Enhanced Depth Imaging Optical Coherence Tomography: A Study of the Choroid in High Axial Myopia

Samar O Zayed, Sherif Z Mansour, Ayman A Gaafar, Abdel Rahman G Salman
Department of Ophthalmology, Faculty of Medicine, Ain Shams University
Corresponding author: Samar O Zayed, Mobile: 01001729041; Email: samar_os_zayed@hotmail.com

ABSTRACT

Background: High myopia is one of the main causes of visual impairment worldwide. About 1% of the population has high myopia. There is significant evidence from research with animal models and humans that the development of refractive errors is associated with changes in the structural characteristics of the choroid. Studies from a range of different animal species, including chicks, macaque monkeys, indicate that alterations in choroidal thickness (CT) can precede and accompany the development of myopic refractive errors. **Aim of the Work:** The aim of this study was to evaluate the choroid by Enhanced Depth Imaging OCT, as regards to its morphology and thickness in high axial myopic patients. **Patients and Methods:** The controlled cross sectional study that was conducted on a consecutive series of subjects attending outpatient clinic of Ophthalmology Department, Ain Shams University. The patients were divided into two groups: Study group (group I): includes 100 high axial myopic eyes (more than -6.00 diopters) and Control group (group II): includes 100 emmetropic eyes. **Results:** According to ANOVA test and Tukey HSD post ANOVA test), choroidal thickness changed significantly with different measurement location, with the thinnest choroid observed in the 3 mm nasal and the thickest choroid in the 3 mm upper. CT varied significantly across the myopic subgroups and the emmetropic control group at all the locations (^P Ia,b,c,d,II <0.001 and #P I/II <0.001 for all locations).By plotting multiple regression analyses for myopic patients to show which factor in the study was the most important determinant of subfoveal CT and CT in different positions. It was found UCVA (LogMar) was the most important determinants for SFCT and all other locations in all study groups.SFCT (β =162.66), (p<0.001) and (95% CI=147.62–177.70), CT 2 mm nasal (β =156.29), (p<0.001) and (95% CI=141.40–171.18), CT 2 mm temporal (β =122.88) (p <0.001) and the (95% CI = 109.83–135.92), CT 2 mm upper (β = 183.27), (p<0.001) and (95% CI=168.30–198.24) and CT 2 mm lower (β = 164.5), (p<0.001)and the (95% CI=149.74–179.39). **Conclusion:** Our study along with the comprehensive meta-analysis showed that the choroidal thickness is significantly lower in high myopic eyes than control emmetropic eyes. UCVA, AL and the presence of posterior staphyloma are the significant predictors of CT in high myopia and must be taken into account when interpreting the data on CT. Given the large number of people with myopia in the world, these findings seem to have widespread implications.

Keywords: enhanced depth imaging, OCT, choroid, axial myopia.

INTRODUCTION

High myopia (defined as -6.00 diopter or more) is one of the leading causes of visual impairment in the world [(1)]. The prevalence of high myopia, varies according to ethnic groups and countries. It is more common in Asian population with rates of 9-12% in comparison to 2-4 % in white population [(2)].

In high myopia, excessive high axial elongation of the globe can cause biomechanical stretching and thinning of choroid and RPE (retinal pigmented epithelium [(3)]. The axial length is a parameter that rarely changes after growth period, around 20 years of age, whereas posterior staphyloma can increase with high myope at adulthood [(4)].It was found that the choroidal thickness is related to high myopia, the choroid in high myopia has been demonstrated to be markedly thinner compared to normal eye (170-220 um) both histologically [(5)] and with Spectral Domain-Ocular Coherence Tomography (SD-OCT). Histologic studies demonstrated that this choroidal thinning is due to significant thinning of the choriocapillaris and focal lack of vessels [(6)].

Choroidal thickness is important for understanding and evaluating various choroidal pathologies. With increasing knowledge and technological advances, SD-OCT becomes an important imaging modality used in routine practice. Choroidal pathology has been shown to be part of some common diseases in ophthalmology, such as diabetic retinopathy and age related macular degeneration, which is the leading cause of irreversible severe central visual acuity loss in people older than 50 years in the developed world [(7)].It was reported the successful examination and measurement of choroidal thickness in normal and pathological states [(8)]. They also demonstrated the ability of the SD-OCT to show an inverted OCT image by moving image closer to the patient eye. Since the SD-OCT detection has the highest sensitivity near zero delay, the choroid is closer to the zero delay line

Received: 14/10/2017
Accepted: 24/10/2017
DOI: 10.12816/0043823

providing enhance sensitivity and increase the imaging depth.OCT is based on a broad band light source that illuminates the eye. Backscattered light is combined with light reflected from a reference arm to generate an interference signal [(9)]. The frequency of the reflected light is correlated to the depth of its origin, whereby the greater the depth the higher the frequency. Because increased depth is associated with reduced signal intensity and resolution, both the retina and the RPE prevent clear demonstration of the choroid by OCT. It has been shown that increased wavelength allows greater tissue penetration by OCT [(10)]. SD-OCT uses a wavelength of 840 nm and a technique where the light source is brought closer to the eye can produce an inverted image focusing on the choroid and inner sclera, for allowing an accurate image of the choroid [(11)]. This technique that enables high-resolution visualization of the choroid is termed "enhanced depth imaging." It has also been performed with OCT prototypes using a 1,060-nm wavelength [12)].Enhanced depth imaging OCT is becoming an accurate method for measuring choroidal thickness. In the future, it may become a useful clinical tool for the diagnosis and monitoring of various ocular diseases that involve choroidal pathology [(13)].

The correlation of these new anatomical findings with other imaging modality results increases understanding of many eye diseases and recognizes of new ones. The status of the choroid appears to be a crucial determinant in the pathogenesis of diseases such as age-related choroidal atrophy, myopic chorioretinal atrophy, central serous chorioretinopathy, chorioretinal inflammatory diseases, and tumors [(14)].

The aim of this study was to evaluate the choroid by Enhanced Depth Imaging OCT, as regards its morphology and thickness in high axial myopic patients.

PATIENTS AND METHODS

The study is a controlled cross-sectional study that was conducted on a consecutive series of subjects attending the outpatient clinic of Ophthalmology Department, Ain Shams University .It was conducted from June 2015 till October 2017.

The patients were divided into two groups:

Study group (group I): includes 100 high axial myopic eyes (more than -6.00 diopters). This group was subdivided according to the level of myopia into:

- Group Ia: from -6 Diopters till -10 Diopters
- Group Ib: more than -10 diopters till -15 diopters
- Group Ic: more than -15 Diopters till -20 Diopters
- Group Id: above or equal to -20 Diopters

Control group (group II): includes 100 emmetropic eyes

The inclusion criteria

- **Study group:**
  High axial myopic patients.
- **Control group**:
  Emmetropic healthy volunteers.

The exclusion criteria

- Patients with systemic disease as hypertension, diabetes and other vascular diseases.
- Pregnant women.
- Patients with cataract affecting the quality of vision
- Patients with previous ocular surgeries
- Patients with previous retinal diseases, preexisting glaucoma, choroidopathies.
- Uncooperative patients with questionable reliability

A written informed consent was taken from the subjects and their parents/guardians (if they were 21 years old and below). Ethics approval was obtained from the Institutional Review Board of the Faculty of Medicine, Ain Shams University. The study was conducted in accordance with the tenets of the World Medical Association's Declaration of Helsinki.

Full ophthalmic history was taken from each patient, such as previous ocular trauma or surgery, history of ocular diseases. Each patient underwent full ophthalmic examination; including refraction, visual acuity testing, IOP measurement, anterior segment examination and fundus examination. Visual acuity was recorded using Snellen charts, this was confirmed with manifest refraction in which the best corrected visual acuity, which was measured monocularly using a logarithm of the minimum angle of resolution (Log-MAR). The refractive error was screened with Autorefractometer RM8900 (Top con). Each patient underwent IOP measuring by using Air Puff tonometry (NT-3000; Nidek, Gamagori, Aichi, Japan).

Patients underwent slit-lamp examination, binocular indirect ophthalmoscopy was performed approximately 30 min after topical instillation of 10% phenylephrine.

Dilated fundus examination was carried out to each patient. The presence and type of peripheral retinal degenerations and vitreous degenerations were systematically documented.

Biometry measurements, that is axial length (AL), anterior chamber depth (AC), were obtained using PAC scan 300A, Digital biometric ruler (SONOMED).Choroid was measured by the SD-OCT (Cirrus-5000 HD OCT, Zeiss), at five locations: subfoveal, 3mm nasal to the fovea, 3 mm temporal to the fovea, 3 mm inferior to the fovea, and 3 mm superior to the fovea. Thickness was measured as the vertical distance between the outer margin of the hyper reflective retinal pigment epithelium layer and the chorioscleral interface. All OCT examinations and measurements were performed by a single examiner and made to the nearest 1 µm.

All collected data was subjected to statistical analysis and presented.

Statistical analysis

All data analyses were performed using the Statistical Package for Social Sciences version 15.0 (SPSS Inc., Chicago, IL, USA). Quantitative data are presented as mean ± SD. Sex differences were analyzed using chi-square analysis. Multiple group means of parametric datasets were compared using one-way analysis of variance (ANOVA) test. A Tukey honestly significant difference (HSD) post hoc test was performed if an overall significance was found. Regression analyses were done on the different factors that influence CT.

The study was approved by the Ethics Board of Ain Shams University.

RESULTS

As seen in table (1), participants were classified based upon subjective noncycloplegic SE:

- **Control group:** (male/female = 50/51)(right eye/left eye=48/53)
- **Study group Ia:** (>-10.0 D to -15.0 D) (male/female = 23/25) (right eye/left eye=23/25)
- **Study group Ib:** (>-10.0 D to -15.0 D)(male/female = 4/14) (right eye/left eye=10/8)
- **Study group Ic:** (>-15.0 D to -20.0 D) (male/female = 7/18) (right eye/left eye=9/16)
- **Study group Id:** (>-20.0 D) (male/female = 6/4) (right eye/left eye=6/4).

Sex is not significantly different within or between groups (#P I/II = 0.157, ^P = 0.072) and side of the eye is not significantly different within or between groups (#P I/II =0.627), (^P = 0.673).

Table (1): Comparison between study groups regarding sex and eye side

Group	Sex (n, %)		Side (n, %)	
	Male	Female	Right	Left
Group-I	40(39.6%)	61(60.4%)	48(47.5%)	53(52.5%)
Group-Ia	23(47.9%)	25(52.1%)	23(47.9%)	25(52.1%)
Group-Ib	4 (22.2%)	14(77.8%)	10(55.6%)	8(44.4%)
Group-Ic	7 (28.0%)	18(72.0%)	9(36.0%)	16(64.0%)
Group-Id	6 (60.0%)	4 (40.0%)	6(60.0%)	4(40.0%)
Group-II	50(49.5%)	51(50.5%)	51(50.5%)	50(49.5%)
^P Ia,b,c,d,II	0.072		0.627	
#P I/II	0.157		0.673	

^ANOVA test, #Chi square test

Regarding table (2) there is no significant differences between study groups regarding age as (^P Ia,b,c,d,II) is 0.357 and the (#P I/II) is 0.672.

Table (2): Comparison between study groups regarding age (years)

Group	Mean±SD	Range
Group-I	34.9±7.9	22.0–56.0
Group-Ia	31.5±5.9	25.0–46.0
Group-Ib	37.8±7.9	26.0–49.0
Group-Ic	36.4±9.3	22.0–56.0
Group-Id	42.1±4.6	33.0–48.0
Group-II	32.4±6.1	22.0–47.0
^P Ia,b,c,d,II	0.357	
#P I/II	0.672	

#Independent t-test, ^ANOVA test

Visual acuity as shown in table (3) was changed to LogMar scale as Mean±SD.

- **The control group:** (0.1±0.1)
- **Study group Ia**: (1.1±0.0)
- **Study group Ib:** (1.3±0.1)
- **Study group Ic:** (1.5±0.1)

It is considered significantly different among different groups as the (^P Ia,b,c,d,II is <0.001) and the (#P I/II is <0.001).

Table (3): Comparison between study groups regarding UCVA (LogMar)

Group	Mean±SD	Range	95% CI	HG
Group-I	1.2±0.2	1.0–1.7	1.2–1.2	--
Group-Ia	1.1±0.0	1.0–1.1	1.0–1.1	a
Group-Ib	1.3±0.1	1.3–1.4	1.3–1.4	b
Group-Ic	1.5±0.1	1.4–1.7	1.4–1.5	c
Group-Id	--	--	--	--
Group-II	0.1±0.1	0.0–0.3	0.1–0.1	d
^P Ia,b,c,d,II	<0.001*			
#P I/II	<0.001*			

#Independent t-test, ^ANOVA test, HG: Homogenous groups have the same letter (Tukey HSD post ANOVA test).

Axial length as shown in table (4) as Mean±SD.

- **The control group:(**21.9±0.8)
- **Study group Ia :**(25.5±1.2)
- **study group Ib**:(27.9±0.5)
- **study group Ic**: (30.6±0.9)
- **Study group Id:** (32.2±0.2)

It is considered significantly different among different groups as the (^P Ia,b,c,d,II is <0.001) and the (#P I/II is <0.001).

Table (4): Comparison between study groups regarding AXL (mm)

Group	Mean±SD	Range	95% CI	HG
Group-I	27.8±2.7	23.7–32.7	27.3–28.4	--
Group-Ia	25.5±1.2	23.7–27.6	25.1–25.8	a
Group-Ib	27.9±0.5	26.8–28.7	27.7–28.2	b
Group-Ic	30.6±0.9	29.0–32.0	30.2–30.9	c
Group-Id	32.2±0.2	32.0–32.7	32.1–32.4	d
Group-II	21.9±0.8	20.5–23.1	21.8–22.1	e
^P Ia,b,c,d,II	<0.001*			
#P I/II	<0.001*			

#Independent t-test, ^ANOVA test, HG: Homogenous groups have the same letter (Tukey HSD post ANOVA test

Fundus examination revealed the presence of posterior staphyloma in all subjects of study group Ic and Id and 50 % of cases in study group Ib. Staphyloma was significantly different among the studied groups as the(^P Ia,b,c,d,II is <0.001) and the (#P I/II is <0.001).

Table (5): Comparison between study groups regarding fundus findings

Group	Normal	Myope	Staphyloma	HG
Group-I	(0.0%)	56 (55.4%)	45 (44.6%)	--
Group-Ia	(0.0%)	47 (97.9%)	1 (2.1%)	A
Group-Ib	(0.0%)	9 (50.0%)	9 (50.0%)	B
Group-Ic	(0.0%)	0 (0.0%)	25 (100.0%)	c
Group-Id	(0.0%)	0 (0.0%)	10 (100.0%)	c
Group-II	101 (100.0%)	0 (0.0%)	0 (0.0%)	d
^P Ia,b,c,d,II	<0.001*			
#P I/II	<0.001*			

#Independent t-test, ^ANOVA test, HG: Homogenous groups have the same letter (Tukey HSD post Dunn's test).

According to ANOVA test and Tukey HSD post ANOVA test),choroidal thickness changed significantly with different measurement location, with the thinnest choroid observed in the 2 mm nasal and the thickest choroid in the 2 mm upper. CT varied significantly across the myopic subgroups and the emmetropic control group at all the locations (^P Ia,b,c,d,II <0.001 and #P I/II <0.001 for all locations)

Regarding the choroidal thickness of all groups at different locations; ***as seen in table (6), regarding the subfoveal thickness at different groups:***

- **Control group**: (348±59.0).
- **Group Ia**: (228.8±54.5).
- **Group Ib:** (197.7±84.8).
- **Group Ic:** (143.7±48.1).
- **Group Id:** (133.6 ±28.3).

Table (6): Comparison between study groups regarding subfoveal choroidal thickness (µm)

Group	Mean±SD	Range	95% CI	HG
Group-I	191.0±69.4	67.0–390.0	177.3–204.7	--
Group-Ia	228.8±54.5	132.0–353.0	213.0–244.7	A
Group-Ib	197.7±84.8	91.0–390.0	145.5–229.8	a,b
Group-Ic	143.7±48.1	67.0–261.0	123.9–163.6	b,c
Group-Id	133.6±28.3	101.0–166.0	113.4–153.8	C
Group-II	348.0±59.0	223.0–512.0	336.3–359.6	D
^P Ia,b,c,d,II	<0.001*			
#P I/II	<0.001*			

#Independent t-test, ^ANOVA test, HG: Homogenous groups have the same letter (Tukey HSD post ANOVA test).

Table (7): Comparison between study groups regarding nasal-3mm choroidal thickness (µm)

Group	Mean±SD	Range	95% CI	HG
Group-I	145.9±58.7	48.0–299.0	134.3–157.5	--
Group-Ia	185.0±46.9	90.0–299.0	171.4–198.7	A
Group-Ib	136.3±55.9	74.0–240.0	108.5–164.1	A
Group-Ic	97.8±29.9	48.0–182.0	85.5–110.2	B
Group-Id	95.8±31.1	66.0–176.0	73.6–118.0	C
Group-II	294.3±47.7	165.0–428.0	284.9–303.7	D
^P Ia,b,c,d,II	<0.001*			
#P I/II	<0.001*			

#Independent t-test, ^ANOVA test, HG: Homogenous groups have the same letter (Tukey HSD post ANOVA test), significant.

Table (8): Comparison between study groups regarding temporal-3mm choroidal thickness (µm)

Group	Mean±SD	Range	95% CI	HG
Group-I	184.5±66.9	49.0–320.0	171.3–197.7	--
Group-Ia	225.0±49.8	142.0–320.0	210.5–239.5	A
Group-Ib	196.0±69.5	90.0–309.0	161.4–230.6	A
Group-Ic	127.0±33.6	77.0–209.0	113.1–140.8	B
Group-Id	112.9±26.4	49.0–142.0	94.0–131.8	B
Group-II	338.1±52.9	212.0–535.0	327.6–348.5	C
^P Ia,b,c,d,II	<0.001*			
#P I/II	<0.001*			

#Independent t-test, ^ANOVA test, HG: Homogenous groups have the same letter (Tukey HSD post ANOVA test), *Significant

Table (9): Comparison between study groups regarding upper-3mm choroidal thickness (µm)

Group	Mean±SD	Range	95% CI	HG
Group-I	218.9±61.8	109.0–341.0	206.6–231.1	--
Group-Ia	258.0±49.9	138.0–341.0	243.5–272.5	A
Group-Ib	219.4±54.5	113.0–330.0	192.4–246.5	A
Group-Ic	167.9±37.5	109.0–271.0	152.4–183.4	B
Group-Id	157.5±22.9	124.0–188.0	141.1–173.9	B
Group-II	352.7±55.7	206.0–501.0	341.8–363.7	C
^P Ia,b,c,d,II	<0.001*			
#P I/II	<0.001*			

#Independent t-test, ^ANOVA test, HG: Homogenous groups have the same letter (Tukey HSD post ANOVA test), *Significant

Table (10): Comparison between study groups regarding lower-3mm choroidal thickness (µm)

Group	Mean±SD	Range	95% CI	HG
Group-I	197.7±63.4	90.0–357.0	185.2–210.2	--
Group-Ia	233.3±56.6	90.0–357.0	216.9–249.8	A
Group-Ib	181.9±45.2	99.0–307.0	159.4–204.3	A
Group-Ic	163.1±59.0	91.0–292.0	138.8–187.5	A
Group-Id	141.6±25.8	104.0–182.0	123.1–160.1	B
Group-II	331.0±46.9	221.0–454.0	321.8–340.3	C
^P Ia,b,c,d,II	<0.001*			
#P I/II	<0.001*			

#Independent t-test, ^ANOVA test, HG: Homogenous groups have the same letter (Tukey HSD post ANOVA test), *Significant.

Table (11): Comparison between cases with and without staphyloma

Items	Group-I			Group-Ib		
	Present (N=45)	Absent (N=56)	^P	Present (N=9)	Absent (N=9)	^P
Age (years)	38.1±8.5	32.3±6.4	<0.00*	38.1±9.3	37.6±6.7	0.886
Sex (n, %) - Male - Female	 16 (35.6%) 29 (64.4%)	 24 (42.9%) 32 (57.1%)	 ¤0.456	 2 (22.2%) 7 (77.8%)	 2 (22.2%) 7 (77.8%)	 # 1.000
Side (n, %) - Right - Left	 20 (44.4%) 25 (55.6%)	 28 (50.0%) 28 (50.0%)	 ¤0.578	 4 (44.4%) 5 (55.6%)	 6 (66.7%) 3 (33.3%)	 # 0.637
UCVA (LM)	1.4±0.1	1.1±0.1	<0.00*	1.4±0.1	1.3±0.0	0.372
RSEq	-16.1±8.2	-7.8±2.9	<0.00*	-13.4±1.6	-12.3±1.6	0.155
IOP (mmHg)	16.1±1.5	15.0±1.5	<0.00*	16.4±1.4	16.4±1.1	1.000
AXL (mm)	30.4±1.6	25.8±1.4	<0.00*	28.1±0.6	27.8±0.4	0.202
ACD (mm)	2.4±0.2	2.9±0.1	<0.00*	2.6±0.1	2.7±0.1	0.118
Subfoveal	146.7±45.2	226.6±65.1	<0.00*	169.4±50.7	205.9±109.3	0.383
Nasal (mm)	102.9±34.7	180.5±50.6	<0.00*	124.4±46.7	148.1±64.3	0.386
Temporal	138.6±48.8	221.3±55.9	<0.00*	199.1±59.5	192.9±81.9	0.856
Upper (mm)	178.5±43.8	251.3±54.9	<0.00*	231.0±41.5	207.9±65.4	0.386
Lower (mm)	160.1±47.7	227.9±58.3	<0.00*	174.1±24.9	189.7±59.8	0.487

^Independent t-test, ¤Chi square test, #Fisher's Exact test

According to table (12);

Group-I: there significant positive correlation between subfoveal choridal thickness and refraction spherical equivalent, ACD& other choridal thickness sites. There is significant negative correlation with age, UCVA, IOP& AXL.

Group-II: there was significant positive correlation between subfoveal choridal thickness and AXL& temporal and upper choridal thickness.

Table (12): Correlation between subfoveal choridal thickness and other variables

Items	Group-I		Group-II	
	R	P	R	P
Age	-0.360	<0.001*	-0.051	0.616
UCVA	-0.447	<0.001*	-0.070	0.488
RSEq	0.340	0.001*	0.102	0.313
IOP	-0.234	0.019*	-0.015	0.881
AXL	-0.554	<0.001*	0.395	<0.001*
ACD	0.587	<0.001*	0.069	0.491
Nasal	0.798	<0.001*	0.144	0.151
Temporal	0.789	<0.001*	0.262	0.008*
Upper	0.751	<0.001*	0.295	0.003*
Lower	0.666	<0.001*	-0.072	0.475

Pearson correlation, *Significant

As seen in table (13):

In group-I: there was significant positive correlation between nasal-3mm choridal thickness and refraction spherical equivalent, ACD& other choridal thickness sites and significant negative correlation with age, UCVA, IOP& AXL.

In group-II: there was significant positive correlation between nasal 3-mm choridal thickness and AXL& temporal and upper choridal thickness.

Table (13): Correlation between nasal-3mm thickness and other variables

Items	Group-I		Group-II	
	R	P	r	P
Age	-0.375	<0.001*	-0.126	0.208
UCVA	-0.589	<0.001*	-0.091	0.363
RSEq	0.425	<0.001*	-0.010	0.921
IOP	-0.337	0.001*	-0.058	0.563
AXL	-0.686	<0.001*	0.272	0.006*
ACD	0.669	<0.001*	-0.164	0.102
Temporal	0.815	<0.001*	0.649	<0.001*
Upper	0.726	<0.001*	0.265	0.007*
Lower	0.715	<0.001*	0.110	0.273

Pearson correlation, *Significant

Regarding table (14):

In group-I: there was significant positive correlation between temporal-3mm choridal thickness and refraction spherical equivalent, ACD& other choridal thickness sites and significant negative correlation with age, UCVA, IOP& AXL.

In group-II: there was significant positive correlation between temporal -3mm choridal thickness and AXL& lower and upper choridal thickness**.**

Table (14): Correlation between temporal-3mm thickness and other variables

:Items	Group-I		Group-II	
	R	P	r	P
Age	-0.391	<0.001*	0.018	0.860
UCVA	-0.548	<0.001*	0.016	0.872
RSEq	0.416	<0.001*	-0.093	0.358
IOP	-0.300	0.002*	-0.030	0.766
AXL	-0.684	<0.001*	0.216	0.030*
ACD	0.678	<0.001*	-0.026	0.795
Upper	0.815	<0.001*	0.649	<0.001*
Lower	0.778	<0.001*	0.335	0.001*

Pearson correlation, *Significant

According to table (15):

In group-I: there was significant positive correlation between upper-3mm choridal thickness and refraction spherical equivalent, ACD& other choridal thickness sites and significant negative correlation with age, UCVA, IOP& AXL.

In group-II: there was significant positive correlation between upper 3-mm choridal thickness and AXL& lower choridal thickness.

Table (15): Correlation between upper-3mm thickness and other variables

Items	Group-I		Group-II	
	R	P	R	P
Age	-0.469	<0.001*	0.117	0.242
UCVA	-0.575	<0.001*	0.199	0.046*
RSEq	0.424	<0.001*	-0.188	0.062
IOP	-0.251	0.011*	0.109	0.279
AXL	-0.690	<0.001*	0.175	0.080
ACD	0.710	<0.001*	0.166	0.097
Lower	0.853	<0.001*	0.549	<0.001*

Pearson correlation, *Significant

As regards to table (16):

In group-I: there was significant positive correlation between lower-3mm choridal thickness and refraction spherical equivalent& ACD and significant negative correlation with age, UCVA, IOP& AXL.

Table (16): Correlation between lower-3mm thickness and other variables

Items	Group-I		Group-II	
	R	P	r	P
Age	-0.408	<0.001*	0.129	0.197
UCVA	-0.515	<0.001*	0.125	0.212
RSEq	0.341	<0.001*	-0.183	0.070
IOP	-0.241	0.015*	-0.039	0.697
AXL	-0.596	<0.001*	-0.180	0.071
ACD	0.594	<0.001*	-0.027	0.790

Pearson correlation, *Significant

As shown in table (17), by plotting multiple regression analyses for myopic patients to show which factor in the study was the most important determinant of subfoveal CT and CT in different positions. It was found UCVA (LogMar) was the most important determinants for SFCT and all other locations in all study groups.

- SFCT (β =162.66), (p<0.001) and (95% CI=147.62–177.70).
- CT 2 mm nasal (β =156.29), (p<0.001) and (95% CI=141.40–171.18).
- CT 2 mm temporal (β =122.88) (p <0.001) and the (95% CI = 109.83–135.92).
- CT 2 mm upper (β = 183.27), (p<0.001) and (95% CI=168.30–198.24)
- CT 2 mm lower (β = 164.5), (p<0.001)and the (95% CI=149.74–179.39).

Table (17): Linear regression for factors affecting choroidal thickness in group-I

Factors	B	SE	P	95% CI	R^2
Subfoveal					
UCVA (LM)	162.66	7.56	<0.001*	147.62–177.70	0.848
Temporal					
UCVA (LM)	122.88	6.56	<0.001*	109.83–135.92	0.809
Nasal					
UCVA (LM)	156.29	7.49	<0.001*	141.40–171.18	0.840
Upper					
UCVA (LM)	183.27	7.53	<0.001*	168.30–198.24	0.877
Lower					
UCVA (LM)	164.56	7.45	<0.001*	149.74–179.39	0.854

β: Regression coefficient, SE: Standard error, CI: Confidence interal, *Signiicant

As shown in table (18), according to linear regression analysis of all studied factors in group-II, only age was a significant factor that increases choroidal thickness as there is a positive relationship between age and choroidal thickness for emmetropes.

Table (18): Linear regression for factors affecting choroidal thickness in group-II

Factors	B	SE	P	95% CI	R^2
Subfoveal					
Age (years)	10.36	0.27	<0.001*	9.82–10.89	0.937
Temporal					
Age (years)	8.74	0.23	<0.001*	8.28–9.20	0.935
Nasal					
Age (years)	10.08	0.24	<0.001*	9.60–10.57	0.945
Upper					
Age (years)	10.55	0.24	<0.001*	10.07–11.03	0.950
Lower					
Age (years)	9.90	0.22	<0.001*	9.47–10.33	0.954

β: Regression coefficient, SE: Standard error, CI: Confidence interval, *Significant

DISCUSSION

Enhanced depth imaging OCT is becoming an accurate method for measuring choroidal thickness. In the future, it may become a useful clinical tool for the diagnosis and monitoring of various ocular diseases that involve choroidal pathology. It has already made

meaningful contributions in research and clinical practice [(15)]. The results of this study unite and ascertain previous knowledge of choroidal thickness, aid in establishing normal values of choroidal thickness in healthy adults, and describe its relations between different macular locations. The results strengthen the correlation between increased axial length and myopia, decrease choroidal thickness.

In this cross-sectional study, we measured the choroidal thickness (CT) in different degrees of high myopia and in normal control eyes. Overall, CT was significantly lower in myopes compared to emmetropes. Moreover, CT varied by location. In group Ia, Ic and Id, the thickest CT is in the upper 2mm, followed by the lower 2mm then subfoveal area, then temporal 2mm and lastly the nasal 2mm. However, in group Ib, the thickest measurements were found in the upper 2mm followed by the temporal 2mm and then subfoveal area, then followed by the lower 2mm and lastly the nasal 2mm.

This is in agreement with many studies, such as, who found that the thickest location for eyes with high myopia is found in the lower region while the thinnest region is in the nasal direction [(16)]. While in our study the thickest measures were found in the upper region in the advanced myopic eyes, but the thinnest region persisted in the nasal direction .This difference could be because Zhang et al. [(16)], included 20 myopic patients (40 eyes) and they did not include a control group (emmetropic participants) while our work included 101 eyes with myopia, with 101 matched healthy emmetropic subjects as a control group. Zhang et al [(16)] included 20 eyes between -6 and -10, 10 eyes between >10- and -15 D, 5 eyes between >-15 and -20 D and 5 eyes >-20D. We classified our study group into Group-Ia: 48 myopic cases (-6D to -10D), group-Ib: 18 myopic cases (-10D to -15D), group-Ic: 25 myopic cases (-15D to -20D) and group-Id: 10 myopic cases (> -20D).The control group (group--II): 101 emmetropic controls.

While the observed pattern of CT distribution in our study is similar to the previous studies, in high myopes [(17)] and [(18)] and in emmetropes [19].

Two possible reasons for the relative choroidal thinning nasally and inferiorly in normal eyes are the choroidal watershed and the fetal choroidal fissure, which closes inferiorly at 7 weeks [(20)]. In summary, the current thickness data agreed with the previous studies.

Multiple regression analyses showed that UCVA (LogMar) was the most important determinants for SFCT and all other locations in all study groups. SFCT (β =162.66), (p<0.001) and (95% CI=147.62–177.70). Regarding CT 2 mm nasal (β =156.29), (p<0.001) and (95% CI=141.40–171.18). As for CT 2 mm temporal (β =122.88) (p <0.001) and the (95% CI = 109.83–135.92). Regarding CT 2 mm upper (β = 183.27), (p<0.001) and (95% CI=168.30–198.24), while the CT 2 mm lower (β = 164.5), (p<0.001)and the (95%CI=149.74–179.39).

However metaregression analysis of various other studies to quantify the change in mean CT with UCVA , found no significant association between UCVA and mean CT (b = 0.429, p = 0.952) indicating AL to be a more

important predictor of CT than UCVA, also the mean SFCT in emmetropes was 348.0 um which is also thicker than previous studies that reported a mean thickness of 272–354 um [8,11,12,19].

The differences in CT in our study compared to other studies could be because of differences in participants' characteristics, such as age, refractive error and ethnicity. In addition, variations in OCT device characteristics such as wavelength, eye tracking method and averaging software among studies. In our results, CT decreased with increase in severity of myopic refractive error. The findings suggest that thinning or abnormalities of choroid play a role in the pathogenesis of myopic degeneration and thus visual impairment.

The AL showed a significant positive correlation with refraction, but showed a significant negative correlation with SFCT, CT 3 mm nasal, CT 3 mm temporal, CT 3 mm upper, and CT 3 mm lower.

Presence of posterior staphyloma, a hallmark of high myopia, was significantly associated with choroidal thinning. Regarding our study, all study groups; cases with staphyloma had significant higher UCVA, IOP& AXL and significant lower choroidal thickness.

This association is probably because in myopic eyes with posterior staphyloma, choroidal circulation is altered with marked attenuation and reduction in number of large choroidal vessels[21]. In addition, there is a shift in the entry site of the posterior ciliary arteries towards the staphyloma's border leading to scarce choroidal arterial network in the area occupied by staphyloma [22]. Thus, all these changes lead to choroidal thinning in eyes with staphyloma.

Population-based investigations, histologic and clinical studies have shown a marked thinning of the choroid with increasing axial elongation [3]. This indicates that with increasing axial elongation, the distance between the Bruch membrane and the sclera was markedly decreased [23].

Studies found that the choroidal volume was lower in highly myopic eyes without vitreoretinal or choroidal pathologies than in emmetropic eyes ($p<0.001$) and choroidal thinning is present in highly myopic eyes compared with emmetropic eyes [24].

In a histologic study on the macular region of highly myopic eyes, the detected macular regions was found without Bruch membrane and (consequently) without adjacent RPE and without choriocapillaris. The photoreceptor layer was markedly diminished or rudimentary, as was the remaining choroid, with only a few large choroidal vessels present. In these regions with this secondary macular opening of Bruch membrane, the globe wall consisted of a markedly thinned sclera, some melanin-bearing cells on the inner surface of the sclera (lamina fusca sclerae), and remnants of the middle layer and inner layer of the retina, including the inner limiting membrane [20].

We present a new correlation that choroidal thickness is significantly greater superior to the fovea than subfoveally and inferior to it. Further research is needed to focus on documenting the progression over time of choroidal thickness in eyes with ocular conditions, or comparing choroidal thickness between eyes of patients with unilateral conditions**.**

Our study has several strong points, such as relatively large sample size, and EDI SD-OCT images were enhanced using to improve CSI visibility. Therefore, the CT measurements obtained in our study are likely more reliable and accurate. Unlike other studies like [16]**,** our study included an emmetropic group, and therefore, we could examine the differences between highly myopic eyes and non-myopic eyes in our case–control study. The study also has some limitations. First, due to our cross-sectional study design, we were unable to determine the causal relationships between the various risk factors and CT. Secondly, only horizontal and vertical scan lines were used to determine the CT profile.

A denser scanning protocol is likely to provide further insights regarding the thickness profile across the posterior pole. While denser scanning protocols may not be feasible with manual segmentation and large subject numbers, the development of automated choroidal segmentation methods opens the door for potential future studies to use denser scanning protocols to determine the topographical thickness profile of the choroid, which will likely provide additional insights into the changes in the choroid associated with myopia. Also, it is not a prospective study with follow-up; it is a single center rather than multicenter study; and it has a small sample size.

CONCLUSION

Our study along with the comprehensive meta-analysis showed that the choroidal thickness is significantly lower in high myopic eyes than control emmetropic eyes. UCVA, AL and the presence of posterior staphyloma are the significant predictors of CT in high myopia and must be taken into account when interpreting the data on CT. Given the large number of people

with myopia in the world, these findings seem to have widespread implications.

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