Measurement of choroidal thickness and volume with spectral domain optical coherence tomography: variation with age, gender and ethnicity.

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***Objective**: To evaluate the subfoveolar choroidal thickness (SFCT) and choroidal volume (CV) in variation to age, gender and ethnicity among healthy individuals.*

***Study design and method**: This was a cross sectional hospital based study done in Selayang Hospital. A total number of 113 healthy subjects were recruited. All subjects were scanned using the spectral domain-optical coherence tomography (SD-OCT) machine using the enhance depth imaging (EDI) mode. The subfoveolar choroidal thickness and choroidal volume were then measured using the build-in thickness map software of the proprietary machine and were then evaluated in variation to age, gender and ethnicity.*

***Results**: The overall mean age was 39.58 (±14.71) years. Mean SFCT was 320.08 (±56.08) µm and mean CV was 8.10 (±1.212) mm^3. Linear regression analysis showed reduction of 1.78 µm of thickness and 0.042 mm^3 of volume respectively per year of age. The mean SFCT in males was 335.13(±58.93) µm and 307.25(±50.55) µm in females. Mean CV was 8.52(±1.35) mm^3 for males and 7.74(±0.96) mm^3 for females. Indians had mean SFCT 342.18 (±55.08) µm and CV 8.58(±1.01) mm^3. There were no significant differences of these values between Malay and Chinese groups with p values >0.95.*

***Conclusion**: SFCT and CV decreases with age. Females had generally thinner SFCT and lesser CV as compared to males. There were no significant variations of SFCT and CV between ethnic groups. However Indian subgroup had a greater SFCT and CV.*

***Keywords**: choroidal thickness;choroidal volume;enhance depth imaging;OCT*

EyeSEA 2017 ; 12 (1) : 40-49
Full text. https://www.tci-thaijo.org/index.php/eyesea/index

Introduction

Adequate visualization of the choroid using OCT has been made possible by using the enhanced depth imaging (EDI) mode. Spaide et al[1] reported successful examination and measurement of choroidal thickness with this technique using the Heidelberg Spectralis (Heidelberg Engineering, Heidelberg, Germany) OCT instrument.

The EDI employs the ability of the spectral domain (SD) OCT systems to show an inverted image when the device is moved close to the patients' eye, allowing images of deeper structures such as the choroid to be closer to the zero-delay line. This technique produced an enhanced sensitivity for the deeper ocular structures which increase the imaging depth and the resultant visibility of the choroidal layer.

Previous reports had demonstrated variations of choroidal parameters in normal and pathologic states using the SD-OCT instruments. The choroid thickness is found to be increased in cases of active Vogt-Koyanagi-Harada disease and central serous chorioretinopathy. In age related macular degeneration and diabetic macula edema, the choroidal thickness is often decreased. These variations suggested that the choroidal thickness and volume could be important parameters in the evaluation of ocular disease.

To understand the significance of these potential differences, normative values for choroidal thickness and volume would appear to be important for reference purposes. Accordingly, a number of investigators have studied and reported normative values for choroidal thickness and volume in different populations.[2,3,4,5,6] The values between different studies were observed to be variable. This limits application of the available data on patients from different backgrounds and thus difficult to establish a clear threshold between normal and pathologically choroidal profile in a clinical setting

Therefore, our study was done to contribute in developing a locally based normative data to help clinicians in evaluating patients with various chorioretinal disorders by providing them a normative value for references. In this study, we measured the subfoveal choroidal thickness and choroidal volume as well as to evaluate its relation to age, gender, and ethnicity among healthy individuals.

Methodology

This cross sectional study was performed between 1st November 2014 until 30th October 2015 with subjects randomly recruited from staffs and visitors of Selayang Hospital, Selangor, Malaysia. Eligible individuals were selected and written consent was obtained from each volunteers. The study was conducted in accordance to the Malaysian Guidelines for Good Clinical Practice (GCP) and the Declaration of Helsinki. and the Declaration of Helsinki. Sample size was calculated using Power and Sample Size Calculation software version 3.0.43 (Dupont WD, Plummer WD: 'Power and Sample Size Calculations: A Review and Computer Program', Controlled Clinical Trials 1990; 11:116-28). Based on mean differences from previous studies[5,8] with the Confidence

Interval of 95%, Power 80% and ratio of sample size 1, the calculated sample size was 114 subjects.

All volunteers underwent screening test for blood pressure, sugar level and ophthalmologic examination. Accepted blood pressure level was ≤140/90mmHg and blood sugar level ≤11.1mmol/l. The inclusion criteria were individuals aged 18 years old and above of either gender. Subjects were either Malay, Chinese or Indian ethnicity with ocular axial length between 23.00 to 24.50 mm. Exclusion criteria were individuals who were diagnosed with systemic illness such as diabetes mellitus, hypertension, connective tissue diseases and malignancies; any co-existing ocular disease except age related cataract with good fundus view and subjects who had undergone any form of previous ocular surgery, laser procedures or intra/peri ocular injections. Subjects with poor image quality scans i.e poor demarcation of choroidoscleral interface and signal strength of less than 7 were excluded as well.

Eligible subjects had their eyes scanned by an experienced operator using the Heidelberg Spectralis Spectral Domain Optical Coherence Tomography, Software version 1.9.10.0 (Heidelberg Engineering, Heidelberg, Germany). Data from either the right or left eye were used and analyzed for the study purposes.

All subjects were scanned twice, each for choroidal volume and subfoveal choroidal thickness evaluation. Scanning for choroidal volume were done using a standardized scanning protocol as described previously by Barteselli G et al[7]. A 31 high-resolution B- scans (9.0mm in length) covering an area of 30° x 25 ° centered on the fovea spaced 240µm apart from each other was performed in each eye. An internal fixation light was used to center the scanning area on the fovea. A minimum of 50 frames were automatically averaged and used to obtain a choroidal image using the built-in TruTrack Active Eye Tracking software of the device (Heidelberg Engineering). The enhanced depth imaging (EDI) mode were used to optimize choroidal sensitivity and enhance visualization of the full choroidal thickness.

For subfoveal choroidal thickness, a standardized scanning protocol of 7 high resolution B-scans, covering an area of 30° x 5 ° centered at the fovea with 100 frames averaged were done using the EDI mode.

To assess the choroidal volume, choroidal segmentations were performed manually after the automated retinal layer segmentation software was disabled. The reference lines of the built- in automated segmentation were moved from the retinal boundaries to the choroidal boundaries. The internal limiting membrane line was moved to the outer part of the hyper- reflective line of Bruch's membrane. The basement membrane line, which was the reference line for the posterior edge of the retina, was shifted to the posterior edge of the choroid as demarcated by the hyper-reflective margin line corresponding to the choroidoscleral interface. This method would allow the use of the automatic retinal thickness/volume map features of the proprietary built-in software to calculate the choroidal volume.

The standardized grid which followed the ETDRS grid that divides the macula into three circles with diameters of 1 mm (central), 3 mm (inner), and 6 mm (outer) were positioned automatically by the Spectralis OCT software that designed to map macular thickness. Both inner and outer rings were further divided into nasal, temporal, superior and inferior quadrants. The values for overall total average choroidal volume and volume within each subfield of the standardized grid were then evaluated. Refer Figure 1.

The subfoveal choroidal thickness was assessed by selecting the horizontal section of choroid corresponding at the foveal center. Manual segmentation of the choroidal layer was done in the similar manner as described for choroidal volume measurement. The choroidal thickness were measured perpendicularly from the Bruch membrane line to the choroidoscleral interface line at the subfoveola region using the automatic built in measurement software.

22 eyes were selected randomly for a repeat measurement of choroidal parameters to assess the reproducibility and reliability of method of measurement. The choroidal parameters were measured by the principle researcher and

medical retina specialist, in which both were masked from each other's measurements.

All data were analyzed using SPSS V 22 (SPSS Inc, Cary, NC), with the level of significance set at less than 0.05%.

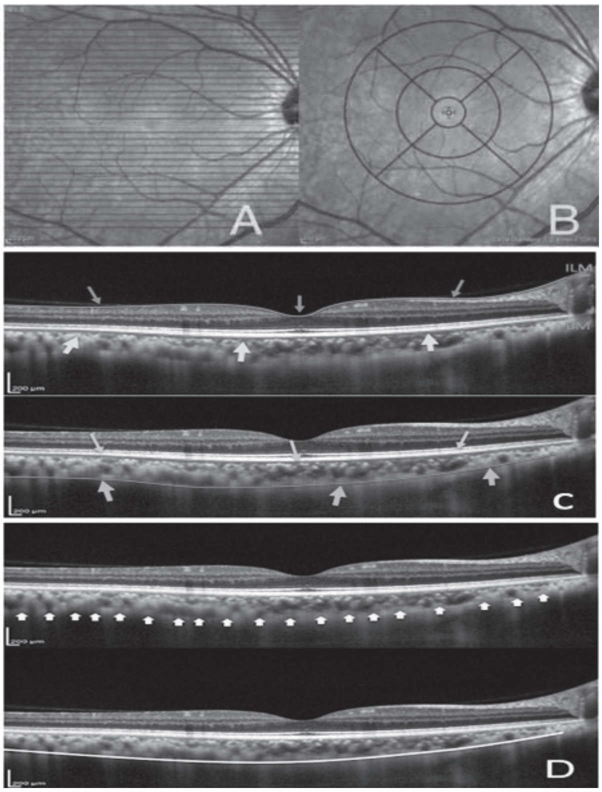

Figure 1 EDI OCT macula A: 31 B scans protocol. B: Standardized grid including three concentric rings with a total of nine subfields centered on the fovea. C: Automated retinal segmentation and manual choroidal segmentation. Internal limiting membrane line (red arrows) and basement membrane line (blue arrows) on automated retinal segmentation is moved to the base of retinal pigment epithelium (orange arrows) and choroidoscleral interface (green arrows) to demarcate choroidal boundaries. D: Delineation of posterior edge of choroid. A curve line is constructed at the inner most zone of the hyper-reflective margin line corresponding to the choroidoscleral interface using the built in segmentation software.

Results

113 out of 118 healthy eyes were included. Five were excluded due to poor delineation of choroidoscleral junction. There were 61 females and 52 males. 41 were Malays, 39 Chinese and 33 Indians respectively. Mean age was 39.58 (± 14.71) years old.

The overall mean subfoveal choroidal thickness was 320.08 µm (±56.08) and choroidal volume was 8.10 (± 1.212) mm^3.

The mean subfoveal choroidal thickness (SFCT) of subjects <40 years old was 335.42µm, between 40 to 60 years old was 302.85µm and > 60 years old was 262.22µm. Further Post hoc (Bonferroni) analysis test noted a significant difference between subjects <40 years old compared to subjects in the other two groups of ≥40 years old with p value of 0.011 and p<0.001 respectively.

The mean choroidal volume (CV) among subjects of <40 years old was 8.47 mm^3. Subjects within the 40-60 years old group had a mean CV of 7.74 mm^3 whereas the older age group >60 years old had a lower CV, with mean of 6.46 mm^3. These differences of mean values were statistically significant in all 3 groups with $p < 0.05$.

Linear regression analysis showed that subfoveal choroidal thickness declined by 1.78 µm and choroidal volume decline by 0.042 mm3 with every year increase in age.

The mean SFCT in males was significantly thicker as compared to females with the value of 335.13um (±58.93) µm and 307.25 (±50.55) µm respectively, p = 0.008. The mean CV in males was also significantly higherµ at 8.52 (±1.35) mm^3 in comparison to 7.74 (±0.96) mm^3 in females, p= 0.001.

Indian subjects had mean SFCT 342.18 (±55.08) µm and CV 8.58(±1.01) mm^3. There were no significant differences of these values between Malay and Chinese subjects with p values >0.95.

Refer table 1 for summary of results.

Table 1 Demographic characteristic, mean SFCT and mean CV of study subjects

Variables	n (%)	Mean SFCT (SD) µm	Mean CV (SD) mm^3
Age group			
< 40 years old	71 (62.8)	335.42(50.48)	8.47 (1.08)
40 – 60 years old	33 (29.2)	302.85 (54.68)	7.74 (1.11)
> 60 years old	9 (8.0)	262.22 (51.99)	6.46 (0.84)
Gender			
Female	61 (54.0)	307.25 (50.55)	7.74 (0.95)
Male	52 (46.0)	335.13 (58.93)	8.52 (1.35)
Ethnic group			
Malay	41 (36.3)	311.56 (51.38)	7.84 (1.26)
Chinese	39 (34.5)	310.33 (9.24)	7.97 (1.23)
Indian	33 (29.2)	342.18 (55.08)	8.58 (1.01)

Discussion

Many studies measuring the choroid using SD OCT had been done in both healthy and in various ocular diseases over recent years. However, only a handful of studies on healthy Asian subjects had been published. These previous studies had observed the healthy mean subfoveal choroidal thickness, as scanned by Spectralis SD-OCT, to be ranging from 261.93µm to 340 µm.[8,9,10,11] Please refer Table 2.

Our study produced the mean SFCT of 320.08 ±56.08 µm which is within the normal variations of choroidal thickness values reported. These variations between studies could be due to the difference in study population in which choroidal thickness was influenced by age, gender, refraction, axial length as well as ethnicity.12

It had been suggested in literature that choroidal thickness decreased with increasing age.[8,12,13] Margolis and Spaide[13] quoted 15.6 µm decrease in choroidal thickness for every 10 years. The current study also showed similar results in which a reduction of SFCT of 1.78 µm per year was observed across both gender and all ethnic groups when the entire cohort was compared.

We found that the SFCT was significantly thicker in males as compared to females, similar to studies done by Li[5] in 93 Danish students and Ding and colleagues.[8] In contrast, some studies did not observe any gender-related differences in choroidal thickness.[11,14]

Our results have also shown that Indian subjects had thicker SFCT as compared to Chinese with P value of 0.046. We propose a study with larger sample size to look further into the ethnicity factor. Bafiq et al[11] had categorized their subjects into white, black and south Asian (Indian subcontinents) with 30 subjects in each group. They observed no difference of SFCT between those groups but noted that the temporal choroid in eyes of black to be significantly thinner compared to whites and South Asians.

Sanchez et al[14] reported overall mean choroidal volume of 8.99 ±1.88 mm3 (mean age 23.8 ±3.2 years), similar to our results 8.10 ±1.212 mm^3 (mean age 39.58 ±14.71 years). Hirata and associates[6] reported lower values of 5.411 ±2.097mm^3 (mean age 65 years), The variations in the mean value between these studies could be related to the difference in the mean age of the study population.

We found that similar to the SFCT, the choroidal volume was negatively related to age as noted in other studies.[4,14,15] The exact mechanisms behind choroidal thinning with age are still not clear. Previous studies on histologic evaluation had shown a reduction in vascular density, luminal area, and diameter of the choriocapillaries in aging eyes.[16]

The choroidal volume in males were observed to be higher when compared to females. The difference of these values could be related to the influence of sex hormones on the choroidal blood flow. Kavroulaki D et al[17] had observed that premenopausal females have higher choroidal blood flow as compared to postmenopausal females.

Our study has provided normative data on subfoveal choroidal thickness and choroidal volume amongst healthy individuals of Malay, Chinese and Indian ethnicity in a single tertiary hospital in Selangor, Malaysia. Strengths of this study include the inclusion criteria for subjects with axial length between 23.00-24.50 mm (mean 23.76 ±0.46mm), which was within the range of emmetropic eyes. Readings of blood pressure and random blood sugar level were also taken, apart from the subject's self-declaration that they were healthy.

Another limitation of this study was a small sample size among subjects above 60 years old.

In this current study, the choroidal segmentations were done manually and thus would subject to error compared to automatic segmentations technique. However, although the choroidoscleral junctions were delineated manually, our data showed good inter-grader agreements with the ICC values ranging between 0.83 to 0.99 indicating a high degree of reliability. Refer Table 3.

We recommend future studies with larger sample sizes to establish a local choroidal normative database including pediatric and elderly age group.

Table 2: Comparison of mean SFCT in different studies among healthy Asians

	X Ding et al[8]	**Kim MK et al[10]**	**Tan CSH et al[9]**	**Bafiq R et al[11]**	**Our study**
Mean Age (SD) years	49.73(±17.9)	40.18 (±17.9)	23.0 (±1.9)	35.0 (±15)	**39.58(± 14.7)**
Ethnicity	Chinese (China)	Korean (Seoul)	Chinese (Singapore)	Indian (UK)	**Malay, Chinese, Indian (Malaysia)**
Mean SFCT (SD) µm	261.93 (±88.42)	307.26 (±95.18)	326.4 (±95.2)	340.0 (±44.6)	**320.08 (±56.08)** ***M-311.56 (±51.38)** ***C- 310.33 (±57.71)** ***I- 342.18 (±55.14)**
OCT type	Spectralis SD OCT	Spectralis SD OCT	Spectralis SD OCT	Spectralis SD OCT	**Spectralis SD OCT**
Scan Protocol	EDI: 100 ART	EDI: 100 ART	EDI:25-35 ART	EDI: 24 ART	**EDI: 100 ART**

- **M-**Malay **C-**Chinese **I-**Indian

Table 3 Reliability of measurements by two raters

Measurements	ICC*	95% CI	P-value
SFCT100	0.83	0.59, 0.93	<0.001
SFCT50	0.94	0.80, 0.98	<0.001
Central CV	0.97	0.92, 0.99	<0.001
Inner nasal (IN)	0.98	0.94, 0.99	<0.001
Inner temporal (IT)	0.98	0.93, 0.99	<0.001
Inner superior (IS)	0.97	0.94, 0.99	<0.001
Inner inferior (II)	0.83	0.60, 0.93	<0.001
Outer nasal (ON)	0.97	0.89, 0.99	<0.001
Outer temporal (OT)	0.99	0.97, 1.00	<0.001
Outer superior (OS)	0.98	0.95, 0.99	<0.001
Outer inferior (OI)	0.98	0.96, 0.99	<0.001
Total CV	0.99	0.92, 1.00	<0.001

*ICC (2,k): Two way random, average measures

The ICC values for all the measurements were high (ranges from 0.83 to 0.99) indicating a high degrees of reliability.

Conclusion

This study has profiled the choroidal thickness and volume among healthy adults which has been evaluated by age, sex, and ethnicity. We found that the subfoveal choroidal thickness and choroidal volume decreases with age. Females had generally thinner SFCT and lower CV as compared to males. There were little variations between ethnic groups however Indian subgroup has a slightly greater subfoveal choroidal thickness and volume. We hope that this will provide basic information that could be useful for further studies evaluating choroidal changes and for facilitation in managing patient with various choroidal disorder.

Acknowledgement

We would like to thank the Director General of Health Malaysia for his permission to publish this article.

References

1. Spaide RF, Koizumi H, Pozzoni MC. (2008).Enhanced depth imaging spectral-domain optical coherence tomography. Am J Ophthalmol;146:496–500.
2. Agawa T, Miura M, Ikuno Y, et al.(2011). Choroidal thickness measurement in healthy Japanese subjects by three-dimensional high-penetration optical coherence tomography. Graefes Arch Clin Exp Ophthalmol.;249:1485–1492.
3. Barteselli G, Chhablani J, El-Emam S, Wang H, Chuang J, Kozak I, et.al.(2012). Choroidal

volume variations with age, axial length, and sex in healthy subjects: A three-dimensional analysis. Ophthalmology;1-7

4. Wen Bin Wei , Liang Xu, Jost B. Jonas, Lei Shao, Kui Fang Du, Shuang Wang, et al.(2010).Subfoveal Choroidal Thickness: The Beijing Eye Study. Ophthalmology;120:175–180
5. Li XQ, Larsen M, Munch IC1. (2011). Subfoveal choroidal thickness in relation to sex and axial Length in 93 Danish University Students. Investigative Ophthalmology & Visual Science; Vol. 52 (11): 8438-8441
6. M Hirata, A Tsujikawa, A Matsumoto, M Hangai, S Ooto, K Yamashiro, M Akiba, N Yoshimura.(2011). Macular Choroidal Thickness and Volume in Normal Subjects Measured by Swept-Source Optical Coherence Tomography. Invest Ophthalmol Vis Sci.;52:4971–4978
7. Barteselli G, Chhablani J, El-Emam S, Wang H, Chuang J, Kozak I, et.al.(2012). Choroidal volume variations with age, axial length, and sex in healthy subjects: A three-dimensional analysis. Ophthalmology;1-7
8. X Ding, J Li, J Zeng, W Ma, R Liu, T Li, S Yu, S Tang.(2011). Choroidal Thickness in Healthy Chinese Subjects. Invest. Ophthalmol. Vis. Sci.: 52 :9555-9560
9. Tan CSH, Cheong KX.(2014). Macular choroidal thicknesses in healthy adults-relationship with ocular and demographic factors. Invest Ophthalmol Vis Sci ;55:6452–6458.
10. Kim MK, Sung Soo, Koh HJ, Lee SC. (2014).Choroidal Thickness, Age, and Refractive Error in Healthy Korean Subjects. Optometry & Vision Science: Volume 91 - Issue 5 - p 491–496
11. Bafiq, R., Mathew, R., Pearce,E., Abdel-Hey Ahmed, Richardsone, M., Bailey,T. & Sivaprasad,S. (2012).Age, Sex, and Ethnic Variations in Inner and Outer Retinal and Choroidal Thickness on Spectral-Domain Optical Coherence TomographyAm J Ophthalmol 2015
12. Ikuno Y, Kawaguchi K, Nouchi T, Yasuno Y. (2010).Choroidal thickness in healthy Japanese subjects. Invest Ophthalmol Vis Sci;51:2173–2176.
13. Margolis, R., Spaide, RF. (2009).A pilot Study of Enhanced Depth Imaging Optical Coherence Tomography of the choroid in normal eyes. Am J Ophthalmol.; 147(5):811-5.
14. Sanchez, CA.,Orduna, E., Segura, F., Lopez,C., Cuenca, NA., Abecia, E. & Pinilla,I. (2014). Choroidal Thickness and Volume in Healthy Young White Adults and therelationships between them and Axial Length, Ammetropy and Sex. Am J Ophthalmol;158:574–583.

15. Shin, JW., Shin,YU., Lee,BR. (2012) Choroidal Thickness and Volume Mapping by a Six Radial Scan Protocol on spectral Domain Optical Coherence Tomography.Ophthalmology ;119:1017–1023.
16. Ramrattan RS, van der Schaft TL, Mooy CM, et al.(1994). Morpho- metric analysis of Bruch's membrane, the choriocapillaris, and the choroid in aging. Invest Ophthalmol Vis Sci ;35: 2857– 64.
17. Kavroulaki D, Gugleta K, Kochkorov A, Katamay R, Flammer J, Orgul S. (2010) Influence of gender and menopausal status on peripheral and choroidal circulation. Acta Ophthalmol.;88:850 – 853