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Choroidal volume variations with age, axial length, and sex in healthy subjects: a three-dimensional analysis

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Abstract

Purpose—To demonstrate the three-dimensional choroidal volume distribution in healthy subjects using enhanced depth imaging (EDI) spectral-domain optical coherence tomography (SD-OCT) and to evaluate its association with age, sex, and axial length.

Design—Retrospective case series.

Participants—One hundred and seventy six eyes from 114 subjects with no retinal or choroidal disease.

Methods—EDI SD-OCT imaging studies for healthy patients who had undergone a 31-raster scanning protocol on a commercial SD-OCT device were reviewed. Manual segmentation of the choroid was performed by two retinal specialists. Macular choroidal volume map and three-dimensional topography were automatically created by the built-in software of the device. Mean choroidal volume was calculated for each Early Treatment Diabetic Retinopathy Study (ETDRS) subfield. Regression analyses were used to evaluate the correlation between macular choroidal volume and age, sex, and axial length.

Main Outcome Measures—Three-dimensional topography and ETDRS-style volume map of the choroid.

Results—Three-dimensional topography of the choroid and volume map was obtained in all cases. The mean choroidal volume was $0.228 \pm 0.077 \text{ mm}^3$ for the center ring and $7.374 \pm 2.181 \text{ mm}^3$ for the total ETDRS grid. The nasal quadrant showed the lowest choroidal volume, and the superior quadrant the highest. The temporal and inferior quadrants did not show different choroidal volume values. Choroidal volume in all the ETDRS rings was significantly correlated with axial length after adjustment for age ($P < 0.0001$), with age after adjustment for axial length ($P < 0.0001$) and with sex after adjustment for axial length ($P < 0.05$). Choroidal volume decreases by 0.54 mm^3 (7.32%) for every decade and by 0.56 mm^3 (7.59%) for every mm of axial length. Males have a 7.37% greater choroidal volume compared to that of females.

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This article contains online-only material. The following should appear online-only: Table 1, Table 2, Figure 1, Figure 4.

Conclusions—EDI SD-OCT is non-invasive and well-tolerated procedure with an excellent ability to visualize three-dimensional topography of the choroid and to measure choroidal volume at the posterior pole using manual segmentation. Age and axial length are inversely correlated with choroidal volume, most likely leading to changes in retinal metabolic support in old and high myopic patients. Sexual differences should be considered when interpreting an EDI SD-OCT scan of the choroid.

Introduction

The choroid has various valuable functions in the eye, including metabolic support of the retinal pigment epithelium (RPE) and the retina¹ and blood supply to the outer retinal layers. However, it is also involved in the pathogenesis of several vision-threatening diseases, such as age-related macular degeneration (AMD)², polypoidal choroidal vasculopathy (PCV)³, central serous chorioretinopathy (CSR)⁴, Vogt–Koyanagi–Harada (VKH) disease⁵, and high myopia-related chorioretinopathy.⁶

Visualization of the choroid by indirect ophthalmoscopy and fluorescein angiography is difficult since pigment in the RPE and choroid obstructs the view. Indocyanine green angiography allows for visualization of choroidal vessel perfusion but does not provide three-dimensional anatomical and quantitative evaluations. Recently, Spaide et al., by using a spectral-domain optical coherence tomography (SD-OCT) device, developed the enhanced depth imaging (EDI) technique, which enables *in-vivo* imaging and measurement of the choroid.⁷ Since then, many investigators have performed a bi-dimensional detailed analysis of the choroid among healthy patients^{8–12} as well as patients with chorio-retinal pathologies,^{13–27} using the EDI technique on various SD-OCT devices. Since automated choroidal segmentation software remains unavailable, choroidal thickness measurements were performed manually, and choroidal thickness was measured only at selected points along a single, horizontal and/or vertical SD-OCT B-scan passing through the fovea. As a result, exhaustive information about the real volume of the choroid using a SD-OCT is limited.

Previous studies have reported choroidal thickness measurements at the fovea and selected points of the choroid in healthy eyes.^{8,26,28–30} However, the choroidal thickness measurements in these studies differ from each other, possibly due to limited sample size, different image acquisition techniques and inconsistencies in choosing the locations for repeated measurement. Moreover, the irregularity of the inner chorio-scleral border influences the measurement at few sampling points.^{26,27} To overcome this problem, evaluation of the choroid over the entire posterior pole would be a better tool to evaluate chorio-retinal diseases.

Recently, choroidal thickness mapping has been reported by Sadda et al.³¹, in which they utilized an EDI SD-OCT and used manual segmentation. Choroidal volume mapping was introduced by Yoshimura et al.³² using an experimental swept-source OCT (SS-OCT) at 1050 nm, which is not commercially available. In a recent study³³, Shin et al. calculated an interpolated choroidal volume measurement using a 6-radial scan protocol on a conventional SD-OCT (3D OCT-2000, Topcon, Tokyo, Japan). However, the chorio-scleral boundary was not detected in all the cases because of scattering and low penetration of the used wavelength through the RPE. Moreover, inadequate averaging (eight images) and disproportionate interpolation due to few (six) scans used may have compromised the validity of the measurements.

In a previous report by our group³⁴, we devised an innovative method of choroidal volume measurement using the built-in software for retinal volume measurement of an EDI SD-

OCT after manual choroidal segmentation on a 31-raster scan protocol. Inter-observer and intra-observer reproducibility and repeatability of this method were excellent.³⁴

The aim of the present study was to perform a three-dimensional topographic visualization of the choroidal volume of the posterior pole in a large sample of healthy subjects and to assess correlation of the volume with age, sex and axial length.

Methods

Study population

Starting in July 2011, all patients undergoing SD-OCT scans at the Jacobs Retina Center at Shiley Eye Center, University of California San Diego (La Jolla, CA) underwent choroidal imaging as part of their evaluation. A raster scan of the macula using a SD-OCT device in EDI-mode (Heidelberg Spectralis HRA2; Heidelberg Engineering, Carlsbad, CA) was used to study the choroid. The raster scan required approximately thirty seconds of additional time and was therefore incorporated into the standard scanning protocol. After approval by the Institutional Review Board of the University of California at San Diego for chart review and data analysis, we retrospectively reviewed charts and images of 176 healthy eyes from 114 patients who underwent multimodal examination to rule out retinal pathologies or to document floaters and posterior vitreous detachment over a three-month period (July 2011 to September 2011). To be considered eligible for data and image analysis as part of this study, patients' eyes must have had no pathology other than floaters and posterior vitreous detachment. We excluded eyes/patients with any systemic or local disease that could affect the choroid including uncontrolled hypertension, diabetes, coagulopathies, AMD, PCV, CSR, VKH disease, or other conditions that have been shown to affect the choroid.

Patients underwent ophthalmic evaluation including best-corrected visual acuity (BCVA), slit lamp biomicroscopy, axial length measurement using ocular biometry (IOLMaster; Carl Zeiss Meditec, Jena, Germany), and a raster scan of the macula using the SD-OCT device in EDI-mode without pupillary dilation. The study was conducted in adherence with the tenets of the Declaration of Helsinki.

Choroidal volume scanning protocol

The scanning protocol included thirty-one high-resolution B-scans centered at the fovea, associated to a simultaneous near-infrared image with undilated pupils. An internal fixation light was used to center the scanning area on the fovea. Each scan was approximately 9.3 mm in length and spaced 240 microns apart. All thirty-one B-scans were acquired in a continuous, automated sequence and covered a 30×25 degrees area centered on the fovea. A minimum of twenty-five frames were automatically averaged and used to obtain a good-quality choroidal image using the built-in TruTrack™ Active Eye Tracking software of the device (Heidelberg Engineering, Carlsbad, CA).

Choroidal volume image analysis

Two retinal specialists manually performed the choroidal segmentation, applying a previously described method.³⁴ A 6mm diameter choroidal volume map, centered on the fovea, was automatically generated by the built-in software of the device, by applying the grid used by the Early Treatment Diabetic Retinopathy Study (ETDRS).³⁵ The ETDRS grid divides the macula into three concentric rings (center, inner and outer), the inner ring measuring 1 to 3 mm and the outer ring measuring 3 to 6 mm from the center (referring to a ring with a diameter of 1 mm centered on the fovea). The grid further divides inner and outer rings into four quadrants (superior, inferior, temporal, and nasal); thus, the ETDRS grid divides the macula into nine subfields. After generating thickness and volume maps,

three-dimensional topography of the choroid was obtained using the same built-in software of the device, and color-coded thickness map was superimposed on the inner surface of the choroid in the topographic image using Photoshop CS3 (Adobe, San Jose, CA).

Choroidal volume maps were grouped by axial length, age and sex to facilitate the clinical applications of our findings. To determine the axial length, we judged the eyes' refraction to be myopic (axial length ≥ 24.5 mm), emmetropic ($24.5 > \text{axial length} \geq 23.4$ mm), or hyperopic (axial length < 23.4 mm), on the basis of a normal axial length variation with refraction and age found in the literature.^{36,37} Eyes were divided into three age groups: eyes of patients 40 years old, 41 to 60, and ≥ 61 years old.

Statistical analysis

Statistical analysis was performed using SPSS statistical software version 20 (SPSS Inc., Chicago, IL). All values are presented as a mean $\pm$ the standard deviation (SD). Fisher's Least Significant Difference test was used to compare the choroidal volume at different ETDRS subfields. Pearson's correlation, independent samples *t*-test, and partial correlation were calculated to assess the relationship of the choroidal volume in the three ETDRS rings of the macula³⁵ with three independent factors, including age, axial length, and sex. Multiple linear regression analysis was used to evaluate the correlation between choroidal volume of each ring and the same grouped factors, dividing eyes by age, axial length and sex of the patients. A *p*-value of <0.05 was considered to be statistically significant.

Results

One hundred and seventy six eyes of 114 healthy subjects (51 men and 63 women), with a mean age of 50 years (range 14 to 89 years), were included in the study. Ethnic distribution included 75 Caucasians subjects, 20 Asians subjects, 18 Hispanics subjects and 1 Black subject. One hundred and sixty eyes were phakic and 16 were pseudophakic. BCVA ranged from 20/63 to 20/20 (Snellen equivalent). Axial length measurement was available in 146 out of 176 eyes (83%); the mean axial length was 24.6 ± 1.6 mm (range: 21.03–31.56 mm).

Using high-resolution B-scans and a minimum averaging of twenty-five frames, the choroidal borders were clearly detected in all cases; no eye was excluded because of poor-quality choroidal images. The basement membrane of the RPE appeared as a regular hyper-reflective line, with a concave aspect toward the choroid. Differently, the chorio-scleral interface (outer border of the choroid) appeared irregular and corrugated, following the course of the deepest choroidal vessels (Figure 1, available at <http://aaojournal.org>). Three-dimensional choroidal topography and volume map were obtained in all eyes (Figure 2). In none of the cases did the built-in software fail to reconstruct the map or topography.

Table 1 (available at <http://aaojournal.org>) shows the mean choroidal volume in each area of the ETDRS map. The mean choroidal volume of the fovea was 0.228 ± 0.077 mm³; the inner ring choroidal volume was 1.748 ± 0.558 mm³ while for the outer ring the choroidal volume was 5.398 ± 1.566 mm³. The choroidal volume in the nasal quadrant was significantly lower than all the other quadrants ($p < 0.0001$), while the superior quadrant had a significantly higher choroidal volume than all the others. No differences were noted in choroidal volume between the inferior and temporal quadrants. The mean choroidal volume of the total ETDRS map was 7.374 ± 2.181 mm³.

Table 2 (available at <http://aaojournal.org>) shows correlation analysis between mean choroidal volume of each ring, age, axial length, and sex. The mean choroidal volume showed a negative correlation with age ($p < 0.01$) and with axial length ($p < 0.01$) in the fovea, inner and outer rings (Pearson's correlation). Considering the total macular area, a low-

grade correlation was found with age ($p < 0.01$, $r = -0.387$) and axial length ($p < 0.01$, $r = -0.349$). No correlation with sex was noted (independent samples t -test). After adjustment for axial length using partial correlation analysis, the mean choroidal volume correlated significantly with age ($p < 0.0001$) and also with sex ($p < 0.05$) in all the rings. After adjustment for age, the mean choroidal volume in all the rings highly correlated with axial length ($p < 0.0001$).

Table 3 shows results of the multiple linear regression analysis for mean choroidal volume of the fovea, inner ring, outer ring and total macula. A stepwise method was used to determine the most unexpected factors. The model determined by age, axial length and sex had the best regression. The model showed a good coefficient of determination, which was 0.568 ($R^2 = 0.323$) for the total macular choroidal volume.

The mean choroidal volume of the total macula (Table 4) was $8.311 \pm 2.199 \text{ mm}^3$ in patients 40yo, $7.258 \pm 1.886 \text{ mm}^3$ in patients ranging in age between 41 and 60yo, $6.526 \pm 2.108 \text{ mm}^3$ in patients 61yo (Figure 3, A–C). Dividing the eyes by axial length, it was $8.355 \pm 2.243 \text{ mm}^3$ in hyperopic eyes, $7.645 \pm 2.186 \text{ mm}^3$ in emmetropic eyes, $6.761 \pm 2.005 \text{ mm}^3$ in myopic eyes (Figure 3, D–F). Males presented a mean macular choroidal volume of $7.664 \pm 2.283 \text{ mm}^3$, while females $7.138 \pm 2.077 \text{ mm}^3$.

Figure 4 (available at <http://aaojournal.org>) shows a significant ($p < 0.01$) negative correlation between the total choroidal volume in the ETDRS map and the axial length ($R^2 = 0.122$). Univariate regression analysis showed an approximate decrease in choroidal volume of 0.56 mm^3 (7.59%) for every mm of axial length. Age tended to have a negative correlation of high significance ($p < 0.01$, $R^2 = 0.150$, Figure 4, available at <http://aaojournal.org>). Univariate regression analysis showed an approximate decrease in choroidal volume of 0.54 mm^3 (7.32%) every 10 years.

Discussion

In the present study, a three-dimensional visualization of the choroid of the macular area in a large sample of healthy eyes was performed using an EDI SD-OCT, and allowed a comprehensive analysis of the choroidal anatomy. Manual segmentation of the choroidal borders was performed following a well-reproducible method described in a previous report by our group.³⁴ Volume of the analyzed choroid was automatically calculated by the built-in software of the SD-OCT.

So far, no previous report has provided *in-vivo* data regarding volume of the choroid in normal eyes using EDI SD-OCT. Yoshimura et al.³² recently reported measurement of the choroidal volume of the macula using a prototype of SS-OCT, which is not yet available commercially. In that report, mean choroidal volume of the center ring (within the 1.0-mm diameter ETDRS circle) was $0.159 \pm 0.066 \text{ mm}^3$, $1.412 \pm 0.567 \text{ mm}^3$ within the ETDRS inner ring, and $5.411 \pm 2.097 \text{ mm}^3$ within the ETDRS outer ring. In our study, results of the choroidal volume measurement are higher: mean choroidal volume of the center ring was $0.228 \pm 0.077 \text{ mm}^3$, $1.976 \pm 0.634 \text{ mm}^3$ within the ETDRS inner ring and $7.374 \pm 2.181 \text{ mm}^3$ within the ETDRS outer ring. Explanations for this difference may be the smaller sample size (31 eyes) or the older mean age (64 years) of the population studied by Yoshimura³²; moreover, we cannot exclude ethnic variations in the choroidal volume. However, they did not analyze the correlation between macular choroidal volume and age, axial length, and sex. In our study, results of multiple regression analysis showed a good coefficient of determination for the macular choroidal volume in the model determined by age, axial length and sex ($R^2 = 0.323$).

By stepwise analysis, we found that age was highly associated with choroidal volume in each ETDRS ring. Univariate regression analysis showed an approximate decrease in volume of 0.54 mm^3 (7.32%) for every 10 years. Although the reductions were similar, the R^2 value was low (0.150), suggesting great inter-individual variations. With the increasing age and the regressing choroidal volume, the ability of the choroid to supply sufficient levels of oxygen and other metabolites to the RPE and outer retina may decrease⁷, contributing to the onset of AMD in elderly people.

We also found a significant negative correlation with axial length in all ETDRS rings. Univariate regression analysis showed an approximate decrease in volume of 0.56 mm^3 (7.59%) for every mm of axial length. Similar to the regression of the age, the R^2 was low (0.122), suggesting great inter-individual variations. Choroidal thinning appears to be prominent in highly myopic eyes; this may play a role in the pathophysiologic features of vision loss in high myopia, such as a relative ischemia of the outer retina, RPE and the choroid itself.¹³

Moreover, our study is the first to report inter-sexual differences in choroidal volume in healthy subjects: males have a significantly greater choroidal volume than females (7.37% greater than females). The influence of sex in choroidal thickness and volume was not assessed in previous reports.^{7,9,13,29,31–33} Clinic-based studies have previously documented that the retina is thicker in men than in women^{38–41}; thus, we can speculate a similar finding for the choroid. However, a longitudinal follow-up study is needed to address the clinical significance of this finding.

The present study also showed that nasal choroid volume in the inner ring was significantly lower than the superior choroid; similarly, nasal choroidal volume of the outer ring was significantly lower than the one of all the other outer-ring quadrants. This loss of choroidal tissue in the nasal quadrant could be a contributing cause for the development of peripapillary atrophy and may play a role in glaucoma, as previously speculated by Margolis and Spaide.⁷

Our study has some limitations. First, it is retrospective in nature; however, we carefully excluded eyes/patients with conditions that have been suggested to affect the choroid, and we included only normal eyes and eyes with only floaters and posterior vitreous detachment in this study. Second, we performed manual segmentation of choroidal borders on SD-OCT B-scans because reliable software to perform automated choroidal segmentation is not available. Although manual segmentation may at first appear to be less reliable, we did show in a previous report that our manual technique is highly reproducible.³⁴ In the future, automated choroidal segmentation software may reduce the risk of errors of the manual segmentation still further. Third, we did not study the potential effect of ethnicity, diurnal variation, blood pressure, hydration status, and other systemic or genetic factors on macular choroidal volume; further studies are warranted to evaluate those factors.

In conclusion, our study shows that EDI SD-OCT is a non-invasive and well-tolerated procedure with an excellent ability to visualize choroidal anatomy and to measure choroidal volume at the posterior pole using manual segmentation without pupillary dilation. Age, axial length and sex are highly associated with choroidal volume in normal patients, most likely leading to insufficient metabolic supplements for the macula especially in elderly high-myopic patients. Our study provides a normative database for choroidal volume, which may be useful for future choroidal analysis studies in various chorio-retinal diseases. A larger, prospective, multi-center study would help to evaluate variations of macular choroidal volume related to ethnicity and other systemic or genetic factors. Assessment of

choroidal volume may provide an innovative way to understand their patho-physiology and to evaluate their clinical course.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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References

1. Linsenmeier RA, Padnick-Silver L. Metabolic dependence of photoreceptors on the choroid in the normal and detached retina. *Invest Ophthalmol Vis Sci.* 2000; 41:3117–3123. [PubMed: 10967072]
2. Grossniklaus HE, Green WR. Choroidal neovascularization. *Am J Ophthalmol.* 2004; 137:496–503. [PubMed: 15013874]
3. Gomi F, Tano Y. Polypoidal choroidal vasculopathy and treatments. *Curr Opin Ophthalmol.* 2008; 19:208–212. [PubMed: 18408495]
4. Gupta B, Mohamed MD. Photodynamic therapy for variant central serous chorioretinopathy: efficacy and side effects. *Ophthalmologica.* 2011; 225:207–210. [PubMed: 21325872]
5. Rajendram R, Evans M, Rao NA. Vogt-Koyanagi-Harada disease. *Int Ophthalmol Clin.* 2005; 45(2):115–134. [PubMed: 15791162]
6. Fitzgerald ME, Wildsoet CF, Reiner A. Temporal relationship of choroidal blood flow and thickness changes during recovery from form deprivation myopia in chicks. *Exp Eye Res.* 2002; 74:561–570. [PubMed: 12076077]
7. Spaide RF, Koizumi H, Pozzoni MC. Enhanced depth imaging spectral-domain optical coherence tomography. *Am J Ophthalmol.* 2008; 146:496–500. [PubMed: 18639219]
8. Margolis R, Spaide RF. A pilot study of enhanced depth imaging optical coherence tomography of the choroid in normal eyes. *Am J Ophthalmol.* 2009; 147:811–815. [PubMed: 19232559]
9. McCourt EA, Cadena BC, Barnett CJ, et al. Measurement of subfoveal choroidal thickness using spectral domain optical coherence tomography. *Ophthalmic Surg Lasers Imaging.* 2010; 41(suppl):S28–S33. [PubMed: 21117598]
10. Manjunath V, Taha M, Fujimoto JG, Duker JS. Choroidal thickness in normal eyes measured using Cirrus HD optical coherence tomography. *Am J Ophthalmol.* 2010; 150:325–329. [PubMed: 20591395]
11. Ding X, Li J, Zeng J, et al. Choroidal thickness in healthy Chinese subjects. *Invest Ophthalmol Vis Sci.* 2011; 52:9555–9560. [PubMed: 22058342]
12. Rahman W, Chen FK, Yeoh J, et al. 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. [PubMed: 21087970]
13. Spaide RF. Enhanced depth imaging optical coherence tomography of retinal pigment epithelial detachment in age-related macular degeneration. *Am J Ophthalmol.* 2009; 147:644–652. [PubMed: 19152869]
14. Fujiwara T, Imamura Y, Margolis R, et al. Enhanced depth imaging optical coherence tomography of the choroid in highly myopic eyes. *Am J Ophthalmol.* 2009; 148:445–450. [PubMed: 19541286]
15. Yasuno Y, Okamoto F, Kawana K, et al. Investigation of multifocal choroiditis with panuveitis by three-dimensional high-penetration optical coherence tomography. *J Biophotonics.* 2009; 2:435–441. [PubMed: 19575418]

16. Imamura Y, Fujiwara T, Margolis R, Spaide RF. Enhanced depth imaging optical coherence tomography of the choroid in central serous chorioretinopathy. *Retina*. 2009; 29:1469–1473. [PubMed: 19898183]
17. Maruko I, Iida T, Sugano Y, et al. Subfoveal choroidal thickness after treatment of central serous chorioretinopathy. *Ophthalmology*. 2010; 117:1792–1799. [PubMed: 20472289]
18. Yeoh J, Rahman W, Chen F, et al. Choroidal imaging in inherited retinal disease using the technique of enhanced depth imaging optical coherence tomography. *Graefes Arch Clin Exp Ophthalmol*. 2010; 248:1719–1728. [PubMed: 20640437]
19. Reibaldi M, Boscia F, Avitabile T, et al. Enhanced depth imaging optical coherence tomography of the choroid in idiopathic macular hole: a cross-sectional prospective study. *Am J Ophthalmol*. 2011; 151:112–117. [PubMed: 20970113]
20. Maruko I, Iida T, Sugano Y, et al. Subfoveal choroidal thickness after treatment of Vogt-Koyanagi-Harada disease. *Retina*. 2011; 31:510–517. [PubMed: 20948460]
21. Imamura Y, Iida T, Maruko I, et al. Enhanced depth imaging optical coherence tomography of the sclera in dome-shaped macula. *Am J Ophthalmol*. 2011; 151:297–302. [PubMed: 21129729]
22. Fong AH, Li KK, Wong D. Choroidal evaluation using enhanced depth imaging spectral-domain optical coherence tomography in Vogt-Koyanagi-Harada disease. *Retina*. 2011; 31:502–509. [PubMed: 21336069]
23. Vance SK, Imamura Y, Freund KB. The effects of sildenafil citrate on choroidal thickness as determined by enhanced depth imaging optical coherence tomography. *Retina*. 2011; 31:332–335. [PubMed: 20975620]
24. Mwanza JC, Hochberg JT, Banitt MR, et al. Lack of association between glaucoma and macular choroidal thickness measured with enhanced depth imaging optical coherence tomography. *Invest Ophthalmol Vis Sci*. 2011; 52:3430–3435. [PubMed: 21357398]
25. Maruko I, Iida T, Sugano Y, et al. Subfoveal retinal and choroidal thickness after verteporfin photodynamic therapy for polypoidal choroidal vasculopathy. *Am J Ophthalmol*. 2011; 151:594–603. [PubMed: 21295766]
26. Chung SE, Kang SW, Lee JH, Kim YT. Choroidal thickness in polypoidal choroidal vasculopathy and exudative age-related macular degeneration. *Ophthalmology*. 2011; 118:840–845. [PubMed: 21211846]
27. Koizumi H, Yamagishi T, Yamazaki T, et al. Subfoveal choroidal thickness in typical age-related macular degeneration and polypoidal choroidal vasculopathy. *Graefes Arch Clin Exp Ophthalmol*. 2011; 249:1123–1128. [PubMed: 21274555]
28. Ikuno Y, Maruko I, Yasuno Y, et al. Reproducibility of retinal and choroidal thickness measurements in enhanced depth imaging and high-penetration optical coherence tomography. *Invest Ophthalmol*. 2011; 52:5536–5540.
29. Ikuno Y, Kawaguchi K, Nouchi T, Yasuno Y. Choroidal thickness in healthy Japanese subjects. *Invest Ophthalmol Vis Sci*. 2010; 51:2173–2176. [PubMed: 19892874]
30. Esmaeelpour M, Povazay B, Hermann B, et al. Threedimensional 1060-nm OCT: choroidal thickness maps in normal subjects and improved posterior segment visualization in cataract patients. *Invest Ophthalmol Vis Sci*. 2010; 51:5260–5266. [PubMed: 20445110]
31. Ouyang Y, Heussen FM, Mokwa N, et al. Spatial distribution of posterior pole choroidal thickness by spectral domain optical coherence tomography. *Invest Ophthalmol Vis Sci*. 2011; 52:7019–7026. [PubMed: 21810980]
32. Hirata M, Tsujikawa A, Matsumoto A, et al. Macular choroidal thickness and volume in normal subjects measured by swept-source optical coherence tomography. *Invest Ophthalmol Vis Sci*. 2011; 52:4971–4978. [PubMed: 21622704]
33. Shin JW, Shin YU, Lee BR. Choroidal thickness and volume mapping by a six radial scan protocol on spectral-domain optical coherence tomography. *Ophthalmology*. 2012; 119:1017–1023. [PubMed: 22281089]
34. Chhablani J, Barteselli G, Wang H, et al. Repeatability and reproducibility of manual choroidal volume measurements using enhanced depth imaging optical coherence tomography. *Invest Ophthalmol Vis Sci*. 2012; 53:2274–2280. [PubMed: 22427584]

35. Early Treatment Diabetic Retinopathy Study Research Group. Photocoagulation for diabetic macular edema: Early Treatment Diabetic Retinopathy Study report number 1. *Arch Ophthalmol*. 1985; 103:1796–1806. [PubMed: 2866759]
36. Strang NC, Schmid KL, Carney LG. Hyperopia is predominantly axial in nature. *Curr Eye Res*. 1998; 17:380–383. [PubMed: 9561829]
37. Llorente L, Barbero S, Cano D, et al. Myopic versus hyperopic eyes: axial length, corneal shape and optical aberrations. *J Vis* [serial online]. 2004; 4:288–298. Available at: <http://www.journalofvision.org/content/4/4/5.long>.
38. Kelty PJ, Payne JF, Trivedi RH, et al. Macular thickness assessment in healthy eyes based on ethnicity using Stratus OCT optical coherence tomography. *Invest Ophthalmol Vis Sci*. 2008; 49:2668–2672. [PubMed: 18515595]
39. Wong AC, Chan CW, Hui SP. Relationship of gender, body mass index, and axial length with central retinal thickness using optical coherence tomography. *Eye (Lond)*. 2005; 19:292–297. [PubMed: 15258609]
40. Duan XR, Liang YB, Friedman DS, et al. Normal macular thickness measurements using optical coherence tomography in healthy eyes of adult Chinese persons: the Handan Eye Study. *Ophthalmology*. 2010; 117:1585–1594. [PubMed: 20472290]
41. Song WK, Lee SC, Lee ES, et al. Macular thickness variations with sex, age, and axial length in healthy subjects: a spectral domain-optical coherence tomography study. *Invest Ophthalmol Vis Sci*. 2010; 51:3913–3918. [PubMed: 20357206]

Figure 1.

Example of enhanced depth imaging of the choroid on a horizontal B-scan passing through the fovea in a left eye, before (A) and after (B) manual segmentation. The basement membrane of the retinal pigment epithelium (inner border of the choroid) appeared as a regular hyper-reflective line, with a concave aspect towards the choroid. Differently, the chorio-scleral interface (outer border of the choroid) appeared irregular and corrugated, following the course of the deepest choroidal vessels.

Figure 2.

A three-dimensional topographic visualization of the choroid with superimposed color-coded choroidal thickness map (microns) in an eye with axial length of 23.2 mm (**A–D**) and in an eye with axial length of 26.5 mm (**E–H**). The superior quadrant of the macula appears thicker than the other quadrants, while the nasal quadrant is the thinnest.

Figure 3.

Effect of age (A–C) and axial length (D–F) on color-coded choroidal thickness map and mean choroidal volume of each subfield of the Early Treatment Diabetic Retinopathy Study (ETDRS) grid. (A) Right eye of a 30 years old patient: total choroidal volume is 8.53 mm³; (B) Right eye of a 50 years old patient: total choroidal volume is 7.39 mm³; (C) Right eye of a 70 years old patient: total choroidal volume is 6.36 mm³; (D) Hyperopic eye (axial length = 22.5 mm): total choroidal volume is 8.61 mm³; (E) Emmetropic eye (axial length = 24.5 mm): total choroidal volume is 7.47 mm³; (F) Myopic eye (axial length = 26.5 mm): total choroidal volume is 6.54 mm³.

Figure 4.

Left: scatterplot of axial length (AXL) and macular choroidal volume of all subjects shows a significant negative correlation ($P < 0.01$; $R^2 = 0.122$). **Right:** scatterplot of age and macular choroidal volume of all subjects shows a significant negative correlation ($P < 0.01$; $R^2 = 0.150$).

Table 1 Choroidal volume measurements (mm³) for each ETDRS area.

	Mean	Standard Deviation	Median
Subfields			
Center	0.228	0.077	0.220
Inner Superior	0.458 ^o	0.141	0.465
Inner Nasal	0.411	0.149	0.390
Inner Inferior	0.431	0.149	0.420
Inner Temporal	0.448	0.142	0.450
Outer Superior	1.535 ^{†‡§}	0.434	1.550
Outer Nasal	1.082	0.419	1.000
Outer Inferior	1.382 [†]	0.442	1.345
Outer Temporal	1.398 [†]	0.401	1.385
Rings			
Center	0.228	0.077	0.220
Inner	1.748	0.558	1.690
Outer	5.398	1.566	5.290
Quadrants			
Superior	1.994	0.568	2.010
Nasal	1.493 [*]	0.561	1.385
Inferior	1.813 ^{**}	0.584	1.780
Temporal	1.846 ^{***}	0.537	1.835
Total ETDRS map			
	7.374	2.181	7.145

ETDRS, Early Treatment Diabetic Retinopathy Study

^o P<0.05 compared to values of inner nasal subfield.[†] P<0.0001 compared to values of outer nasal subfield.[‡] P<0.01 compared to values of outer inferior subfield.[§] P<0.05 compared to values of outer temporal subfield.^{*} P<0.001 compared to values of other quadrants.^{**} P<0.01 compared to superior quadrant.^{***} P<0.05 if compared to superior quadrant

Table 2

Correlation analysis between mean choroidal volume and age, axial length, and sex for each ETDRS ring.

	Pearson's Correlation Coefficient	P	Partial Correlation Coefficient	P
Fovea				
Age (y)	−0.297	<0.01	−0.340	<0.0001 (adjusted for AXL)
Axial length (mm)	−0.389	<0.01	−0.429	<0.0001 (adjusted for age)
Sex	n/a	>0.05 *	−0.170	<0.05 (adjusted for AXL)
Inner ring				
Age (y)	−0.325	<0.01	−0.376	<0.0001 (adjusted for AXL)
Axial length (mm)	−0.374	<0.01	−0.420	<0.0001 (adjusted for age)
Sex	n/a	>0.05 *	−0.164	<0.05 (adjusted for AXL)
Outer ring				
Age (y)	−0.409	<0.01	−0.453	<0.0001 (adjusted for AXL)
Axial length (mm)	−0.333	<0.01	−0.396	<0.0001 (adjusted for age)
Sex	n/a	>0.05 *	−0.213	<0.05 (adjusted for AXL)
Total macular area				
Age (y)	−0.387	<0.01	−0.434	<0.0001 (adjusted for AXL)
Axial length (mm)	−0.349	<0.01	−0.408	<0.0001 (adjusted for age)
Sex	n/a	>0.05 *	−0.202	<0.05 (adjusted for AXL)

y, years; AXL, axial length; D, diopters; ETDRS, Early Treatment Diabetic Retinopathy Study; n/a, not applicable.

* Independent samples *t*-test

Table 3

Multiple linear regression analysis for choroidal volume of the macula by age, axial length and sex for each ETDRS ring.

Factor	Coefficient	Standard Error	R ²	P
Center				
Intercept	0.861	0.094	0.275	<0.0001
Age	−0.001	0.000	0.275	<0.0001
Axial length	−0.021	0.003	0.275	<0.0001
Sex	−0.025	0.011	0.275	<0.05
Inner circle				
Intercept	6.346	0.693	0.285	<0.0001
Age	−0.011	0.002	0.285	<0.0001
Axial length	−0.153	0.026	0.285	<0.0001
Sex	−0.180	0.084	0.285	<0.05
Outer circle				
Intercept	18.300	1.866	0.334	<0.0001
Age	−0.038	0.006	0.334	<0.0001
Axial length	−0.405	0.069	0.334	<0.0001
Sex	−0.664	0.226	0.334	<0.01
Total ETDRS map				
Intercept	25.507	2.621	0.323	<0.0001
Age	−0.051	0.009	0.323	<0.0001
Axial length	−0.579	0.097	0.323	<0.0001
Sex	−0.869	0.317	0.323	<0.01

ETDRS, Early Treatment Diabetic Retinopathy Study

Table 4

Choroidal volume measurements for ETDRS rings dividing by age, axial length, and sex.

	Center		Inner Ring		Outer Ring		Total ETDRS map		P
	Mean (mm ³)	SD	Mean (mm ³)	SD	Mean (mm ³)	SD	Mean (mm ³)	SD	
Age									
<40 y (n=59)	0.255	0.080	1.950	0.576	6.106	1.561	8.311	2.199	
41–60 y (n=60)	0.222	0.067	1.714	0.491	5.322	1.346	7.258	1.886	<0.001
>61 y (n=57)	0.206	0.076	1.576	0.550	4.744	1.504	6.526	2.108	
Axial length *									
Hyperopic (n=35)	0.273	0.076	2.052	0.564	6.030	1.623	8.355	2.243	
Emmetropic (n=42)	0.237	0.073	1.810	0.550	5.599	1.593	7.645	2.186	<0.01
Myopic (n=69)	0.202	0.068	1.570	0.510	4.989	1.442	6.761	2.005	
Sex									
Males (n=79)	0.235	0.080	1.802	0.587	5.627	1.636	7.664	2.283	
Females (n=97)	0.222	0.073	1.705	0.533	5.211	1.489	7.138	2.077	<0.05

* Data are available for 146 eyes

SD, standard deviation; ETDRS, Early Treatment Diabetic Retinopathy Study; y, years.