Changing Hyperelastic Properties of the Tree Shrew Sclera during Visually-Guided Remodeling

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Introduction: Myopia (“nearsightedness”) is the most common type of refractive error affecting approximately 40% of the U.S. adult population and is associated with an increased risk of blinding diseases such as glaucoma [1]. A myopic eye is too long for its own optics, and the axial length is primarily determined by the size of the scleral shell. In tree shrews, humans, and other mammals the sclera is comprised of interwoven layers of (primarily) type I collagen fibrils. We have previously shown that the creep rate of the tree shrew sclera increases during lens-induced myopia and decreases after removing the lens as the eye recovers from the induced myopia [2]. This finding supports the notion that the induced myopia is due to a visually-guided mechanism that involves active remodeling. The aim of this study is to further explore this theory by investigating the changes in the hyperelastic material properties of the sclera during lens-induced myopia and recovery from the myopia.

Methods: To reveal changes in the collagen fibril dominated material response, quasi-static uniaxial tensile tests on 3-mm wide scleral strips were performed at super-physiological loading conditions (3 cycles 0-50 g, 30 sec). Scleral strips were obtained from juvenile tree shrews exposed to three different visual conditions: (i) normal development; (ii) monocular -5 D lens wear to induce axial elongation and myopia; and (iii) recovery from -5 D lens wear, mediated by slowed axial elongation. We assume that collagen fibrils are cramped in the unloaded scleral strips and uncrimp as the tissue stiffens under load. Inverse numerical analyses were performed to estimate the crimp angle (unloaded) and elastic modulus of collagen fibrils using a microstructure-based constitutive formulation [3]. The crimp angle determines the stretch level at which the collagen fibrils straighten and the sclera stiffens, while the elastic modulus of collagen fibrils mainly determines the tissue stiffness in the linear region of the stress-strain response.

Results: Compared to the control eye, the fitted collagen fibril crimp angle was significantly higher in the treated eye after 2 days and peaked after 4 days of -5D lens wear (Figure A). This difference was slowly reduced with continuous -5 D lens wear but remained significantly higher after 11 days. In contrast, the difference in crimp angle rapidly decreased after the lens was removed and was not significant after 1 day of recovery. Compared to normally developing eyes, a rapid increase in the elastic modulus (up to 2-3 fold) was seen in both eyes (control and treated) after starting or stopping the -5 D lens wear (Figure B). The increase was highly transient during lens wear, but more sustained during recovery. Compared to normally developing eyes, this stiffening effect was significant during the first 2 days of monocular -5 D lens wear in both eyes, while it remained significant up to day 4 and 10 of recovery in the treated and control eye, respectively.
Figure. Fitted material parameters (mean, standard deviation) versus days of visual experience during compensation for a -5 D lens (n = 5 per group) and recovery (n = 3 per group). A: Difference in fitted collagen fibril crimp angle between the deprived or recovering eye and the control eye. (T vs C) indicates a significant difference (paired t-test, p < 0.05) between the deprived eye and the control eye. No significant differences were found between the recovering eye and its control. The average value and 95% confidence interval are shown for the difference between the right and left eye of normal animals. B: Fitted elastic modulus of collagen fibrils during compensation for a -5 D lens and recovery. Compared to a normal eye, significant differences (unpaired t-test, p < 0.05) are indicated with text labels for the deprived eye (T vs N), the control eye (C vs N), the recovering eye (RT vs N), and the recovering control eye (RC vs N).

Conclusions: The estimated change in the unloaded crimp angle of scleral collagen fibrils is temporally associated with the change in axial elongation rate during myopia development and recovery. This finding suggests that axial eye elongation may be controlled by a remodeling mechanism that modulates the collagen fibril crimp as well as the creep rate [2]. The rapid and extensive changes in collagen fibril elastic modulus support the existence of a dynamic biomechanical mechanism that leads to transient scleral stiffening. However, this binocular changes in scleral stiffness during monocular lens treatment and recovery are not temporally associated with the change in axial elongation, indicating that scleral stiffening may not be causally related to axial elongation in myopia.

REFERENCES