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Retinal and choroidal thickness measurement in myopic eyes by spectral domain optical coherence tomography and enhanced depth imaging: OCT

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Abstract
Background: Early detection and timely intervention of high myopia and associated maculopathy can prevent long term complications in myopics. Measurement of retinal thickness by Spectral Domain-Occular Coherence Tomography (SD-OCT) and choroidal thickness by Enhanced Depth Imaging-Occular Coherence Tomography (EDI-OCT) was undertaken in this study.
Material and Methods: Total 92 patients (46 high myopic, 46 normal vision as controls) recruited for the study. Correlation among retinal and choroidal thickness with age, refractive error in dioptres and co-relation of visual acuity measured in log MAR with choroidal and retinal thickness were analyzed with linear mixed models.
Results: The mean age of the 46 patients with high myopia was 35.3 $\pm$ 7.941, the mean axial length was 26.73 $\pm$ 1.584 mm in myopes. The mean subfield RT thickness was found to be 240.72 $\pm$ 32.581 µm. The subfoveal CT was found to be 115 $\pm$ 87.8 µm. The mean photoreceptor layer thickness including the RPE layer was 98.6 $\pm$ 9.8 µm.
Conclusion: OCT was helpful in detecting early macular changes in the myopic retina, which could be precursors to various forms of myopic maculopathy. OCT can serve as a useful guideline in early diagnosis, management, prognostication and research for high myopia patients.

Keywords: High myopia; retinal thickness; choroidal thickness; OCT

Introduction

High myopia, defined as a spherical equivalent equal to or greater than -6 diopters (D), is associated with excessive and progressive elongation of the globe, resulting in a variety of fundus changes that lead to visual impairment, including lacquer cracks in the Bruch membrane, choroidal neovascularization (CNV), and chorioretinal atrophy [1, 2, 3] and is one of the leading causes of low vision worldwide [4, 5].

'Pathological' or degenerative myopia is characterized by progressive antero-posterior elongation of the scleral envelope associated with a range of secondary ocular changes, principally thought to relate to mechanical stretching of the involved tissue. It is a major cause of legal blindness, with myopic maculopathy being the most common cause of visual loss. Histological studies have shown thinner retina, choroid and sclera compared with age-matched control patients [5, 6]. Based on these findings, retinal dysfunction would be expected to correlate with the degree of myopia regardless of the patient's age. However, visual function tends to be normal in highly myopic children regardless of the degree of myopia, and worsens with age [7, 8, 9].

The higher the myopia, the more likely vision-threatening complications can occur [10, 11]. Choroidal neovascularisation, retinal detachment, macular hole, foveoschisis, epiretinal membrane, vitreomacular traction syndrome, chorioretinal atrophy are some complications that are often seen in these patients. Recent studies have demonstrated that asymptomatic macular holes and myopic tractional maculopathy often precede the development of such complications [12, 13].

The choroid is an integral structure in the eye that accounts for most of the ocular blood flow. Thus, the choroid is of paramount importance to retinal and visual function because it supplies nutrients to retinal pigment epithelial cells and the outer retina. In addition, the choroid also contributes to the blood supply of the prelaminar portion of the optic nerve. Compromised choroidal circulation may account for the retinal dysfunction and vision loss that is observed in highly myopic and glaucomatous patients. However, it is difficult to image the full thickness of the choroid because of pigments in the retinal pigment epithelium

(RPE) layer [14]. Its physiochemical nature impedes visualization by ophthalmoscopy, fundus photography, and fluorescein angiography. Direct choroidal layer visualization and measurement could be obtained through enhanced depth imaging (EDI) spectral-domain optical coherence tomography [15, 16, 17].

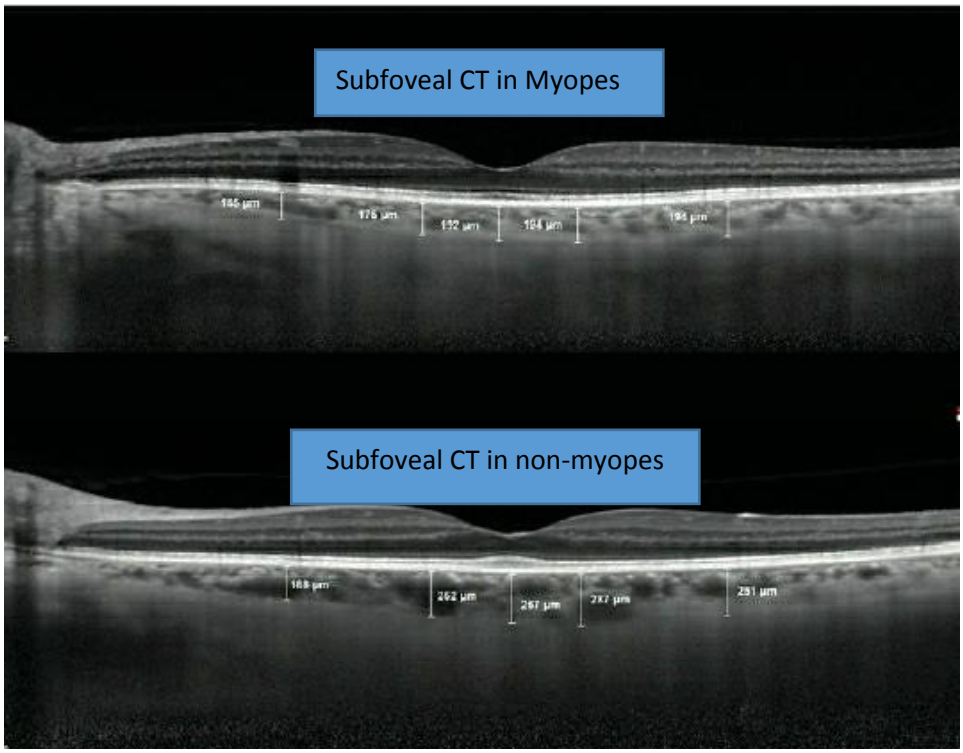
Optical coherence tomography (OCT) is a non-invasive interferometric technique, typically employing near-infrared light to provide useful objective information regarding macular characteristics and relative morphological changes [18-21]. Recent developments of OCT technology have made it possible to accurately image and measure the thickness of inner structures of the eye such as the retina (and its various layers), and choroid using reflected or backscattered light and low coherence interferometry [18, 19].

Materials and Methods

This study had review board approval from the Ethics committee of our institution. This study was a cross-sectional analysis involving myopic patients in our center. Consecutive patients with a refractive error of at least 6 diopters (D) were recruited in the Department of Ophthalmology in our hospital from February 2018 to March 2019. Recruited patients underwent retinal thickness (RT) measurement by SD-OCT and choroidal thickness (CT) measurement by EDI-OCT. Inclusion criteria for age range were from 10 to 70 years old. Automated refraction was obtained for phakic patients. Imaging results for RT and CT in patients with spherical equivalence of more than 6 D were evaluated. Also Non-myopic controls having spherical equivalence of ±0.5 D were included in the study.

In patients who underwent cataract or refractive surgery, the preoperative records of automated refraction were adopted. Snellen visual acuities were converted to logarithm of the minimum angle of resolution (log MAR) for statistical analysis. Any intraocular procedures, including intravitreal injection of anti-vascular endothelial growth factor, cataract surgery, or vitrectomy, were recorded. Exclusion criteria included history of proliferative retinopathy, retinal hemorrhage, epiretinal membrane, retinal detachment, choroidal neovascularization, macular hole, myopic macular atrophy, or amblyopia. Patients with other causes of loss in vision other than high myopia, such as significant cataract or corneal pathologies were also excluded. Only patients who had normal-looking fundi and macula and who did not receive any intraocular operations including cataract operation within 12 months were recruited.

OCT was performed using Cirrus SD-OCT machine (Carl Zeiss Meditec, Dublin, CA). Pupils were dilated to atleast 5mm prior to the examination. Correction for refractive error was provided by means of the Littman formula-based correction factors implemented in the software. Retinal thickness was measured automatically by the inbuilt algorithm which determines the anterior and posterior extent at the internal limiting membrane and retinal pigment epithelium respectively. Atleast three good quality (signal strength ≥7) scans were retained for analysis of each eye. Choroidal thickness was measured by EDI using the spectral-domain OCT (v. 1.6.4.0, Heidelberg Engineering, Heidelberg, Germany) and by placing the instrument close enough to the eye to obtain an inverted image. Every section, consisted of 30 average scans was obtained by placing a 15×30-degree rectangle which was centered at the macula. Choroidal thickness was determined as the distance from the outer surface of the hyper-reflective line, referred to as the "RPE" layer, to the hyper-reflective line of the inner sclera border [21]. The scan was measured in a horizontal section from 3 mm temporal to the fovea to 3 mm nasal to the fovea at 500-µm intervals. Mean RT and CT in relation to the fovea was documented.



Statistical Analysis: The datas obtained were analyzed using SPSS. The association between the foveal, photoreceptor layer thickness and subfoveal choroidal thickness with age and refractive power, and the relationship between visual acuity and foveal and subfoveal thickness were analyzed with linear mixed models. $P<0.05$ was

considered statistically significant.

Results

There were 46 myopes (24 female and 22 male) and 46 patients with normal eyes (20 male and 26 female) were recruited for the study. We excluded any cases that included a history of macula off retinal detachment (2 eyes), a history of myopic choroidal neovascularization (1 eye), or posterior staphyloma (1 eye). 32 eyes were pseudophakic, 60 eyes were phakic, and no cases were aphakic. The mean age was 35.3 ± 7.941 years in myopics and 43.4±12.800 years in normal subjects, and the mean refractive error was −8.7 D (range −6.1 to −15 D).

The ranges of visual acuity of recruited patients were from 20/10 to 20/200. Any patients with observable myopic atrophy were excluded from the study. Patients who underwent cataract operation within 3 months and those with clinically observable cataracts were excluded from the study.

The mean axial length was 26.73 ± 1.584 mm in myopes and 22.80 ± 0.412 mm in normal patients. The mean subfield RT thickness was found to be 240.72 ± 32.581 µm in myopes and 230.42 ± 18.702 µm in non-myopes. The subfoveal CT was found to be 115 ± 87.8 µm standard deviation. This agreed with currently available studies in patients with high myopia [22] and was significantly thinner than the subfoveal CT of normal eyes (265 ± 25.350µm) found in our study [23]. The mean CT was computed on the basis of the thickness at the subfoveal region and varied significantly at different locations. The mean photoreceptor layer thickness including the RPE layer was 98.6 ± 9.8 µm as compared to controls (96.4 ± 7.9 µm). All the parameters between high myopes and normal patients were found to be statistically significant (p <0.0001).

In this study the axial length was found to increase with increasing diopters of myopia whereas the foveal thickness, photoreceptor and subfoveal choroidal thickness were found to decrease with increasing degrees of high myopia.

Table 1: Age distribution in myopes versus normal patients

	High Myopia Patients		Normal Patients	
Age (in years)	**No**	**Percentage (%)**	**No**	**Percentage (%)**
10-19	13	28.26	4	8.7
20-29	21	45.65	12	26.09
30-39	7	15.21	16	34.78
40-49	2	4.34	10	21.74
50-59	1	2.17	3	6.52
60-69	2	4.34	1	2.17
Mean ± S D	35.3 ± 7.941		43.4 ± 12.800	

Table 2: Gender distribution among the cases and controls

	High Myopia Patients		Normal Patients	
Gender	**Number**	**Percentage (%)**	**Number**	**Percentage (%)**
Male	22	47.83	20	43.48
Female	24	52.17	26	56.52
Total	46	100	46	100

Table 3: Mean of axial length, foveal thickness, photoreceptor layer thickness and choroidal thickness in myopes and normal patients

Variables	High Myopes	Normal patients	P value
Axial length (mm)	26.73 ± 1.584	22.80 ± 0.412	<0.0001
Foveal thickness (µ)	240.72 ± 32.581	230.42 ± 18.702	<0.0001
Photoreceptor layer thickness (µ)	98.6 + 9.8	96.4 ± 7.9	<0.0001
Subfoveal choroidal thickness(µ)	115 ± 87.8	265 ± 25.350	<0.0001

Table 4: Correlation of visual acuity with axial length, foveal thickness, choroidal thickness and photoreceptor (plus RPE) thickness

Visual Acuity (Dioptres)	AL(mm)	FT(µ)	CT(µ)	PT(µ)
6-9	26.08	250.18	121.85	99.52
9-12	27.25	230.52	119.27	99.10
12-15	27.55	235.71	115.35	98.62
>15	28.12	227.65	112.78	97.85

Discussion

In this study, the visual acuity in high myopic eyes with no evidence of myopic maculopathy or any other retinal disorder correlated well with foveal thickness, photoreceptor layer thickness and subfoveal choroidal thickness. Photoreceptor layer thickness had a statistical correlation with all the variables measured, mean choroidal thickness, subfoveal choroidal thickness and foveal thickness, but not with age. From the table above we can see that the axial length showed significant increase with increasing degree of myopia, other macular thickness parameters showed significant decrease with increasing degrees of myopia.

Similarly our study showed that thinner choroidal thickness is associated with poorer visual acuity in high myopic eyes and this correlated well with other similar studies published previously [22-25]. With regard to the outer retinal layer, defined as photoreceptor layer thickness plus RPE thickness, measured from the ELM to the outer border of the RPE, a negative correlation was found between BCVA (Log MAR) and this parameter similar to that seen with choroidal thickness, that is as the photoreceptor including the RPE layer thickness decreased in high myopia it led to further decline in visual acuity. In the study by Nishida *et al*, the Japanese group found significant correlation between visual

acuity and the inner segment to RPE aggregate thickness as was seen in our study [25].

Macular choroidal thickness and subfoveal choroidal thickness showed a positive correlation with the photoreceptors and RPE aggregate, so as the outer retina thickness increases the choroid is thicker. It remains to be established whether the outer retina determines a thicker choroid due to an increased energy consumption, or vice versa, a thicker choroid means more and better outer retinal metabolism and thus increased cellular survival.

The age-dependent decrease in choroidal thickness described in this report suggests a role for choroidal atrophy in the pathogenesis of visual dysfunction in high myopia. The findings in this study suggest that in addition to undergoing choroidal thinning resulting from progressive stretching from increasing axial elongation, highly myopic eyes also experience the same age-related choroidal attenuation that affect normal eyes. Because both the choroid and the retina are stretched in highly myopic eyes, the choroid—although thinner than normal—still may be able to supply the proportionally thin retina adequately with necessary oxygen and nutrients. This is consistent with fairly normal visual function in adolescents and young adults with high myopia. The relatively thin choroids seen in younger myopes may be physiologically sufficient, even though if the same CT was found in an eye without myopia, such a condition may be considered pathologic. However, as the choroid undergoes age-related attenuation, the available supply may not be sufficient to support the outer retina, the RPE, and even the choroid itself. Accordingly, the logMAR VA in this study was correlated inversely with subfoveal CT.

High myopia as well as macular hole and retinal detachment are diseases wherein the outer retina layers, from ELM to the basal border of RPE, are the retinal main predictor factors for visual prognosis [26-28]. From a pathological point of view, this measurement corresponds with the inner (including ellipsoid and myoid portion of the inner segments) and the outer segments of photoreceptors and RPE, structures that transform the light into nerve impulse [29].

Limitations of the study: In this study the design was retrospective and the choroidal thickness neasurements were done manually as there are no in-built automated software in the OCT machine to measure the choriodal thickness. The visual acuity has been compared with choroidal thickness only in a horizontal scan and not in a vertical one; we have not studied the RPE status. However, patchy or diffuse chorioretinal atrophy was an exclusion criterion. Futures studies comparing retinal/choroidal thickness and autofluorescence images would enhance these results. Studies of choroidal circulation are needed to correlate CT with perfusion, which may guide future therapies aimed at increasing oxygen and nutrient delivery to the choroid and outer retina. At last the sample size in our study was small, a larger population size and standardization can improve the reliability of results.

Conclusion

This study demonstrates that subfoveal choroidal thickness, mean macular choroidal thickness and outer foveal thickness (at the same time dependent of the axial length), and not outer nuclear layer and foveal thickness, are the most important predictive factors for visual acuity in highly myopic eyes without macular pathology. The mechanism of how increasing axial length affects choroidal and external retinal thickness remains inadequately understood.

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