

## IMI The Dynamic Choroid: New Insights, Challenges, and Potential Significance for Human Myopia

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There is increasing interest in the role the choroid plays in the regulation of eye growth and the potential implications this has on the development and treatment of myopia.

#### What has been learned from animal models?

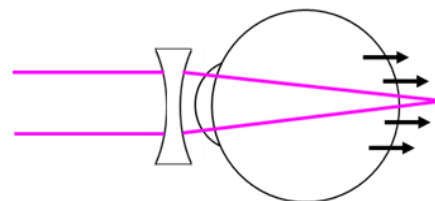
Extensive work has been performed in animal models, guiding and informing what is known about the dynamic nature of the choroid and its potential role in eye growth and myopia. Three key findings from animal models regarding the choroid and its relevance to human myopia are:

- (1) Bidirectional compensatory changes in choroidal thickness occur in response to optical defocus, which predict longer term changes ocular growth rate;

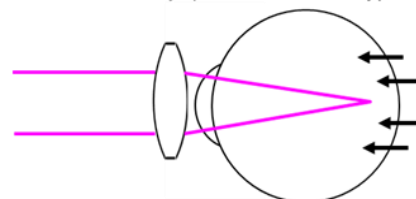
Hyperopic defocus (- lens) → **choroidal thinning** → increased scleral growth → myopia

Myopic defocus (+ lens) → **choroidal thickening** → decreased scleral growth → hyperopia

-3 D lens → hyperopic defocus → myopia



+3 D lens → myopic defocus → hyperopia



- (2) The choroid of animal models is influenced by physiological factors, such as diurnal oscillations in thickness. When normal diurnal variations are disrupted, refractive errors develop.
- (3) The choroid secretes growth factors and neurotransmitter molecules that regulate angiogenesis, matrix turnover, and ocular growth, providing potential targets for myopia control.

In animals, the immediate bidirectional changes of the choroid predict longer term changes in eye growth. Further research is needed to understand the mechanisms underlying these findings and explore the feasibility of optically or pharmacologically manipulating the choroid to prevent myopia development.

### How do we measure choroidal changes?

The choroid can be difficult to visualise and quantify. Axial length can serve as a proxy for changes in choroidal thickness, but this approach has its limitations. Optical coherence tomography (OCT) enables high-resolution imaging of the choroid and provides direct measurements of choroidal thickness. However, the posterior border of the choroid is often difficult to detect and the analysis of OCT images often requires manual segmentation; researchers are actively working on developing automated methods. Additionally, alternative imaging techniques like laser doppler velocimetry and optical coherence tomography angiography (OCT-A) are available for evaluating choroidal blood flow. To advance the field, it is crucial to continue developing and validating relevant instrumentation, establish standardized measurement protocols, and enhance imaging techniques to precisely quantify even subtle changes in choroidal thickness.

### What are the clinical implications of choroidal imaging?

There is no clear consensus on the role of choroidal imaging in the clinical management of myopia. In addition, for most clinicians, there remain significant barriers to measuring choroidal thickness, and current approaches are both challenging and time-consuming.

### What have we learned from human studies?

Thinner choroids are generally associated with higher levels of myopia and longer axial lengths. Gender and ethnicity may influence choroidal thickness, but findings are inconsistent. There is nasal-temporal asymmetry, with the nasal choroid consistently shown to be thinner.

#### (1) Physiological factors affect choroidal thickness

- Diurnal rhythm – several studies have demonstrated that the choroid is thicker during the night and thinner during the day
- Physical activity – findings are conflicting regarding the influence of physical activity, with some studies reporting that thickness may be affected and others reporting no effect
- Pregnancy – the choroid likely thickens during some months of pregnancy
- Water intake – the choroid may undergo a small increase in thickness after 5 minutes of ingesting one liter of water

#### (2) Pharmacological agents affect choroidal thickness – small and transient changes observed:

- Increased thickness has been observed with Atropine, Homatropine and Alcohol
- No change has been observed with Phenylephrine
- Thinning has been observed with Tropicamide and Caffeine
- Conflicting evidence for Cyclopentolate and Nicotine (thinner or no change) and Pilocarpine (thicker or no change)

#### (3) Optical factors affect choroidal thickness – small and transient changes observed:

- Increased thickness when exposed to 1000 lux or when reading white text on a darker background
- Thinning with accommodation or when reading black text on a lighter background
- Conflicting evidence for changes in choroidal thickness when exposed to hyperopic defocus (thickening or no change), myopic defocus (thinning or no change), or exposure to various spectral compositions of light or virtual reality

### What are the implications in myopia and myopia control?

There is currently **insufficient evidence** to either support or refute the hypothesis that changes in choroidal thickness to short-term optical or environmental cues or after instillation of pharmacological agents (i.e., 5-60 minutes) are reliable predictors of longer-term changes in axial length and thus whether a stimulus is myopiagenic or protective, as a marker of efficacy for myopia control treatments

### What further research questions remain to be answered?

- What is the exact nature of the choroid's role in eye growth regulation? Is it an active mediator, a passive signal relay, a diffusion barrier, or a combination of these functions?

- Do the short-term changes in choroidal thickness observed in various conditions have a long-lasting impact on the rate of ocular growth?
- Are the associations between thicker choroids and shorter eyes or less myopic refractive errors, as well as thinner choroids and longer eyes or more myopia, causal or merely a by-product of altered growth?

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### REFERENCE

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