Analysis of Widefield Choroidal Thickness Maps of Healthy Eyes using Swept Source Optical Coherence Tomography

Masatoshi Hirano
Kyoto University

Yuki Muraoka (✉️ muraoka@kuhp.kyoto-u.ac.jp)
Kyoto University

Takahiro Kogo
Kyoto University

Masaharu Ishikura
Kyoto University

Naomi Nishigori
Kyoto University

Naoko Ueda-Arakawa
Kyoto University

Manabu Miyata
Kyoto University

Masayuki Hata
Kyoto University

Ayako Takahashi
Kyoto University

Masahiro Miyake
Kyoto University

Akitaka Tsujikawa
Kyoto University

Article

Keywords:

Posted Date: March 9th, 2023

DOI: https://doi.org/10.21203/rs.3.rs-2626368/v1
Abstract

We aimed to obtain widefield (WF) swept source optical coherence tomography (SS-OCT) data and examine the features of choroidal thickness maps of healthy eyes. The posterior pole choroidal thickness was examined for 127 eyes using enhanced-depth imaging (EDI) of SS-OCT with a viewing angle of 20 (vertical) × 23 (horizontal) mm, and choroidal thickness maps were generated. For SS-OCT image analysis, we developed a grid with inner and outer rings, each divided into superotemporal, inferotemporal, superonasal, and inferonasal quadrants, respectively, making up a total of nine subfields including the central 3-mm ring. The posterior pole choroidal thicknesses were significantly lesser at the periphery than in the central area, in the inferior field than in the superior field, and in the nasal field than in the temporal field (p < 0.001 for all). We also evaluated the effects of age and axial length (AL) on the WF choroidal thickness. Choroidal thicknesses in all subfields were negatively associated with advanced age (p < 0.05). Choroidal thicknesses in the central subfield and the inferonasal inner and outer subfields were negatively associated with AL (p = 0.042, 0.034, and 0.022, respectively). These findings provide insights into the two-dimensional characteristics of the choroidal thickness and their associations with age and AL.

Introduction

The choroid, which forms the posterior part of the uvea, is a melanin-rich membranous tissue with abundant vasculature and stroma. It lies between the retina and sclera and plays important roles in the supply of oxygen and nutrients to the outer retina, regulation of intraocular pressure, and absorption of excess light [1–5]. Considering these functions, the characteristics of the choroidal structure in eyes with pathologies, such as age-related macular degeneration (AMD), central serous chorioretinopathy (CSC), and high myopia, have been discussed [6–9].

Highly sensitive and early detection of pathological changes in the choroid requires thorough knowledge of the anatomical features of the normal choroid. Previous studies using optical coherence tomography (OCT) B-scans showed that the macular choroidal thickness was negatively associated with aging and an increase in the axial length (AL) [10, 11], and that the macular choroid was the thickest on the superior side, followed by the foveal area and the temporal, inferior, and nasal sides [12].

Recent technological advances in OCT imaging, particularly enhanced-depth imaging (EDI) and swept-source (SS) OCT, have facilitated widefield (WF) and quantitative evaluations of the choroidal structure [13, 14]. Recent studies using WF SS-OCT imaging of eyes with CSC showed choroidal thickening from the vicinity of the vortex vein ampulla along the course of the vertically and asymmetrically dilated choroidal veins, which was suggestive of the pathogenesis [15–17]. However, the characteristics of the WF choroidal thickness in healthy eyes have not been fully elucidated.

Accordingly, the aim of the present study was to obtain WF SS-OCT data and examine the features of the generated choroidal thickness maps for healthy eyes.
Results

Table 1 shows the background characteristics of the 127 participants (58 men and 69 women). The mean age was 59.9 ± 17.3 years, and the mean AL was 24.19 ± 1.08 mm. Figure 1 shows the mean choroidal thickness in each examined subfield. For each participant, a clear choroidal thickness map was generated, in which the choroid at the posterior pole showed continuous thinning from the macula to the periphery. However, the area along the choroidal large vessels (vortex veins) was thicker than the surrounding area (Supplementary Fig. S1 online).

Table 1
Characteristics of Healthy Eyes Included in the Study

<table>
<thead>
<tr>
<th>Number (men/women)</th>
<th>127 (58/69)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years (range, years)</td>
<td>59.9 ± 17.3 (20–87)</td>
</tr>
<tr>
<td>Height, cm (range, cm)</td>
<td>161.4 ± 8.0 (146–178)</td>
</tr>
<tr>
<td>Weight, kg (range, kg)</td>
<td>61.6 ± 11.5 (40.9–96.1)</td>
</tr>
<tr>
<td>Axial length, mm (range, mm)</td>
<td>24.19 ± 1.08 (22.01–25.95)</td>
</tr>
<tr>
<td>LogMAR visual acuity (Snellen equivalent)</td>
<td>0.0 ± 0.2 (20/100–20/13)</td>
</tr>
</tbody>
</table>

The data are shown as mean ± standard deviation unless otherwise indicated. LogMAR: logarithm of minimum angle of resolution

We compared the choroidal thicknesses between the corresponding subfields in the inner and outer rings, between the corresponding areas in the superior and inferior subfields, and between the corresponding areas in the temporal and nasal subfields (Fig. 1). The choroidal thicknesses were significantly lesser in the outer ring than in the corresponding subfields in the inner ring (p < 0.001 for all), in the inferior subfields than in the corresponding areas in the superior subfields (p < 0.001 for all), and in the nasal subfields than in the corresponding areas in the temporal subfields (p < 0.001 for all; Fig. 1).

We then evaluated the effects of age and AL on the WF choroidal thickness (Table 2). Choroidal thicknesses in all subfields were negatively associated with age (p < 0.05, Table 2, Fig. 2, Supplementary Fig. S2 online), while those in the central subfield and inferonasal subfields in the inner and outer rings were negatively associated with AL (p = 0.042, 0.034, and 0.022, respectively; Table 2, Fig. 3).
Table 2  
Effects of Age and Axial Length on the Choroidal Thickness in Healthy Eyes

<table>
<thead>
<tr>
<th></th>
<th>Age</th>
<th>Axial length</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>( B )</td>
<td>( p )</td>
</tr>
<tr>
<td>Central (3 mm)</td>
<td>-2.0</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Inner ring (3-9 mm)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Superotemporal</td>
<td>-2.7</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Inferotemporal</td>
<td>-2.6</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Superonasal</td>
<td>-1.9</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Inferonasal</td>
<td>-1.9</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Outer ring (9-18 mm)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Superotemporal</td>
<td>-1.7</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Inferotemporal</td>
<td>-1.8</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Superonasal</td>
<td>-1.7</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Inferonasal</td>
<td>-1.3</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

Discussion

In the present study, EDI of WF SS-OCT enabled the generation of posterior pole choroidal thickness maps for healthy eyes and facilitated quantitative evaluation of the choroidal thickness. The posterior pole choroidal thickness was significantly lesser at the periphery than in the central area, in the inferior area than in the superior area, and in the nasal area than in the temporal area. Moreover, the choroidal thicknesses in all subfields were negatively associated with advanced age, whereas those in the central and inferonasal subfields were negatively associated with AL.

Recent studies described the morphological features of the choroid of eyes with pathologies using SS-OCT with or without EDI [15, 17, 18]. The macular choroid has been shown to be thicker in eyes with AMD [6] and CSC [7] and thinner in eyes with high myopia [9]. Mori et al. recently examined the choroidal thickness in healthy eyes using macular cross-scanning OCT with a length of 6 mm or 9 mm and showed the associations with age, sex, AL, and the spherical equivalent [12]. Funatsu et al. most recently examined the choroidal structure in healthy eyes using 12 long radial scans and reported the WF choroidal thickness features [19]. Their results were fairly consistent with the main results of the present study. However, with the imaging protocol used to acquire the radial scans, it might be difficult to capture fine changes in the choroidal thickness, particularly at the periphery, because the scanned area is sparser than the more central area (Supplementary Fig. S1 online). In contrast, WF choroidal thickness map
analysis performed using the same protocol showed choroidal thickening along the dilated vortex veins in eyes with CSC, which was suggestive of the pathogenesis [15].

In this study, the choroidal thickness was greater in the macular area than at the periphery; the course of the short posterior ciliary arteries (SPCAs) may have played a role in this. The SPCAs enter the sclera a short distance away from the optic nerve and run radially toward the equator [20]. The temporal distal SPCAs pierce the sclera to enter the eyeball in the macula and diverge toward the distal portion [20, 21]. The choroidal thicknesses in the inferior subfields were lesser than those in the superior subfields. A previous study showed that the peripapillary choroidal thickness in the inferior area was significantly lesser than that in the superior area [22–24], similar to the results of the present study. The choroid was the thinnest in the inferonasal area in the present study; this may be associated with the development of the eye. The optic fissure is located at the inferior aspect of the optic cup and is the last point at which the globe closes [25].

In addition to the SPCAs, the course of the choroidal veins may affect the choroidal thickness. In healthy eyes, the vortex veins extend along the uveal tracts, and the vertical watershed between the temporal and nasal vortex veins passes just temporal to the optic disc. In contrast, the horizontal watershed between the superior and inferior vortex veins passes between the optic disc and macula [26, 27]. The location of the vertical watershed may affect the horizontal choroidal thickness. In the superior area above the horizontal watershed, blood in the superior vortex veins flows against gravity; in contrast, in the inferior area below the horizontal watershed, the blood in the inferior vortex veins flows in the direction of gravity. Thus, the superior vortex veins might be more congested, and the superior choroid might be thicker than the inferior choroid.

In the present study, the choroidal thicknesses in all subfields were negatively associated with advanced age. This finding was similar to the results of previous studies using OCT B-scans [11, 12, 19, 22, 23]. Ocular blood flow decreases with advanced age [28], probably because of age-related increases in systemic vascular resistance. These changes in the ocular and systemic blood flow may affect the age-related decrease in the WF choroidal thickness. In the present study, the choroidal thicknesses in the central and inferonasal subfields were negatively associated with AL. This finding was also consistent with previous findings obtained by OCT B-scans [11, 12]. However, in the previous reports, morphological changes in the choroid were examined only in the macular area, and the present study may provide additional information on the choroidal thickness outside the macular area. The significant association between increased AL and decreased choroidal thickness may be attributed to the location of the optic fissure.

Of late, the role of the choroid in ocular growth regulation has received increasing attention [1, 29]. Nickla et al. studied the choroidal histology in animal eyes and suggested the ability of the choroid to substantially change the blood flow [1]. In another animal study using guinea pigs, reduced choroidal blood flow caused a hypoxic environment that could lead to various changes in the sclera and retina, contributing to the onset and progression of myopia [29]. The association between the choroidal blood
flow and the choroidal thickness is undetermined, although related evidence is accumulating [30, 32]. The choroidal thickness may be an indicator of the choroidal blood flow. Previous studies showed that the choroidal thickness decreased the myopic shift in children and suggested that choroidal thinning may be associated with eye lengthening [32, 33]. In the present study, the inferonasal choroid was thin, and it became thinner with an increase in AL. The preferential location of an inferior posterior staphyloma [34] may be associated with the two-dimensional features of the choroidal thickness observed in the present study.

This study had several limitations. First, the number of participants was smaller than that in other studies using a normal database. Second, the choroidal thickness was measured using a viewing angle of 20 (vertical) × 23 (horizontal) mm, which was wider than the viewing angle used in previous studies. However, the areas outside this viewing angle were not evaluated. Third, we did not perform real-shape correction of the measurement error in the choroidal thickness. Real-shape correction may be useful for thickness maps generated from dense radial scans. Instead, we corrected the AL-related magnification using the modified Littmann formula (Bennett procedure) while developing the evaluation grid.

Despite these limitations, we could examine the two-dimensional features of the WF choroidal thickness in healthy eyes using thickness map analysis and determine negative associations with advanced age and increased AL. Replication of the current findings is expected in larger cohorts, such as epidemiologic consortiums.

**Methods**

**Participants**

This observational study was approved by the Institutional Review Board of Kyoto University Graduate School of Medicine (Kyoto, Japan) and adhered to the tenets of the Declaration of Helsinki. Written informed consent was obtained from each participant during the first visit before the start of the study.

We included healthy participants without any ocular diseases other than cataract who were examined at Kyoto University Hospital between October 2021 and September 2022. One eye from each participant was examined for analysis. The exclusion criteria were as follows: history of chorioretinal disease, macular neovascularization, uveitis, scleritis, or corticosteroid use; pregnancy; ocular hypertension (> 21 mmHg) or hypotension (< 5 mmHg); keratoconus; high myopia with a spherical equivalent of < − 6 diopters; hyperopia > + 4 diopters; astigmatism > ± 3 diopters; and poor-quality OCT images (signal strength index, < 5) due to eye movements or media opacities. Eventually, a total of 127 eyes of 127 participants met the inclusion criteria.

**Choroidal Thickness Evaluations Using Edi Of Wf Ss-oct**
We examined the choroidal structure using SS-OCT (Xephilio OCT-S1, Canon Medical Systems, Japan) with a near-infrared illumination of 1010–1110 nm (scanning laser ophthalmoscope, 780 nm) and a scanning speed of 100,000 A-scans per second. We set the focus spot at 30 mm to ensure that the device scanned a large area. No additional lenses or device modifications were required during image acquisition.

To capture WF choroidal thickness features, we acquired three-dimensional volume data using EDI of SS-OCT with the following parameters: 20 mm (vertical, 128 B-scans) × 23 mm (horizontal, 1024 pixels) with a 5.3-mm scan depth (1396 pixels). For segmentation of the choroid, we set the choroidal thickness as the vertical distance from Bruch's membrane to the choriocapillary interface. Segmentation was automatically performed using built-in software supported by artificial intelligence. Because the eyes were free of any pathologies, automatic segmentations of the inner and outer borders of the choroid were correctly performed.

We analyzed choroidal thickness maps based on our recently reported method [15], which is briefly described below. A grid comprising three circles with diameters of 3, 9, and 18 mm, respectively, was used; the grid center was always set at the center of the fovea (foveal bulge) without any rotation (Fig. 4). The inner and outer rings were defined as the fields enclosed between the 3- and 9-mm circles and the 9- and 18-mm circles, respectively. Each ring was divided into superotemporal, inferotemporal, superonasal, and inferonasal quadrants, and measurements were performed for a total of nine subfields including the central 3-mm ring (Fig. 4).

For choroidal thickness measurements, we unified the measurement range for all participants by correcting the AL-related magnification using the modified Littmann formula (Bennett procedure) [35, 36].

**Statistical Analysis**

All statistical analyses were performed using JMP pro version 16.2 (SAS Institute Inc., Cary, NC, USA). Values are presented as mean ± standard deviation. Comparisons between the outer and inner, inferior and superior, and nasal and temporal subfields were performed using the Wilcoxon signed-rank test. To evaluate the association of age and AL with the choroidal thickness, we performed multiple linear regression analysis to adjust for each factor. A P-value of < 0.05 was considered statistically significant.

**Declarations**

**ACKNOWLEDGEMENTS:**

This work was supported in part by a grant-in-aid for scientific research (no. 20K09771) from the Japan Society for the Promotion of Science (Tokyo, Japan) and Canon Inc. (Tokyo, Japan). These organizations had no role in the design or conduct of this research. The funders had no role in the study design, data collection and analysis, decision to publish, or preparation of the manuscript.
AUTHOR CONTRIBUTION:

Conception and design of the study, MHi, YM, TK; data analysis and interpretation, MHi, YM, TK, MI, NN; writing of the article, MHi, YM, TK; critical revision of the article, NUA, MMiyata, MHa, ATa, MMiyake, and ATs; All authors have approved the final version of the manuscript.

DATA AVAILABILITY

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests


References


Figures
Figure 1

Choroidal thickness map analysis using enhanced-depth imaging of widefield swept-source optical coherence tomography

A. Mean choroidal thickness in each subfield

B. Comparisons of widefield (WF) choroidal thicknesses between corresponding quadrants in the inner and outer rings

Choroidal thicknesses in the outer ring are significantly lesser than those in the corresponding quadrants in the inner ring ($p < 0.001$ for all).

C. Comparisons of WF choroidal thicknesses between corresponding superior and inferior subfields

The choroidal thicknesses in the inferior subfields are significantly lesser than those in the corresponding superior subfields ($p < 0.001$ for all).

D. Comparisons of WF choroidal thicknesses between corresponding temporal and nasal subfields
The choroidal thicknesses in the nasal subfields are significantly lesser than those in the corresponding temporal subfields ($p < 0.001$ for all).

Figure 2

Differences in choroidal thickness with age

A, B. A widefield (WF) choroidal thickness map for a 38-year-old man. The axial length (AL) of the eye is 24.78 mm.

C, D. A WF choroidal thickness map of a 64-year-old man. The AL of the eye is 24.64 mm.

These findings suggest that the choroid in all subfields is thinner in elderly individuals than in young individuals.
**Figure 3**

**Differences in choroidal thickness according to the axial length**

**A, B.** A Widefield (WF) choroidal thickness map of a 70-year-old woman. The axial length (AL) of the eye is 22.98mm.

**C, D.** A WF choroidal thickness map of a 68-year-old man. The AL of the eye is 25.61 mm.

The findings suggest that the choroid in all subfields is significantly thinner in eyes with a greater AL (C, D) than in eyes with a smaller AL (A, B).
Figure 4

Thickness map analysis of the healthy choroid using enhanced-depth imaging of widefield swept-source optical coherence tomography

A. A grid has been developed for measuring changes in the widefield choroidal thickness. It comprises nine subfields divided by three circles with diameters of 3, 9, and 18 mm, respectively, and four lines. Circumferential and zonal areas enclosed by these circles are divided into superotemporal, inferotemporal, superonasal, and inferonasal subfields, with consideration of the arrangement of the vortex veins.

B. Infrared scanning laser ophthalmoscopy images with the measurement grids overlaid.

C. A choroidal thickness map

D. Choroidal thickness values measured using the grid

The value for each subfield depicts the mean choroidal thickness (μm) in that subfield.
Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- FigureS1.tif
- FigureS2.tif
- SupplementaryFigurelegend.docx