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Major review

# State of science: Choroidal thickness and systemic health

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ABSTRACT

The choroid is a highly vascular structure; therefore, a wide range of systemic conditions can affect it. Conversely, choroid health may also give us insight into systemic health. With the emergence of optical coherence tomography, there has been a surge in the research on choroidal thickness and factors affecting it. Studies regarding the effect of systemic health on the choroid have largely been in the form of cross-sectional, prospective, and case studies. We offer a summary of recent findings on the topic.



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## 1. Introduction

The choroid is the most vascular layer of the eye and plays an instrumental role in the physiology of the eye and in the pathogenesis of various ocular diseases. Per unit weight, the choroid has the highest blood flow of any tissue in the body[7] and is the vascular supply to the outer retina, retinal pigment epithelium, possibly a portion of the optic nerve,[44] and is the only source of metabolic exchange for the avascular fovea.[80]

A structurally and functionally normal choroidal vasculature is essential for retinal function. Abnormal choroidal blood volume and/or compromised flow may result in photoreceptors dysfunction and death with resultant vision loss.[16] Consequently, the choroid plays a vital role in the pathophysiology of many conditions, such as central serous chorioretinopathy,[27] choroidal neovascularization related to age-related macular degeneration,[68,74] polypoidal choroidal vasculopathy,[68,74] multifocal choroiditis,[55] angioid streaks,[6] and high myopia-related chorioretinal atrophy.[20] In addition, the high flow of blood in the choroid predisposes it as a site for metastatic and embolic spread of tumors and infections.[80] Basically, as a result of the vascular nature of the choroid, potentially any disease affecting vasculature could also affect choroid health.

Quantitative assessment of the choroid has always been a challenging task with conventional imaging modalities such as indocyanine green angiography and ultrasonography because of limited image resolution and repeatability.[22,43] Histological evaluation is difficult because of the lack of samples and may not be accurate owing to changes in the choroid after fixation; however, our understanding of the choroid has been vastly augmented in recent times since the introduction of imaging the choroid *in vivo* using enhanced depth imaging technique of optical coherence tomography (EDI-OCT).[104]

This innovation in technology has sparked a rise in the amount of research done with regard to choroidal thickness,[71,86,104] which is measured on the EDI-OCT from the outer border of the retinal pigment epithelium, represented by a hyperreflective line, to the inner border of the suprachoroidal space, represented by a hyporeflective line. There is, however, only limited literature published on systemic diseases affecting choroidal health.[10] We consolidate the current knowledge on the effects of systemic health on choroidal thickness and attempt to provide insights on how choroid thickness may be an indicator of systemic health (Table 1). Infections and diseases limited to the eye without any systemic involvement have been excluded.

## 2. Physiological changes in choroidal thickness

### 2.1. Diurnal variation

There have been few studies determining the diurnal variation of choroidal thickness in healthy patients.[17,106,109,113] A prospective study conducted by Tan et al of 12 healthy volunteers studied the choroidal thickness over 2 separate days in 5 fixed, 2-hour intervals.[106] This study revealed that there is a significant variation in choroidal thickness, with mean amplitude of 33.7 ± 21.5 μm. A progressive decrease in choroidal thickness occurred from 9 AM till 5 PM, with good reproducibility of the diurnal pattern between 2 visits. A study conducted in Japanese patients by Usui et al[113] performed over a 24-hour period showed a similar decreasing trend in choroidal thickness from 9 AM to 6 PM The amplitude reported, 33.0 ± 14.3 μm, was also similar to the reported values in Tan et al. In contrast, a study by Toyokawa et al[109] on Japanese subjects showed a smaller mean amplitude of 20.3 μm and an apparent increase in choroidal thickness from morning to evening. Current literature suggests that there is pattern of change of choroidal thickness; however, the exact pattern remains uncertain. Findings suggest that the time of measurements is important to consider when assessing choroidal thickness in clinical practice and in trials. A possible hypothesis is that diurnal variation occurs because of the circadian rhythm of hormonal changes affecting the blood supply of the body,[67] reflected in the vascular supply of the choroid, influencing its thickness. Increased vascular supply from sympathetic over activity in the morning[67] may be reflected in the vascularity of the choroid and hence results in a thicker choroid in the morning.

### 2.2. Age-related changes

Age is one of the biggest contributing factors to choroidal thickness (Fig. 1).[37,102] Previous histologic studies have shown a decrease in vascular density, overall luminal area, and diameter of the choriocapillaris with age.[34,87,97] This leads to a decrease in physiological functions of the choroid, that is, the ability of the choroid to provide sufficient levels of oxygen and other metabolites to the retinal pigment epithelium and outer retina may decrease,[104] contributing to the onset of many diseases in the elderly. Similar to histologic studies, age-related choroidal thinning in healthy eyes is confirmed by numerous clinical studies.[11,37,49,70,71,91,96] In healthy eyes, Margolis et al and Ikuno et al reported a decrease in choroidal thickness by 15.6 μm and 14 μm, respectively, for each decade of life.[49,71] Ding et al reported that age-related thinning occurs only after age 60.[31] Barteselli et al reported decrease in choroidal volume by 7.32% for every decade.[11] There are increasing data from recent population-based studies that indicate that both choroidal thickness and choroidal volume decrease with advancing age.[42,115]

A study[84] involving 96 eyes from 48 healthy children (mean age of 6.7 years) and 54 eyes from 27 healthy adults (mean age of 30.7 years) analyzed the choroidal thickness of the 2 populations and found that choroidal thickness was significantly greater in adults than in children. Thus, it is essential that age be taken into consideration when choroidal thickness is evaluated; however, no nomogram with age existents, and it may be time to develop one.

### 2.3. Gender differences

There are gender differences in the epidemiology of certain macular diseases. For example, a large number of studies have shown that central serous chorioretinopathy is more common in men, with a male-to-female ratio of up to 8:1.[66] Several