




Article

# Retinal and Choroidal Thickness in Myopic Young Adults

Enrique J. Fernández <sup>1,\*</sup> , José A. Villa-Carpes <sup>1,2</sup>, Rosa M. Martínez-Ojeda <sup>1</sup>, Francisco J. Ávila <sup>3</sup>   
and Juan M. Bueno <sup>1</sup> 

- <sup>1</sup> Laboratorio de Óptica, Instituto Universitario de Investigación en Óptica y Nanofísica, Campus de Espinardo (Ed. 34), Universidad de Murcia, 30100 Murcia, Spain; joseantonio.villa1@um.es (J.A.V.-C.); rosamaria.martinez9@um.es (R.M.M.-O.); bueno@um.es (J.M.B.)  
<sup>2</sup> Servicio de Oftalmología, Hospital Virgen de la Arrixaca, 30120 Murcia, Spain  
<sup>3</sup> Departamento de Física Aplicada, Universidad de Zaragoza, 50009 Zaragoza, Spain; avila@unizar.es  
\* Correspondence: enriquej@um.es

**Abstract:** The retinal and the choroidal thickness were measured at four locations along the horizontal direction (foveola, one nasal to the fovea and two temporal) in a group of 43 young adults (mean age:  $27.1 \pm 3.9$  years), with ocular refraction ranging from emmetropia to high myopia (0 to  $-10$ D). Thickness values were obtained from OCT images centered at the foveal depression. The retinal thickness exhibited a correlation with refraction at all eccentricities but not at the fovea. When different subgroups of refraction were considered, the analysis of such correlations indicated that only the retinal thickness in the group of high myopia (refraction  $\leq -6$ D) was statistically different from the other two groups (emmetropes:  $[-0.5, 0]$  D, and myopes:  $(-6, -0.5)$  D). No significant differences were found between emmetropic and myopic groups. In contrast to the retina, the choroidal thickness exhibited a significant correlation with refraction at the fovea, although such dependency only stood for high myopes (the choroid of myopes and emmetropes exhibited similar thickness). Correlation with refraction was also found at the nasal location, arising between emmetropic and high myopia groups. Other choroidal locations among groups did not exhibit relationship with the refraction. It is concluded that the differences in the choroid and retina thickness along the horizontal meridian as a function of refraction do not characterize the onset and progression of myopia at early stages, since they only manifest in the group of high myopia.

**Keywords:** retina; choroid; myopia; adult eye



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## 1. Introduction

Myopia raises a significant health problem worldwide. Its prevalence is expected to further augment in the next decades, with projections indicating that practically a half of the World population will suffer from any degree of myopia in 2050 [1,2]. This enormous prevalence makes economic and social impacts of myopia a major challenge [3,4]. Beyond the mere refractive effect of myopia, its associated complications, including the developing of pathological myopia, may cause permanent blindness or severe vision impairment through its concomitant retinal disorders [5]. Consequently, there is a significant interest in characterizing and understanding the myopic eye, with the prospect of finding an efficient intervention to halt the myopia progression once expressed, or even preventing its onset when possible.

In this direction, the anatomical changes of the eye associated to myopia have been intensively investigated in recent years. The monotonic axial length increase with refraction is the first key feature in the myopic ocular globe [6]. Nevertheless, other subtle changes occur at the back of the posterior eye, in particular at the retina. The advent of ophthalmic optical coherent tomography (OCT) techniques provided a significant burst into the characterization of the myopic retina [7]. OCT boosted the study of the retinal morphology, allowing establishing correlations between thickness and other factors, such

as ocular refraction and axial length. In this context, the possible association between retinal thickness in the macular area and myopia in adults was early investigated [8,9], resulting in weak or no dependency. Later, other studies targeted possible early signs of myopia, or indicators of progression in children, finding some degree of correlation between the retinal thickness and myopia [10]. Soon after the characterization of the foveal region, the retinal thickness was measured at other eccentricities to determine any possible relationship with the myopia level at different retinal locations [11,12]. The advances in OCT ophthalmic devices, with the incorporation of the swept-source modality and near infrared illumination in the range of 1000 nm, provided enhanced capabilities for the visualization of deeper layers at the posterior part of the eye, allowing resolving the choroid [13,14].

The study of both the structure and thickness of the choroid was then incorporated into the quest of characterizing the morphology of the myopic eye [15,16]. Some studies attempted to find changes in retinal and choroidal thickness at different regions as a function of myopia. The results in the literature are not conclusive. In some cases, comparisons were performed only between high myopes and emmetropes [17,18], while in other studies children were targeted [19,20]. Despite the number of works published in the last years, the questions of whether and to what extent the thickness of the retina and the choroid are related, and their correlation with myopia at distinct eccentricities, remain open. These questions are particularly important in normal values of myopia, and how it compares to emmetropes, since this is precisely the range of interest to understand myopia onset and its progression.

In this work we tackle all these questions in a population of young adults with steady refraction, including subjects exhibiting a wide range of refraction from emmetropia to high myopia. We measured and analyzed possible changes and correlations not only between subgroups exhibiting different refraction (emmetropes, myopes, and high myopes), but also investigating the trends when all the subjects are taken without distributing them into subgroups. This approach might help to better understand the origin of some apparently contradictory results found in the literature. At the same time this might cover the existing gap between emmetropes and myopes groups in the fully developed eye of young adults, capital to understand the progression from myopia to high myopia. In addition, we propose a straightforward protocol to obtain thicknesses from OCT images that will contribute to objectively compare results across different studies in the future.

## 2. Materials and Methods

### 2.1. Subjects

A total of 43 volunteers with normal vision participated in the study. They were free from any pathology compromising vision or ocular function. The participants were recruited from the staff of a local hospital (Hospital Universitario Virgen de la Arrixaca, Murcia, Spain). All the volunteers were adults (mean age:  $27.1 \pm 3.9$  years) with steady refraction during the previous year. Ocular refractions ranged from 0 to  $-10$ D. No distinction or classification based on the subjects' genre was applied. The participants were informed of the purpose of the study, and they signed an informed consent following the regulations of the Ethical Committee of the institution, which had previously approved the study. The entire experiment followed the tenets of the Declaration of Helsinki and the European regulations in management and storage of clinical data, assuring privacy and rights of the participants in this regard.

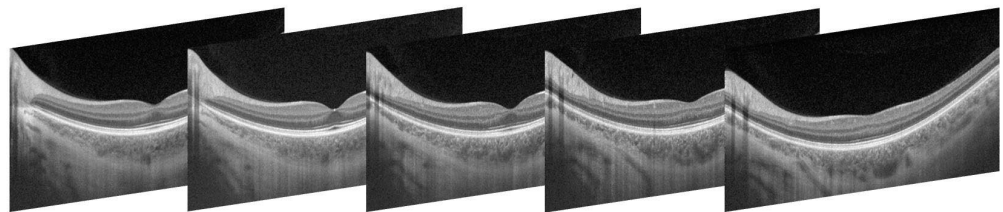
The participants were separated into 3 groups according to their spherical equivalent (SE). The first group, named as Emmetropia Group ( $SE \in [0.00, -0.50$ D]), included 10 subjects. A second group of 24 volunteers was referred to as Myopia Group ( $SE \in (-0.50, -6.00$ D)). The third one ( $N = 9$ ) corresponded to the High Myopia Group ( $SE \in [-6.00, -10.00$ D]).

### 2.2. Experimental Protocol

The experimental protocol included measurements of the refractive error, estimation of the monocular VA and OCT image acquisition in the right eye of all the participants.

For the refractive error a commercially available autorefractor (Topcon KR-8900<sup>®</sup>, Topcon Corporation, Japan) was used under normal viewing conditions. The SE was calculated as the average from 3 consecutive runs. VA was assessed by means of the free platform Freiburg Visual Acuity Test (FrACT) [21]. During VA testing, all participants wore their habitual optical corrections, either spectacles or contact lenses and the left eye was occluded. Details on the VA protocol can be found in [22]. Additional measurements of intraocular pressure (IOP) were conducted on every subject with a commercial non-contact tonometer (Topcon CT-80<sup>®</sup>, Topcon Corporation, Japan) to detect possible signs of glaucoma or other pathologies associated to high pressure. None of the subjects exhibited high IOP (>21 mm Hg). The average value of IOP for all participants was  $13.8 \pm 2.3$  mm Hg, with a range from 10 to 20 mm Hg.

A commercial swept-source OCT ophthalmoscope (ADRI OCT Triton<sup>®</sup>, Topcon Europe Medical) was employed to image the retinal structures. This instrument scans a narrow beam with central wavelength of 1050 nm onto the retina to render B and C-scan high resolution fundus images. The use of this near infrared wavelength permits a deeper penetration into the retinal tissues, even covering the choroid and part of the sclera. Five B-scans centered around the fovea were acquired on every eye. The separation across adjacent scans was 0.15 mm. The length of each B-scan image was set to 9 mm. According to the technical specifications, a pixel in the image along the horizontal (vertical) direction corresponds to  $8.79 \mu\text{m}$  ( $2.02 \mu\text{m}$ ) in distance. Figure 1 shows a representative example of a set of the B-scan images acquired in one of the subjects. The central frame containing the maximum foveal depression (i.e., the foveal pit) can be identified. This frame was selected following the protocol described below.



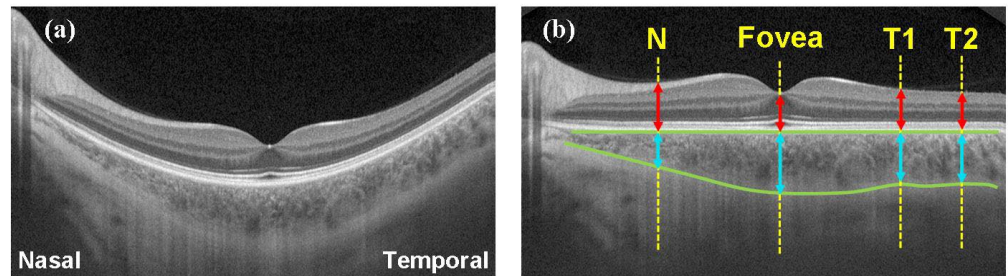
**Figure 1.** Set of raw OCT fundus images (B-scans) provided by the instrument in one of the participants. The separation among images was 0.15 mm. The left side of each panel corresponds to the nasal retinal location.

The selected OCT fundus images underwent a specific digital processing to avoid the curvature of the retinal structures. The laboratory-made software used for this was written in Matlab<sup>™</sup>. The aim was to establish an objective reference to measure distances (choroidal and retinal thickness at different eccentricities). In the present work, the retinal pigment epithelium (RPE) was chosen as the reference layer. For each B-scan the algorithm automatically identifies the RPE layer of every A-scan as the brightest signal. Once the RPE was detected for each A-scan, this was shifted in the vertical direction to match the RPE across adjacent columns in the B-scan. This approach generated a new version of the OCT fundus image where the RPE appeared as a “horizontal line”, with the rest of the morphological structures and layers maintaining their size and relative position. An example of this flattening process is displayed in Figure 2.

Four locations (i.e., retinal eccentricities) were selected to measure the thickness of the retina and the choroid (see Figure 2b): central fovea ( $0 \mu\text{m}$ ),  $2250 \mu\text{m}$  nasal to the fovea (location N),  $2250 \mu\text{m}$  (location T1) and  $3375 \mu\text{m}$  (location T2) temporal to the fovea. Choroidal thickness was measured from the RPE (outer border of the hyper-reflective line) to the inner sclera border [23]. Neural retinal thickness was defined as the distance between the inner surface of the hyper-reflective line corresponding to the internal limiting membrane and the RPE.

The distances were semi-manually obtained with the help of custom software written in the open platform ImageJ<sup>™</sup>. One of the authors (J.A.V.-C.) manually marked the outer

limit of the choroid following a random order in the selection of frames. Then, the software automatically displayed the pre-designated locations and the distances from the RPE layer. The procedure was repeated 3 times. For each location, the final thicknesses were computed as the mean values of those consecutive measurements.

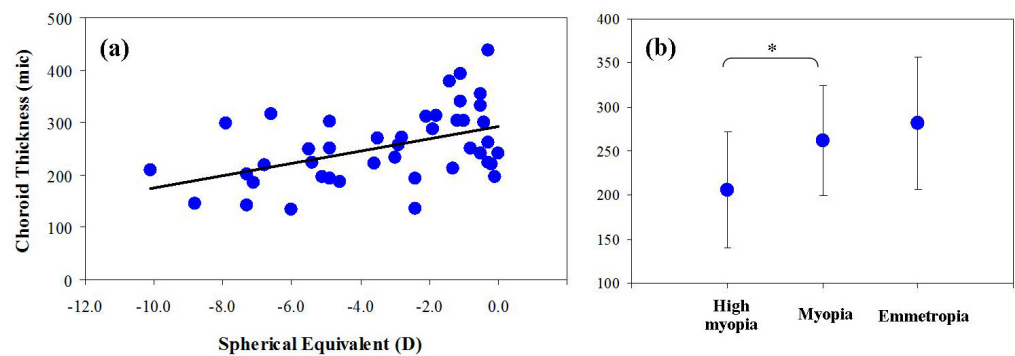


**Figure 2.** Example of OCT fundus images (B-scans) of the retina of one of the participants before (a) and after (b) the flattening operation. The horizontal distribution of the RPE is easily observed in panel (b). The four locations of interest where the neural retina (red) and choroid (blue) thickness values were: N, nasal; Fovea; T1, temporal 1; and T2, temporal 2. See text for further details.

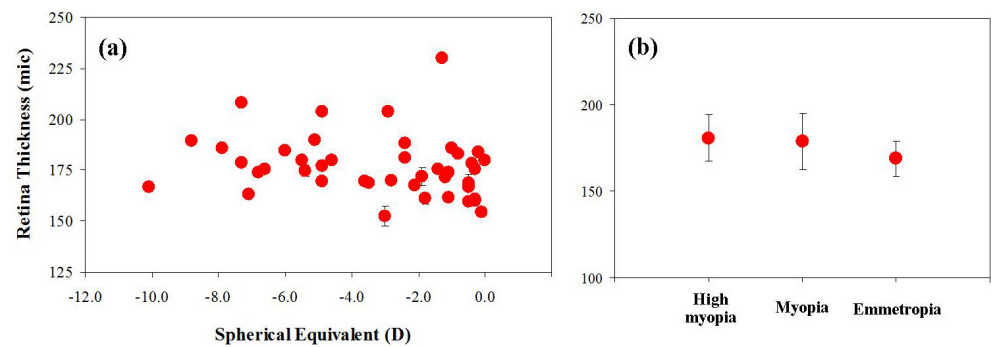
### 3. Results

The mean VA from all the subjects was  $1.22 \pm 0.41$  in decimal scale. The mean SE values for the groups of emmetropes, myopes and high myopes were  $-0.3 \pm 0.2$ ,  $-2.9 \pm 1.6$ , and  $-7.5 \pm 1.2D$ , respectively.

The relationship between the values of subfoveal choroidal thickness and the corresponding SE is shown in Figure 3a. Values were within the interval  $[134, 438] \mu\text{m}$ . A significant linear relationship was found ( $R = 0.47, p = 0.002$ ). This represents a thickness decrease of  $\sim 12 \mu\text{m}/D$ . Figure 3b depicts the averaged values for group, where the comparison high myopia and myopia groups presents statistical differences ( $t$ -test,  $p = 0.031$ ). Unlike what occurs with the choroid, the thickness of the retina at the central fovea was not correlated with the ocular refraction (Figure 4).

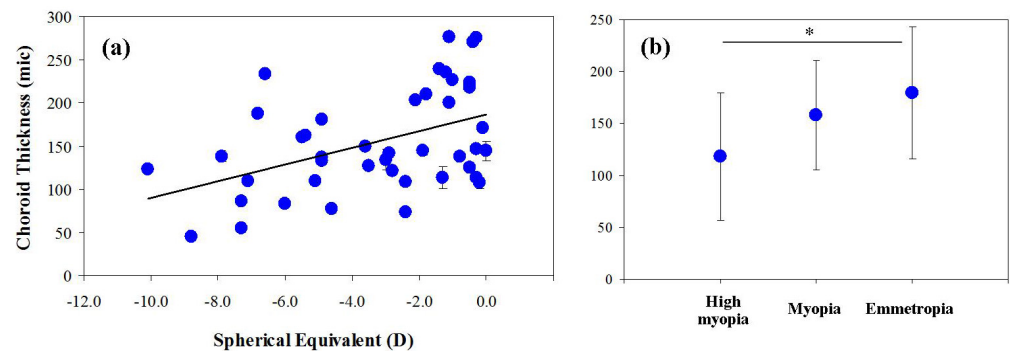


**Figure 3.** (a) Subfoveal choroidal thickness ( $\mu\text{m}$ ) versus the SE. Best linear fit:  $T_{\text{cor}} = 11.66 \cdot \text{SE} + 292.59$ . For each refraction value, the symbol represents the mean across three measurements (error bars were always within the blue dots). (b) Averaged thickness values for the experimental groups defined according to their refraction. Error bars indicate the standard deviation. (\*:  $p = 0.03$ ).

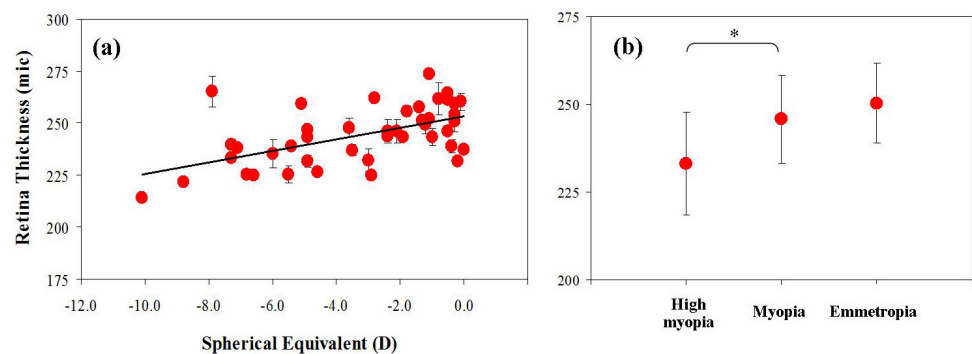


**Figure 4.** (a) Retinal thickness at the foveal location as a function of the ocular refraction. (b) Averaged retinal thickness for each myopia group. Error bars in both panels represent the standard deviation. In some cases (left panel), the size of the error bars are within the red symbols.

Following the experimental protocol described in Methods, the thickness for both choroid and retina was also measured at location N (see Figure 2b). For the choroid, Figure 5 depicts the individual thickness values and the averages for each experimental set of subjects. Although a linear significant correlation is present ( $R = 0.45, p = 0.002$ ; best linear fit:  $T_{cor} = 9.70 \cdot SE + 186.6$ ), choroidal thickness at this location only differs significantly comparing high myopes and emmetropes ( $t$ -test,  $p = 0.04$ ). Similar to the choroid, retinal thickness also decreases with the SE ( $R = 0.56, p < 0.0001$ ) (Figure 6a). Values were between 214 and 274  $\mu\text{m}$ . However, differences were statistically significant also when comparing high myopic and myopic subjects ( $t$ -test,  $p = 0.01$ ) (Figure 6b).

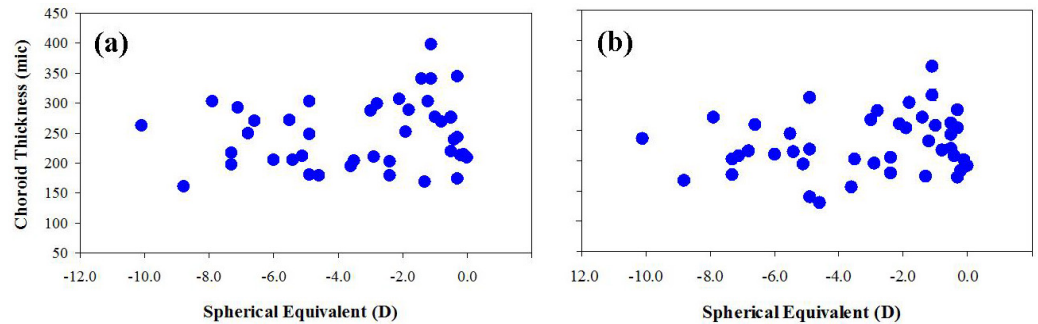


**Figure 5.** (a) Choroidal thickness as a function of the SE at the location N. (b) Averaged thickness values for each experimental group (\*:  $p = 0.04$ ). Error bars indicate the standard deviation in both panels. In some cases, left panel, the diameter of the experimental points surpasses the magnitude of the corresponding error bar.



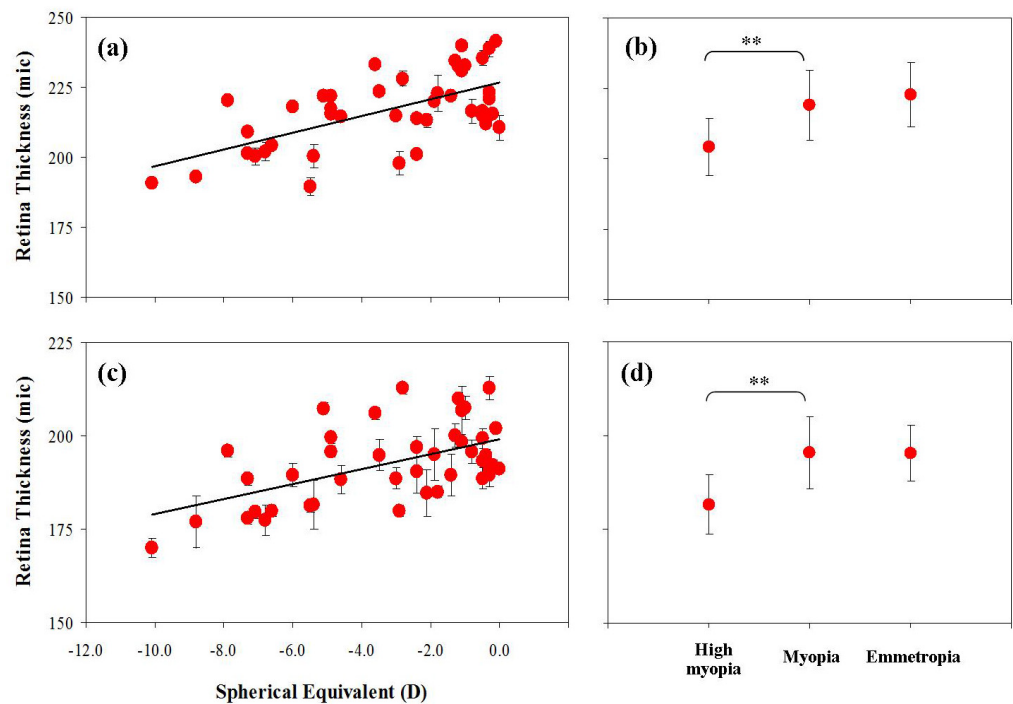
**Figure 6.** (a) Relationship between retinal thickness and refraction at the nasal location. Best linear fit:  $T_{ret} = 11.66 \cdot SE + 292.59$ . (b) Averaged retinal thickness for each group of subjects (\*:  $p = 0.01$ ). Error bars indicate the standard deviation in both panels. In some cases, left panel, the diameter of the experimental points surpasses the magnitude of the corresponding error bar.

For the two temporal locations, the choroidal thickness hardly varies as a function of the SE (Figure 7). Although, on average, the choroid at location T2 was thinner ( $226 \pm 48 \mu\text{m}$ ) than at location T1 ( $249 \pm 55 \mu\text{m}$ ), this difference was not statistically significant ( $t$ -test,  $p > 0.05$ ).



**Figure 7.** Choroidal thickness versus refraction for locations T1 (a) and T2 (b). No significant differences were found for both sets of data.

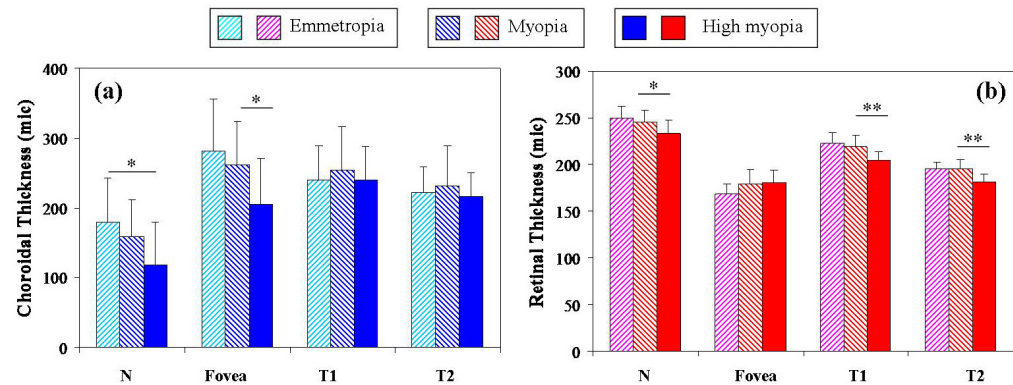
On the opposite, the retinal thickness presents a linear and significant decrease with increasing myopia for both temporal locations (T1:  $R = 0.63$ ,  $p < 0.0001$ ; T2:  $R = 0.55$ ,  $p = 0.0001$ ) (Figure 8). When splitting the data into the pre-defined refraction groups, values for high myopes were statistically different from those corresponding to myopes ( $p = 0.004$  and  $p = 0.001$  for locations T1 and T2 respectively).



**Figure 8.** Retinal thickness at locations T1 (a) and T2 (c) as a function of the SE for every patient. (b,d) Averaged retinal thickness values for the three groups of patients: location T1 (b); location T2 (d). In panels (b,d) \*\*:  $p < 0.004$ . Error bars indicate the standard deviation in all panels. For some data in left panel, the size of the error bars are within the red symbols.

For the sense of completeness and to facilitate direct comparisons, Figure 9 presents the averaged thickness values for the groups at the selected eccentricities. The choroid was thickest at the fovea and decreased towards nasal and temporal directions, reaching a minimum nasal to the fovea. The mean subfoveal choroidal thickness was  $206 \pm 66 \mu\text{m}$

and  $261 \pm 62 \mu\text{m}$  for high myopes and myopes respectively. The retina was thinnest at fovea, with a mean foveal thickness of  $181 \pm 13 \mu\text{m}$  in high myopic eyes ( $179 \pm 16 \mu\text{m}$  for myopic ones). The thickest retina was found at location N.



**Figure 9.** Choroidal (a) and retinal (b) thickness versus location in myopic and high myopic eyes. Each bar corresponds to the mean value for all eyes of an experimental group at the indicated location.

#### 4. Discussion

This study has shown measurements of both retinal and choroidal thickness in a cohort of healthy young subjects as a function of the SE at different locations using OCT images. Custom software was developed to flatten the curvature of the original images and to assess the distances between the retinal structures of interest, minimizing possible geometrical distortions arising due to the beam scanning during image acquisition.

At the foveal depression, or foveola, the retinal thickness was significantly thinner than at the nasal and temporal locations in all groups ( $p < 0.0001$ ), exhibiting no difference as a function of SE. Our results are in the same direction of those presented in the work of Wakitani et al. [8], where subjects ranging in age from 12 to 74 years showed that the average retinal thickness in areas surrounding the central fovea was not significantly correlated with refraction. Similar results were later reported by Ikuno et al. (age range 33–75 years) [17]. Even when adjusted by sex, age and axial length, SE (range [3.75, −23.50] D) had no significant influence on retinal thickness [12]. Some measurements restricted to children [24] and young subjects with similar age to that used herein also reported that retinal thickness of the fovea did not vary with myopia [25]. Other works have reported weak correlation between foveal thickness and axial length or refraction, not only in young eyes [9,26], but also when middle-aged subjects [11], children [10,27,28] and within a wide age range are involved [29]. Recent studies have reported that the fovea is thicker in moderate/high myopic eyes than in the non-myopic eyes [30,31]. In most of the studies where certain correlation was found, thickness was confronted to axial length, rather than to refraction. In the cases showing dependency with refraction [29], thickness was obtained as an average in the foveal region, not as a measurement at certain specific location as we have reported in the present work. Thus, according to our results, the retinal thickness at the foveola is independent of refraction. Consequently, it should not be adopted as a differentiating feature in the myopic eye.

For the present work, the retina thickness at the central fovea was  $177 \mu\text{m}$  on average. However, this value presents large variability in the literature, even in sets of young subjects:  $141 \mu\text{m}$  [9],  $178\text{--}206 \mu\text{m}$  [26],  $235\text{--}283 \mu\text{m}$  [25] and  $238\text{--}261 \mu\text{m}$  [30]. Since SE ranges do not differ significantly from ours, differences might originate from the method employed to measure the thickness. Most of those tests used the reticules (rings and areas) defined by the software provided by the commercial instrument, where the central area is about 1 mm in diameter. Such a large area averages retinal locations around the fovea with very different thicknesses and then, the final value provided by the instrument could be overestimated since the neural retina increases in a radial direction from the foveola.

It can be noted that the estimation of actual distances from ophthalmic OCT retinal images is still an open issue. OCT modality records changes in refractive index, but the conversion to physical distance from optical path requires of the knowledge of the refractive index. This index is typically assumed to be constant across the retina, what produces a deformation in the relative thickness of the different layers. This fact is often neglected in the interpretation of the images in the clinical/medical context, although it arises very evident when retinal OCT images are confronted with their histological pairs [32–34]. Accordingly, the numerical results provided in this and other works for the retina and choroid thickness using OCT modality must be taken cautiously.

In a different direction to what we found at the foveola, retinal thickness did show a significant correlation with SE at every other selected location. In all these eccentricities the retinal thickness declined with negative SE, showing a robust trend when all the subjects were considered. Essentially, as the eye exhibited larger myopia levels, the retina presented thinner thickness out of the fovea. The highest decline was found at location N, with an estimated rate of 3  $\mu\text{m}/\text{D}$  in the myopic direction. When the analysis was performed across groups, N and T regions were systematically thinner in the high myopic group than in the myopia group ( $p < 0.01$ ). However, values were similar when comparing myopic and emmetropic eyes ( $p > 0.05$ ). Mean values for each subgroup are interesting, since they unveil the origin of the correlation found when all the subjects were presented together without distributing them into subgroups. The association between thinner retinas and myopia only emerges when high myopes were considered. The myopia group presented indistinguishable thickness as compared to the emmetropic group. Then, it can be concluded that such morphological marker should not be targeted for myopia onset investigation, for it only exhibits a differential trend when myopia has been well developed and reached high values.

Unlike the central fovea, for perifoveal/macular locations, results previously reported by other authors (involving subjects with age similar to those of the present study) mostly agree to each other when correlating retinal thickness and refraction. Lim et al. suggested that retinal thinning in myopia is more common in the peripheral retina [9]. This conclusion is supported by Lam and co-authors [11], who found that macular thickness decreased in eyes with a greater degree of myopia in a 3–6 mm outer ring (not in the 1–3 mm inner ring). Othman and co-workers [26] found positive correlations between the outer macular thickness (all quadrants within the perifoveal area) and SE. Liu and co-workers also proposed that macular retinal thickness was significantly lower in the high myopia group compared with the low to moderate myopia group, except at the fovea [25].

The present study goes a step further since the actual change in retinal thinning found herein occurs only for high myopic eyes. This agrees well with Lam et al.'s data where macular thickness was shown to be significantly lower in the high myopic eyes than in the low to moderate myopic and the non-myopic eyes [11]. Also using the instrument's software, Zereid and colleagues reported thinner parafoveal and perifoveal regions in moderate to high myopic eyes than in non-myopic eyes [30]. Although our myopia groups are not the same, those results seem also to be fairly coherent with these.

It must be said that glaucoma can cause a pathologic thinning of the retina, specifically in the zone close to the optic disc, which eventually could affect the results. We conducted measurements of IOP to account for this possibility, and none the subjects exhibited abnormal values of IOP. However, it is a fact that some subjects might suffer from glaucoma even presenting normal values of IOP, so a more specific test can be programmed in the future to fully exclude this possibility.

In this study a detailed assessment of the topographical variations in choroidal thickness has also been provided. The mean subfoveal choroidal thickness here obtained was  $254 \pm 70 \mu\text{m}$ , a value similar to the one reported by Ding et al. [25], but below others provided by different authors [23,24,35–37]. The thinner values of our study may result from differences in the sets of subjects, such as age, refractive state, ethnic group [38], image processing software or the OCT light source. Compared with a conventional 850-nm OCT



source, the long-wavelength (1050-nm) source used herein has a higher penetration and, consequently, increased sensitivity, what facilitates the visualization of the choroid-scleral interface not only at the subfoveal location but also at any other region.

When using an OCT device with a swept-source, the mean subfoveal choroidal thickness found in other works was  $299 \pm 131 \mu\text{m}$  [39]. This value is above ours, although it may be affected by the range of age (19–60 years), refraction (from +4 to –6D), the ethnicity (Indians) or the period of the day when the OCT image was acquired (10 a.m.–2 p.m.).

When analysing the relationship with the SE, the subfoveal choroidal thickness linearly reduced with the amount of myopia (slope of  $11.66 \mu\text{m}/\text{D}$  from the best linear fit). However, significant differences were only found between high myopes and myopes ( $p = 0.031$ ). These results are consistent with other studies that reported a similar correlation with refractive error, in both adults [17,35,40] and children [34,37,41]. Previous studies showed that central choroidal thickness decreased by  $8.7\text{--}13.6 \mu\text{m}/\text{D}$  of myopia [17,35,42,43]. However, the linear regression analysis carried out by Tunzer et al. showed a change of  $50.24 \mu\text{m}/\text{D}$  [44], although they did not provide clues to explain such a different value.

To the best of our knowledge studies exploring normal young eyes are scarce in the literature. When only those subjects were involved, the central choroidal thickness was significantly lower in the high myopia group than in the other groups (myopes and emmetropes): 34% [18] and 10% [45], what agrees well with the 23% of reduction found in the present work when comparing high myopes and myopes.

Choroid was found to reduce with increasing eccentricity from the fovea towards the periphery. Moreover, location N was significantly thinner than the rest of analyzed areas ( $p < 0.0001$ ), what is consistent with the trends found in previous studies [17,35,42,46–48]. This significant choroidal thickness decrease nasal to the fovea could be explained by the anatomical location of the optic nerve [49] or because of the high metabolic demand at the central macular area [43,50]. Since eccentric locations were often different from those here used, it is also difficult to directly compare the present numerical results with those from other studies.

As above stated, previous literature was mainly centred on exploring choroidal changes with refraction at the subfoveal location. Although results on choroidal thickness at eccentric locations were provided, there is a lack of analyses of the effects of the ocular refraction. Most studies only compared eccentricity-dependent differences in choroidal thickness for two refractive groups (myopia vs. non-myopia), but they did not show the trend for the entire set of subjects ranging from emmetropes to high myopes as we did here.

It is interesting to note that we also found a linear decrease between choroidal thickness and SE at location N ( $p < 0.002$ ). In addition, high myopes differed ( $p = 0.04$ ) from emmetropes. For locations T1 and T2 high myopic choroids were also thinner, but differences among groups were not significant. That is, at temporal regions, SE and choroidal thickness were not correlated.

This result is consistent with other studies in young adults where choroidal thinning was not significantly associated with refraction in the peripheral regions [45,46,51]. This lack of correlation at temporal eccentricities might also partially agree with Read et al. findings [37]. They claimed that choroidal thickness differences between myopic and non-myopic children (10–15 years) was significantly greater in central than in more peripheral regions. In that sense, Jin et al. reported that, compared to emmetropic children (7–13 years), the myopic group had a significantly thinner choroid in all regions ( $p < 0.01$ ) [41]. Similar results were found by Teberik and co-authors in a group of Turkish patients (13–66 years) [18]. Although the analyzed locations of these previous studies were overall similar to ours, differences in age and refraction range might be more critical issues in terms of myopia development and associated morphological changes.

Recent results on wide-field choroidal thickness comparing myopes and emmetropes have been reported by Collins' group [45,46]. They examined macular (fovea, parafovea, and perifovea) and extra-macular areas in healthy young adults. It was shown that myopes

exhibited a thinner choroid than emmetropes in the macular region (~72 mic of difference on average), this difference diminished towards the periphery (~26 mic). Although this behaviour also occurred in the present work (changes of 65  $\mu\text{m}$  and 12–54  $\mu\text{m}$  for the fovea and peripheral locations respectively), differences were not statistically significant.

It must be remarked that the precise estimation of the choroidal thickness cannot be accomplished due to the lack of a true outer border. The inner limit of the choroid is precisely defined by the RPE. On the contrary, the outer choroid structure is progressively interlaced with the scleral tissue. This imposes an additional complication in the characterization of this layer. Consequently, the estimations of choroidal thickness in this and other works must be taken with care since optical methods provide solely a first approximation to the problem. Future advances in ophthalmic OCT, with enhanced penetration capabilities and resolution, might enable to establish a more objective outer limit for the choroid, perhaps based on a pre-set percentage of interlaced scleral tissue.

In addition, data here presented involved young healthy subjects and OCT images were acquired during a similar and narrow time frame of the day. Therefore, no further adjustments for age [24,44] and circadian variations [52] needed to be applied on the results. Myopia was expected to be fully developed and steady in this cohort [53]. Other ocular changes associated to normal aging, as presbyopia, were not compromising vision for this age range [54]. Moreover, the subjects were around the turning point in the refraction evolution associated to internal changes in the lens [55–57]. All these reasons made this age range a particularly interesting group to study myopia. We adopted the refractive ranges to distribute subjects (as emmetropes, myopes and high myopes) proposed in the work of Flitcroft [58]. This is highly recommended to allow for direct comparison of results across different studies.

Moreover, our OCT retinal images were digitally flattened to establish a reliable protocol to estimate distances. In contrast to the thickness values obtained using the software supplied by the company with the commercial instruments, the estimates presented in this work did not average extended areas. Then, they were not affected by large geometrical distortions inherent to the scanning of the laser beam in ophthalmic OCT modality.

We strongly recommend using this image flattening protocol in future works, since an ideal thickness requires to be assessed along a direction perpendicular to the layers of interest. This fact has not always been considered in the existing literature. In that sense, we are fairly convinced that the results presented in this work are more accurate than those obtained from commercial software in the existing literature.

## 5. Conclusions

We have measured both the choroid and the retina thickness at 4 locations along the horizontal meridian (fovea, 2250  $\mu\text{m}$  nasal to the foveal depression; 2250  $\mu\text{m}$  and 3375  $\mu\text{m}$  temporal) in a group of 43 young healthy subjects with refractions ranging from emmetropia to high myopia. To the best of our knowledge no prior work had specifically targeted such a population group. It was found that the retinal thickness at the foveola was independent from refraction, while variations only emerged at other eccentricities. We shed light in the origin of the correlation between myopia and retinal thickness, specifically showing that it only aroused for high myopes. There was no difference between myopes and emmetropes in the retinal thickness. Consequently, we conclude that such a parameter does not provide a clue in the onset of myopia and early stages of progression.

When looking at the choroid, a kind of reverse result was found: changes in choroidal thickness were mostly present at the fovea. In the nasal eccentricity the correlation was due to differences between the emmetropic and high myopia subgroups. Other eccentricities did not exhibit changes as a function of refraction. When present, changes in choroidal thickness exclusively occurred in the high myopia subgroup. Consequently, choroid thickness changes neither provide a useful marker to track early stages of myopia.

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**Informed Consent Statement:** Informed consent was obtained from all subjects involved in the study.

**Data Availability Statement:** Requests for materials should be addressed to J.M.B. or E.J.F.

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