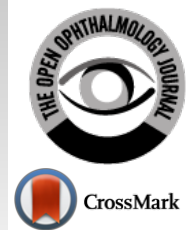




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REVIEW ARTICLE

The Effect of Optical Defocus on the Choroidal Thickness: A Review

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Abstract:

The choroid is a heavily vascularized tissue located between the retina and sclera and plays a primary role in ocular metabolism. It has recently been suggested that the choroid has the ability to change its thickness and secretion of growth factors. This may play an important role during visual development by adjusting retinal position during growth to support emmetropisation; however, the mechanism by which changes in choroidal thickness (ChT) occur is unclear.

This relationship becomes an interesting topic in the clinical field, although conflicting evidence found that these changes in the choroidal thickness may not be associated with the development of refractive errors. Many reports have investigated the changes in the choroid and related factors that affect the ChT. Thus, this review will summarize the current literature related to choroidal thickness in different refractive error groups, determine the factors that influence the thickness of the choroid, and discuss in detail the relationship between the changes in the ChT and ocular elongation, and therefore, the effect of optical defocus on ChT and the development of the refractive error.

Keywords: Choroid, Choroidal thickness, Emmetropization, Ocular elongation, Optical defocus, Refractive errors.

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1. INTRODUCTION

The choroid of the human eye is mainly a vascular structure located between the retina and the sclera. It plays an important role in ocular metabolism by supplying the outer retina and retinal pigment epithelium with oxygen and nutrients [1]. It has been proposed that the choroid has other functions, such as thermoregulation of ocular temperature, adjustment of the position of the retina by changes in choroidal thickness (ChT), and regulation of eye growth [2 - 4]. These functions could play an important role during the emmetropization process by changing retinal position during eye growth to correct refractive errors [1]. However, the changes in choroidal thickness, as well as the secretion of growth factors and the relationship between these two mechanisms, remain unclear [5 - 8]. Thus, this relationship becomes an interesting topic in the clinical field, although conflicting evidence found that these changes in the choroidal thickness may not be associated with the development of refractive errors.

This review will summarize the current literature related to choroidal thickness in different refractive error groups, determine the factors that influence the thickness of the choroid, and discuss in detail the relationship between

the changes in the ChT and ocular elongation, and therefore, the effect of optical defocus on ChT and development of the refractive error.

1.1. Method of Literature Search

The literature search was carried out in the following databases: PubMed, Embase, Google Scholars, and ISI Web of Science. The search terms used were: choroid, ChT, optical coherence tomography, OCT, choroidal thickness, choroid thickness, choroid thinning, choroidal thickening, choroidal volume, choroidal change. This review focused on published studies and reports in English that included choroidal thickness measured by OCT. The search included the studies examining the changes in choroidal thickness, and the results retrieved a total of 33 articles. Abstracts, comments, duplicate data, letters, case reports, and full texts with insufficient data on choroidal thickness were excluded.

1.1.1. Choroidal Thickness in Different Refractive Error Groups

Previous reports on the choroid in human eyes found a significant association between refractive error and/or axial length and ChT [9 - 17]. These studies found a thinner choroid for the myopic subjects with longer axial length, whereas a thicker choroid was associated with shorter hyperopic eyes.

A study used spectral-domain optical coherence

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tomography (SD-OCT) to examine the correlation between the sub-foveal choroidal thickness (SFCT) and the different refractive error groups [15]. The measurements were collected from 3468 Chinese subjects, with a mean age of 64.6 ± 9.8 years (range, 50–93 years). They found a significant correlation between SFCT and the myopic group ($15 \mu\text{m}$ per diopter of myopia, $p < 0.001$), but no relationship was found for the hyperopic group. The results also showed that the myopic group had a reduction in the SFCT by $4.1 \mu\text{m}$ per year.

Another study was conducted to observe the differences in the ChT between high myopia subjects ($> -6\text{D}$) and subjects with spherical equivalent refraction between -3D to $+3\text{D}$ [16]. Measurements of ChT were obtained by the use of enhanced depth imaging optical coherence tomography (EDI-OCT). Data were collected from two groups; the first group involved 171 high myopic subjects with $\text{MSE} = 7.56 \pm 1.9\text{D}$, and mean age of 22.23 ± 6.5 , whereas the control group included 103 subjects with $\text{MSE} = 0.74 \pm 1.5\text{D}$ and mean age of 23.3 ± 7.4 . They reported a significant thinning of the choroid in the high myopia group compared to the control group at all macular regions ($p < 0.001$ for all comparisons).

Many studies have found a thinner choroid with myopic children compared to other refractive groups. This thinning in the choroid generally occurs at an early stage of refractive error development [17 - 19]. A study used swept-source optical coherence tomography (SS-OCT) to measure both ChT and retinal thickness in 276 Chinese children aged 7-13 years [17]. The results showed a significantly lower thickness in the choroid for the myopic group compared to the healthy group at all macular locations ($p < 0.01$) and found higher thickness in the choroid for the hyperopic group compared to the healthy group in most macular locations ($p < 0.05$).

1.1.2. Factors that Influence the Thickness of the Choroid

In human eyes, many studies have described the diurnal variations in ChT and reported that the choroid was thicker at night and thinner in the morning [20 - 22]. Other studies have found that it is possible to disrupt the diurnal rhythm after imposed retinal defocuses in human subjects [5 - 8, 23].

Numerous researchers, using different OCT devices, have shown that the ChT decreases with the increasing age, with reductions in SFCT by the range of 14 to $54 \mu\text{m}$ per decade [12, 13, 15]. A study was conducted by Ikuno *et al.* to examine the correlation between ChT and refractive error, axial length, and age. Measurements of ocular biometry were obtained from 43 healthy Japanese subjects with a mean age of 39.4 ± 16.0 years (range, 23-88 years) [12]. They found a significant correlation between ChT and age ($P < 0.001$), while ChT was not significantly correlated with refractive error and axial length ($P = 0.22$).

It has been reported that gender could play a role in choroidal thickness [14, 24]. A study examined the association between sub-foveal choroidal thickness (SFCT) and ocular axial length, refractive error, in 93 healthy young women and men (mean age 24.9 ± 2.6 years) [14]. The results showed that the thickness of the choroid was 18% higher in men compared to women. Another study examined the association between choroidal thickness and age, sex, and axial length [24].

Spectral-domain optical coherence tomography (SD-OCT) was used to measure the choroid for 114 healthy subjects (51 men and 63 women) with a mean age of 50 years (range, 14-89 years). They reported a significant increase in choroidal thickness for male subjects by 7.37% than female subjects.

1.1.3. The Effect of Optical Defocus on Choroidal Thickness

In animal studies, it has been found that optical defocus can affect the emmetropization process and lead to the development of refractive error [25 - 28]. They reported that the hyperopic defocus (negative spherical lenses) has the ability to accelerate eye growth and leads to develop myopia in tree shrews and monkeys [25, 26], while myopic defocus (positive spherical lenses) has been shown to slow eye growth leading to hyperopia [27].

Several studies on visual development using human data [10 - 15, 29 - 32] and animal models [28, 33 - 35] have found significant evidence that the changes in ChT are associated with the development of the refractive error. The study conducted by Hung *et al.* examined the influence of optical defocus on the ChT in animal eyes [28]. Myopic and hyperopic lens defocuses (range: -6D to $+12\text{D}$) were imposed on 10 normal rhesus monkeys. These lenses were worn full time for 3 months, and then ChT, refractive error, and axial length measurements were obtained. The results showed that the ChT decreased when myopia developed, while a thicker choroid was found for those developing hyperopia.

Studies on the choroid in human subjects found a decrease in the ChT when negative lenses were imposed, and an increase in the thickness of the choroid with positive lenses was observed [5 - 8]. Other studies have also observed a significant rapid choroidal thinning in response to sustain near-work activities [36].

The response of ChT with short-term monocular defocus has been examined in a series of young adult healthy eyes from different ethnicities (15 Caucasian, 8 East Asian, and 5 Indian subjects) [5]. A total of 28 subjects aged between 20 and 31 years were assigned into two groups (14 myopes/14 emmetropes, mean age 25 ± 3 years). Three different types of optical defocus were imposed, $+3\text{D}$ myopic defocus, -3D hyperopic defocus, and a diffuser, Bangerter filter (foil number 0.2). The measurements of the ChT were obtained by the use of Lenstar LS-900 optical biometer before and after 30 or 60 minutes of exposure to optical defocus. Optical defocus was imposed on the right eye, while the left eye was used to be a control. The results showed a significant choroidal thickening associated with the exposure to 60 minutes of $+3\text{D}$ myopic defocus (mean change, $+12 \pm 16 \mu\text{m}$; $p = 0.004$). They also found small but not significant choroidal thinning in response to 60 minutes of -3D hyperopic defocus (mean change, $-3 \pm 14 \mu\text{m}$) and the optical diffuser (mean change, $-6 \pm 12 \mu\text{m}$).

A study observed the short-term influence of imposed optical defocus on SFCT [8]. A total of 12 East Asian subjects (6 emmetropic and 6 myopic; mean age, 22.9 ± 5.9 years, range 18-34 years old) were examined. The SFCT was measured using spectral-domain optical coherence tomography (SD-OCT) before and after 60 minutes of viewing a distance target (video movie at 6 meters). In two separate sessions,

measurements were taken while subjects were wearing their full distance vision correction in one eye, and the optical defocus (+2D or -2D) was imposed on the fellow eye. They found a significant correlation between SFCT and the degree of myopia (-39 μ m per dioptre of myopia, $R^2=0.67$; $p<0.01$), and the results showed a significant thinning in the SFCT for the myopic group (mean \pm SD 256 \pm 42 μ m) compared to the emmetropic group (mean \pm SD 423 \pm 62 μ m; $p<0.01$). There was also a significant reduction in SFCT with -2D (hyperopic defocus) for the myopic group (-20 μ m) and the emmetropic group (-16 μ m, $p<0.01$), while the SFCT was not found to be significantly changed in the control eye for both subject groups (1 μ m for myopic and -1 μ m for an emmetropic group). Conversely, a significant increase was found in SFCT with +2D (myopic defocus) for the myopic group (+16 μ m) and the emmetropic group (+15 μ m, $p<0.01$) compared to a change in the control eye (-5 μ m for myopic and -9 μ m for emmetropic group).

The study conducted by Woodman *et al.* [36] examined the influence of 30 min accommodative task on SFCT in 59 adult subjects (mean age 21.83 \pm 2.98 years, 37 myopic and 22 emmetropic subjects). Lenstar LS-900 optical biometer was used to measure the ChT before and after 30 min near the task at 4D accommodation demand. The results showed a significant reduction in ChT occurring after the near task (-9 \pm 18 μ m; $p<0.05$) in the myopic group, with non-significant changes in ChT in the emmetropic group (-7 \pm 22 μ m).

1.1.4. The Effect of Peripheral Retinal Defocus on Choroidal Thickness

It has been shown that using orthokeratology lenses may inhibit myopic progression in children due to the peripheral myopic blur [37]. These lenses are worn overnight to reshape and flatten the central corneal curvature. A study was conducted by Chen *et al.* to examine the short-term effect of orthokeratology treatment on ChT and axial length [23]. Measurements of the choroid were obtained using Enhanced depth imaging optical coherence tomography (EDI-OCT) for 77 myopic subjects aged between 7 and 17 years. Subjects were divided into 2 groups; one group was treated with orthokeratology lenses, while the control group wore single vision lenses over 3 weeks. The results showed a significant parafoveal choroidal thickening occurred after 3 weeks of wearing orthokeratology lenses. No significant changes occurred in axial length over time ($p = 0.975$) for both groups ($p = 0.582$). They also found that regional choroidal thickening may be related to the changes in optical defocus associated with orthokeratology treatment. In contrast, one study investigated the influence of long-term peripheral myopic defocus on the choroid of the human eye [38]. Nine children aged between 11 and 15 years (mean age, 13.61 \pm 1.25 years) were treated with orthokeratology lenses. Measurements were obtained by the use of Lenstar LS 900 biometer at baseline and after 1, 3, 6, and 9 months. They reported no choroidal thickening with orthokeratology lenses despite significant amounts of peripheral myopic defocus.

2. DISCUSSION

Previous studies have shown considerable changes in ChT

after imposed optical defocus [5 - 8, 23]. However, one study [38] did not find any association between ChT and peripheral myopic defocus. Gardner *et al.* examined the changes in ChT in response to imposed optical defocus over a longer period of time (9 months) [38], whereas other studies have found rapid choroidal changes after a short period (1 hour) of imposed optical defocus.

The imposition of hyperopic or myopic retinal blur through optical defocus can significantly affect the development of refractive error; however, the mechanism remains unclear. The choroid may decrease in thickness in order to alter the position of a retinal plane towards the defocus, as shown in animal models. Therefore, further work is important to clarify the exact mechanism affecting the emmetropization process when imposing optical defocus upon the choroid.

Another possibility is that the optical defocus can change the accommodative function. However, the data reported by Anstice and Phillips's study [39] have shown variability in the amount of accommodation responses when using the dual-focus contact lenses. The variability of the accommodation responses ranged from 0.75D to 2.75D when wearing these lenses, and it is thought that this variability may decrease the imposed blur effect of optical defocus. This would produce inter-subject variability when imposing optical defocus upon the thickness of the choroid. Further investigation is necessary to observe the accommodation and physiological variability induced by the use of optical defocus over a longer period of time; however, the diurnal variation of the choroid should be taken into account in studies conducted over a longer time frame.

Many studies have suggested that the diurnal variations of the choroid need to be considered during the examination of the effect of imposed optical defocus upon ChT [20 - 22]. One study observed that the choroid increased in thickness at night and decreased in thickness in the morning, and they found that the mean changes in the choroid during one day (from 9.00 am to 9.00 pm) were 29 \pm 16 μ m, ranging from 79 to 11 μ m [21]. The diurnal variations of the choroid within the day were large, making it more difficult to examine the impact of other factors, such as optical defocus, where the total changes observed were much smaller (mean change, +12 \pm 16 μ m) for both emmetropic and myopic groups compared to the study conducted by Read *et al.* [5]. Hence, it is possible that these small changes observed in previous studies were due to physiological changes and were within the normal level of the diurnal variation of the choroid.

In humans, many researchers have observed that the normal choroidal rhythm can be disrupted, and changes in the ChT are found with imposed optical defocus [5 - 8, 23]. However, these changes in the ChT after a short period (1 hour) of imposed optical defocus were found to be very small compared to the changes found in the animal studies, specifically in chicks where larger changes in the choroid have been found after a similarly short period (1 hour) of imposed optical defocus [40 - 42]. In chicks, one study reported that the mean changes in ChT after a short-term (1 hour) exposure to retinal image defocus (+6D and -6D) was 60 μ m [40], and other study found the changes in ChT after 1 hour of imposed optical

defocus (+10D and -10D) to be 89 μm [42], whereas, in rhesus monkeys, it has been shown by Hung *et al.* [28] that the changes in the thickness of the choroid were 50 μm after a long-term (3 months period) exposure to optical defocus (range: -6D to +12D). They also reported that the long-term effect of optical defocus on the thickness of the choroid was substantially larger in chicks [33, 35] compared to primates [28, [34]. These differences in the amount of choroidal changes in animals compared to humans studies conducted previously indicate variations in the nature of the eye of different species to adjust the position of the retina by changes in ChT when imposing optical defocus.

CONCLUSION

This review illustrated the relationship between the ChT and refractive error groups and the other factors that contributed to the changes of the ChT, such as the age of onset, gender, diurnal variation of ChT, and exposure to optical defocus. Future studies should investigate the long-term effect of optical defocus on the thickness of the choroid in human eyes. It is very important to understand the potential role of optical defocus in regulating ocular growth and developing refractive errors. A longitudinal study is also required to observe the choroid changes in younger subjects at an early stage in the development of refractive error, using different methods of a lens-induced retinal blur. In this review, a majority of studies have measured the influence of imposed optical defocus on ChT only in the foveal region, whereas the changes at other locations within the macular area were not examined. Thus, future work must examine the response of choroids at all the macular areas. This may offer an additional explanation regarding the role of retinal blur through optical defocus in the emmetropization process.

CONSENT FOR PUBLICATION

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CONFLICT OF INTEREST

The author declares no conflict of interest, financial or otherwise.

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