Spectralis (Heidelberg Engineering, Heidelberg, Germany) were obtained.

#### Eligibility criteria

Inclusion criteria were; being under 15 years of age and having keratoconus in least one eye. The diagnosis of keratoconus was based on clinical examination and confirmed by corneal topographer. The eye with a higher mean corneal power of each patient was included in the study.

Exclusion criteria were; history of any ocular disease other than keratoconus, having any systemic disease or history of previous intraocular surgery including corneal cross linking or laser therapy, presence of any corneal scarring/opacity which may influence OCT imaging, and contact lens wearing at last month.

We recruited the age-matched controls from subjects who visited our clinic and have no ocular and systemic disease, and also had 20/20 or better visual acuity in both eyes. The right eye was designated as the study eye for subjects with an even birth month number, and the left eye was selected for those with an odd birth month number.

#### Instruments

Sirius corneal topography device was used for measuring the anterior segment parameters. All images were taken and assessed by an experienced refractive surgeon (AA) at the same time of the day, between 9 and 10 am. The Sirius use of Scheimpflug camera and a Placido disk to measure and image the anterior eye segment; including the cornea, anterior chamber, iris, pupil, and lens.<sup>8</sup> The device can acquire 25 Scheimpflug frames and 1 keratoscopy reading in less than 1 second.<sup>9</sup> It is capable of measuring anterior and posterior tangential curvature, sagittal curvature altimetry and refractive power, equivalent refractive power, corneal thickness, and visual quality (spot diagram, point-spread function and optical transfer function).<sup>9</sup> Previous studies showed that good agreement between repeated measurement obtained in the same subjects (repeatability) via Sirius device.<sup>4,8</sup>

Spectralis OCT device was used for measuring the posterior segment parameters. Central macular thickness (CMT), which is define as the distance between the vitreoretinal interface and the anterior surface of the retinal pigment epithelium, was automatically calculated by OCT mapping software. All OCT images were taken and assessed by an experienced retinal specialist (IY), who was masked, at the same time of the day, between 9 and 10 am. The choroid was visualized by standard EDI technique.<sup>10</sup> A single line of 6 mm length centered horizontally on the fovea was used for the visualization of the choroid. Automatic real time (ART) mean function was set for a hundred frames and the images were acquired in high-resolution protocol. CT was measured as the vertical distance from outer surface of the retinal pigment epithelium to the inner surface of the sclera.<sup>11</sup> CT was measured at subfoveal and 500 microns interval to the nasal and temporal to the fovea up to 2000 microns. Previous studies showed that good agreement between repeated measurement obtained in the same subjects (repeatability) via Spectralis OCT device.<sup>5,12</sup>

#### Statistical analysis

The results are expressed as the means  $\pm$  standard deviation (SD). The demographic characteristics of the patient and control groups and the OCT measurements of the eyes were compared using an independent *t*-test. Pearson's correlation analysis was used to evaluate the possible correlation between anterior and posterior segment parameters. Statistical Package for the Social Sciences (Version 20.0, SPSS, Chicago, IL, USA) was used for data analysis and values of p < 0.05 were considered statistically significant.

#### Results

#### Demographic characteristics

The study included 50 eyes of 50 patients (22 female, 28 male) and 50 eyes of 50 age-matched controls (24 female, 26 male). All participants were Caucasians. Clinical characteristics of the all participants are demonstrated in Table 1.

#### Anterior segment parameters

Anterior segment parameters of the patients are demonstrated in Table 2.

#### Macular and choroidal thickness

Sufficient image quality from OCT scans was obtained in all participants. The mean central macular thickness (CMT) measurement and the mean CT measurements are demonstrated in Table 3.

 Table 1. Demographic characteristics of the patient and control groups.

	Patients ( $n = 50$ ) Controls ( $n$		
Age mean min-max	12.4 ± 1.9 (8/14)	12.0 ± 2.1 (8/14)	
Refractive error (se, mean min-max	D) -3.2 ± 3.3 (-14/0)	0.3 ± 0.6 (-0.50/0.50)	
UCVA (logMAR) mean min–max	0.52 ± 0.33 (1/0)	0	
BCVA (logMAR) mean min–max	0.32 ± 0.28 (1/0)	0	

f; female, m; male, se; spherical equivalent, D; diopter, UCVA; uncorrected visual acuity, BCVA; best-corrected visual acuity, IOP; intraocular pressure.

 Table 2. Anterior segment parameters of the patients.

	Patients ( $n = 50$ )	Controls ( $n = 50$ )	p value
SimK Avg. (D mean min–max	) 48.28 ± 3.95 (41.16/61.52)	42.65 ± 1.28 (40.82/43.70)	0.001*
Corneal Volu mean min-max	me 184.26 ± 36.85 (86/264)	160.10 ± 30.10 (128/186)	0.012*
Corneal Ape» mean min–max	< (D) 57.45 ± 11.16 (43.99/112.11)	43.40 ± 8.12	0.001*
Thinnest corr mean min–max	neal pachimetry (μm) 456 ± 57 (334/539)	548 ± 52 (504/594)	0.001*

SimKAvg; simulated keratometry average, D; diopter.

\* *p* values from independent *t*-test.

There was no correlation between anterior segment parameters and CMT. Pearson correlation results were; SimK and CMT ( $r = 0.281 \ p = 0.51$ ), corneal volume and CMT ( $r = -0.014 \ p = 0.93$ ), corneal apex and CMT ( $r = 0.135 \ p = 0.36$ ).

There was no correlation between anterior segment parameters and subfoveal choroidal thickness (SCT); thinnest pachimetry and SCT ( $r = -0.333 \ p = 0.20$ ), SimK and SCT ( $r = 0.164 \ p = 0.26$ ), corneal volume SCT ( $r = -0.11 \ p = 0.94$ ), corneal apex and CMT ( $r = 0.174 \ p = 0.232$ ).

#### Discussion

Although keratoconus is most frequently diagnosed after adolescence, it has been shown that the corneal ectasia process starts at a much younger age.<sup>13</sup> Studies have shown that pediatric keratoconus demonstrates a higher rate and speed of keratoconus progression as compared to adult keratoconus.  $^{\rm 14,15}$  Corneal topographers are essential tools to diagnose keratoconus.  $^{\rm 14}$ 

Normal values of corneal parameters in pediatric population has been studied in literature.<sup>16</sup> Reddy et al evaluated one hundred eyes of 100 patients with a mean age of 10.6  $\pm$  2.7 years and reported that the mean maximum and minimum corneal power (keratometry) were 44.26  $\pm$  1.55 and 4 3.56  $\pm$  1.57 D, the mean astigmatism and refractive power in the 3 and 5 mm zones was 0.64  $\pm$  0.36, 43.85  $\pm$  1.53 and 0.78  $\pm$  0.5, 43.41  $\pm$  1.48.<sup>16</sup> The thinnest site on the cornea, the central cornea, had an average thickness of 540  $\pm$  34.0 3  $\mu$ m and the superonasal cornea had the greatest average thickness of 628  $\pm$  38.94  $\mu$ m.<sup>16</sup> For our study participants of pediatric keratoconus the mean maximum and minimum corneal power were higher as expected 46.28  $\pm$  3.40 and 55.59  $\pm$  4.76 D. Also the thinnest site of the cornea, was thinner as expected, had an average thickness of 456  $\pm$  57  $\mu$ m.

Normal values of CMT in pediatric population has been studied in literature.<sup>17</sup> Yilmaz et al. reported that the mean CMT was 261  $\pm$  27  $\mu$ m (range 223–434) in sixty eyes of 30 healthy pediatric patients, aged  $10.8 \pm 3.1$  years.<sup>17</sup> In our study the mean CMT was  $258 \pm 24 \,\mu\text{m}$  for the patients and  $240 \pm 28 \,\mu$ m for the controls which were both similar with the literature. Normal values of CT in pediatric population has been studied in literature.<sup>18</sup> Bidaut-Garnier et al. worked on three hundred and forty-eight eyes from 174 children aged 3.5 years to 14.9 and reported that the mean SCT was 341.96  $\pm$  74.7  $\mu m.^{18}$  In our study the mean SCT was 34  $2 \pm 30$  µm for the patients and  $358 \pm 35$  µm for the controls which were both similar with the literature. Our study shows that CMT and CT of the pediatric patients with keratoconus are similar with CMT and CT of the normal pediatric subject which means that keratoconus may not affect CMT and CT or vice versa.

Previous studies have shown that CT in healthy eyes may change depending on gender<sup>19</sup> and age.<sup>20</sup> In this study the clinical characteristics of the patients and controls were similar to each other in regards of gender and age. Other previous study has showed that CT may change depending on axial length.<sup>21</sup> However longer axial length of patients with keratoconus are coming from cornea so we do not believe that the axial length is a matter for our study.

Previous studies also have shown that the effect of some ocular disorders on CT.<sup>22–25</sup> Similarly the effect of some medical, laser and surgical treatments may effect on CT.<sup>26–28</sup> However the CT of pediatric keratoconus patients has not been studied previously. In this study, we found out that pediatric patients with keratoconus have a similar CT with normal subjects.

The study has limitations. Current Spectralis OCT equipment does not provide software for the automated measurement of CT, so all identifications of the choroidal borders were conducted manually. Also although we had clear OCT

Table 3. Central macular thickness and choroidal thickness measurements ( $\mu m$ ).

	CMT	T1500	T1000	T500	Subf.	N500	N1000	N1500
Pediatric keratoconus patients	258 ± 24 (191–376)	$306 \pm 32$	$320 \pm 36$	$333 \pm 29$	$342 \pm 30$	321 ± 27 (178–445)	$296 \pm 28$	$263 \pm 29$
Controls	(171=370) 240 ± 28	(103 - 430) 324 ± 39	(177 = 430) 310 ± 35	(201-473) $303 \pm 23$ (2204750)	$(103 \pm 30)$ 358 ± 35	(170 - 443) 301 ± 29	(130 - 444) 279 ± 32	(110-421) 250 ± 33
p values	(170-356) p = 0.89	(165-402) p = 0.69	(200-435) p = 0.78	(220–458) p = 0.67	(100-464) p = 0.91	(155-433) p = 0.70	(149-418) p = 0.72	(131-391) p = 0.84

CMT; central macular thickness, Subf.; subfoveal choroidal thickness.

images for all participants the altered optical properties of the keratoconic eyes may influence the OCT images. In addition, as this was the first study about the CT of the keratoconic children, we were not able to support the study with previous studies. The powerful sides were good patient number for a rare disease as pediatric keratoconus. Also we evaluated both corneal topography and OCT findings of this specific group of patients.

To the best of our knowledge, we have demonstrated for the first time via OCT that CT of pediatric keratoconus patients. Correlations between anterior and posterior segment parameters were performed. As expected the cornea was found to be thinner and steeper in pediatric keratoconus patients than the healthy subjects. The OCT parameters as CMT and CT in different points were not found to be different from the healthy subjects. Therefore we may conclude that keratoconus do not affect the CMT and the CT of pediatric keratoconus patients, and we may propose that we do not need a correction for this group of patients when we need to evaluate the CMT and the CT. Further studies are needed to confirm this data.

#### **Conflicts of interest**

The authors declare that there are no conflicts of interest.

## References

- Shetty R, Nagaraja H, Jayadev C, Pahuja NK, Kurian Kummelil M, Nuijts RM. Accelerated corneal collagen cross-linking in pediatric patients: two-year follow-up results. *Biomed Res Int* 2014;2014:894095. <u>https://doi.org/10.1155/2014/894095</u>, Epub 2014 Sep 11.
- Reeves SW, Stinnett S, Adelman RA, Afshari NA. Risk factors for progression to penetrating keratoplasty in patients with keratoconus. *Am J Ophthalmol* 2005;**140**(4):607–11.
- Ambrósio Jr R, Klyce SD, Wilson SE. Corneal topographic and pachymetric screening of keratorefractive patients. J Refract Surg 2003;19(1):24–9.
- Wang Q, Ding X, Savini G, Chen H, Feng Y, Pan C, et al. Anterior chamber depth measurements using Scheimpflug imaging and optical coherence tomography: Repeatability, reproducibility, and agreement. J Cataract Refract Surg 2015;41(1):178–85.
- Rahman W, Chen FK, Yeoh J, Patel P, Tufail A, Da Cruz L. Repeatability of manual subfoveal choroidal thickness measurements in healthy subjects using the technique of enhanced depth imaging optical coherence tomography. *Invest Ophthalmol Vis Sci* 2011;52(5):2267–71.
- Moschos MM, Chatziralli IP, Koutsandrea C, Siasou G, Droutsas D. Assessment of the macula in keratoconus: an optical coherence tomography and multifocal electroretinography study. Ophthalmologica 2013;229(4):203–7.
- Cankaya AB, Beyazyildiz E, Ileri D, Yilmazbas P. Optic disc and retinal nerve fiber layer parameters of eyes with keratoconus. *Ophthal Surg Lasers Imaging* 2012;43(5):401–7.
- Milla M, Piñero DP, Amparo F, Alió JL. Pachymetric measurements with a new Scheimpflug photography-based system: intraobserver repeatability and agreement with optical coherence tomography pachymetry. J Cataract Refract Surg 2011;37(2):310–6.
- 9. Wang Q, Savini G, Hoffer KJ, Xu Z, Feng Y, Wen D, et al. A comprehensive assessment of the precision and agreement of

anterior corneal power measurements obtained using 8 different devices. *PLoS One* 2012;**7**(9):e45607. <u>https://doi.org/10.1371/journal.pone.004560</u>, Epub 2012 Sep 25.

- Karalezli A, Eroglu FC, Kivanc T, Dogan R. Evaluation of choroidal thickness using spectral-domain optical coherence tomography in patients with severe obstructive sleep apnea syndrome: a comparative study. Int J Ophthalmol 2014;7(6):1030–4.
- Yilmaz I, Ozkaya A, Kocamaz M, Ahmet S, Ozkaya HM, Yasa D, et al. Correlation of choroidal thickness and body mass index. Retina 2015 April 29. Epub ahead of print.
- Ctori I, Huntjens B. Repeatability of foveal measurements using spectralis optical coherence tomography segmentation software. *PLoS One* 2015;**10**(6):e0129005. <u>https://doi.org/10.1371/journal.pone.012900</u>, eCollection 2015.
- 13. Rabinowitz YS. Keratoconus. Surv Ophthalmol 1998;42(4):297, 297-19.
- Léoni-Mesplié S, Mortemousque B, Touboul D, Malet F, Praud D, Mesplié N, et al. Scalability and severity of keratoconus in children. Am J Ophthalmol 2012;154(1):56–62.
- Chatzis N, Hafezi F. Progression of keratoconus and efficacy of pediatric corneal collagen cross-linking in children and adolescents. J Refract Surg 2012;28(11):753–8.
- Reddy SP, Bansal R, Vaddavalli PK. Corneal topography and corneal thickness in children. J Pediatr Ophthalmol Strabismus 2013;50 ():304–10.
- Yilmaz I, Ozkaya A, Karakucuk Y, Perente I, Yazici AT. Macular thickness measurement via heidelberg spectralis SD-OCT in pediatric patients. Ophthalmol Res: Int J 2014;2(6):384–90.
- Bidaut-Garnier M, Schwartz C, Puyraveau M, Montard M, Delbosc B, Saleh M. Choroidal thickness measurement in children using optical coherence tomography. *Retina* 2014;34(4):768–74.
- 19. 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(9):1904–11.
- Margolis R, Spaide RF. A pilot study of enhanced depth imaging optical coherence tomography of the choroid in normal eyes. Am J Ophthalmol 2009;147(5):811–5.
- Zhang C, Tatham AJ, Medeiros FA, Zangwill LM, Yang Z, Weinreb RN. Assessment of choroidal thickness in healthy and glaucomatous eyes using swept source optical coherence tomography. PLoS One 2014; 9(10): e109683. https://doi.org/10.1371/journal.pone.0109683 eCollection 2014.
- Kuroda S, Ikuno Y, Yasuno Y, Nakai K, Usui S, Sawa M, et al. Choroidal thickness in central serous chorioretinopathy. *Retina* 2013;33(2):302–8.
- Laíns I, Figueira J, Santos AR, Baltar A, Costa M, Nunes S, et al. Choroidal thickness in diabetic retinopathy: the influence of antiangiogenic therapy. *Retina* 2014;34(6):1199–207.
- Jonas JB, Forster TM, Steinmetz P, Schlichtenbrede FC, Harder BC. Choroidal thickness in age-related macular degeneration. *Retina* 2014;34(6):1149–55.
- Dhoot DS, Huo S, Yuan A, Xu D, Srivistava S, Ehlers JP, et al. Evaluation of choroidal thickness in retinitis pigmentosa using enhanced depth imaging optical coherence tomography. Br J Ophthalmol 2013;97(1):66–9.
- 26. Yiu G, Manjunath V, Chiu SJ, Farsiu S, Mahmoud TH. Effect of antivascular endothelial growth factor therapy on choroidal thickness in diabetic macular edema. Am J Ophthalmol 2014;158(4):745–51.
- Zhu Y, Zhang T, Wang K, Xu G, Huang X. Changes in Choroidal Thickness after panretinal photocoagulation in patients with type 2 diabetes. Retina 2014 Dec 1. Epub ahead of print.
- Saeedi O, Pillar A, Jefferys J, Arora K, Friedman D, Quigley H. Change in choroidal thickness and axial length with change in intraocular pressure after trabeculectomy. Br J Ophthalmol 2014;98 ():976–9.