THE CHOROID AS AN OPTICAL BIOMARKER FOR EYE GROWTH

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Disclosures:

Inventor on a number of patents related to myopia control.
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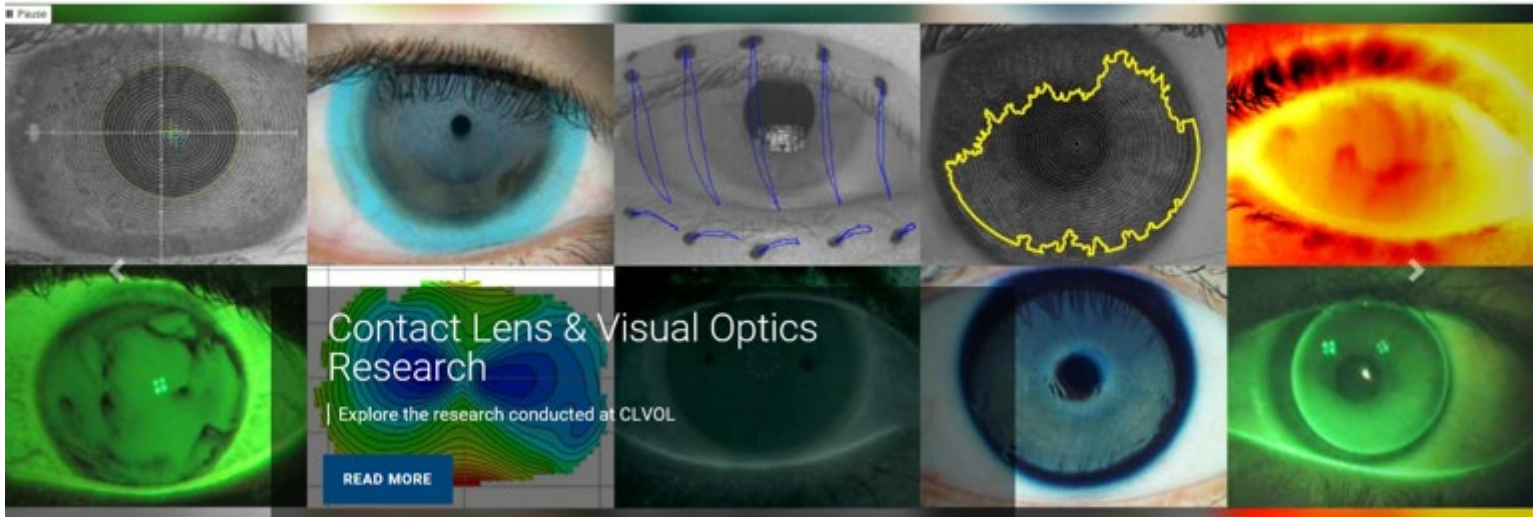
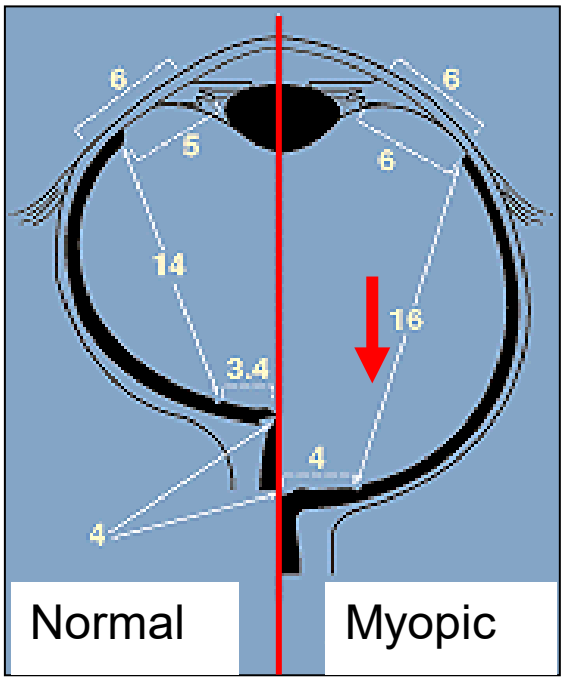
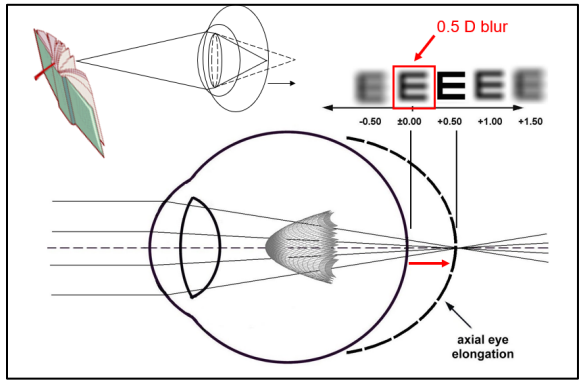


Topics

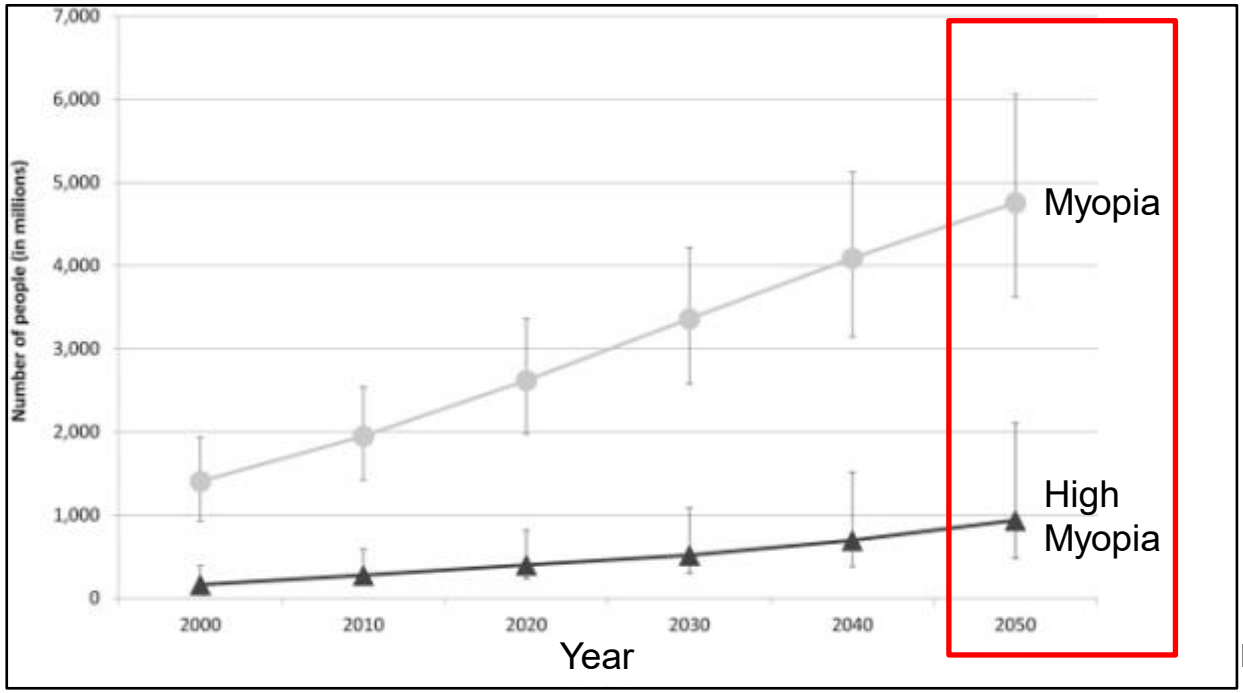
- Myopia background
  - Prevalence
  - Emmetropization
  - Risk factors
- Choroid and myopia
  - Choroid and animal myopia
  - Anatomy of the human choroid
  - Measuring the human choroid and axial length
  - Response of the human choroid to myopiagenic stimuli
- Choroid as a biomarker for eye growth
  - Atropine
  - Orthokeratology
  - Myopia control contact lenses
  - Myopia control spectacles
  - Wavelength of light
  - Sunlight





1 billion high myopes by 2050

- Modelling based on current trends in myopia development and progression, predicts globally by 2050:
  - **5 billion myopes**
  - **1 billion high myopes**
- Public health implications of this ‘myopia boom’ provide significant impetus for myopia control interventions.

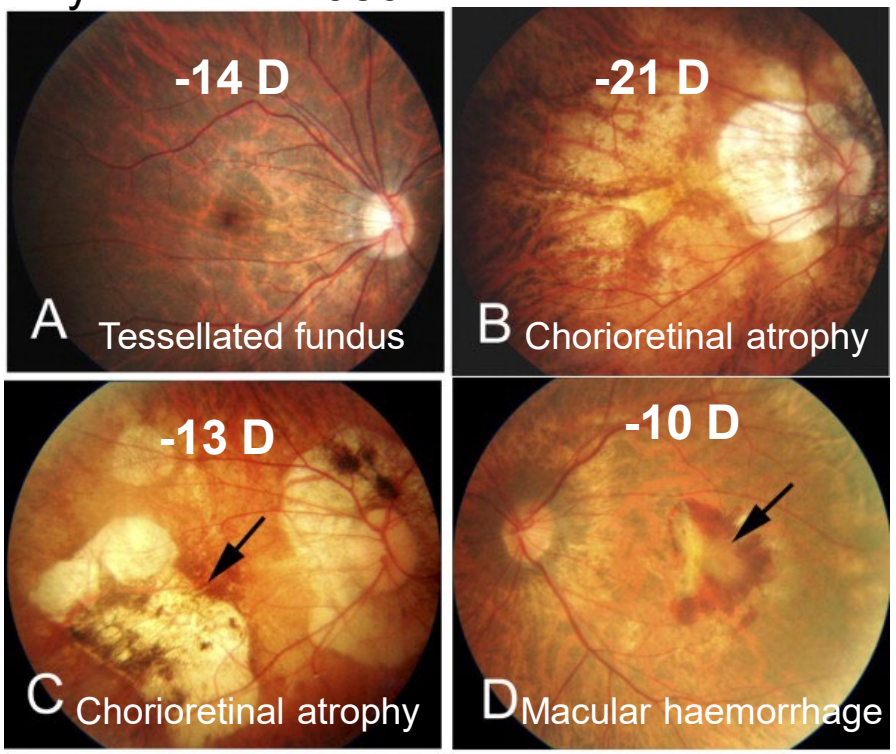


Holden et al. - 2016

Myopia risks

- Prevalence seems to be rising in many countries and >80% prevalence in some developed Asian countries
- Higher prevalence associated with higher dioptric levels of myopia
- Creates significant health care cost to the community
- High levels of myopia are associated with increased risk of glaucoma, cataract and retinal degenerations

Hayashi et al 1980



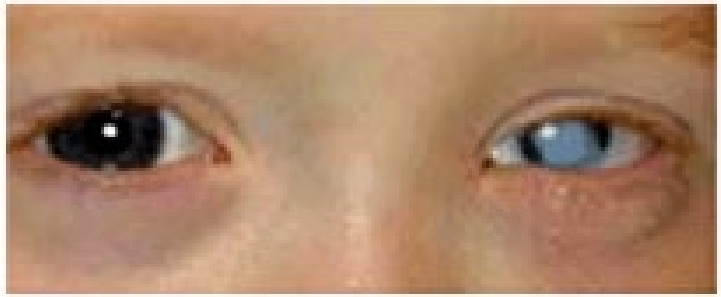
	Glaucoma	Cataract (PSCC)	Retinal detachment	Myopic Maculopathy
-1.00 to -3.00	2.3	2.1	3.1	2.2
-3.00 to -5.00	3.3	3.1	9.0	9.7
-5.00 to -7.00	3.3	5.5	21.5	40.6
<-7.00	-	-	44.2	126.8

TABLE 1: Odds ratios of increased risk of ocular pathology with increasing levels of myopia, summarised from Flitcroft, 2012.

Johnson 2016

Disruption of human eye growth

- Form deprivation
  - Corneal scarring
  - Congenital cataract
  - Vitreous haemorrhage



Refractive error distribution in children

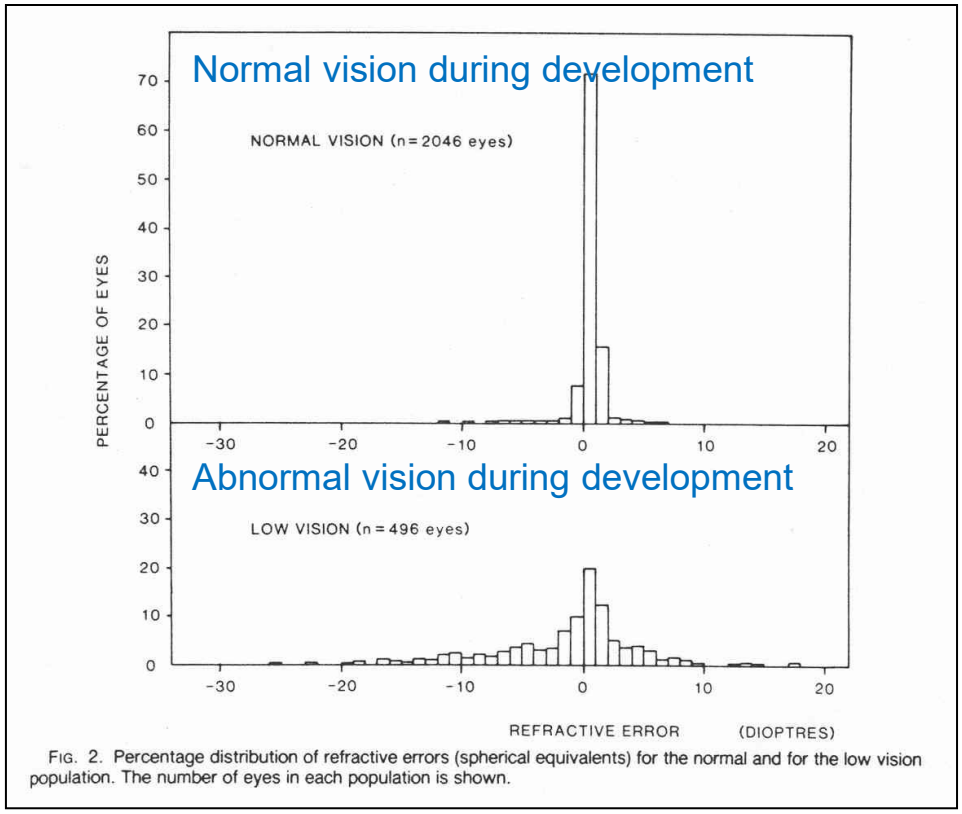
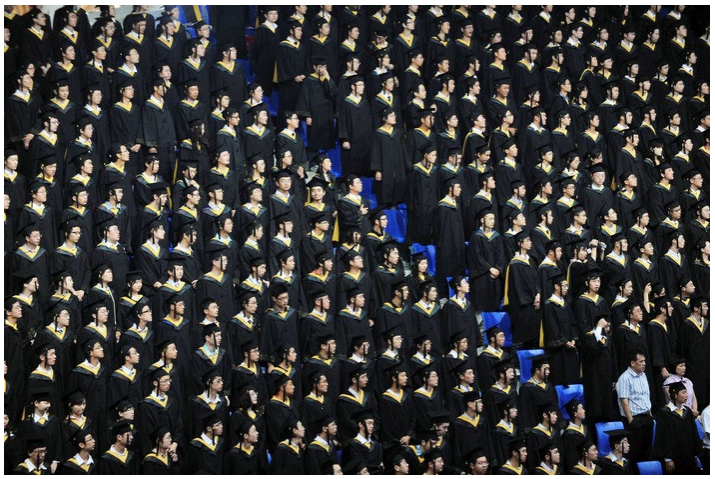


FIG. 2. Percentage distribution of refractive errors (spherical equivalents) for the normal and for the low vision population. The number of eyes in each population is shown.

Nathan et al Am J Optom Physiol Opt 1985

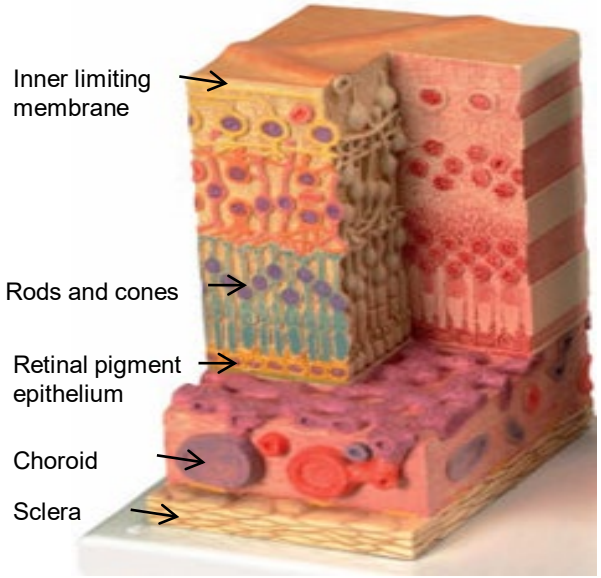
Myopia in humans

- Factors that can influence myopia development include:
  - Genetics
    - Myopic parents increases risk
  - Outdoor activities
    - Sunlight hours offers protection
  - Near work activities
    - Education level increases risk
    - More near work increases risk
  - Optical blur
    - Eye growth is poorly regulated when optical abnormalities present
    - Optical treatments (plus in image) can slow progression of myopia



"Myopia is an environmentally driven condition in genetically susceptible individuals." Hysi et al IOVS 2014

Topics



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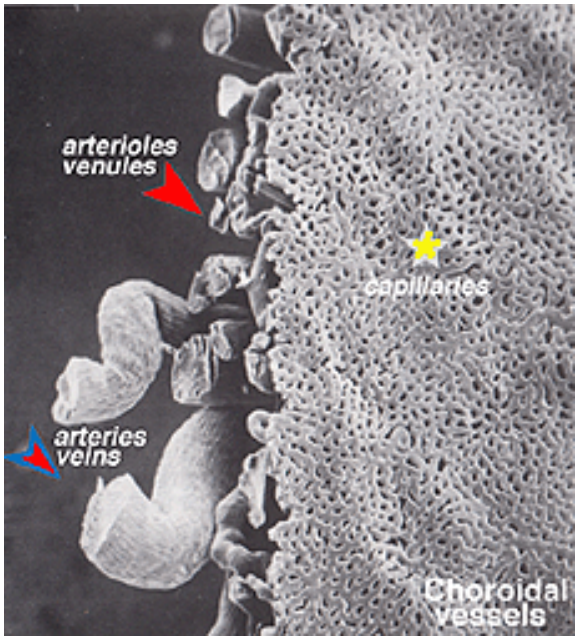
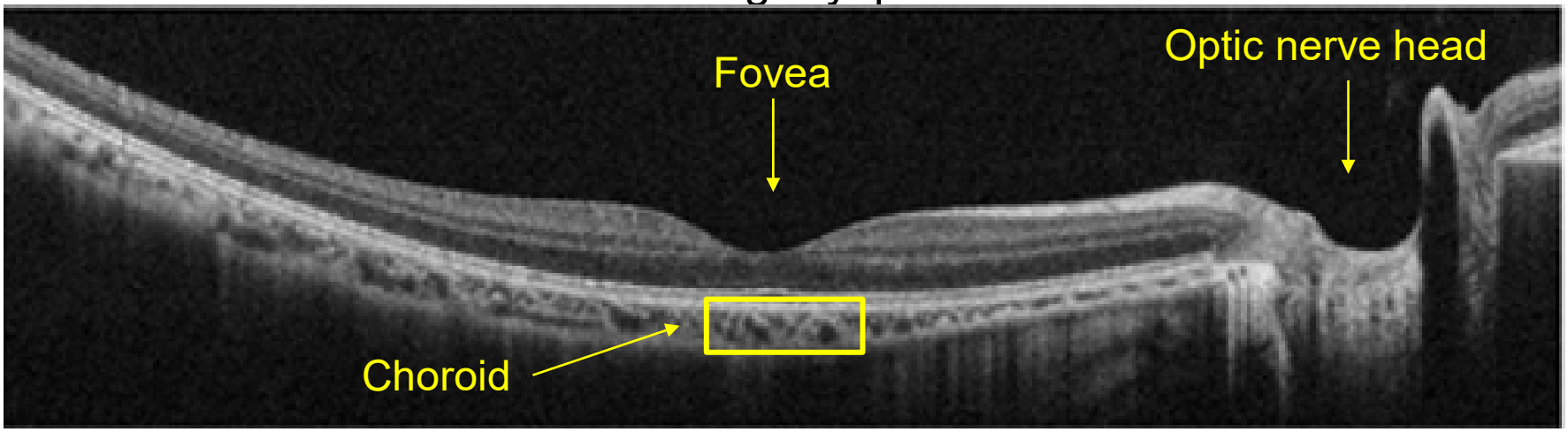
Choroid anatomy

- Normal choroidal thickness between 200-400 microns
- Small capillaries (choriocapillaris), then larger vessels deeper (towards sclera)
- Comprised mostly of blood vessels, but some smooth muscle
- Choroid naturally thins with age
- Choroid is thinner with increasing myopia

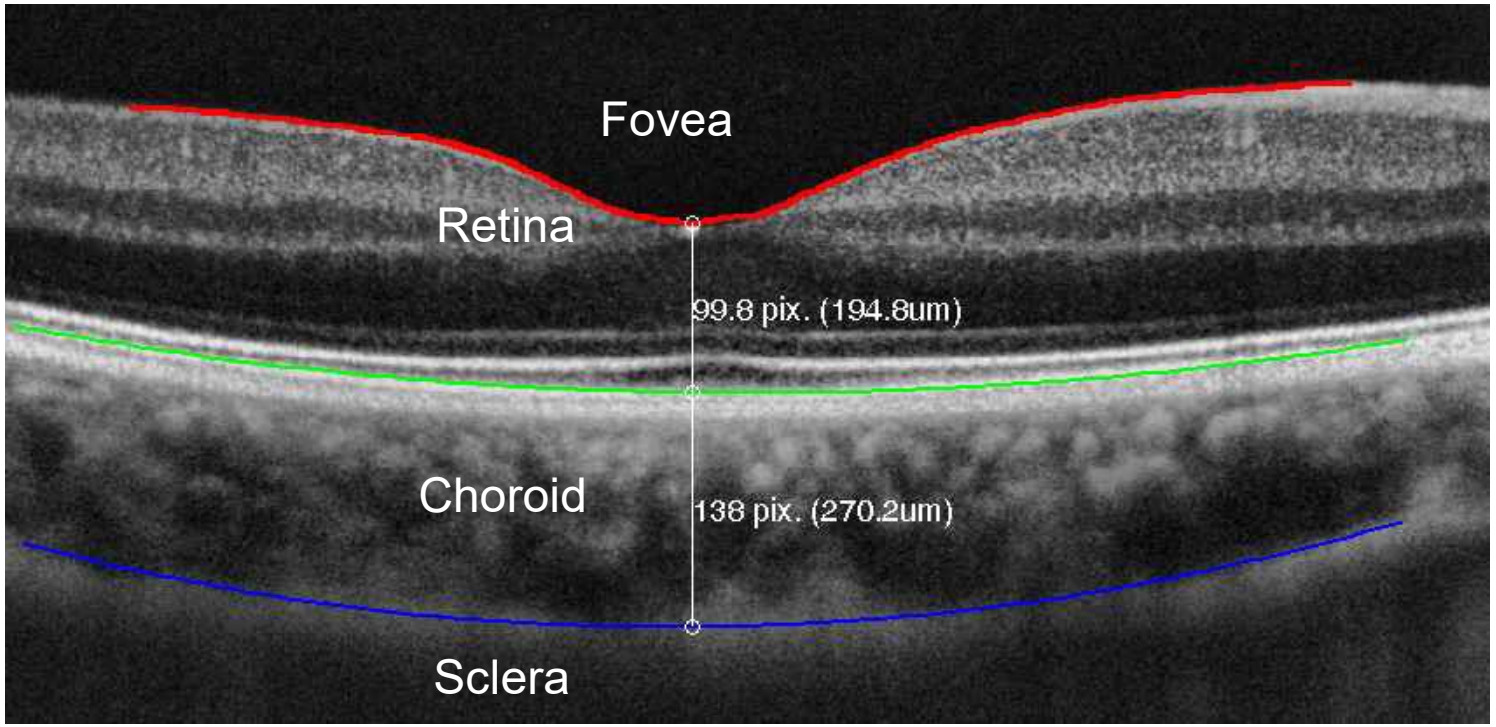
Zhang 1994





Measuring choroidal thickness

- Optical coherence tomography
  - Spectral domain (resolution ~3-5 microns)
- Optical low coherence reflectometry
  - Lenstar optical biometer (resolution ~6-7 microns)



Myopia: Animal Research

- Research with animal models shows that eye growth can be influenced by vision and optical focus
- The principle of emmetropization
  - The eye actively grows to focus light on the retina
  - Lens induced blur
    - Hyperopic (minus) and myopic (plus) lens blur have predictable effects
  - Form deprivation
    - Created by lid suture, translucent occluder, diffuser
    - Lack of clear vision typically causes myopia

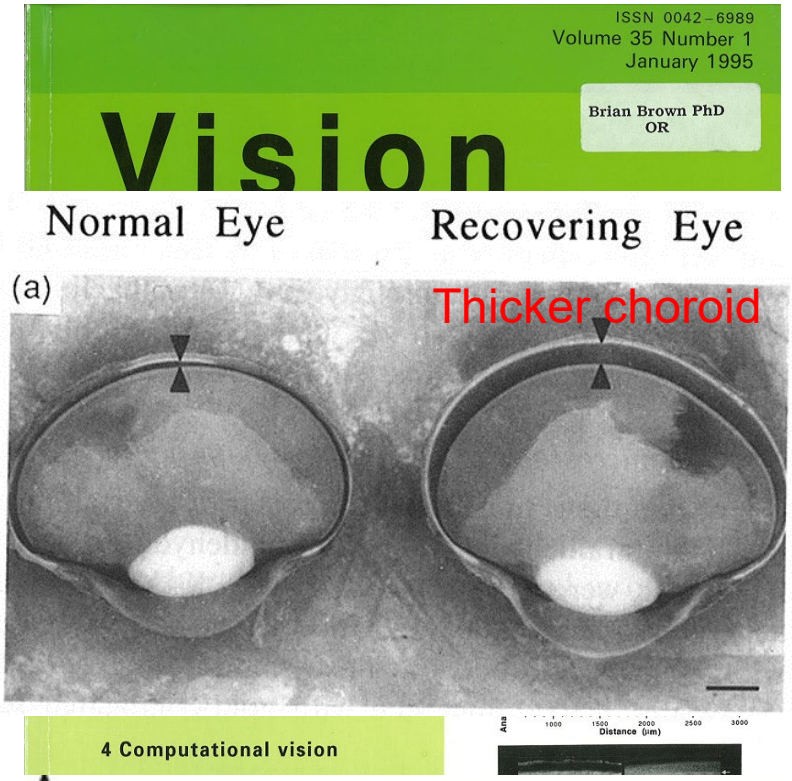
Smith EL

Shen & Sivak, 2007

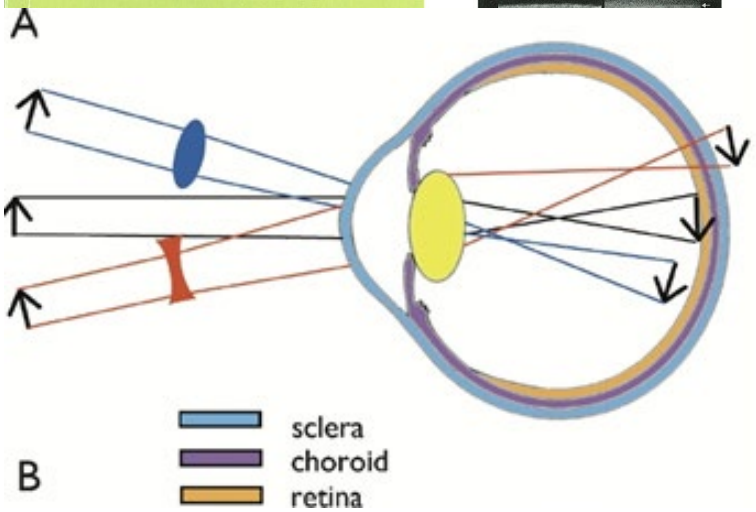
Howlett & McFadden 2006

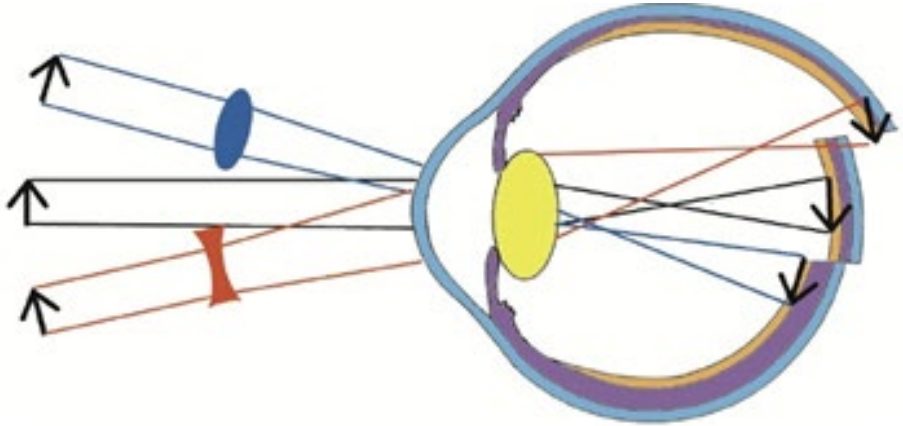
Wildsoet, CF

Optical/form blur and choroidal response in chicks



- Two mechanisms modulate the response:
  - 1. Choroid thickness
    - Rapid, within minutes
  - 2. Scleral remodeling
    - Slower, within hours to days

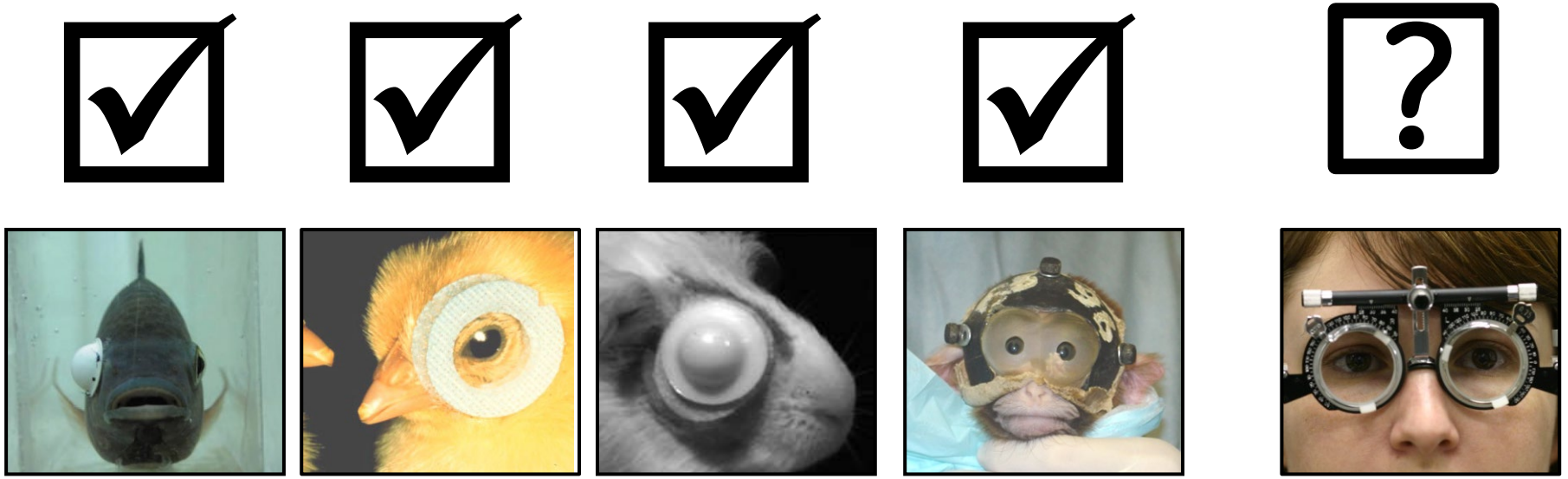




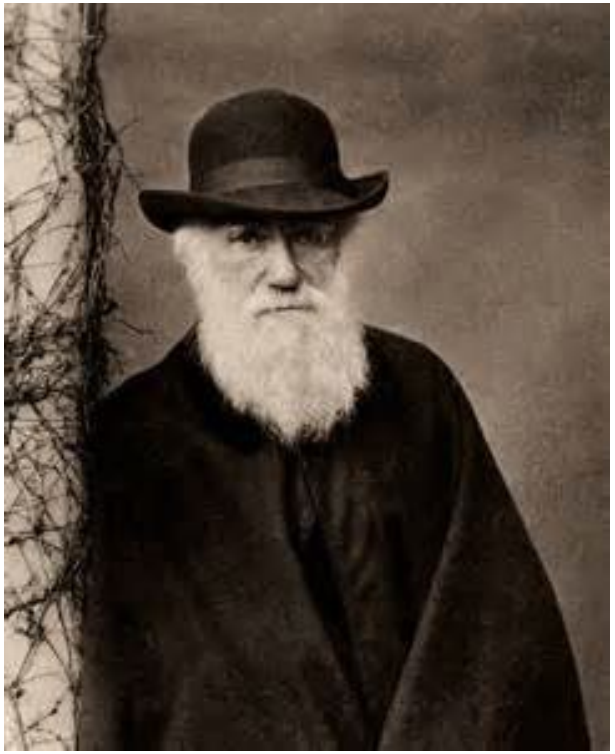
Wallman & Winawer 2004

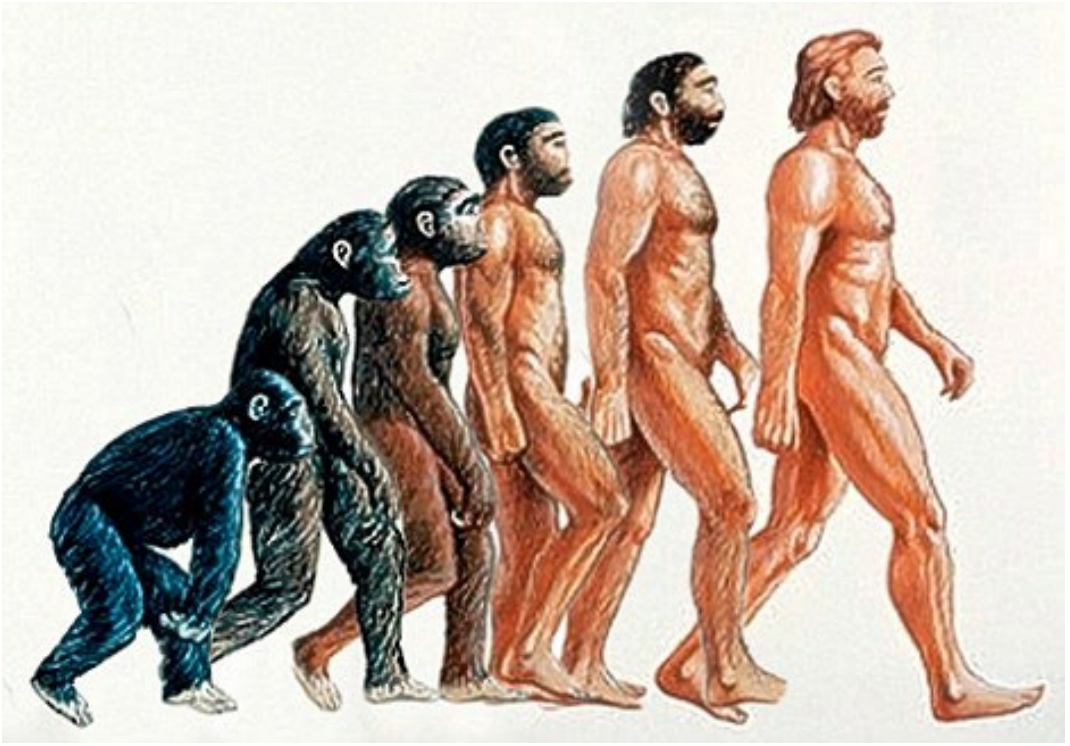
Majority of knowledge regarding visually guided eye growth is from animal research

But does imposing optical defocus upon young adult **human** subjects also lead to short term changes in axial length and the choroid?



EVOLUTION

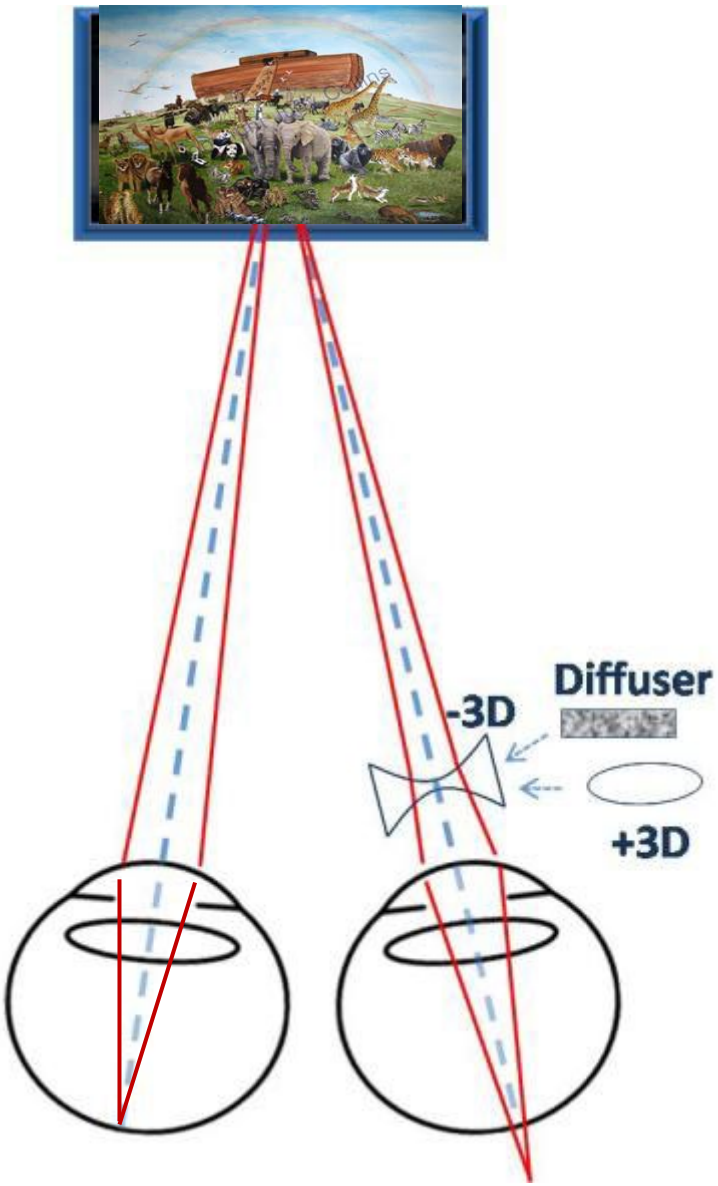




DIVINE CREATION

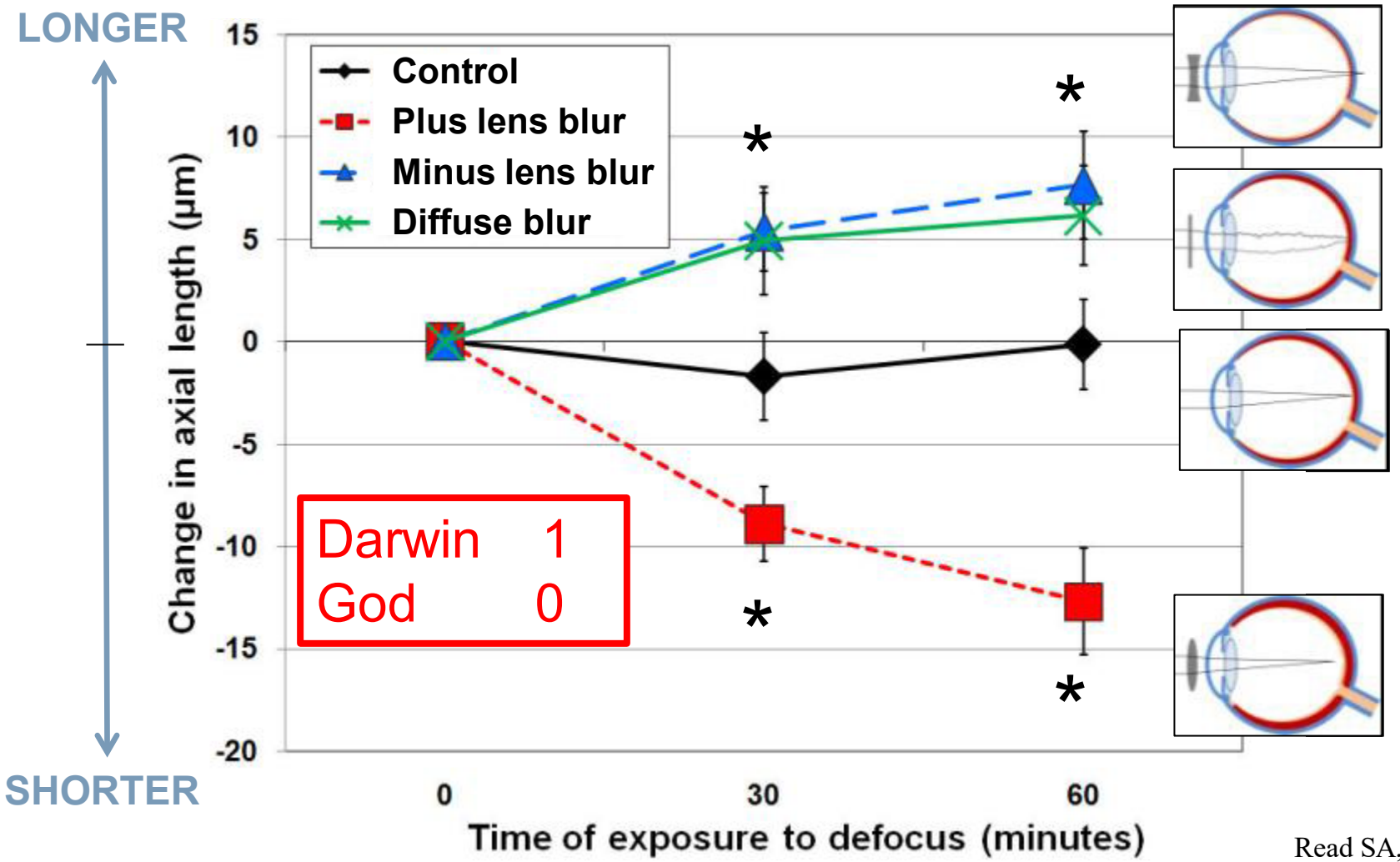
Eye length (choroidal thickness) and optical blur

- 28 young adult subjects
  - 14 myopes and 14 emmetropes
- 20 mins “washout”
- 60 minutes of monocular spectacle lens ‘blur’ conditions
  - Fellow eye in focus
  - Tested eye -3 D, +3 D and diffuser
- Axial length and choroidal thickness measured with Lenstar
  - Before, during and after the blur



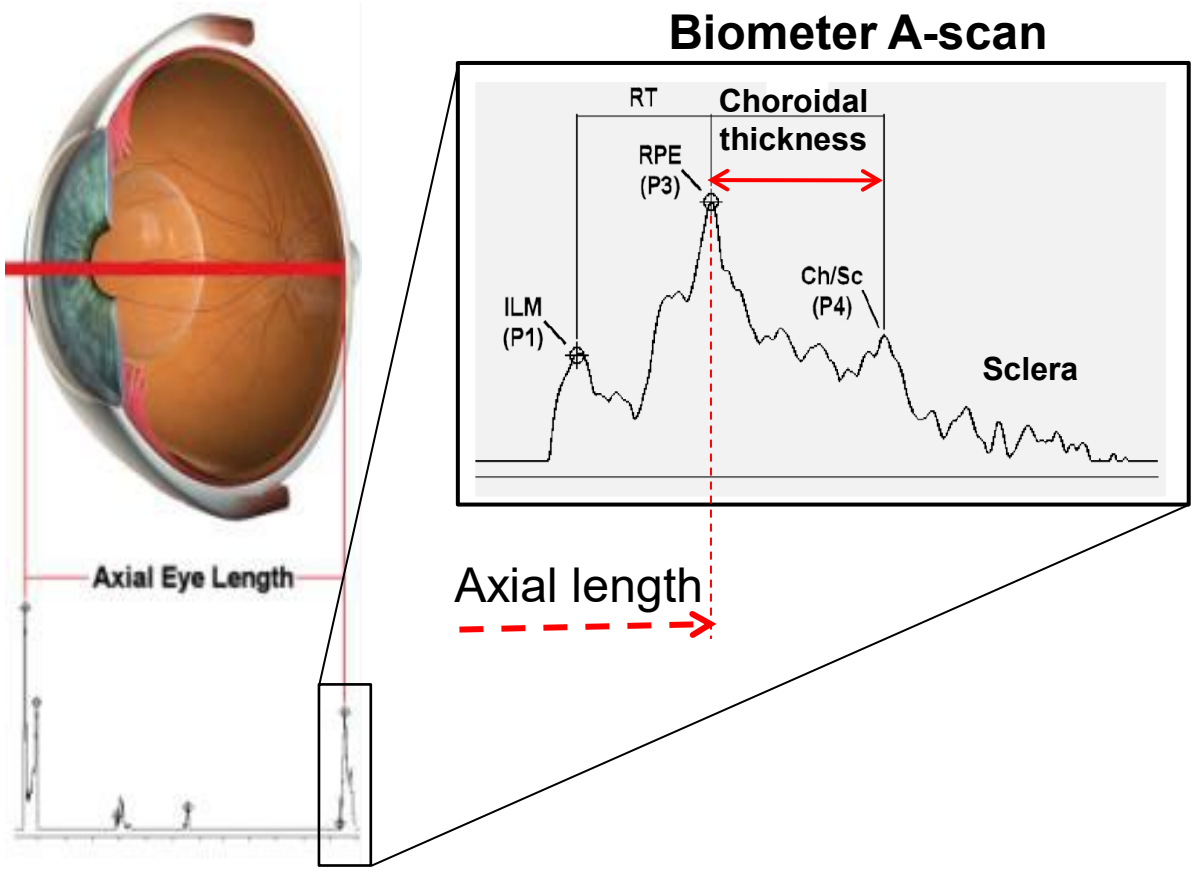
Read SA, Collins MJ and Sander B. *Human optical axial length and defocus.* **Investigative Ophthalmology and Visual Science** 2010; 51(12): 6262-6269.

Eye length and optical blur

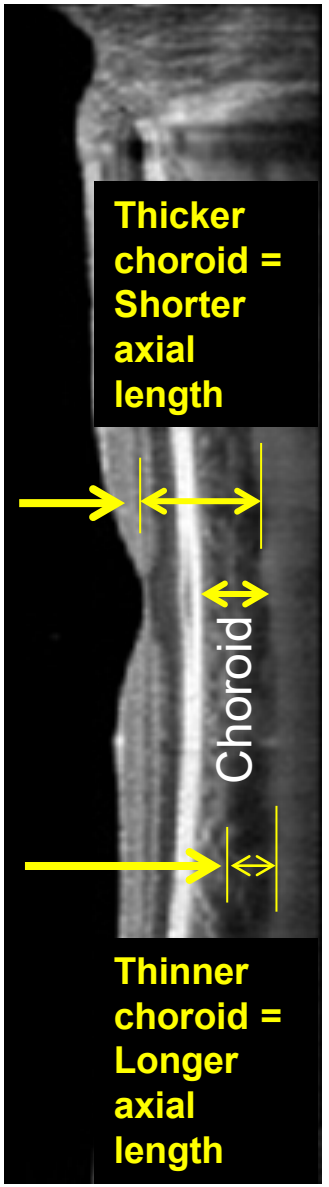


Read SA, Collins MJ, Sander BP. *Human optical axial length and defocus*. **IOVS**. 2010:51;6262-9

Measuring human axial length and choroidal thickness

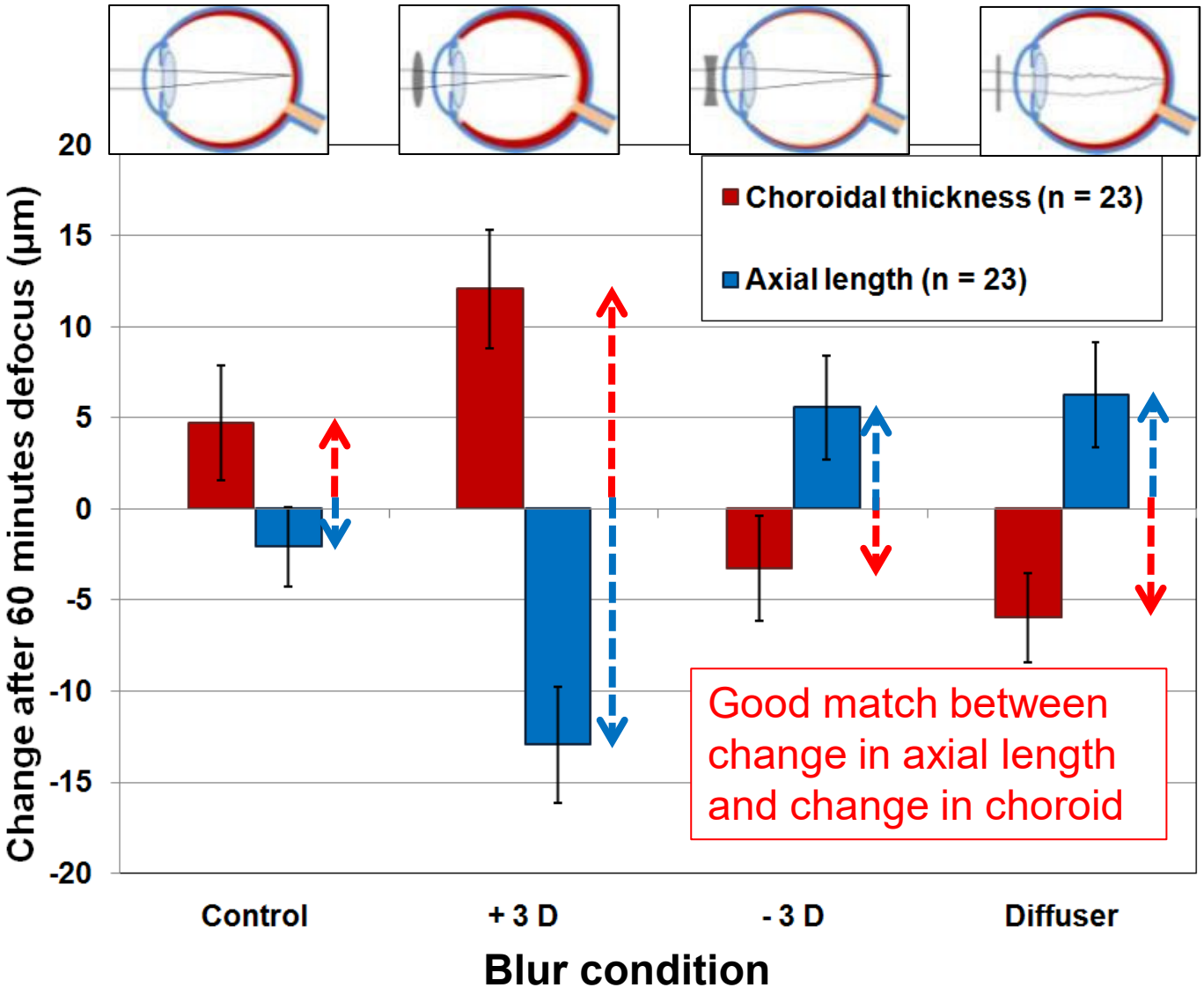


OCT scan



- Biometer measures of axial length (AxL)
  - Distance from surface of the cornea to the retinal pigment epithelium
  - If the sclera and cornea are considered to not move:
  - Then changes in choroid thickness lead to changes in axial length
  - Choroid thickens the RPE moves forward (AxL shortens)
  - Choroid thins the RPE moves backwards (AxL lengthens)

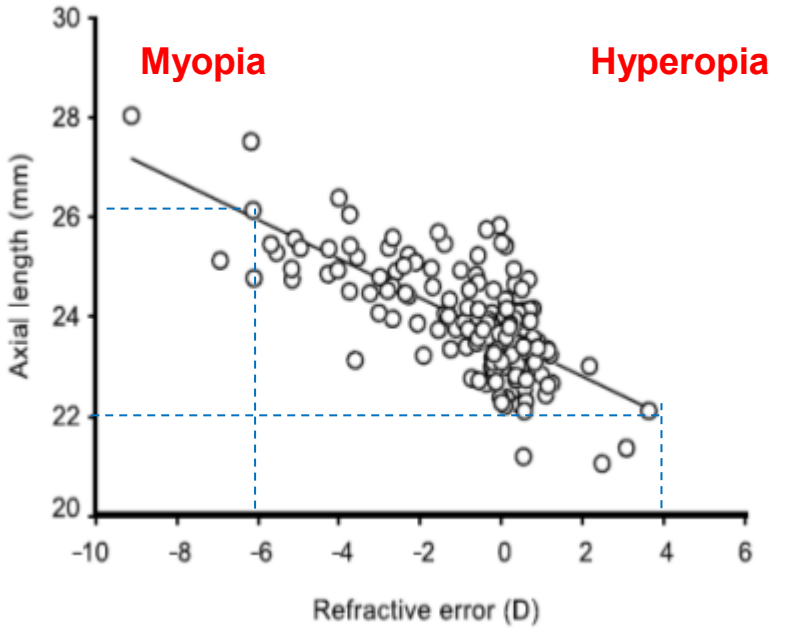
Choroidal thickness and optical blur



Axial Length Longer
Choroid Thicker

Choroid Thinner
Axial Length Shorter

Optical effect of choroidal changes



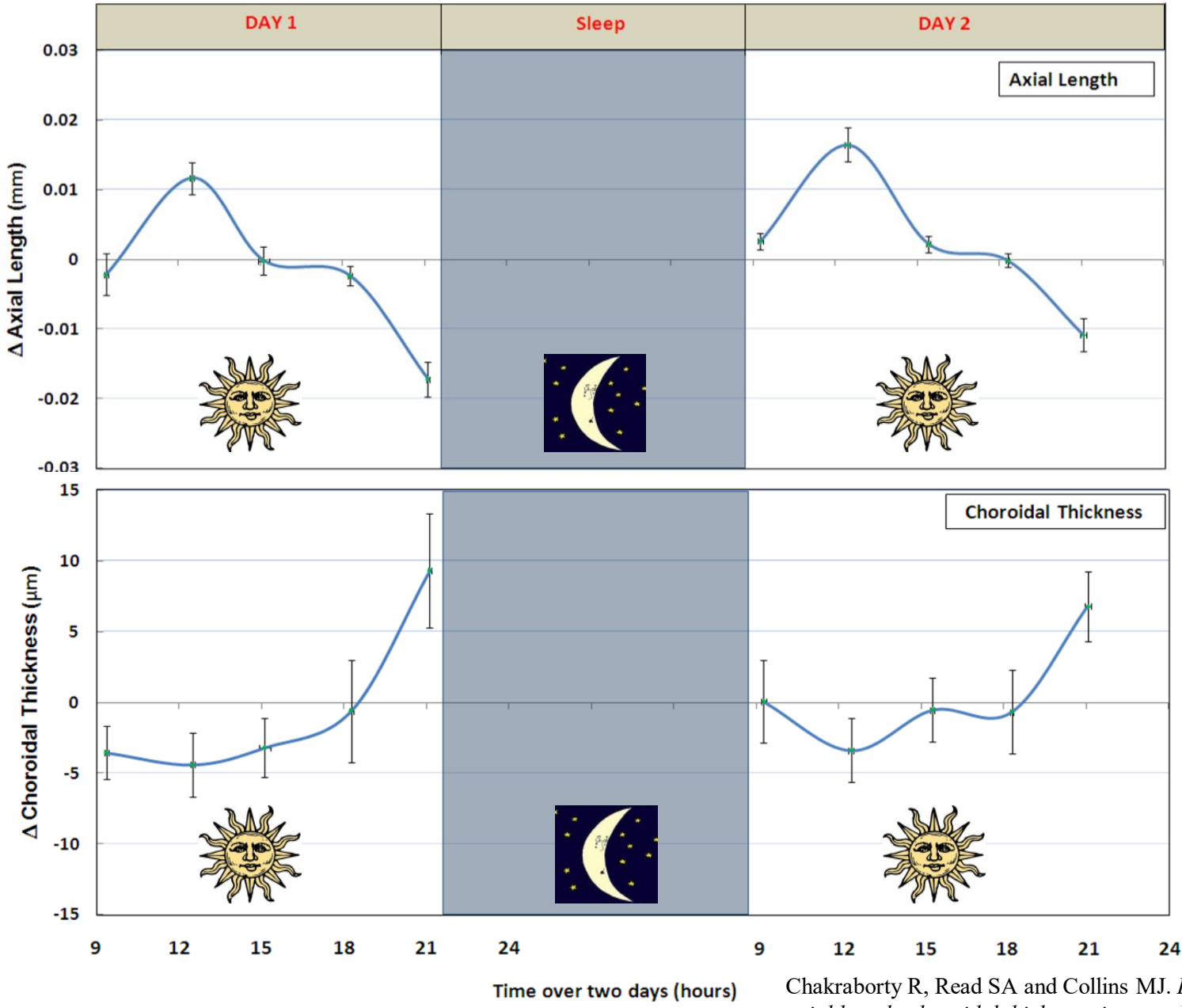
Gilmartin, 2004

10 D = 4 mm
0.25 D = 100 microns
0.05 D = 20 microns

- Normal choroidal thickness is between 200-400 microns
- Maximum changes observed in short-term human studies are ~20-30 microns
- So the optical effects of the axial length changes are very small ~0.05 – 0.07 D
- Therefore the change in choroidal thickness does not appear to be a form of “accommodation” to improve vision (even though it moves the photoreceptors towards the focus)

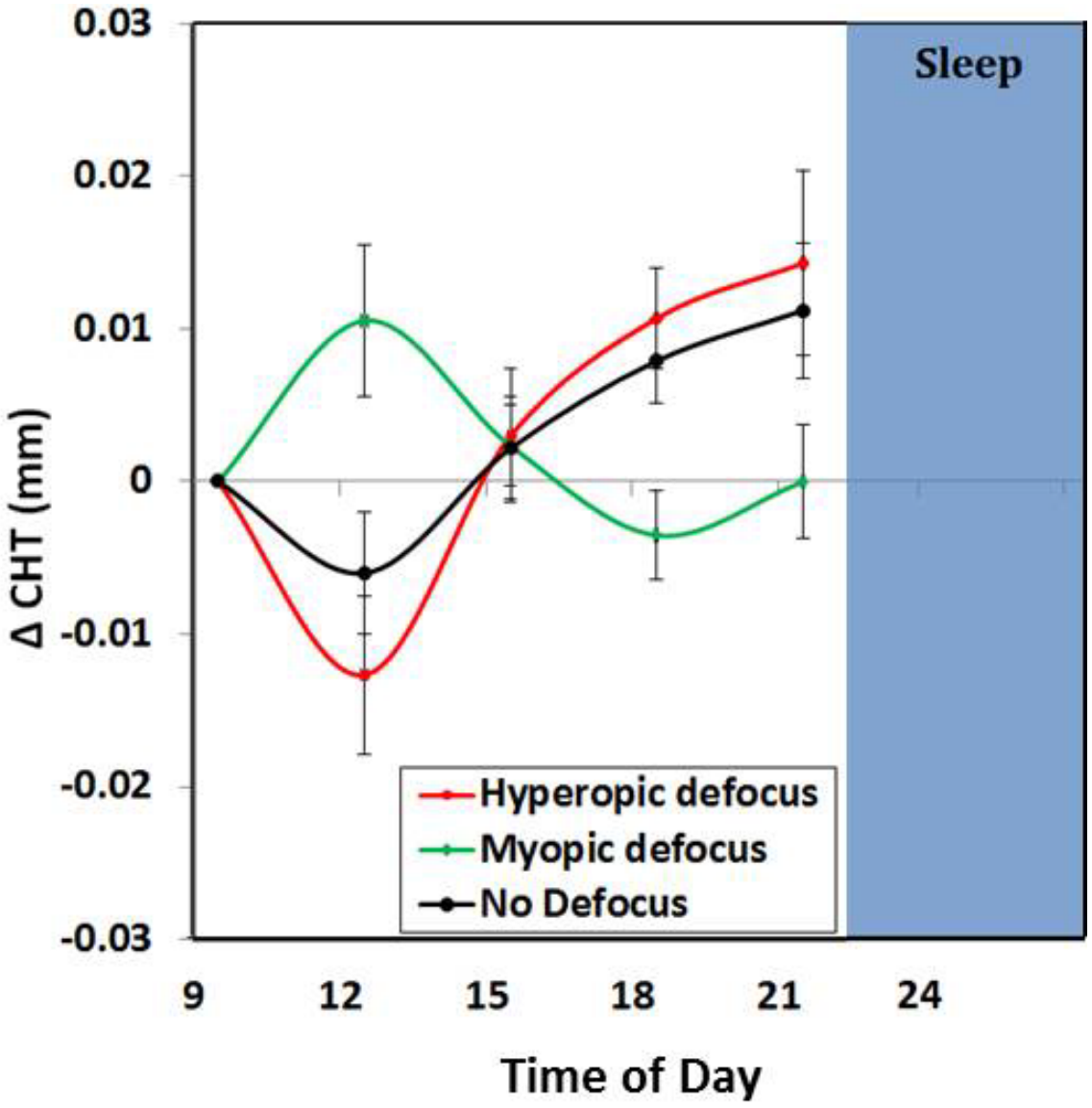
Best guess:
The changes appear to reflect an intermediate step in the process that signals the stimuli from the retina to the sclera to control eye growth (ie. biomarker)

NORMAL DIURNAL RHYTHMS – AXIAL AND CHOROID



Chakraborty R, Read SA and Collins MJ. *Diurnal variations in axial length, choroidal thickness, intraocular pressure and ocular biometrics*. **Investigative Ophthalmology and Visual Science** 2011; 52(8): 5121-5129.

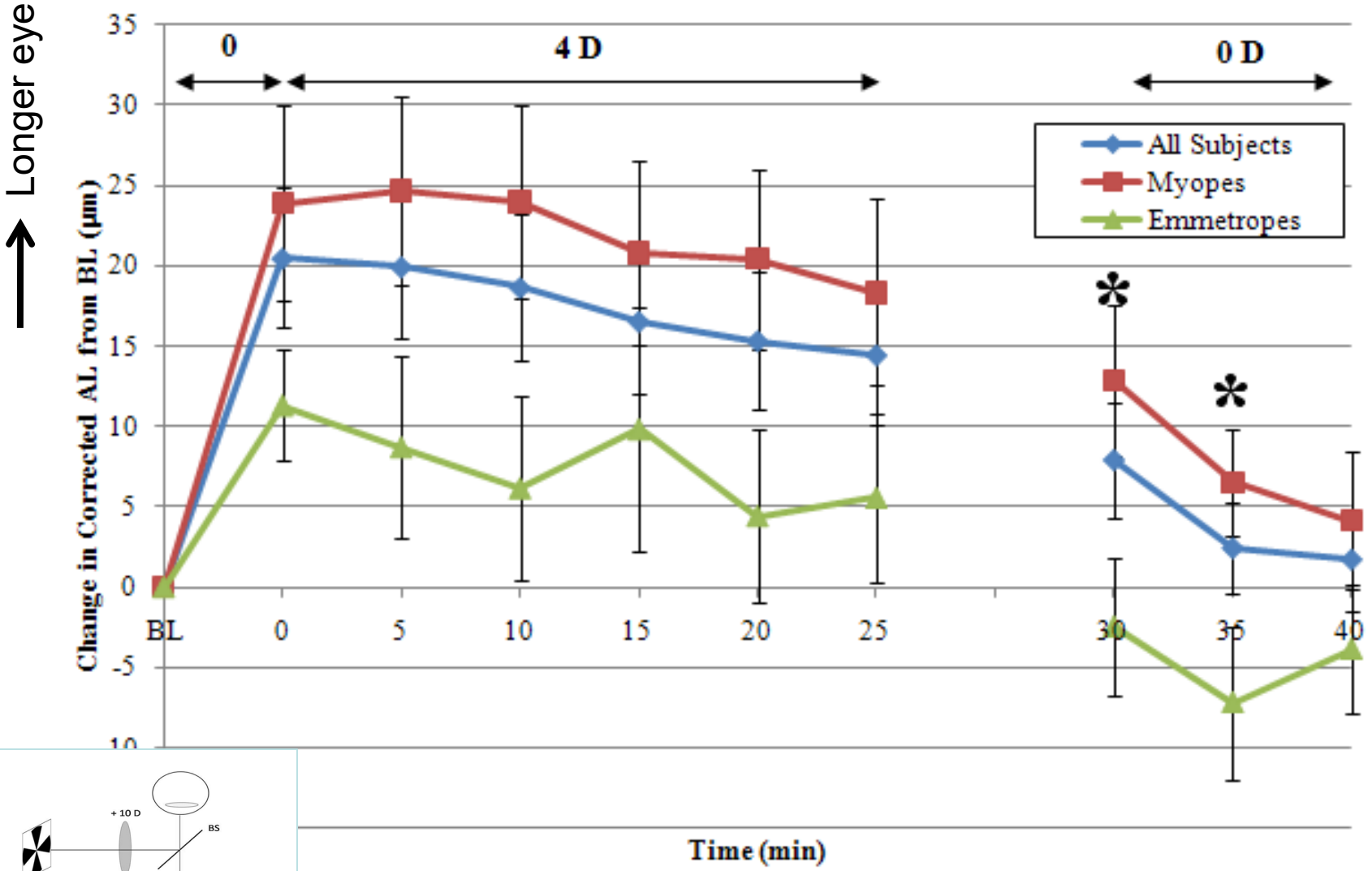
EFFECT OF DEFOCUS ON DIURNAL RHYTHMS

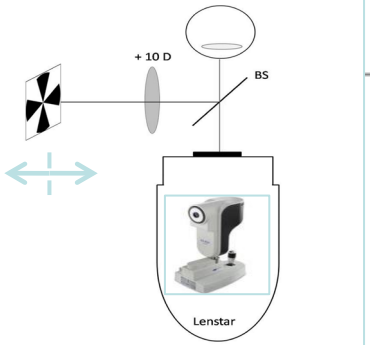


Chakraborty R, Read SA and Collins MJ. *Monocular myopic defocus and daily changes in axial length and choroidal thickness of human eyes*. **Experimental Eye Research** 2012; 103: 47-54.

Chakraborty R, Read SA and Collins MJ. *Hyperopic defocus and diurnal changes in human choroid and axial length*. **Optometry and Vision Science** 2013; 90(11): 1187-1198.

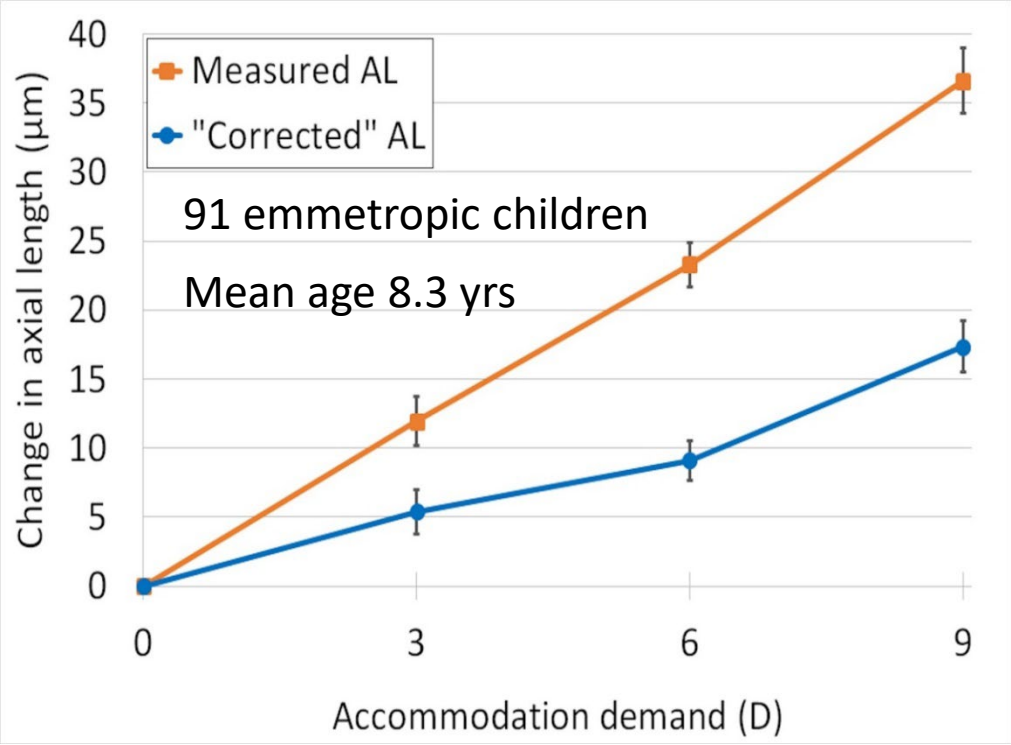
Effect of accommodation on axial length (adults)

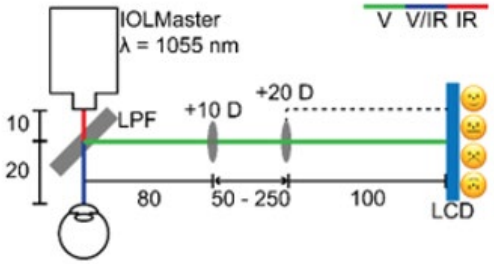


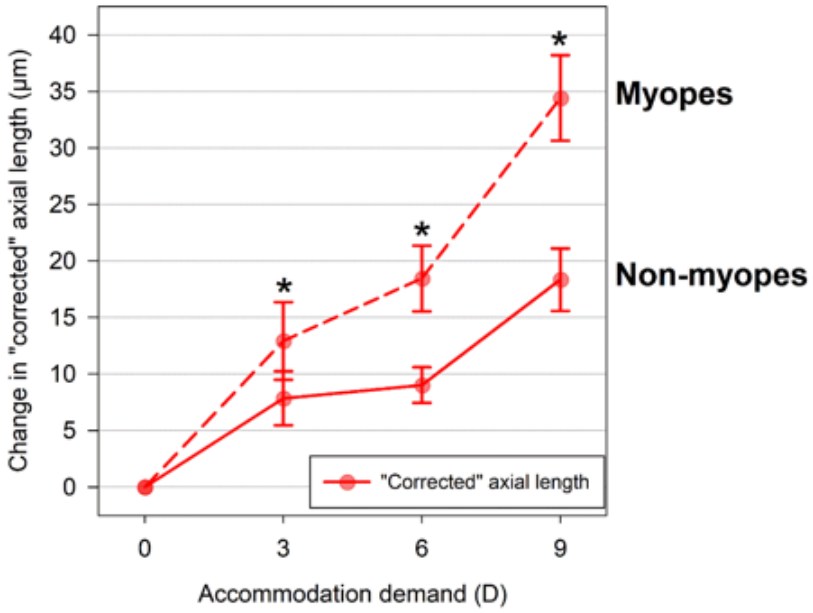


Woodman EC, Read SA and Collins MJ. Axial length and choroidal thickness changes accompanying prolonged accommodation in myopes and emmetropes. Vision Research 2012; 72: 34-41.

Accommodation related changes in axial length in children





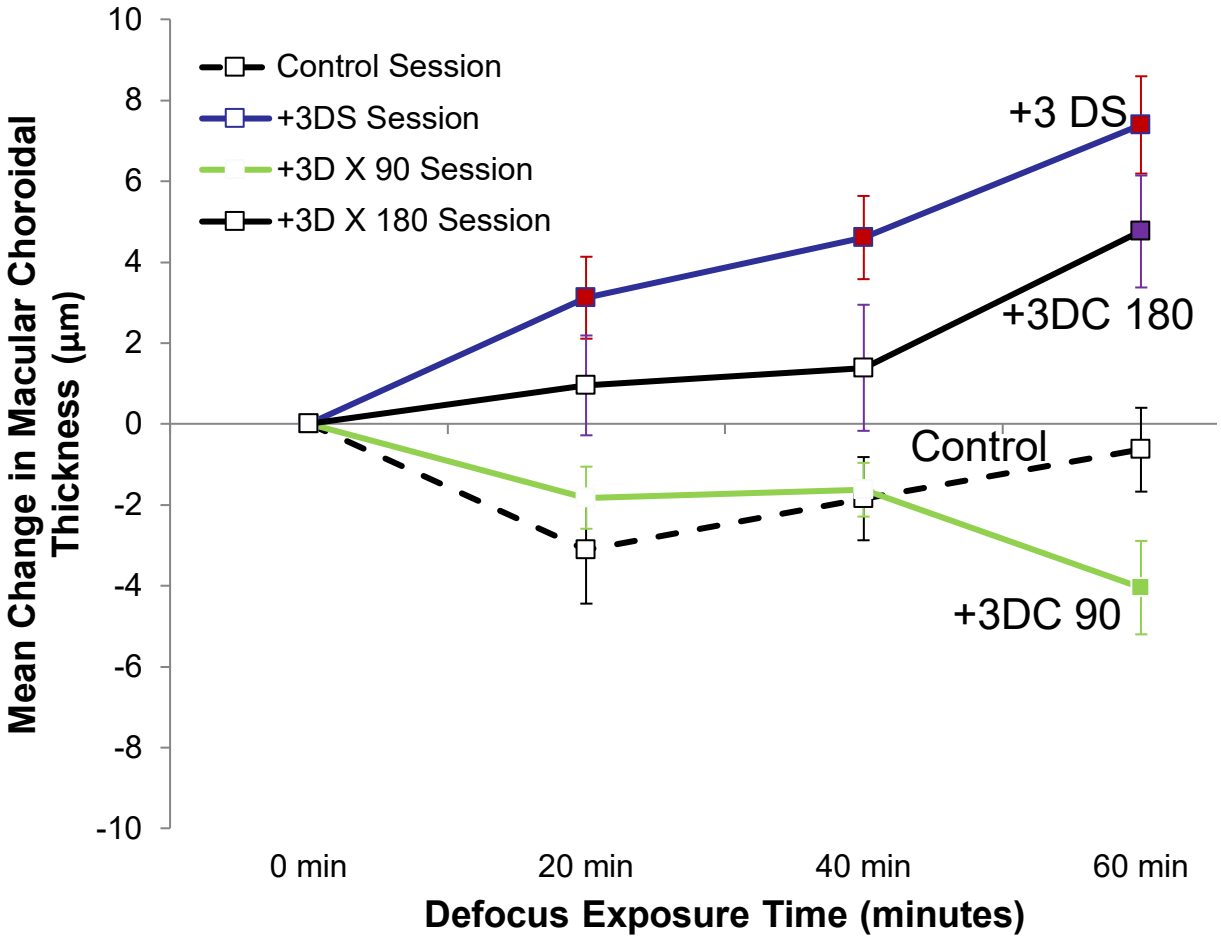


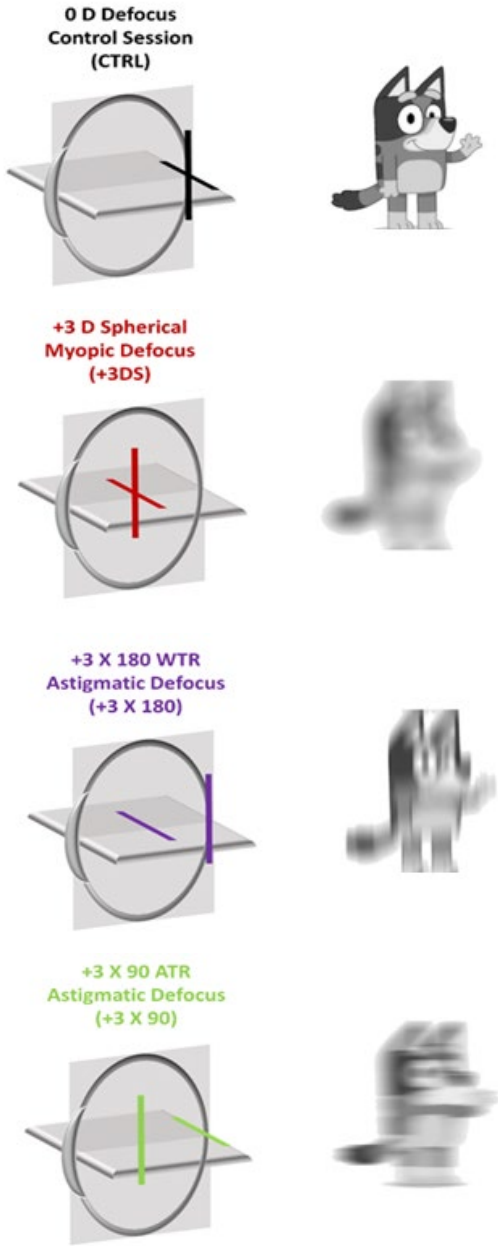
Correction required for increased lens thickness during accommodation.

Hughes RPJ, Read SA, Collins MJ and Vincent SJ. *Changes in ocular biometry during short-term accommodation in children.* **Ophthalmic and Physiological Optics** 2020; 40: 584–594.

Hughes RPJ, Read SA, Collins MJ and Vincent SJ. *Axial elongation during short-term accommodation in myopic and non-myopic children*. **Investigative Ophthalmology and Visual Science** 2022; 63(3): 12.

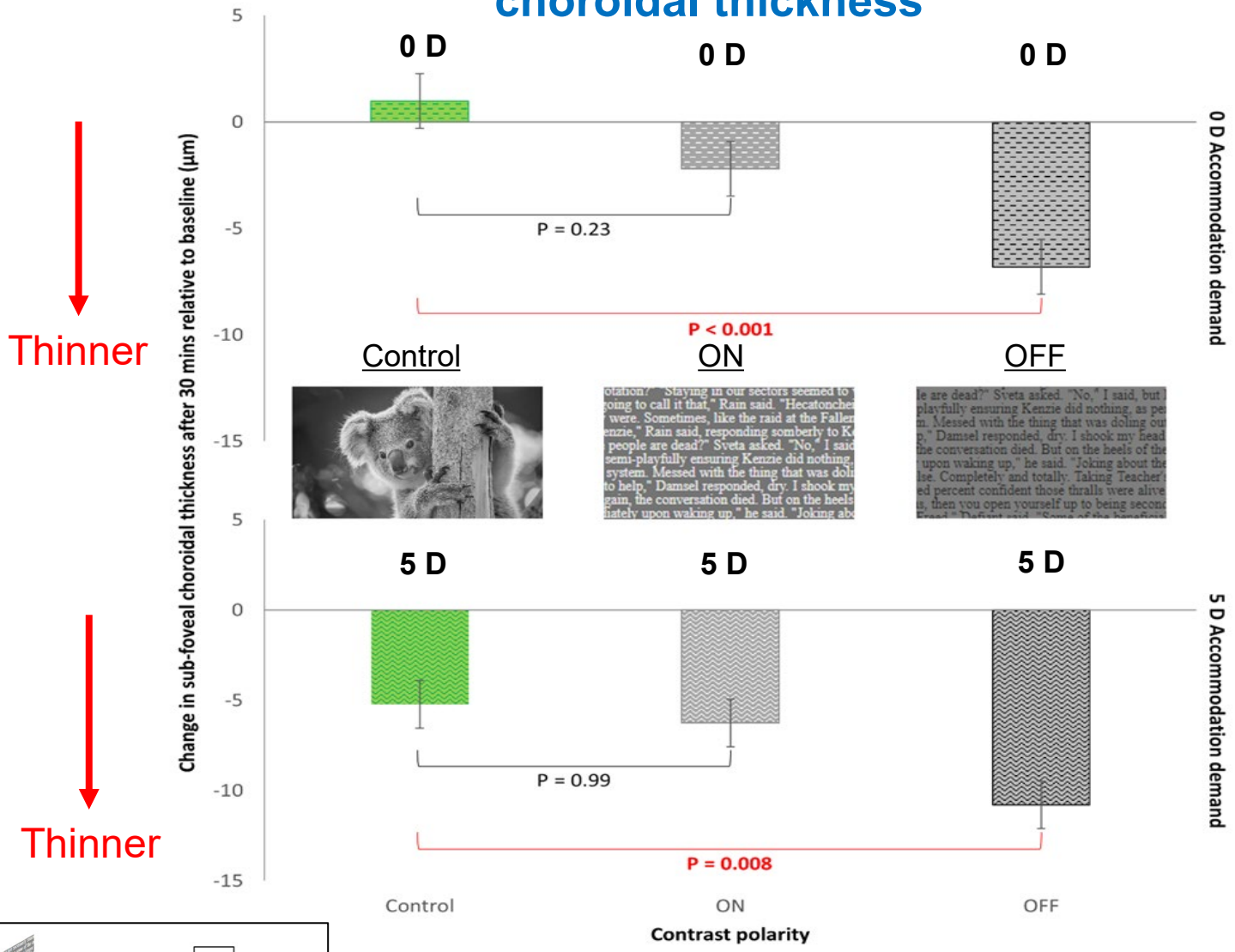
Choroidal thickness changes with imposed astigmatic defocus





Yazdi HH, Read SA, Vincent SJ and Collins MJ. *Astigmatic defocus leads to short-term changes in human choroidal thickness.* **Investigative Ophthalmology and Visual Science** 2020; 61(8): 48.

Retinal ON/OFF pathway activation and accommodation-induced choroidal thickness

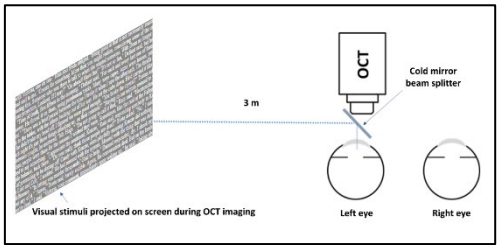


Thinner

Thinner

0 D accommodation

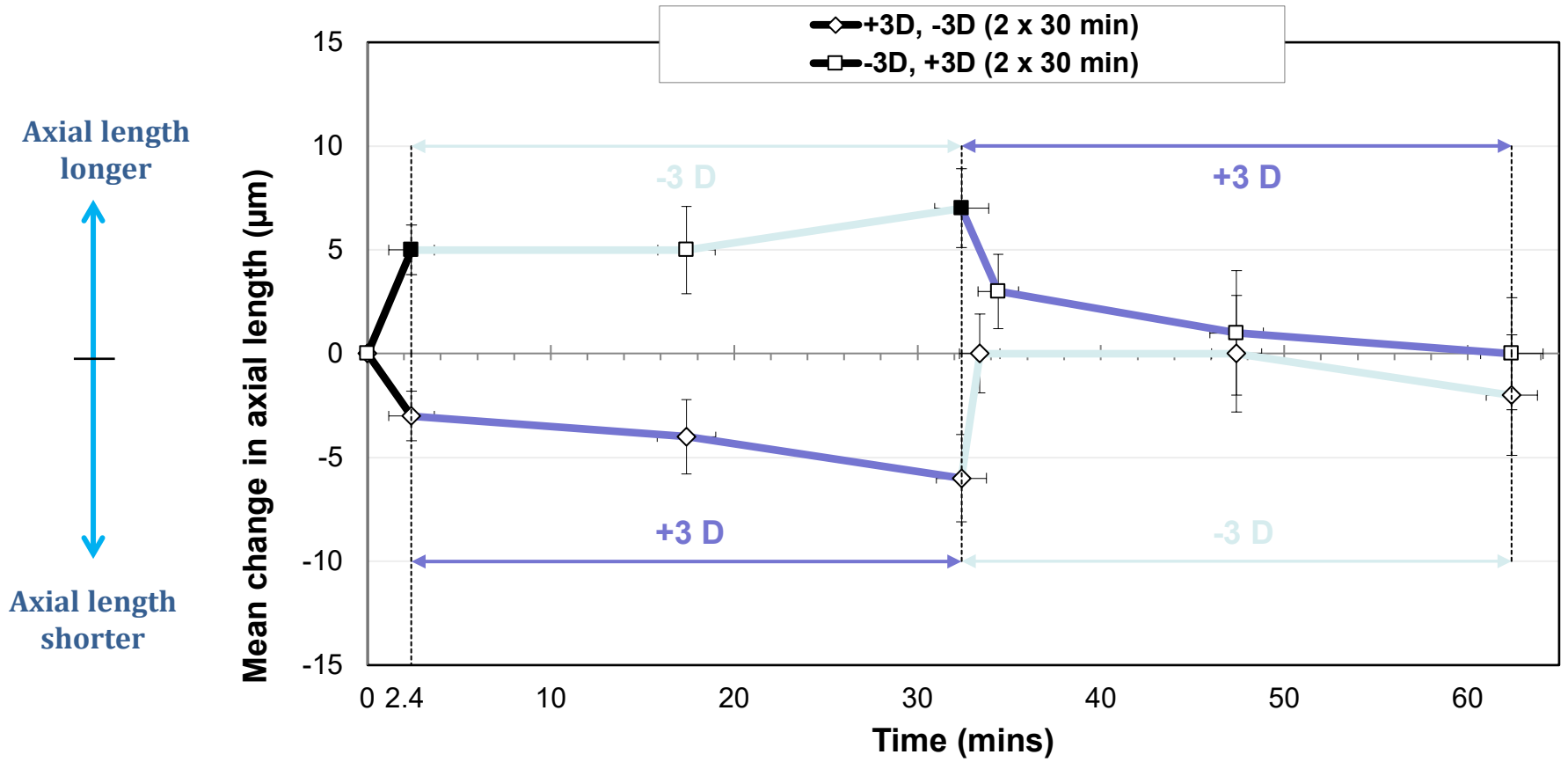
5 D accommodation



Hoseini-Yazdi H, Read SA, Alonso-Caneiro D and Collins MJ. *Retinal OFF-pathway overstimulation leads to greater accommodation-induced choroidal thinning.* **Investigative Ophthalmology and Visual Science** 2021; 62(13):5.

Temporal integration

Axial length during alternating defocus 30 min cycles

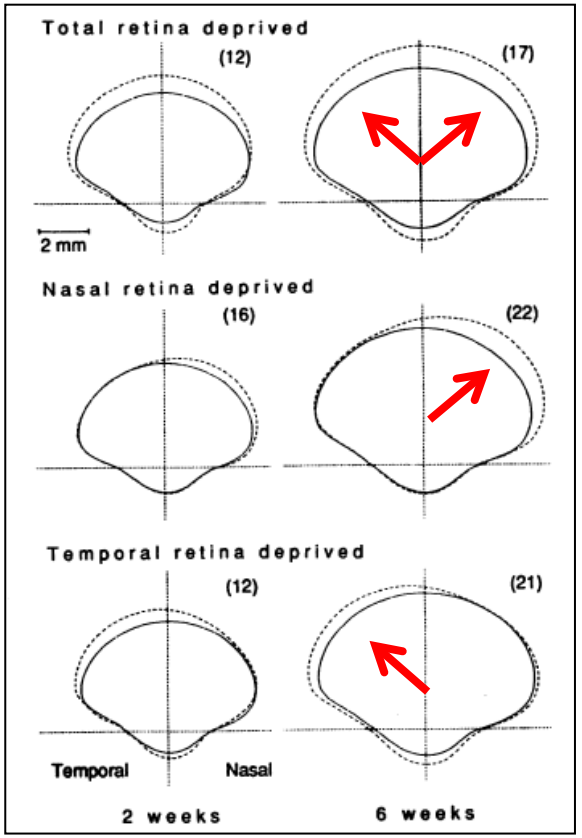


Delshad S, Collins MJ, Read SA and Vincent SJ. *The human axial length and choroidal thickness responses to continuous and alternating episodes of myopic and hyperopic blur*. **PLoS ONE** 2020; 15(12): e0243076

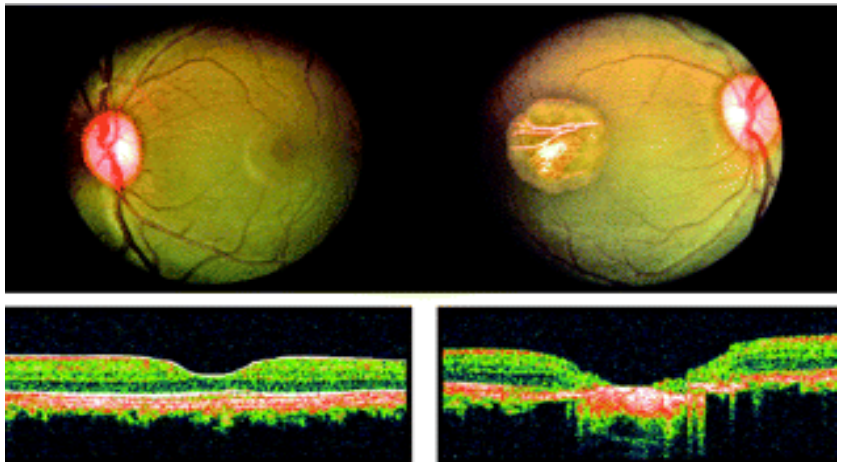
At 30-min alternating frequency, myopic and hyperopic defocus of equal duration effectively cancel the preceding effects on axial length

Peripheral retina theory

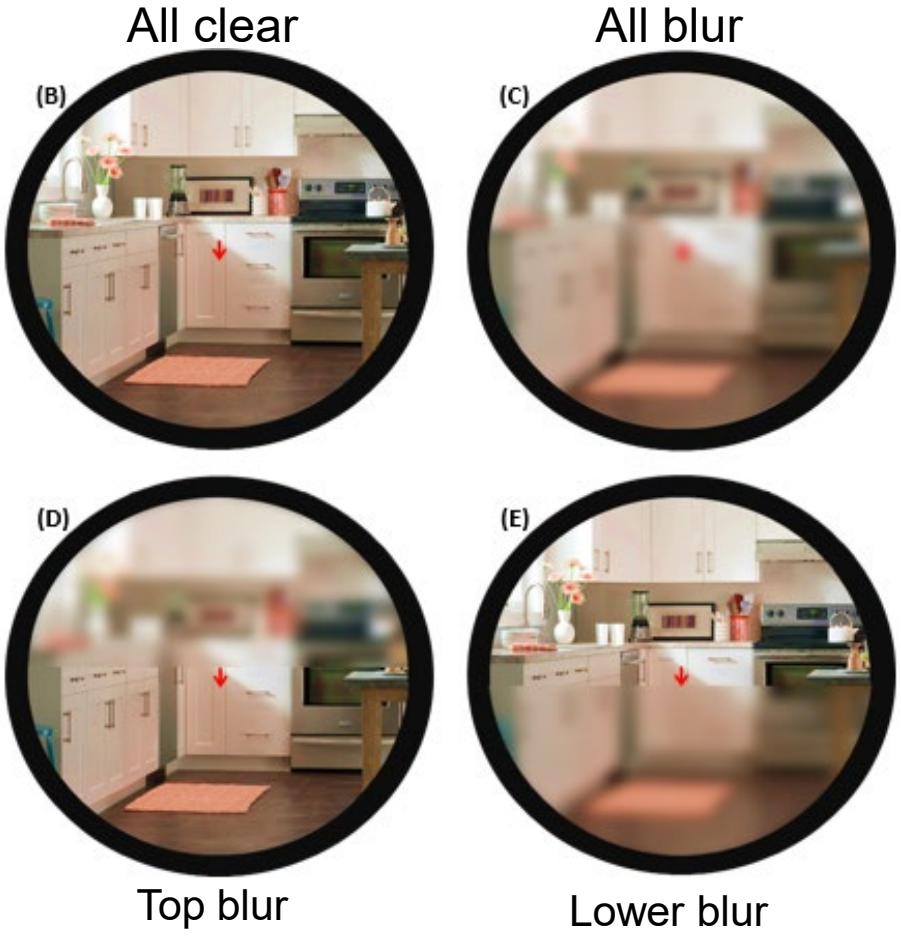
- Local regions of the eye can control local eye growth.
  - After inducing form deprivation in half the visual field/retina of chicks, only that region of the eye grew.
  - Wallman et al 1987
  - Diether and Schaeffel 1997



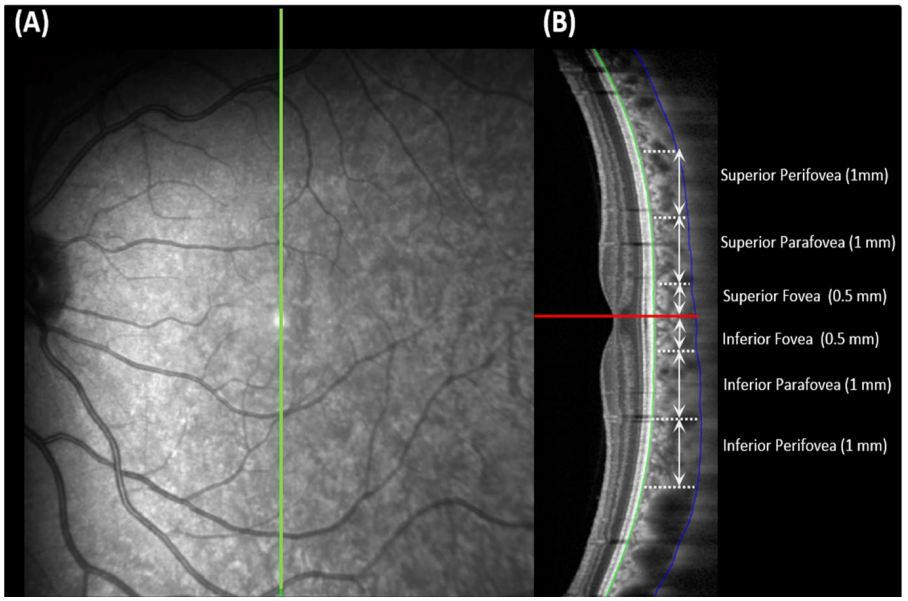
- The peripheral retina, without the fovea, can regulate eye growth.
  - After ablating the fovea, the monkey eyes still grew in response to hyperopic defocus
  - Smith et al 2005 and 2007



Exposure of half the retina to blur (hemifield)



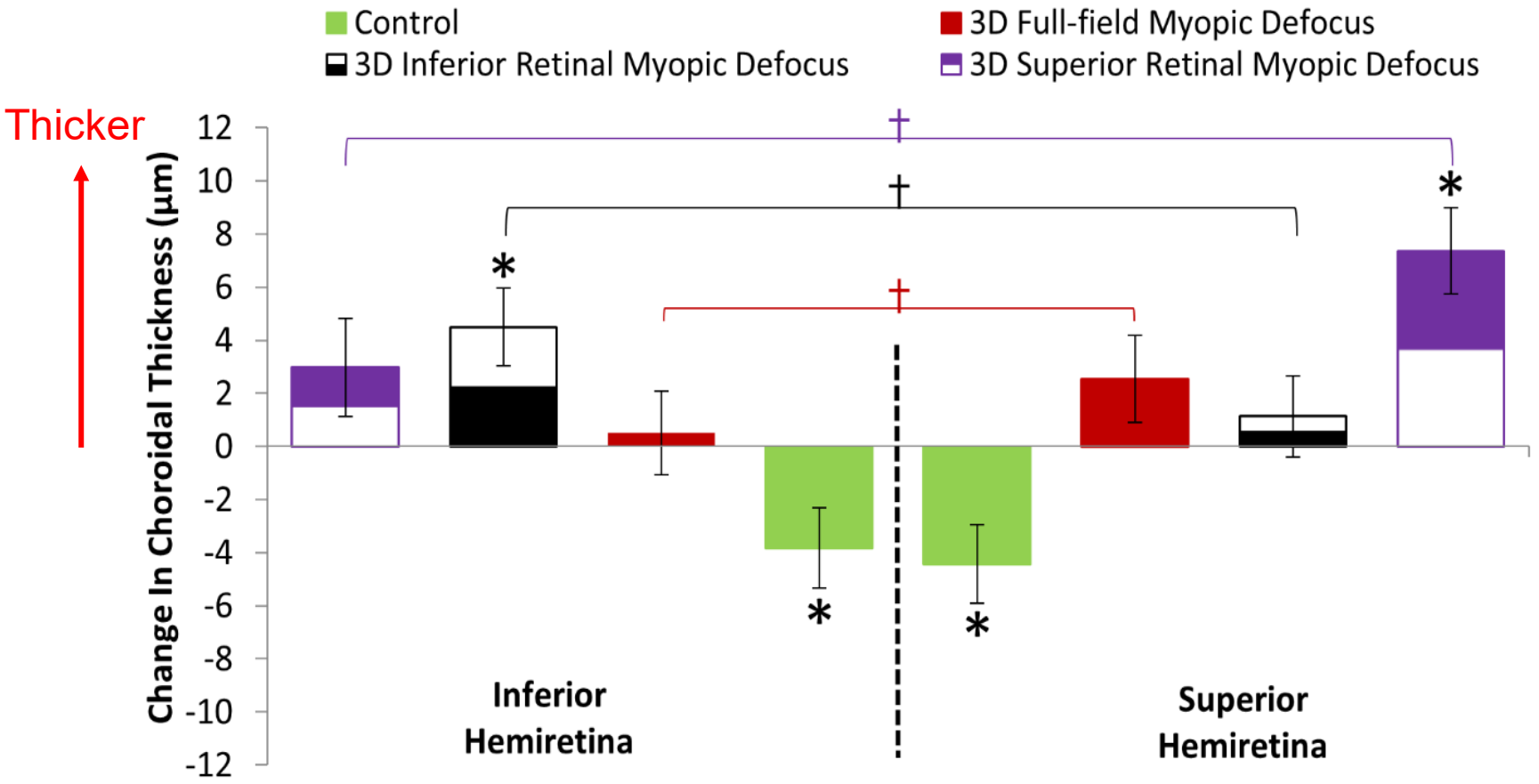
Graphical representation of a visual scene viewed through the Badal optometer and cold mirror system mounted on the OCT instrument during each of the defocus sessions. Subject fixated red arrow continuously (feedback).

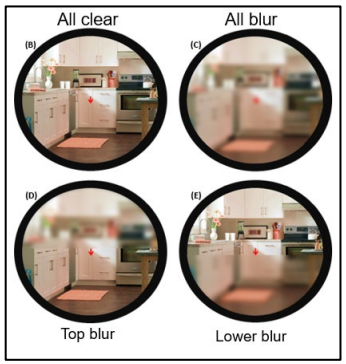


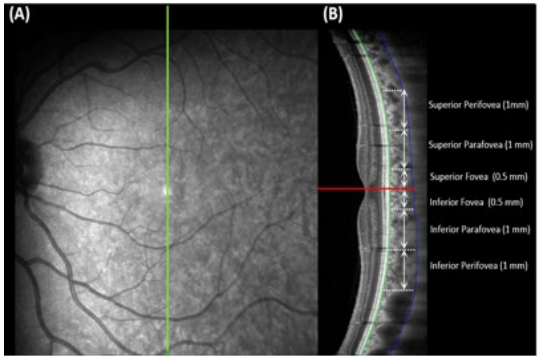
The en-face retinal (A) and B-scan image (B) of a representative subject demonstrating the position of the trans-foveal vertical EDI-OCT line scan (green vertical line in A), the foveal pit as manually marked in the custom written software (horizontal red line in B), and the anterior (green line in the B-scan image) and posterior (blue line in the B-scan image) boundaries of the choroid.

Hoseini-Yazdi H, Vincent SJ, Collins MJ and Read SA. *Regional alterations in human choroidal thickness in response to short-term monocular hemifield myopic defocus*. **Ophthalmic and Physiological Optics** 2019; 39(3): 172-182.

Change in choroidal thickness with hemifield blur







Hoseini-Yazdi H, Vincent SJ, Collins MJ and Read SA. *Regional alterations in human choroidal thickness in response to short-term monocular hemifield myopic defocus*. **Ophthalmic and Physiological Optics** 2019; 39(3): 172-182.

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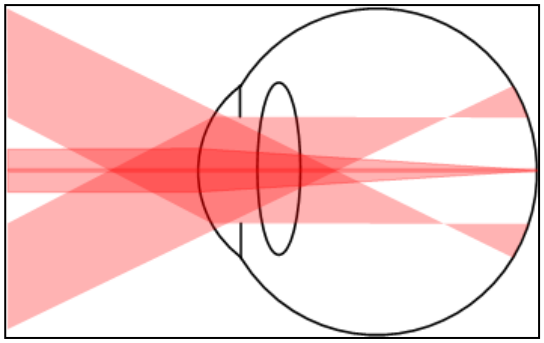
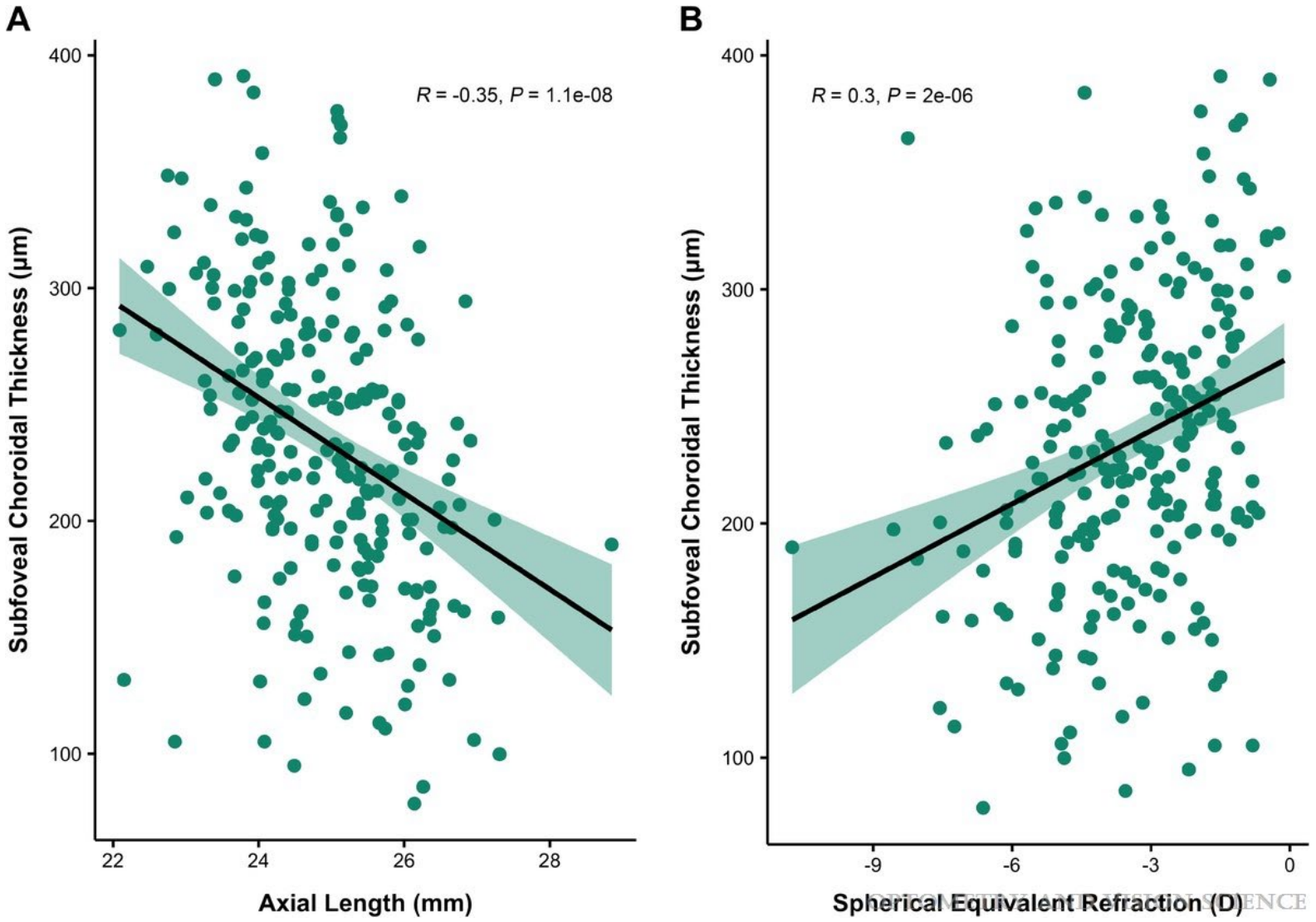
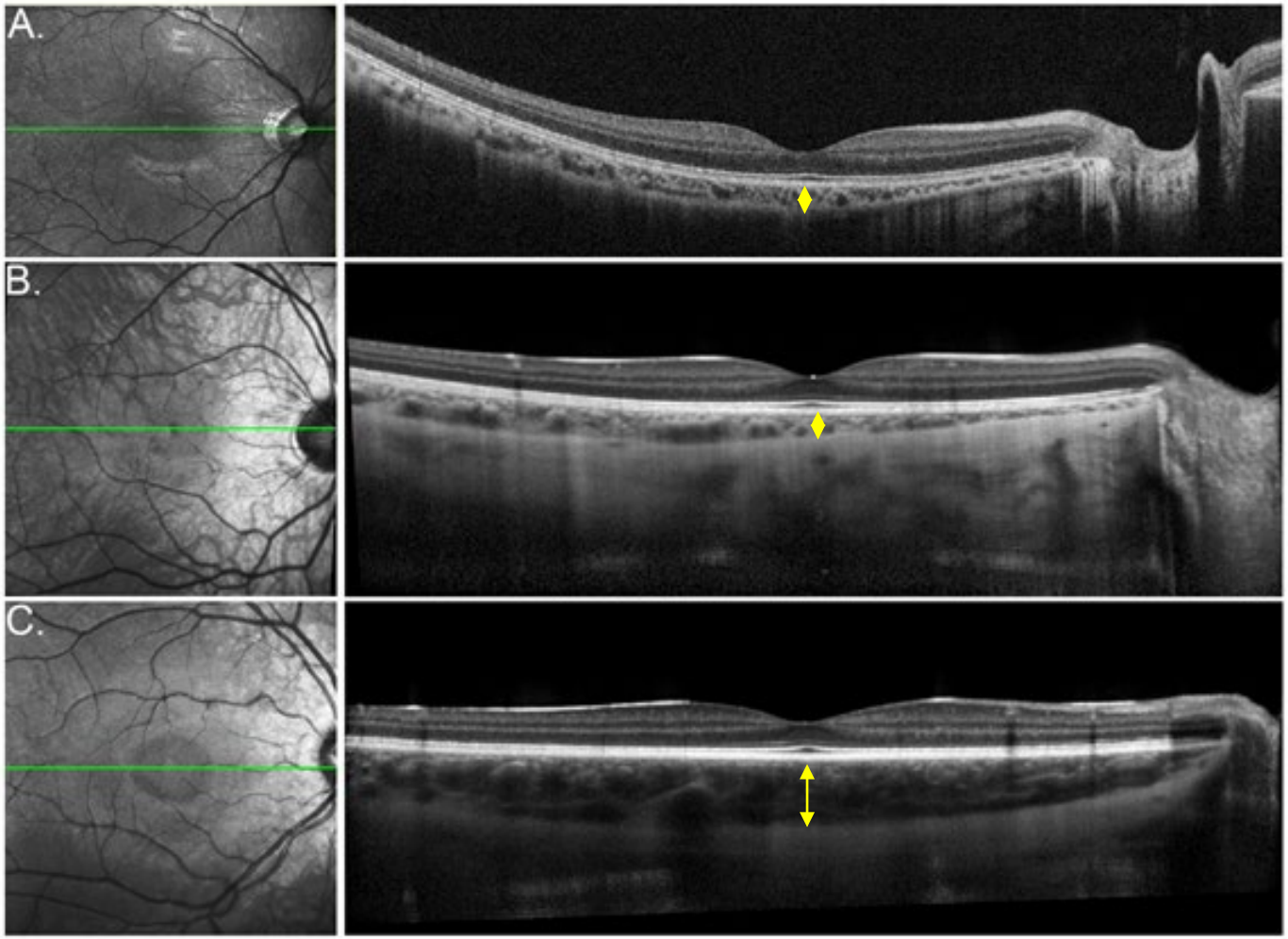


Choroidal thickness in children and myopia



Kobia-Acquah, Emmanuel; Flitcroft, Daniel Ian; Lingham, Gareth; Paudel, Nabin; Loughman, James. Optometry and Vision Science100(1):57-66, January 2023.

Choroidal thickness in children and myopia



11 yr old
Highly myopic child

11 yr old
Highly myopic child

11 yr old
Emmetropic child

Examples of high resolution, foveal centred chorioretinal OCT scans in subjects with high myopia (both aged 11), illustrating the marked choroidal thinning that is typically found with high myopia (A,B). Foveal OCT scan of an age-matched emmetropic subject is shown in C for comparative purposes.

Read SA, Fuss JA, Vincent SJ, Collins MJ and Alonso-Caneiro D. *Choroidal changes in human myopia: Insights from OCT imaging*. **Clinical and Experimental Optometry** 2019; 102(3): 270-285.

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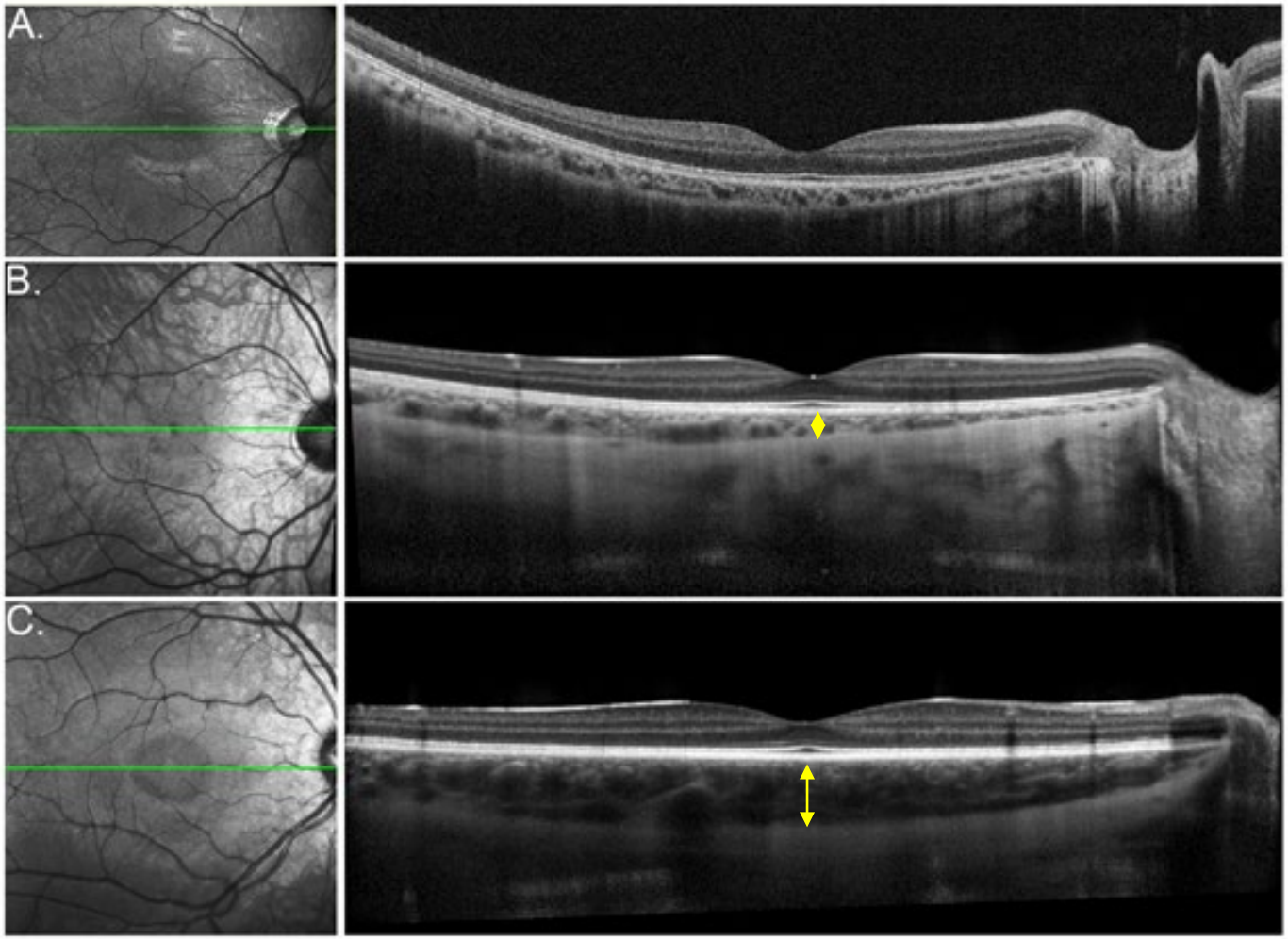
Choroidal thickness in children and myopia



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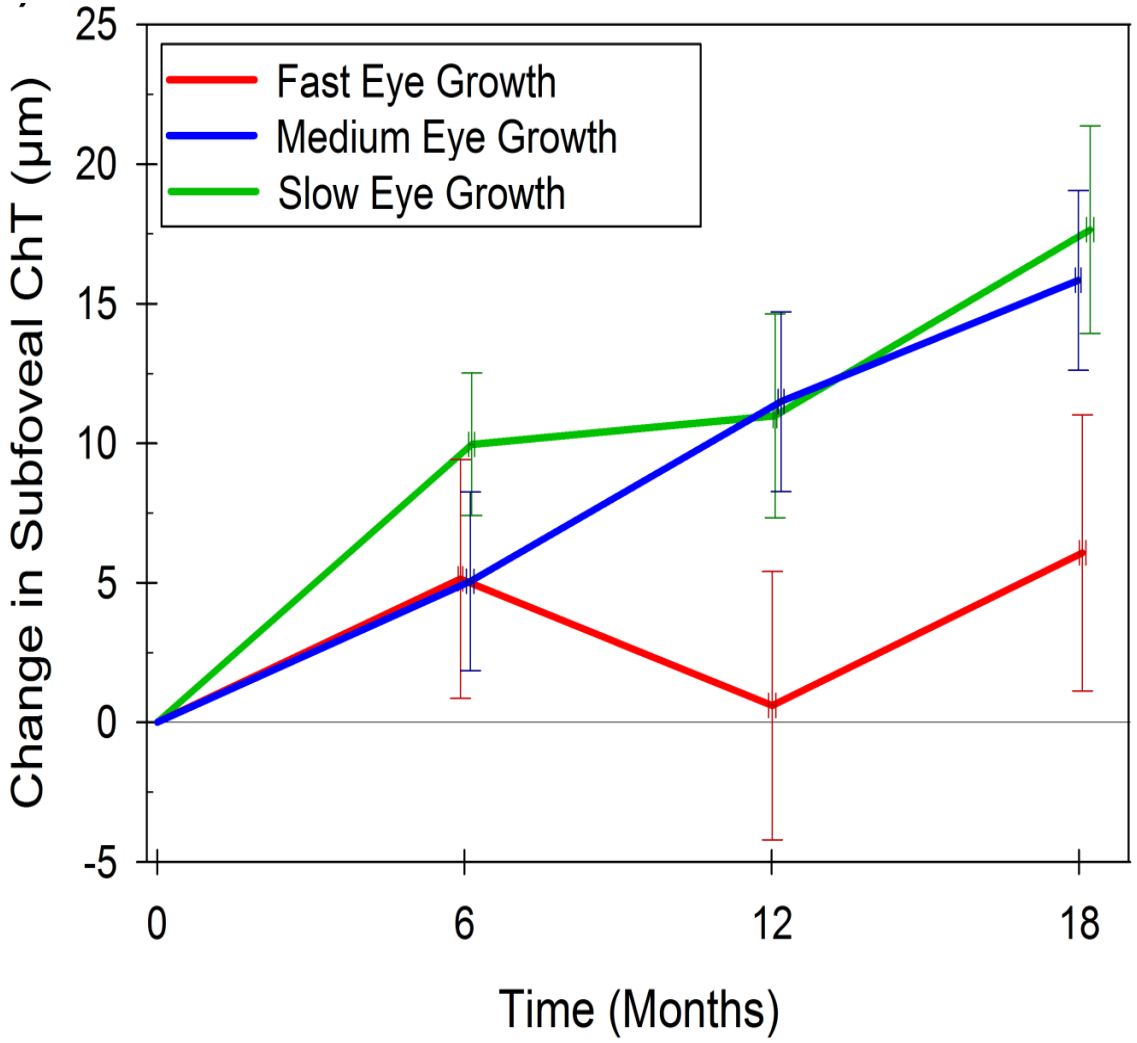
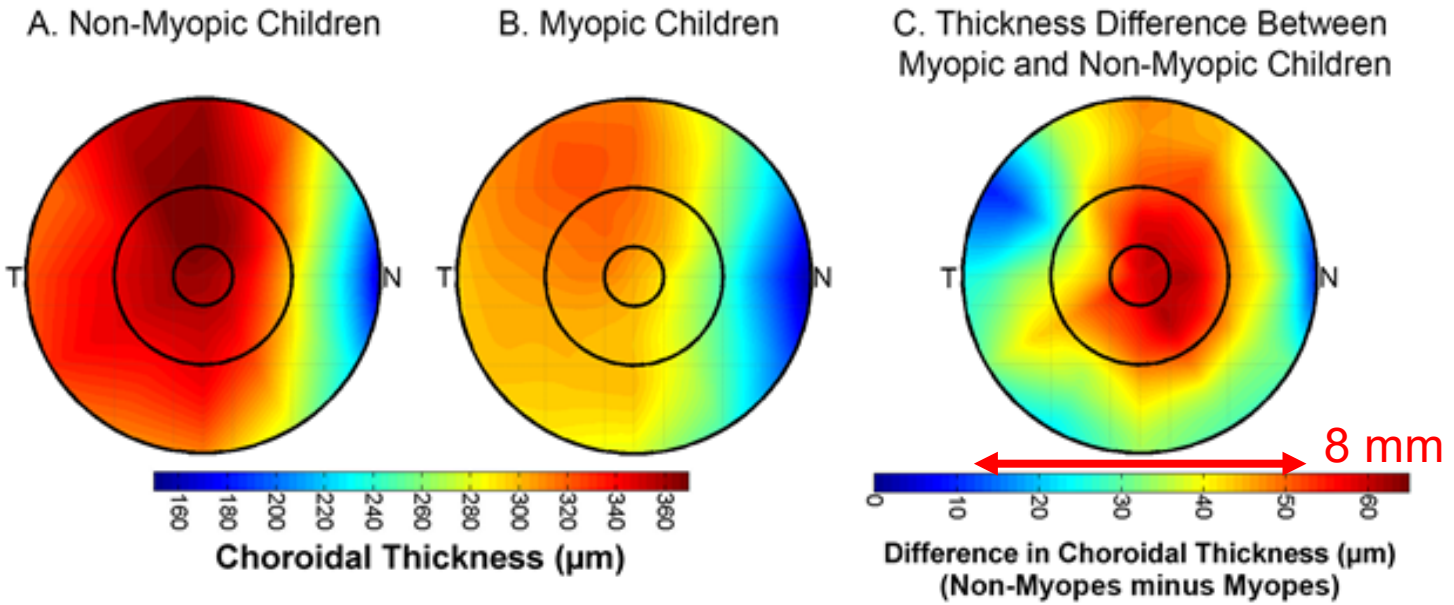
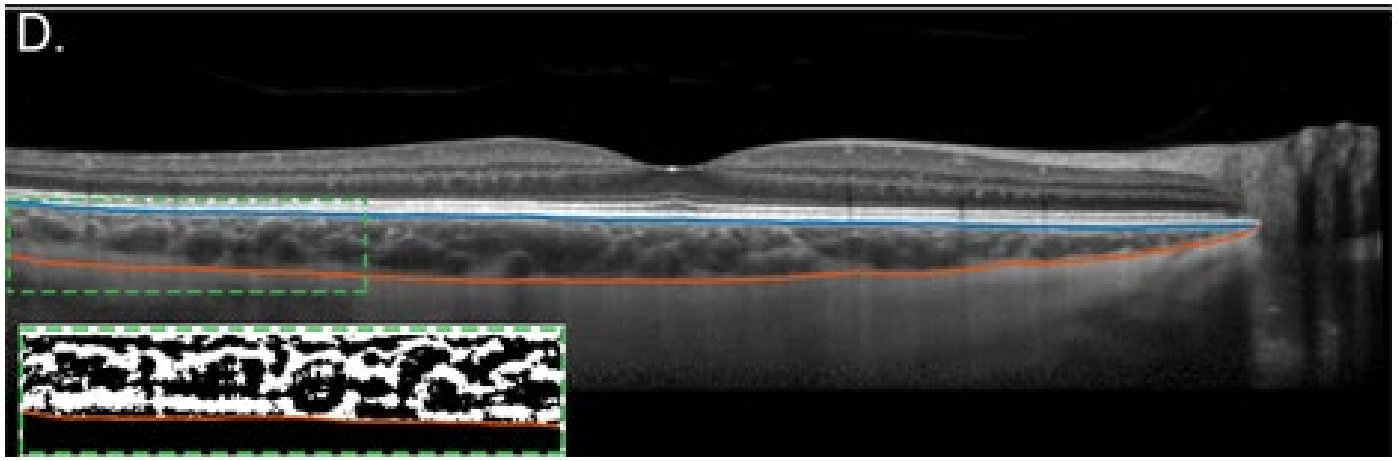
Axial eye growth and choroidal thickness in children



Read SA, Alonso-Caneiro D, Vincent SJ and Collins MJ. *Longitudinal changes in choroidal thickness and eye growth in childhood.* **Investigative Ophthalmology and Visual Science** 2015; 56(5): 3103-3112.

Topographical analysis of choroidal thickness in children





Read SA, Fuss JA, Vincent SJ, Collins MJ and Alonso-Caneiro D. *Choroidal changes in human myopia: Insights from OCT imaging*. **Clinical and Experimental Optometry** 2019; 102(3): 270-285.

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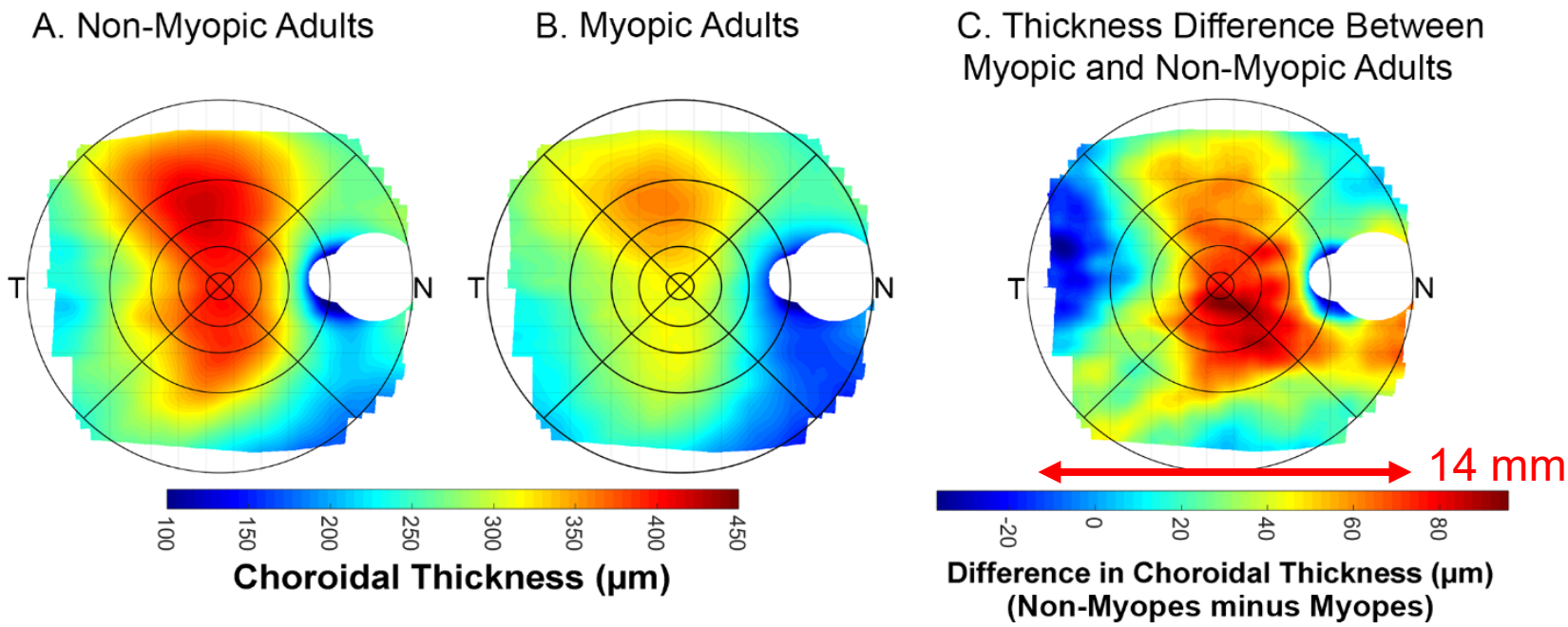
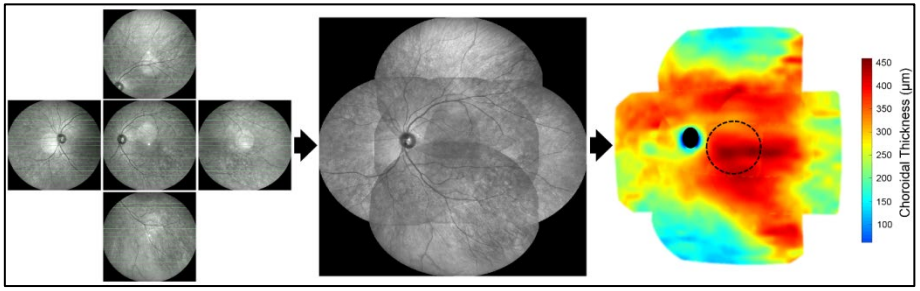
Wide field choroidal thickness in adults





Hoseini-Yazdi H, Vincent SJ, Collins MJ, Read SA, and Alonso-Caneiro D. *Wide-field choroidal thickness in myopes and emmetropes.* **Scientific Reports** 2019; 9: 3474.

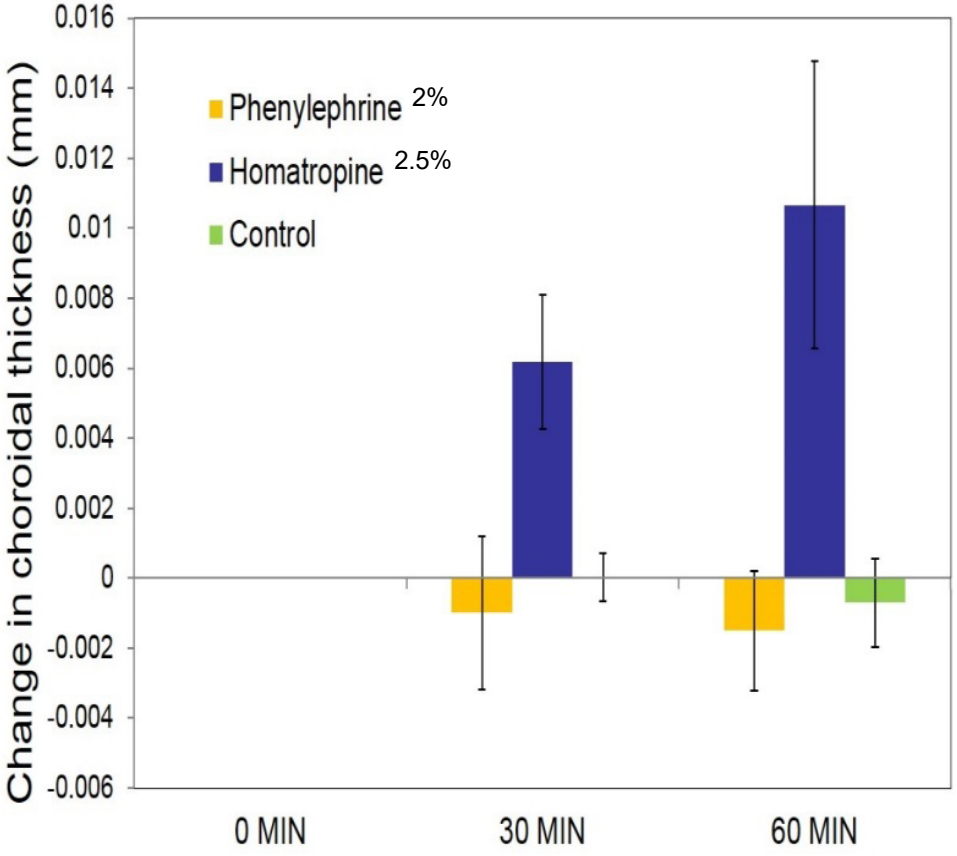
Myopia control strategies

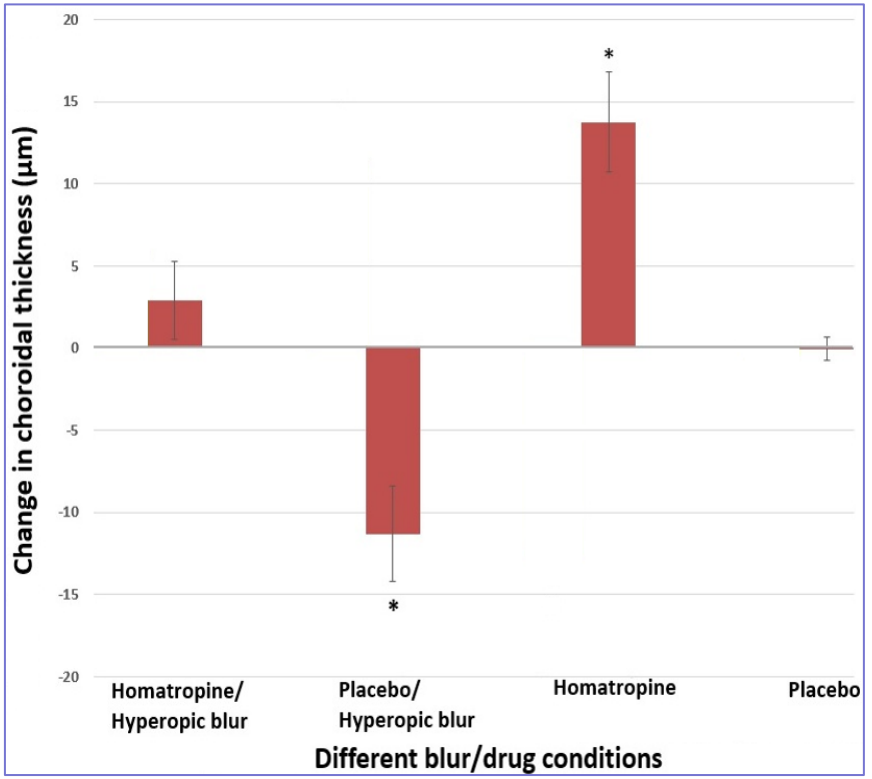
Choroid thickens in response to:

- Atropine
- Orthokeratology
- Myopia control spectacles
- Soft contact lens myopia control
- Light (sunlight, red, violet, blue at optic nerve head)

- Note – evidence is strong (repeated by different labs) for some treatments but still early (initial reports) for others

Choroidal changes and homatropine

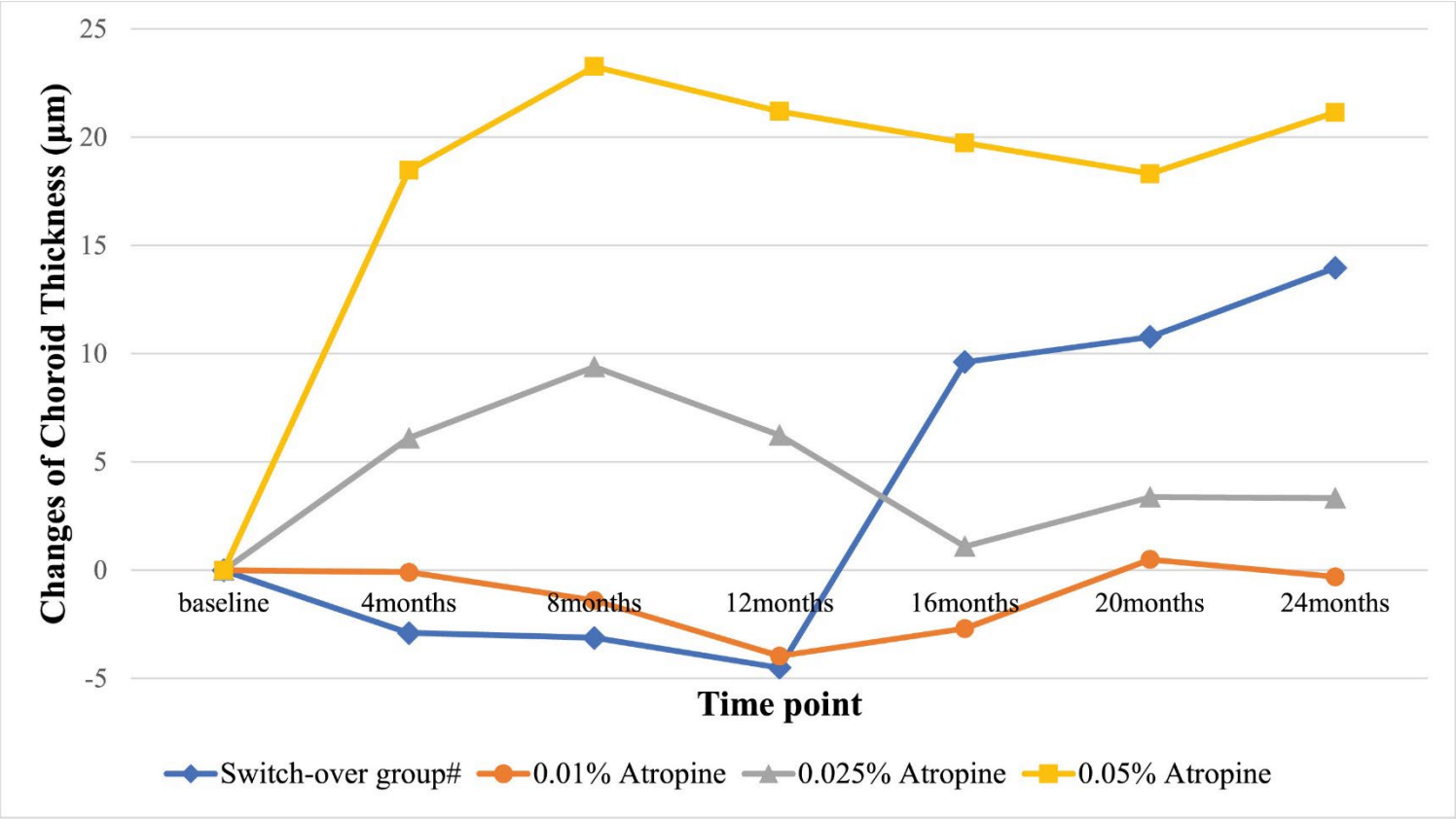




Sander BP, Collins MJ and Read SA. *The interaction between homatropine and optical blur on choroidal thickness*. **Ophthalmic and Physiological Optics** 2018; 38: 257-265.

Sander BP, Collins MJ and Read SA. *The effect of topical adrenergic and anticholinergic agents on the choroidal thickness of young healthy adults*. **Experimental Eye Research** 2014; 128: 181-189.

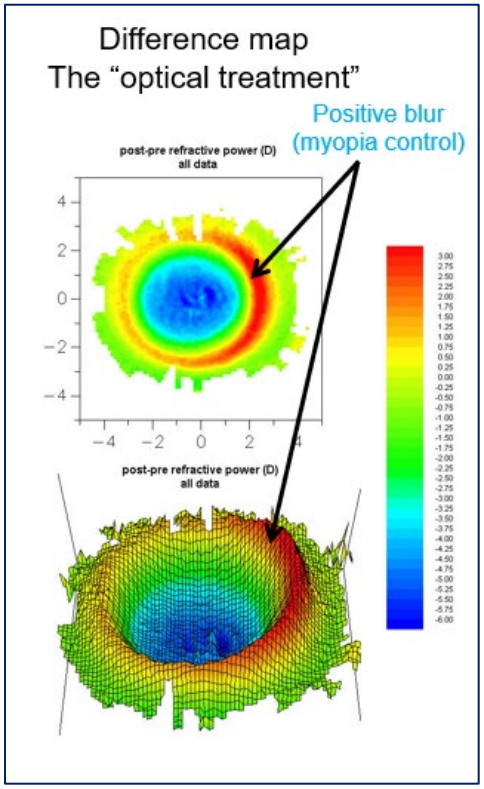
Choroidal changes and atropine

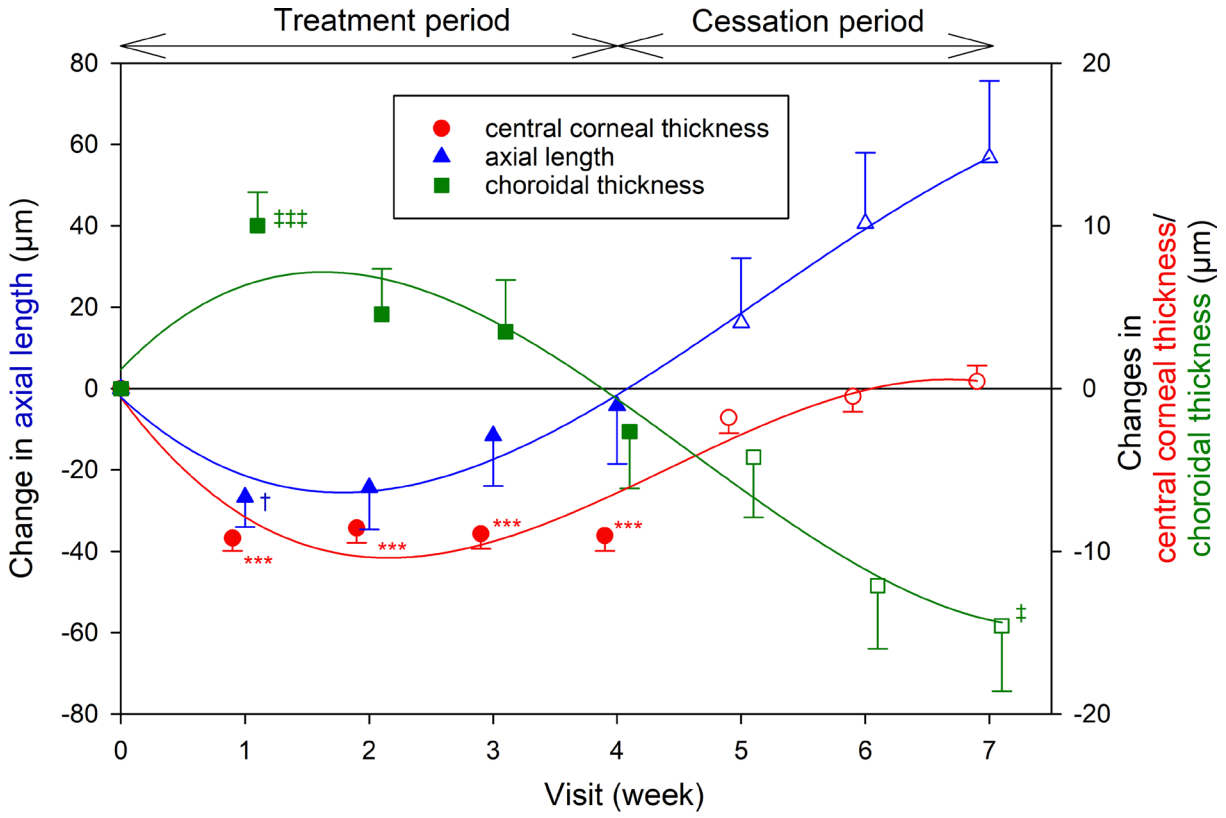


Conclusions: Low concentration atropine induced a choroidal thickening effect along a concentration-dependent response throughout the treatment period. The choroidal thickening was associated with a slower SE progression and AL elongation among all the treatment groups. Choroidal response can be used for assessment of long-term treatment outcomes and as a guide for concentration titrations of atropine.

Yam JC, Jiang Y, Lee J, Li S, Zhang Y, Sun W, Yuan N, Wang YM, Yip BHK, Kam KW, Chan HN, Zhang XJ, Young AL, Tham CC, Cheung CY, Chu WK, Pang CP, Chen LJ. The Association of Choroidal Thickening by Atropine With Treatment Effects for Myopia: Two-Year Clinical Trial of the Low-concentration Atropine for Myopia Progression (LAMP) Study. Am J Ophthalmol. 2022 May;237:130-138.

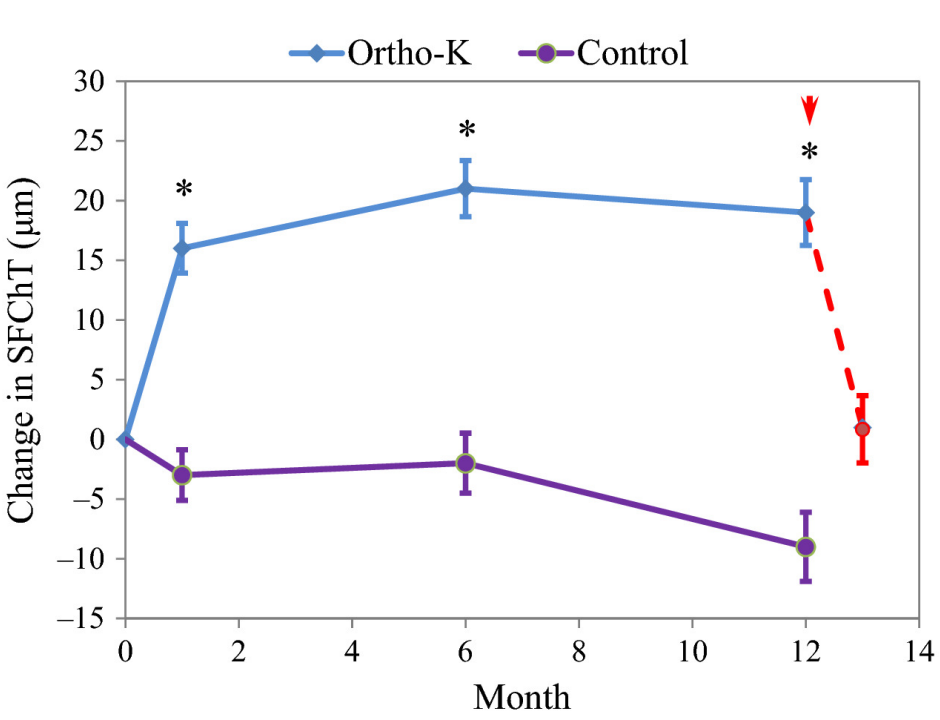
Orthokeratology and choroidal changes

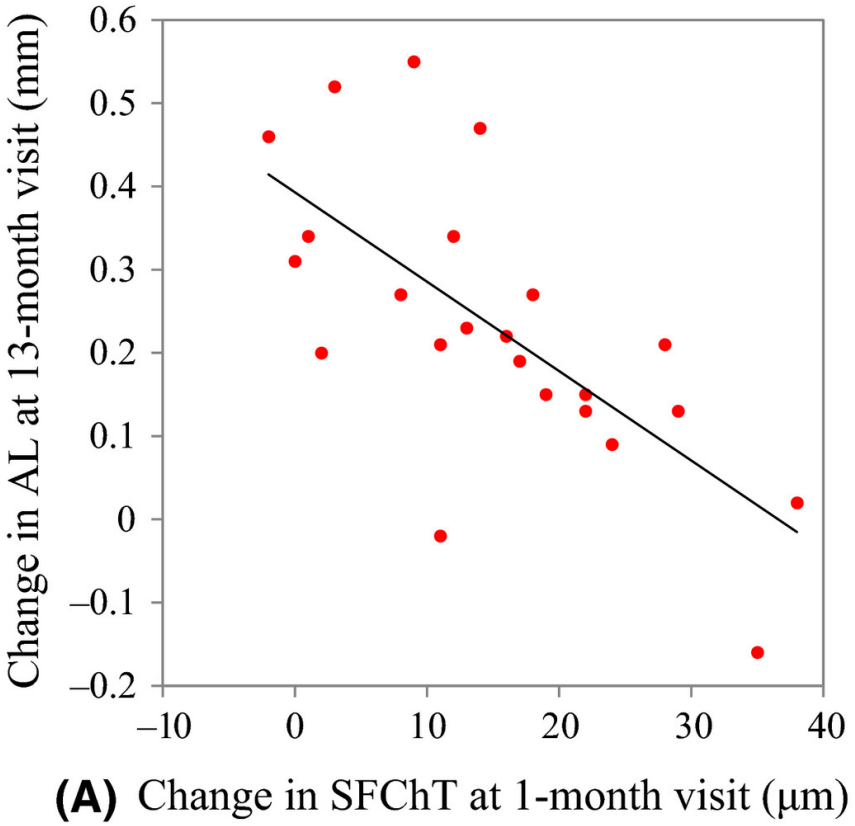




Jason K. Lau, Kin Wan, Sin-Wan Cheung, Stephen J. Vincent, Pauline Cho; Weekly Changes in Axial Length and Choroidal Thickness in Children During and Following Orthokeratology Treatment With Different Compression Factors. *Trans. Vis. Sci. Tech.* 2019;8(4):9.

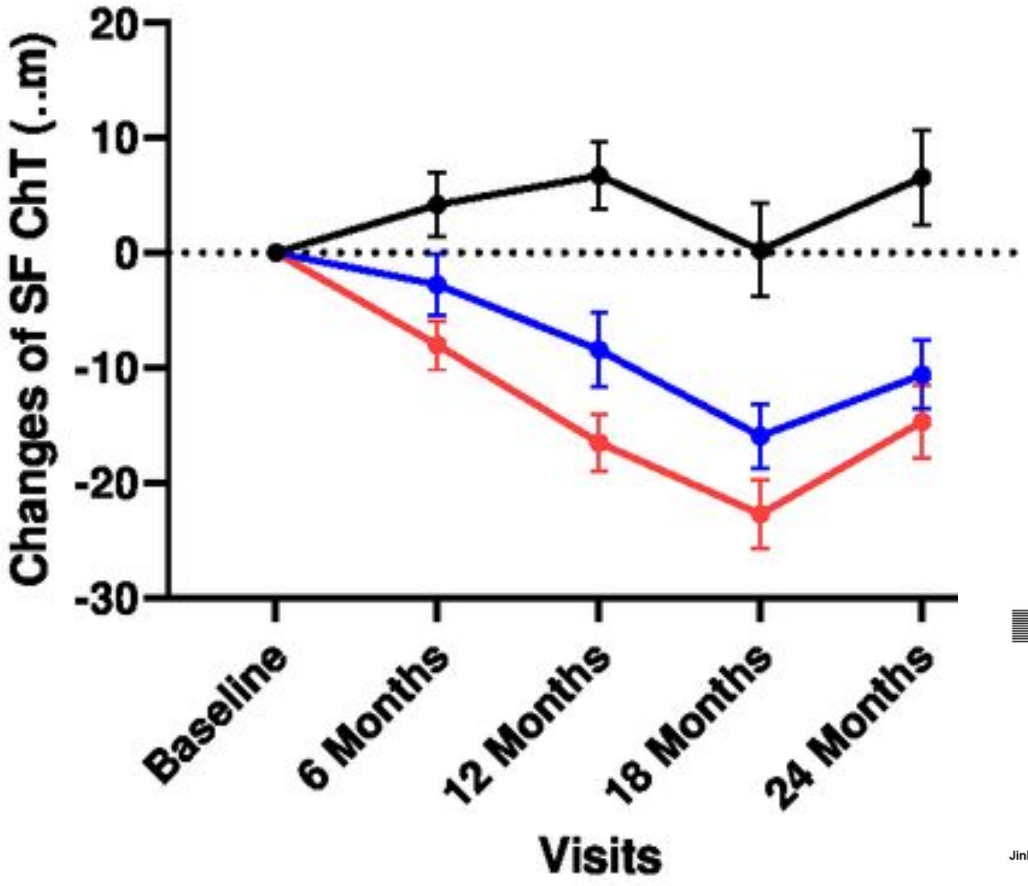
Orthokeratology and choroidal changes

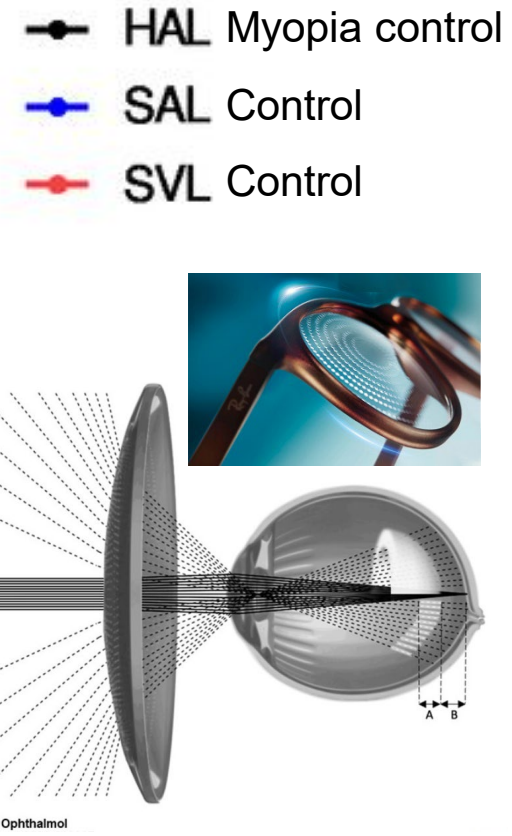




Li, Z., Hu, Y., Cui, D., Long, W., He, M. and Yang, X. (2019), Change in subfoveal choroidal thickness secondary to orthokeratology and its cessation: a predictor for the change in axial length. Acta Ophthalmol, 97: e454-e459.

Myopia control spectacles and choroid



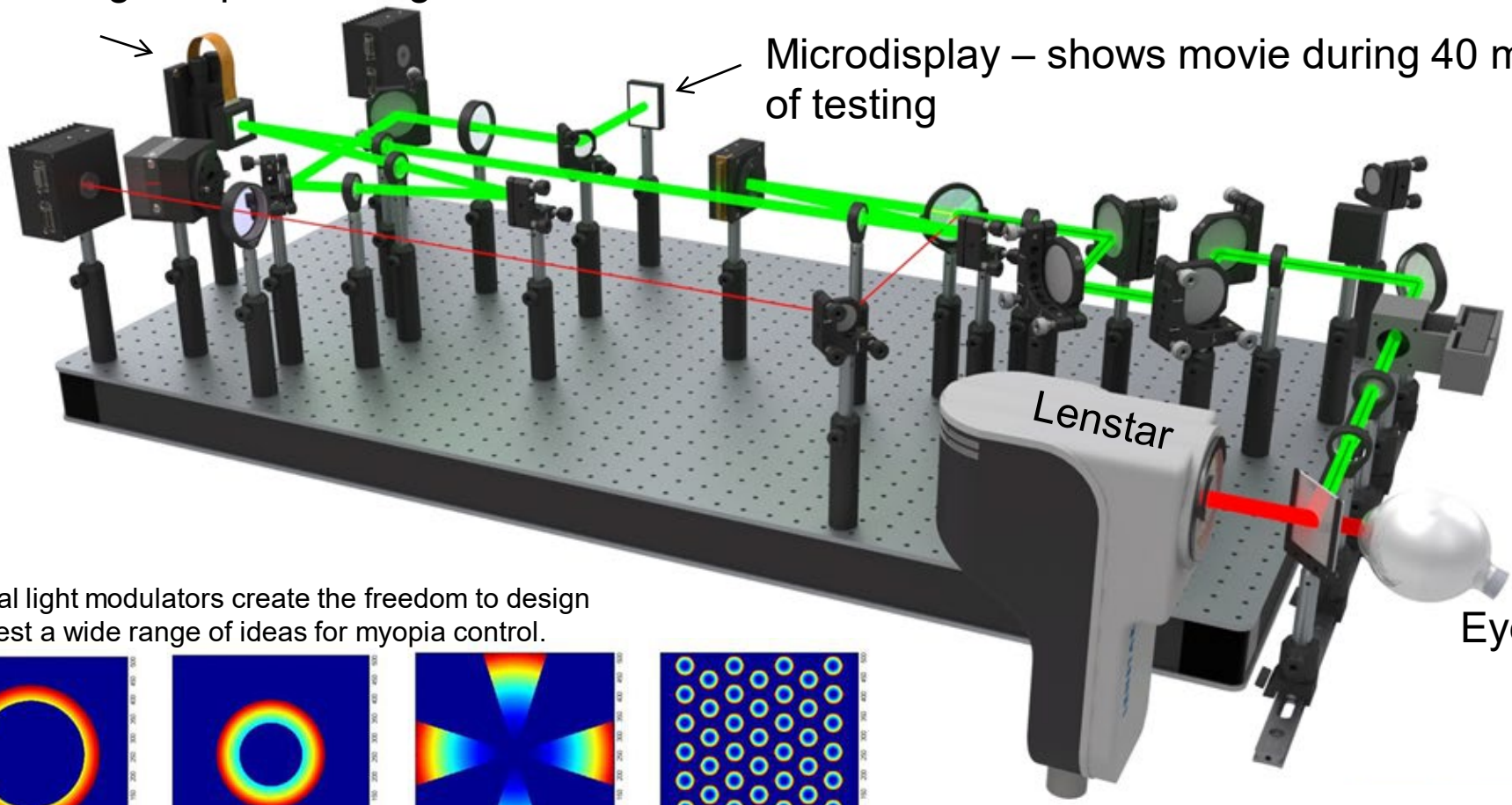


Yingying Huang, XUE LI, Adeline Yang, Daniel Spiegel, Bjorn Drobe, Hao Chen, Jinhua Bao; Effect of Myopia Control Spectacle Lenses with Aspherical Lenslets on Choroidal Thickness in Myopic Children: 1-Year Results. *Invest. Ophthalmol. Vis. Sci.* 2021;62(8):1373.

Axial length changes in response to optics

Spatial light modulator creates digital optical design

Microdisplay – shows movie during 40 mins of testing



Spatial light modulators create the freedom to design and test a wide range of ideas for myopia control.

M.J. Collins, F. Yi and B.A. Davis. ***Apparatus, method and system for measuring the influence of ophthalmic lens designs.***.

Reports at conferences of choroidal thickening with myopia control contact lenses including Abiliti (JJVC), MiSight (CooperVision), Concentric bifocals (BLINK study), Acuvue bifocal

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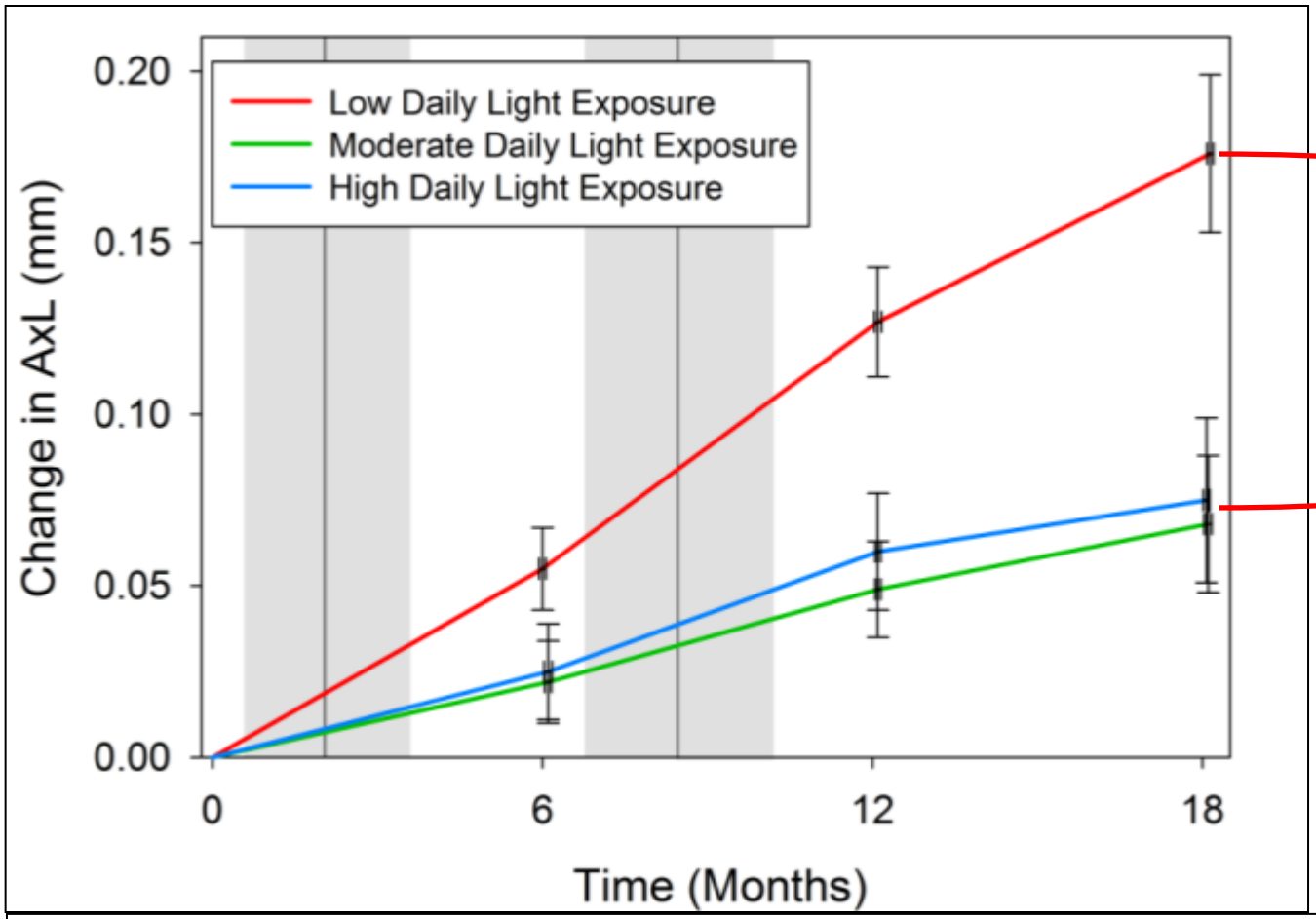
Sunlight exposure and eye growth in children



0.1 mm (59%) = 0.3 D

Faster eye growth in low light exposure group (p<0.05)

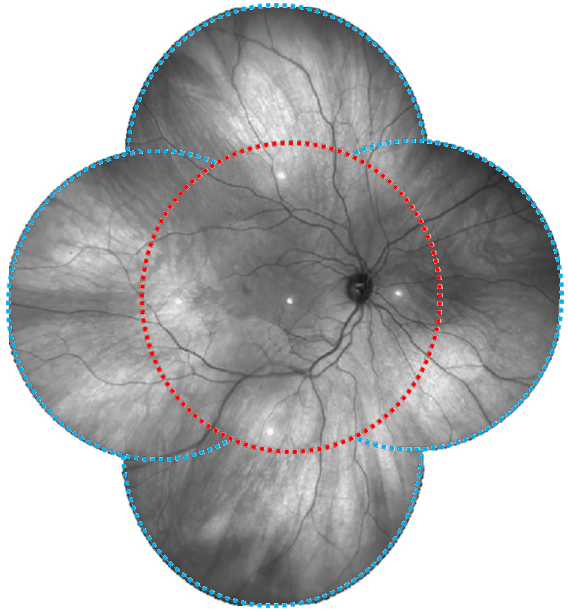
Average Daily Bright Light Exposure (>1000 lux):

High Daily Light: 137 min/day
Moderate Daily Light: 90 min/day
Low Daily Light: 56 min/day

- **Low Light Exposure** ≤*651 lux* (mean: 459 lux, 56 minutes/day exposure >1000 lux) (n = 33)
- **Moderate Light Exposure** *652-1019 lux* (mean 842 lux, 91 mins/day exposure >1000 lux) (n = 33)
- **High Light Exposure** ≥*1020 lux* (mean 1455 lux, 137 mins/day exposure >1000 lux) (n = 33)

Read SA, Collins MJ and Vincent SJ. *Light exposure and eye growth in childhood.* **Investigative Ophthalmology and Visual Science** 2015; 56(11): 6779-6787.

Topics



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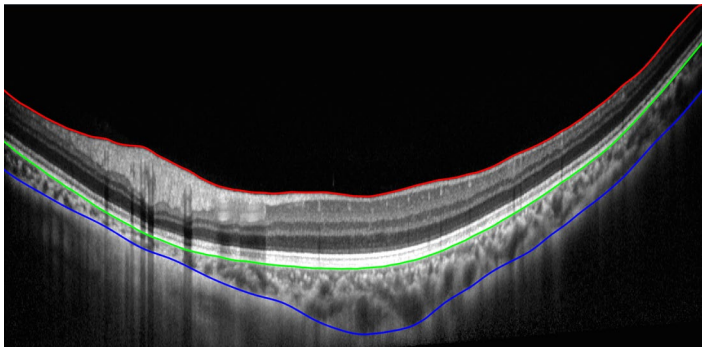

Thanks to my collaborators

Scott Read
Steven Vincent
David Alonso-Caneiro
Hosein Hoseini-Yazdi
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Emily Woodman-Pieterse
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Rohan Hughes
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Swee Chai Teoh
Brett Davis
Fan Yi

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