Purpose: To determine the difference in macular choroidal thickness (CT) profile between eyes in healthy individuals using swept-source optical coherence tomography.

Design: Cross-sectional noninterventional study.

Participants: One hundred and forty eyes from 70 healthy patients with spherical equivalent between ±3 D and with difference ≤0.25 D between eyes were scanned using a swept-source optical coherence tomography (Topcon Corporation).

Methods: Cross-sectional noninterventional study. One hundred and forty eyes from 70 healthy patients with spherical equivalent between ±3 D and with difference ≤0.25 D between eyes were scanned using a swept-source optical coherence tomography (Topcon Corporation). A horizontal CT profile of the macula was created in both eyes by manually measuring the subfoveal CT from the posterior edge of retinal pigment epithelium (RPE) to the choroid/sclera junction. Three determinations were performed at successive points 1,000 mm nasal to the fovea and 5 more temporal to the fovea. The differences in CT between both eyes were analyzed.

Results: Mean age was 25.4 ± 19.9 years (from 4 to 75). The mean spherical equivalent was 0.18 ± 1.37 D (from −3 to +3). Mean macular nasal CT was thicker in the right eye (RE) than in the left eye (LE) (228.11 ± 69.23 µm vs. 212.27 ± 62.71 µm; P = 0.0002; Student’s t-test paired data). Mean subfoveal CT and mean temporal CT was not statistically significantly different between the eyes. No statistically significant differences were observed comparing spherical equivalent in the RE compared with the LE. Both men and women showed a thicker mean nasal choroid in the RE versus the left (men, 226.97 ± 61.56 µm vs. 209.87 ± 60.31 µm; women, 229.63 ± 79.39 µm vs. 211.33 ± 66.92 µm; P = 0.003 and P = 0.03, respectively; Student’s t-test paired data). At each nasal determination, CT in the RE was statistically significantly thicker than the LE (N1: 283.72 ± 81.10 µm vs. 269.76 ± 75.81 µm [P = 0.001]; in N2: 230.45 ± 73.47 µm vs. 211.33 ± 66.92 µm [P = 0.0002]; and in N3: 170.16 ± 61.00 µm vs. 155.72 ± 53.87 µm [P = 0.008], respectively).

Conclusion: To the best of our knowledge, this is the first report suggesting thicker macular nasal choroid in the RE compared with the LE. In contrast, subfoveal CT and temporal CT were not found to be different between eyes.

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The choroid and its involvement in a variety of ocular pathologies has been the subject of intensive study during the past few years. The choroid plays a role in or is affected by pathologies, such as central serous chorior- retinopathy,1–4 age-related macular degeneration,1,5–10 posterior segment tumors,1,11–13 myopic maculopathy,14–17 posterior uveitis,1,6,18–22 and polypoidal choroidal vasculopathy.1,7,8 It may also have influence in glaucoma,23–26 and even in neurologic pathologies, such as migraine27 and Alzheimer disease.28 Advances in optical coherence tomography (OCT) in recent years allows deep high-resolution imaging of the posterior eye layers “in vivo.”4 Optical coherence tomography’s brief acquisition time makes the examination easier for patients who are less cooperative, such as children, the elderly, and those with poor vision.17,31
Recently, with the improvements in spectral domain optical coherence tomography provided by enhanced-depth imaging32 and swept-source optical coherence tomography (SS-OCT) technology,33–36 which is able to image deeper into the choroid, the choroidal thickness (CT) profiles of healthy populations have been studied.31,37–39

The aim of this study is to determine whether there are differences in horizontal macular CT profile between the two eyes in a large population of healthy individuals using SS-OCT.

Patients and Methods

This is a cross-sectional noninterventional study, performed at Castilla La Mancha University Spain. This study followed the tenets of the Declaration of Helsinki. The institutional review board approved this study. All examinations were obtained in the afternoon to avoid diurnal variations.40–42

Choroidal thickness was manually measured in 140 eyes from 70 patients with no known ocular or systemic disease. Their macular area was studied with an SS-OCT system (Topcon Corporation, Tokyo, Japan), after they provided informed consent. Inclusion criteria were best-corrected visual acuity of 20/20, spherical equivalent (SE) between ±3 diopters (D), with difference ≤0.25 D between eyes and no systemic diseases. Eyes with any history of mild retinal diseases were not included.

The SS-OCT device used to image the full-thickness choroid and sclera43 uses a tunable laser as a light source operated at 100,000 Hz, A-scan repetition rate in the 1-μm wavelength region. The device can perform image averaging of up to 96 B-scans at each location. For the macular imaging performed in this study, the reference mirror was placed at the deeper position of the retina so that the sensitivity was higher in the choroid. A one-line scanning mode, which produces an OCT image containing 1,024 axial scans with a scan length of 12 mm was used. This sampling space in object space corresponds to 11.7 μm/pixel. Lateral resolution was set to be 20 μm with 24-mm axial eye length, whereas axial resolution was 8 μm in retina.44 Lateral and axial resolution were independent.

Acquisition time for the scan protocol was 1 second. Both eyes were scanned consecutively. A horizontal CT profile of the macula was manually created measuring CT from the posterior edge of RPE to the choroid/sclera junction under the fovea, in a line perpendicular to the retinal surface. The outer aspect of the lamina fusca/inner border of the sclera rather than the outer limit of the choroidal vessels was determined as the outer limit of the choroid.38,45

Five determinations were performed every 1,000 μm temporal (T1, T2, T3, T4 and T5) and 3 more nasal (N1, N2 and N3) to the fovea (Figure 1).

Fig. 1. Example of choroidal thickness measures at SFCT and N3, N2, and N1 in two eyes of one patient (top RE and bottom LE), from the posterior edge of RPE to the choroid/sclera junction.

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Eyes with SE beyond $\pm 3$ D and with difference $>0.25$ D between eyes were excluded. An experienced technician determined refractive errors and best-corrected visual acuity using an autorefractometer (Nidek, Gamagohri, Japan) that was later checked by a certified optometrist.

The differences in mean CT and CT at each independent location between both eyes were analyzed. Two observers determined CT independently and in a masked fashion.

**Statistical Analysis**

For the statistical treatment of the data, the program used was version 17.0 of SPSS for Windows (SPSS, Chicago, IL). The interobserver reproducibility was evaluated using intraclass correlation coefficient for each variable measured (mean and 95% confidence interval [CI]), coefficient of variation between graders and Bland–Altman plots. The mean of the measures obtained by the two observers was the data used for the rest of calculations. Kolmogorov–Smirnov test was applied for all data samples to check normality. Comparision between groups was performed using the Student’s $t$-test when samples were normally distributed or Mann–Whitney test when parametric statistics were not possible. The level of significance was always the same ($P < 0.05$). The homogeneity of variances was checked using the Levene’s test. Bivariate correlations were evaluated using Spearman correlation coefficients. For the development of predictive models, linear regression was used. Mean macular nasal CT was determined by the arithmetic mean of the values obtained at N3, N2, and N1, whereas the mean macular temporal CT was calculated by the mean of T1, T2, T3, T4, and T5.

**Results**

Forty patients (57.1%) were male (80 eyes) and 30 patients (42.9%) were female (60 eyes). Mean age was 25.4 ± 19.9 years (from 4 to 75). Mean SE was 0.18 ± 1.37 D (from −3 to +3). Mean macular horizontal nasal CT was statistically thicker in the right eye (RE) 228.11 ± 69.23 μm, range 105.33 to 391.33 μm (95% CI: 211.61–244.62) on average, than in the left eye (LE) 212.27 ± 62.71 μm, range 84.17 to 356.83 μm (95% CI: 197.32–229.22) ($P = 0.0002$; Student’s $t$-test paired data; Figure 2). Mean subfoveal CT (SFCT) was 315.86 ± 76.78 μm (95% CI: 297.42–334.41) in the RE versus 308.41 ± 75.51 μm (95% CI: 290.99–325.83) in the LE ($P = 0.138$, Student’s $t$-test paired data) and mean macular temporal CT was 292.02 ± 63.68 μm (95% CI: 276.62–307.31) in the RE versus 294.15 ± 54.69 μm (95% CI: 280.58–307.72) in the LE ($P = 0.602$; Student’s $t$-test paired data). No statistically significant differences were observed comparing SE between the REs (0.18 ± 1.33 D; 95% CI: −0.14 to 0.50) versus the LEs (0.19 ± 1.37 D; 95% CI: −0.13 to 0.51) ($P = 0.517$; Wilcoxon’s test). With respect to sex, there were no statistically significant differences between eyes for SFCT or mean temporal CT (Table 1).

The cohort of males in this population studied had a mean age of 19 years (range, 4 to 74 years). When analyzing mean nasal CT by sex, men manifested a nasal choroid thicker in the RE, 226.97 ± 61.56 μm (95% CI: 207.29–246.66) versus 209.87 ± 60.31 μm in the LE (95% CI: 190.58–229.16) ($P = 0.003$, Student’s $t$-test paired data). In the female cohort group, the mean age was 32.8 ± 18.3 years (from 8 to 75) statistically significantly older than men ($P < 0.05$). The mean nasal CT of 229.63 ± 79.39 μm in the RE (95% CI: 199.99–259.28) versus 215.47 ± 66.68 μm in the LE (95% CI: 190.57–240.368) ($P = 0.03$; Student’s $t$-test paired data).

Studying the CT at each individual location in the nasal sector, CT in the RE at N1 was 283.72 ± 81.10 μm (95% CI: 264.39–303.069) versus 269.76 ± 75.81 μm in the LE (95% CI: 251.68–287.83) ($P = 0.001$, Student’s $t$-test paired data); at N2, RE CT was 230.45 ± 73.47 μm (95% CI: 212.93–247.97) versus 211.33 ± 66.92 μm in the LE (95% CI: 195.37–227.29) ($P = 0.0002$, Student’s $t$-test paired data); at N3, RE CT was 170.16 ± 61.00 μm (95% CI: 155.62–184.71) versus 155.72 ± 53.87 μm in the LE (95% CI: 142.88–168.57) ($P = 0.008$, Student’s $t$-test paired data).

The choroid was thicker in the RE at every nasal location for both sexes except for women at N1, where differences were not statistically significant ($P = 0.259$; Table 2). The correlation of nasal CT between RE and LE at each location (N3, N2, and N1) was $r = 0.853$, 0.842 and 0.822, respectively ($P < 0.001$; Spearman...
A high agreement in the measures taken by the 2 observers was found as can be seen in Table 3. The intraclass correlation coefficient values obtained for the variables evaluated were within the range 0.976 to 0.988. The Bland–Altman plots (Figure 3) also confirmed high agreement between measures.

**Discussion**

Several studies have been published about CT in healthy populations. Ding et al16 analyze the CT in 210 healthy volunteers (420 eyes) with no ophthalmic disease history using enhanced-depth imaging spectral domain optical coherence tomography at multiple locations: SFCT and 1 mm and 3 mm temporal, nasal, superior, and inferior to the fovea. However, the authors did not analyze any differences between the eyes.46

Ikuno et al17 studied CT and its profile with an SS-OCT device in 86 eyes of 43 healthy Japanese subjects as well as the correlation with axial length, refractive error and age, but they also published no data concerning any differences between right and LEs.

In contrast, Chen et al18 reported the factors influencing topographical and interocular variations in CT in a 50 healthy adult population using enhanced-depth imaging spectral domain optical coherence tomography. They measured SFCT and also performed CT measurements at 4 paramacular loci (3 mm superior, inferior, temporal, and nasal to the foveal center). They analyzed the relationship between interocular differences in CT. The differences in CT between RE and LE were 1.0 μm at SFCT, 13.6 μm at nasal and −2.9 μm at temporal location, which was not statistically significant different. Of note, there was a trend toward a thicker nasal CT (14 μm) in REs.

When comparing these data with the series reported in this article, at the same locations (SCFT, N3 CT and T3 CT), we observed that the difference comparing RE and LE was 7.45 μm in mean SFCT, 1.43 μm at T3, and 1.44 μm at N3. The differences between mean nasal CT (P = 0.0002), mean nasal CT in men (P = 0.003) and in women (P = 0.03), and mean CT at each nasal location (P = 0.001, 0.002 and 0.08, the authors did not analyze any differences between the eyes.46

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**Table 1. Choroidal Thickness (μm) at SF, Mean Temporal, T1, T2, T3, T4, and T5 by Eye**

<table>
<thead>
<tr>
<th></th>
<th>RE</th>
<th>LE</th>
<th>P*</th>
</tr>
</thead>
<tbody>
<tr>
<td>SFCT</td>
<td>315.86 ± 76.49 (297.42–334.41)</td>
<td>308.41 ± 75.51 (290.99–325.83)</td>
<td>0.138</td>
</tr>
<tr>
<td>Mean TCT</td>
<td>292.02 ± 63.68 (276.62–307.31)</td>
<td>294.15 ± 54.69 (280.58–307.72)</td>
<td>0.602</td>
</tr>
<tr>
<td>T1 (95% CI)</td>
<td>311.75 ± 78.14 (292.96–330.51)</td>
<td>312.12 ± 68.42 (295.68–328.55)</td>
<td>0.883</td>
</tr>
<tr>
<td>T2 (95% CI)</td>
<td>306.57 ± 73.05 (286.02–321.12)</td>
<td>311.46 ± 63.42 (296.23–312.39)</td>
<td>0.188</td>
</tr>
<tr>
<td>T3 (95% CI)</td>
<td>293.42 ± 71.96 (276.14–310.71)</td>
<td>291.99 ± 61.01 (277.34–306.65)</td>
<td>0.961</td>
</tr>
<tr>
<td>T4 (95% CI)</td>
<td>282.46 ± 68.21 (266.08–298.85)</td>
<td>284.04 ± 67.24 (267.89–300.20)</td>
<td>0.626</td>
</tr>
<tr>
<td>T5 (95% CI)</td>
<td>269.71 ± 72.66 (251.39–287.04)</td>
<td>272.20 ± 75.76 (255.68–291.81)</td>
<td>0.585</td>
</tr>
</tbody>
</table>

*Student’s t-test paired data.

**Table 2. Choroidal Thickness (μm) at N1, N2, and N3 by Eye and Sex**

<table>
<thead>
<tr>
<th></th>
<th>RE</th>
<th>LE</th>
<th>P*</th>
</tr>
</thead>
<tbody>
<tr>
<td>N1</td>
<td>284.08 ± 68.49 (262.17–305.98)</td>
<td>265.51 ± 68.89 (243.48–287.54)</td>
<td>0.006</td>
</tr>
<tr>
<td>Men</td>
<td>283.25 ± 96.63 (247.17–319.33)</td>
<td>275.42 ± 85.06 (243.65–307.18)</td>
<td>0.259</td>
</tr>
<tr>
<td>Total group (95% CI)</td>
<td>283.72 ± 81.09 (111.00–475.00)</td>
<td>269.76 ± 75.81 (251.68–287.83)</td>
<td>0.008</td>
</tr>
<tr>
<td>N2</td>
<td>228.98 ± 64.97 (208.19–249.75)</td>
<td>208.73 ± 65.64 (187.73–229.72)</td>
<td>0.001</td>
</tr>
<tr>
<td>Men</td>
<td>232.42 ± 84.62 (200.82–264.02)</td>
<td>214.80 ± 69.58 (188.82–240.78)</td>
<td>0.026</td>
</tr>
<tr>
<td>Total group (95% CI)</td>
<td>230.45 ± 73.46 (212.93–247.97)</td>
<td>211.33 ± 66.93 (195.37–227.29)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>N3</td>
<td>167.86 ± 58.71 (149.09–186.64)</td>
<td>155.38 ± 53.62 (138.23–172.52)</td>
<td>0.007</td>
</tr>
<tr>
<td>Men</td>
<td>173.23 ± 64.81 (149.03–197.44)</td>
<td>156.18 ± 55.12 (135.60–176.77)</td>
<td>0.016</td>
</tr>
<tr>
<td>Total group (95% CI)</td>
<td>170.16 ± 61.00 (155.62–184.71)</td>
<td>155.72 ± 53.87 (142.88–168.57)</td>
<td>0.001</td>
</tr>
</tbody>
</table>

*Student’s t-test paired data.

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respectively) were statistically significant. The choroid was thicker in the RE at every nasal location for both sexes except for women at N1 ($P = 0.259$; Table 2).

The correlation of the CT obtained by Chen et al between eyes was strongest for SFCT ($r = 0.90$; $P < 0.001$, Spearman correlation test), for nasal locations was $r = 0.83$ ($P < 0.001$, Spearman correlation test), and weakest for temporal locations ($r = 0.49$; $P < 0.001$, Spearman correlation test).

In our patients, the study of correlation for mean CT at SF, N3, and T3 was similar ($r = 0.860, 0.853$ and $0.754$, respectively, $P < 0.001$; Spearman correlation test).

The CT profile described in their article is very similar to the CT profile obtained in our work comparing REs to LEs (Figure 2).

It is difficult to explain the strong and consistent evidence that REs have a thicker nasal choroid than LEs in a healthy young population. One possibility is a differential in blood flow between the two eyes due to lack of anatomic symmetry at the aortic arch. Such asymmetry has been suggested to explain the differences in incidence/prevalence of vascular pathologies between REs and left eyes with respect to metastatic bacterial endophthalmitis and retinal artery occlusion.

Choroidal circulation is generated from short posterior ciliary arteries that penetrate through the sclera around of optical nerve in a variable number between 10 and 20; so the nasal choroid studied in our cases (choroid between fovea and optical nerve) is directly supplied from these short posterior ciliary arteries. Furthermore, short posterior ciliary arteries are branches of the ophthalmic artery, which is a branch of the common carotid artery.

Table 3. Intraclass Coefficient and Coefficients of Variation of Each Observer at Each Measurement Point

<table>
<thead>
<tr>
<th>ICC</th>
<th>95% CI</th>
<th>CV Observer 1</th>
<th>CV Observer 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>N3</td>
<td>0.976</td>
<td>0.962–0.985</td>
<td>0.349</td>
</tr>
<tr>
<td>N2</td>
<td>0.979</td>
<td>0.967–0.987</td>
<td>0.316</td>
</tr>
<tr>
<td>N1</td>
<td>0.988</td>
<td>0.982–0.993</td>
<td>0.282</td>
</tr>
<tr>
<td>SF</td>
<td>0.985</td>
<td>0.975–0.990</td>
<td>0.251</td>
</tr>
<tr>
<td>T1</td>
<td>0.982</td>
<td>0.972–0.989</td>
<td>0.236</td>
</tr>
<tr>
<td>T2</td>
<td>0.976</td>
<td>0.962–0.985</td>
<td>0.213</td>
</tr>
<tr>
<td>T3</td>
<td>0.977</td>
<td>0.964–0.986</td>
<td>0.226</td>
</tr>
<tr>
<td>T4</td>
<td>0.979</td>
<td>0.967–0.987</td>
<td>0.254</td>
</tr>
<tr>
<td>T5</td>
<td>0.976</td>
<td>0.962–0.985</td>
<td>0.284</td>
</tr>
</tbody>
</table>

CV, coefficient of variation; ICC, intraclass correlation coefficient.

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Fig. 3. Bland–Altman plots for interobserver correlation in measurement location from N3 to SFCT. N1 (top left), N2 (top right), N3 (bottom left), and SF (bottom right).
presumably responsible of a more proximal and direct blood flow to the right carotid.49

Given that most of the choroidal structure is vascular tissue (the mean vessel density in outer choroid is 87%54), a supposed higher blood flow in the right versus left short posterior ciliary arteries may explain why the nasal choroid is thicker in RE, as stated in our study, and as described previously by Chen et al.48

In this study, as in previous articles,31 we used SE instead of axial length determinations since the procedure is less invasive and previous indications from the literature show that refraction, which is more convenient to obtain, provides equivalent modeling capability as axial length.55

The limitations of this article are the relatively small number of eyes (140, 70 per group), study of the thickness limited to a line beneath the fovea, the use of SE instead of axial length, the fact that no correction was made for other variables, such as central corneal thickness, intraocular pressure, systemic medication, and blood pressure, and the impossibility to determine whether the vessels of the nasal choroid are wider in the RE than in the left. This is due to the fact the resolution provided by the current technology does not allow a proper and accurate analysis of choroidal vessel thickness, and there is no way to make sure you are analyzing the largest diameter of a vessel because of the irregularity of choroidal vascularization. However, selecting patients with similar SE between eyes, the wide span of ages (from 4 to 75 years) and the high level of statistical significance would support the findings of a thicker choroid nasal to the fovea in the RE versus LE. New studies with larger number of patients and with methods to measure choroidal blood flow (directly or indirectly) will be necessary to verify our results.

Key words: choroidal thickness, choroidal thickness asymmetry, nasal choroidal thickness, healthy population, SS-OCT.

References