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Influence of Macular Choroidal Thickness on Visual Function in Highly Myopic Eyes

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Key Words
Choroid · Choroidal thickness · Retinal sensitivity · Microperimetry · Myopia · Optical coherence tomography

Abstract
Purpose: To explore the retinal and choroidal thicknesses (RT, CT), as measured using enhanced depth imaging (EDI) optical coherence tomography (OCT, Spectralis) in highly myopic eyes and its relationship with visual function. ***Materials and Methods:*** Prospective, case-control, noninterventional clinical study. CT was measured by EDI-OCT in highly myopic eyes (≥6 dpt) without any macular diseases and age-matched control eyes. A complete ophthalmological examination, visual acuity assessment and MP1 microperimetry were obtained. ***Results:*** 38 myopic (15 M/23 F, mean age 51 ± 8.9 years) and 21 control eyes (5 M/16 F, mean age 50 ± 5.4 years) were included. The myopic mean refractive error was –13.3 ± 4.9 dpt and axial length 29.2 ± 2.2 mm. The mean best-corrected visual acuity (BCVA) was lower in highly myopic than in control eyes (77.3 ± 9.25 vs. 84.8 ± 0.6 letters, p = 0.0001, respectively) as was the mean retinal sensitivity (MRS; 16.32 ± 2.6 vs. 19.9 ± 0.2 dB, p < 0.0001). While RT was similar between groups (291.5 ± 24.2 vs. 283.6 ± 13.9 μm, p = 0.06, respectively), subfoveal CT was thinner in highly myopic compared to control eyes (114.3 ± 78.5 vs. 272.6 ± 110.2 μm, p < 0.0001). A significant relationship was found between subfoveal CT and MRS (R^2 = 0.22; p = 0.003) and BCVA (R^2 = 0.13; p = 0.027). ***Conclusions:*** Macular function is reduced in highly myopic eyes without any visible macular diseases compared to controls, and a significant proportion of the macular function variability seems to be related to a reduced CT.

Introduction

Myopia is one of the most common eye diseases (1–2% in the USA, 5–8% in Japan, 15% in Singapore) [1–3], characterized by excessive and progressive elongation of the globe and leading to stretching of retinal tissue and reduced retinal function [4].

The most common fundus changes occurring in highly myopic eyes are lacquer cracks, choroidal neovascularization, chorioretinal atrophy, macular hole and macular schisis [5–7]. Moreover, it has been described by histological studies that both vessel density and diameter are reduced in the choriocapillaris of highly myopic eyes [8, 9]. As the choroid supplies nutrition to retinal pigment epithelial cells and the outer retina, compromised choroidal morphology and circulation may account, in part, for retinal dysfunction and vision loss that is seen in high myopia [10, 11].

Until now it has not been possible to study in vivo noninvasively the morphological characterization of the cho-

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roid. Recently the method called enhanced depth imaging spectral-domain optical coherence tomography (EDI-OCT) has been developed to allow in vivo cross-sectional imaging of the choroid and choroidal thickness (CT) measurement [12].

A good reproducibility of CT measurement has been reported [13, 14], and reduced CT was found in highly myopic compared to control eyes [11, 12, 15]. Moreover, a negative correlation between CT and axial length (AL) has been documented [11, 12, 15, 16]. Previous studies have directly correlated CT and visual acuity in highly myopic eyes [17]. Microperimetry allows a detailed point-to-point evaluation of macular function and fixation stability, and previous studies reported a reduced retinal sensitivity in highly myopic compared to control eyes [18–22].

The purpose of this study is to explore the retinal thickness (RT) and CT, as measured using EDI-OCT in highly myopic eyes without any macular diseases in comparison to emmetropic eyes and its relationship with visual function.

Materials and Methods

In this prospective, noninterventional, case-control clinical study, consecutive highly myopic patients and age-matched control subjects, who visited the Department of Ophthalmology of IRCCS Fondazione G.B. Bietti from November 2011 and April 2012, were enrolled.

The study protocol adhered to the tenets of the Declaration of Helsinki and was approved by the local Institutional Review Board, and each patient signed an informed consent before enrolment.

Our inclusion criteria were: high myopia with a spherical equivalent refraction ≥–6.00 dpt, age between 40 and 60 years, and healthy volunteers with no ophthalmic or systemic pathology and spherical equivalent refraction between ±1 dpt.

The exclusion criteria were the presence of any macular diseases such as foveal lacquer cracks, choroidal neovascularization, chorioretinal atrophy, macular hole, myopic macular schisis, or a history of vitreoretinal surgeries such as scleral buckling procedure and pars plana vitrectomy.

Patients with media opacities such as corneal abnormalities and cataract, which could bias functional and structural retinal testing, were also excluded.

All enrolled patients performed best-corrected visual acuity (BCVA) measurement with Early Treatment Diabetic Retinopathy Study (ETDRS) charts, slitlamp biomicroscopy with intraocular pressure assessment by Goldmann applanation tonometry, AL measurement using IOLMaster (Carl Zeiss Meditec, Jena, Germany), spectral-domain OCT (Spectralis, version 1.5.12.0; Heidelberg Engineering, Heidelberg, Germany) scan acquisition and MP1 microperimetry (Nidek Technologies, Padova, Italy). The patients' mean retinal sensitivity (MRS) was tested using a customized radial grid of 36 stimuli covering the central 10° (centered on the fovea), the time between stimuli was equal to 1 s, stimulus size equivalent to Goldmann III, white background set at 4 asb, a bright red cross of 2° as the fixation target. A 4-2 double staircase strategy was carried out and the first stimulus was presented at the level of 10 dB. MRS was calculated in the whole 10° and in the 2-degree central area. The stability of fixation, graded on the basis of the preferred retinal locus, was reported as *stable, relatively unstable* and *unstable* [23]. In each patient microperimetry was performed twice within 1 week to rule out potential learning effects, and the second test was used for the analysis. Moreover patients underwent a brief training session at the beginning of each test. Tropicamide 1% was used to dilate the pupil in the selected eye.

EDI-OCT images were obtained by Heidelberg Spectralis, and RT and CT were measured with the EDI system. The scanning protocol used was the Volume Fast program. RT measurements of each of the 9 subfields corresponding to the ETDRS areas were considered for the analysis. ETDRS areas are defined by 3 concentric rings centered into the fovea with diameters of 1, 3 and 6 mm, respectively, with the 2 outer rings divided into quadrants by 2 intersecting orthogonal lines. Measurement of central RT, mean thickness in the central 1-mm diameter area, was obtained. The EDI-OCT technique, used to obtain CT, was already described elsewhere [11, 12]. The method involves placing the objective lens of the spectral-domain OCT device closer to the eye such that an inverted image is obtained. By performing this maneuver, the deeper structures are placed closer to zero delay, allowing better visualization of the choroid. Seven horizontal sections were obtained within a 5 × 30-degree area centered at the fovea, with 100 averaged scans for each section using the automatic averaging and eye tracking features to reduce noise and to improve image quality. CT was defined as the distance from the retinal pigment epithelial line to the hyperreflective line behind the large vessel layers of the choroid, presumed to be the choroid-sclera interface. If the choroid was tilted, the distance was measured right to the retinal pigment epithelial line. CT was manually measured behind the fovea (subfoveal CT) and at 500 μm from the fovea on the horizontal and vertical axes. The average CT was then calculated as the mean of the subfoveal CT measurement and 4 CT measurements obtained at 500 μm from the fovea.

The OCT measurements were made by 2 examiners independently, and if the difference in their thickness measurements was greater than 15% of the mean of the 2 values, there was open adjudication with the senior author.

Statistical Analysis

Data were expressed as means ± SD for continuous variables and frequencies for categorical variables. Between-group comparisons were performed by the independent t test after normality check of data distribution by the Shapiro-Wilk test. Relationships between CT and RT and visual function were explored by regression analysis. The analysis was performed with JMP (version 9; SAS Institute Inc., Cary, N.C., USA). $p < 0.05$ was considered statistically significant.

Results

Data analysis included 38 myopic eyes of 38 patients (15 males; 23 females, mean age 51 ± 8.9 years) and 21 emmetropic control eyes of 21 patients (5 males, 16 fe-

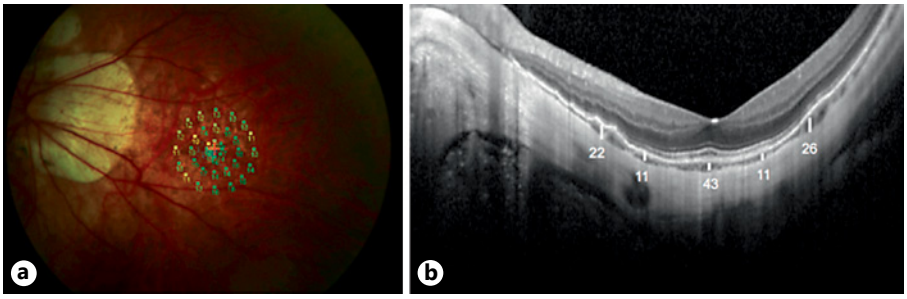

Fig. 1. Retinal sensitivity (**a**) measured using MP1 microperimetry and CT (**b**) with EDI-OCT measured subfoveally and at 500 μm from the fovea in highly myopic eyes.

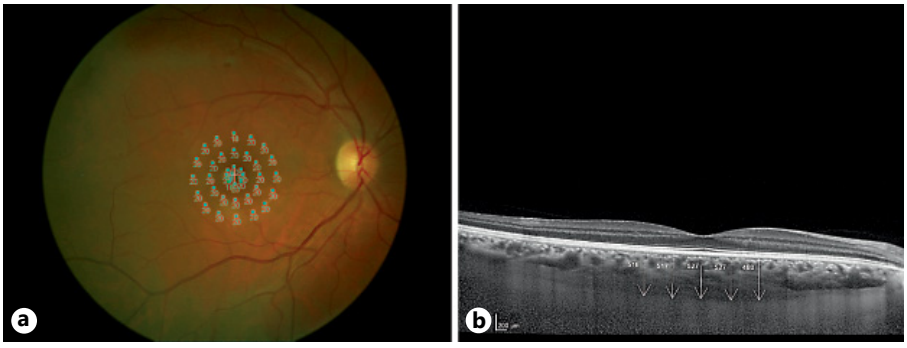

Fig. 2. Retinal sensitivity (**a**) measured using MP1 microperimetry and CT (**b**) with EDI-OCT measured subfoveally and at 500 μm from the fovea in control eyes.

males, mean age 50 ± 5.42 years). The myopic eyes had a mean refractive error of –13.32 ± 4.89 dpt (range 6.5–23) and an AL of 29.23 ± 2.25 mm (range 25.9–33.9). The control eyes had a mean refractive error of 0.21 ± 0.33 dpt (range 0 to +1) and an AL of 23.66 ± 0.91 mm (range 22.2–25.5). The mean BCVA was significantly lower in highly myopic than in control eyes (77.26 ± 9.25 vs. 84.85 ± 0.65 letters, p = 0.0001, respectively). MRS was significantly lower in highly myopic compared to control eyes (16.32 ± 2.57 vs. 19.9 ± 0.25 dB, p < 0.0001, respectively). While the mean central RT was similar between groups (291.5 ± 24.18 vs. 283.57 ± 13.9 μm, p = 0.06), the subfoveal CT was significantly thinner in highly myopic compared to control eyes (114.28 ± 78.48 vs. 272.57 ± 110.25 μm, p < 0.0001, respectively; fig. 1, 2).

MRS, evaluated in the 10°, was found to be directly and significantly related to subfoveal CT (R^2 = 0.22; p = 0.003) and average CT (R^2 = 0.23; p = 0.004). Also the MRS in the central 2-degree area was directly and significantly related to subfoveal CT (R^2 = 0.17; p = 0.0101) and average CT (R^2 = 0.20; p = 0.005). Fixation was stable in 97% (37/38) in highly myopic and in 100% (21/21) in control eyes (21/21) and relatively unstable in 3% (1/38) in highly myopic eyes.

Our data showed also a significant direct relationship between BCVA and subfoveal and average thicknesses and CT (R^2 = 0.13; p = 0.027, R^2 = 0.14; p = 0.031, respectively). Differently no significant relationships have been found between either MRS and BCVA and central RT (R^2 = 0.04; p = 0.2, R^2 = 0.04; p = 0.23, respectively).

A significant relationship was found between AL and CT (R^2 = 0.37; p < 0.0001) and between AL and both BCVA and MRS (R^2 = 0.24; p = 0.0015, R^2 = 0.55; p < 0.0001) while the relationship between AL and CRT was not statistically significant (R^2 = 0.09; p = 0.06).

Discussion

In this study we explored the relationship between visual function and RT and CT in highly myopic eyes. Our data showed an impairment of macular function, as expressed by both visual acuity and retinal sensitivity, in highly myopic eyes without any macular diseases in comparison with control eyes. Moreover visual acuity and retinal sensitivity appeared to be significantly related to macular CT in our population; that is the lower the CT, the lower the expected visual function measures. The same is not true for RT which was not found to be related to macular function in our data.

While BCVA is the gold standard used to assess the functional impact of macular abnormalities and, although useful, quick, economic and reproducible, it represents

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just one of the aspects of macular function. Microperimetry is able to quantify macular sensitivity in an exact fundus-related fashion [18–20, 24, 25] integrating it to BCVA information regarding the degree and pattern of macular functional impairment in highly myopic eyes without any macular diseases with its intersubject variability. In our study highly myopic eyes showed a lower mean BCVA and MRS that were both found significantly related to AL. An impaired retinal sensitivity in young myopes compared to that of emmetropes was reported by Gella et al. [21] and Qin et al. [22]. In agreement with our data, a strong positive relationship of retinal sensitivity also with AL was found. This finding could be partially explained mechanistically by a change in the ocular structure due to increased AL in myopic eyes that determines an increased stretching of the macular area causing a coarser distribution of cones in the posterior retina [26]. Electroretinogram testing, including multifocal electroretinography, has shown decreased b-wave amplitudes with increased AL in eyes affected by nonpathological myopia, which indicates early injury of the cones [27–30].

In our study we found that central RT was similar between highly myopic and control eyes without any relationship with AL and without any significant relationship with either BCVA or MRS. Also Gella et al. [21] evaluated in myopic eyes the retinal sensitivity at microperimetry and the retinal morphological characteristics including photoreceptor layer thickness and retinal pigment epithelial thickness, by means of spectral-domain OCT. The authors found that the retinal sensitivity was significantly reduced in myopes in spite of normal retinal morphology [21], concluding that the observed functional changes may either precede retinal structural changes or that additional morphological elements, such as CT, could contribute to explain the reduced retinal function in these eyes.

For this reason we aimed to study the choroidal characteristics in highly myopic eyes and to explore their relationship with visual acuity and retinal sensitivity. In our study we found that highly myopic eyes had a strongly reduced subfoveal CT that was significantly related to the extent of AL ($R^2 = 0.37$; $p < 0.0001$), compared to control eyes (114.28 ± 78.48 vs. 272.57 ± 110.25 μm, $p < 0.0001$), and this finding is in agreement with the previous reports of a reduced subfoveal CT in myopic eyes [11, 15, 16]. In our study BCVA was directly related to the thickness of the choroid with lower BCVA associated with lower macular choroid thickness. This finding is in agreement with previous reports where CT was found to be the most important predictor for visual acuity in highly myopic eyes without macular pathology [17, 31, 32].

One strength of our work compared to previous reports is the functional assessment performed in the whole macular area by means of fundus-related microperimetry that detected a significant reduction of macular sensitivity in highly myopic eyes compared to controls. Interestingly retinal sensitivity appeared to be related to macular CT in our population and not to RT. These findings suggest that anatomical changes such as choroidal thinning, and not retinal changes, could be related to the decrease in macular sensitivity in highly myopic eyes, without any macular diseases. A possible explanation is that choroidal thinning could determine a reduction in the choroidal blood flow and thus of oxygen and nutrient supply to the outer retina possibly influencing retinal function even in the absence of a manifest macular disease. In experimental settings form-deprived chick eyes decreased choriocapillaris density caused in myopic chick eyes may be due partly to capillary atrophy and partly to overall stretch of the capillary network caused by abnormal enlargement of the myopic eyes [8, 33].

Nevertheless a limitation of our study could be due to magnification errors related to intersubject AL variability that could bias either the structural measurements and the projection of the stimuli of microperimetry, thus weakening the relationships between structure and function.

In conclusion our data showed a reduction of central macular function, as expressed by visual acuity, and a functional impairment in the whole macular area, as evaluated by means of fundus-related microperimetry, in highly myopic eyes without any manifest macular diseases. The observed functional impairment appeared to be directly related to macular CT and not to RT, suggesting that abnormalities of the choroid may play a role in the pathogenesis of myopic macular dysfunction and eventually degeneration.

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Disclosure Statement

The authors declare no conflict of interest. The authors alone are responsible for the content and writing of the paper.

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References

1 Klaver CC, Wolfs RC, Vingerling JR, Hofman A, de Jong PT: Age-specific prevalence and causes of blindness and visual impairment in an older population: the Rotterdam Study. Arch Ophthalmol 1998;116:653–658.

2 Bar Dayan Y, Levin A, Morad Y, Grotto I, Ben-David R, Goldberg A, et al: The changing prevalence of myopia in young adults: a 13-year series of population-based prevalence surveys. Invest Ophthalmol Vis Sci 2005;46:2760–2765.

3 Lin LL, Shih YF, Hsiao CK, Chen CJ: Prevalence of myopia in Taiwanese schoolchildren: 1983–2000. Ann Acad Med Singapore 2004;33:27–33.

4 Chui TY, Yap MK, Chan HH, Thibos LN: Retinal stretching limits peripheral visual acuity in myopia. Vision Res 2005;45:593–605.

5 Lai TY, Fan DS, Lai WW, Lam DS: Peripheral and posterior pole retinal lesions in association with high myopia: a cross-sectional community-based study in Hong Kong. Eye (Lond) 2008;22:209–213.

6 Buch H, Vinding T, La Cour M, Appleyard M, Jensen GB, Nielsen NV: Prevalence and causes of visual impairment and blindness among 9,980 Scandinavian adults: the Copenhagen City Eye Study. Ophthalmology 2004;111:53–61.

7 Iwase A, Araie M, Tomidokoro A, Yamamoto T, Shimizu H, Kitazawa Y: Prevalence and causes of low vision and blindness in a Japanese adult population: the Tajimi Study. Ophthalmology 2006;113:1354–1362.

8 Hirata A, Negi A: Morphological changes of choriocapillaris in experimentally induced chick myopia. Graefes Arch Clin Exp Ophthalmol 1998;236:132–137.

9 Grossniklaus HE, Green WR: Pathologic findings in pathologic myopia. Retina 1992;12:127–133.

10 Kitaguchi Y, Bessho K, Yamaguchi T, Nakazawa N, Mihashi T, Fujikado T: In vivo measurements of cone photoreceptor spacing in myopic eyes from images obtained by an adaptive optics fundus camera. Jpn J Ophthalmol 2007;51:456–461.

11 Fujiwara T, Imamura Y, Margolis R, Slakter JS, Spaide RF: Enhanced depth imaging optical coherence tomography of the choroid in highly myopic eyes. Am J Ophthalmol 2009;148:445–450.

12 Spaide RF, Koizumi H, Pozzoni MC: Enhanced depth imaging spectral-domain optical coherence tomography. Am J Ophthalmol 2008;146:496–500.

13 Rahaman 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;52:2267–2271.

14 Branchini L, Regatieri CV, Flores-Moreno I, Baumann B, Fujimoto JG, Duker JS: Reproducibility of choroidal thickness measurements across three spectral domain optical coherence tomography systems. Ophthalmology 2012;119:119–123.

15 Ikuno Y, Tano Y: Retinal and choroidal biometry in highly myopic eyes with spectral-domain optical coherence tomography. Invest Ophthalmol Vis Sci 2009;50:3876–3880.

16 Flores-Moreno I, Lugo F, Duker JS, Ruiz-Moreno JM: The Relationship between axial length and choroidal thickness in eyes with high myopia. Am J Ophthalmol 2013;155:314–319.

17 Nishida Y, Fujiwara T, Imamura Y, Lima LH, Kurosaka D, Spaide RF: Choroidal thickness and visual acuity in highly myopic eyes. Retina 2012;32:1229–1236.

18 Schneider U, Kuck H, Inhoffen W, Kreissig I: Fundus-controlled microperimetry with the scanning laser ophthalmoscope in macular diseases. Klin Monatsbl Augenheilkd 1993;203:212–218.

19 Varano M, Scassa C: Scanning laser ophthalmoscope microperimetry. Semin Ophthalmol 1998;13:203–209.

20 Midena E, Radin PP, Pilotto E, Ghirlando A, Convento E, Varano M: Fixation pattern and macular sensitivity in eyes with subfoveal choroidal neovascularization secondary to age related macular degeneration. Semin Ophthalmol 2004;19:55–61.

21 Gella L, Raman R, Sharma T: Evaluation of in vivo human retinal morphology and function in myopes. Curr Eye Res 2011;36:943–946.

22 Qin Y, Zhu M, Qu X, Xu G, Yu Y, Witt RE, et al: Regional macular light sensitivity changes in myopic Chinese adults: an MP1 study. Invest Ophthalmol Vis Sci 2010;51:4451–4457.

23 Fujii GY, de Juan E Jr, Sunness J, Humayun MS, Pieramici DJ, Chang TS: Patient Selection for Macular Translocation Surgery using the Scanning laser Ophthalmoscope. Ophthalmology 2002;109:1737–1744.

24 Parravano M, Oddone F, Boccassini B, Chiaravalloti A, Scarinci F, Sciamanna M, et al: Functional and structural assessment of lamellar macular holes. Br J Ophthalmol 2013;97:291–296.

25 Parravano M, Oddone F, Tedeschi M, Chiaravalloti A, Perillo L, Boccassini B, et al: Retinal functional changes measured by microperimetry in neovascular age-related macular degeneration treated with ranibizumab: 24-month results. Retina 2010;30:1017–1024.

26 Horio N, Miyake Y, Horiguchi M: Kinetics of foveal cone photopigment in myopia without chorioretinal degeneration. Jpn J Ophthalmol 1999;43:44–47.

27 Westall CA, Dhaliwal HS, Panton CM, Sigesmun D, Levin AV, Nischal KK, et al: Values of electroretinogram responses according to axial length. Doc Ophthalmol 2001;102:115–130.

28 Kawabata H, Adachi-Usami E: Multifocal electroretinogram in myopia. Invest Ophthalmol Vis Sci 1997;38:2844–2851.

29 Luu CD, Lau AM, Lee SY: Multifocal electroretinogram in adults and children with myopia. Arch Ophthalmol 2006;124:328–334.

30 Chen JC, Brown B, Schmid KL: Delayed mfERG responses in myopia. Vision Res 2006;46:1221–1229.

31 Flores-Moreno I, Ruiz-Medrano J, Duker JS, Ruiz-Moreno JM: The relationship between retinal and choroidal thickness and visual acuity in highly myopic eyes. Br J Ophthalmol 2013;97:1010–1013.

32 Ho M, Liu DT, Chan VC, Lam DS: Choroidal thickness measurement in myopic eyes by enhanced depth optical coherence tomography. Ophthalmology 2013;120:1909–1914.

33 Lin T, Grimes PA, Stone RA: Expansion of the retinal pigment epithelium in experimental myopia. Vision Res 1993;33:1881–1885.