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SCLERAL BIOMECHANICS IN THE GLAUCOMATOUS MONKEY EYE

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INTRODUCTION

The sclera is the outer shell and principal load-bearing tissue of the eye, and consists primarily of avascular lamellae of collagen fibers. Ninety percent of the collagen fibers in the sclera are Type I, which provide the eye with necessary mechanical strength to withstand intraocular pressure (IOP). A small hole pierces the posterior sclera, known as the scleral canal, through which the retinal ganglion cell axons turn and pass out of the eye on their path to the brain. The scleral canal is spanned by a fenestrated connective tissue called the lamina cribrosa that provides structural and nutritional support to the axons as they leave the eye. This region, including the peripapillary sclera (the sclera closest to the canal), the lamina cribrosa, and the contained retinal ganglion cell axons, is collectively known as the optic nerve head or ONH.

Glaucoma is the second leading cause of blindness worldwide and manifests as damage to the neural and connective tissues of the ONH at normal and elevated levels of IOP. We have previously shown that the biomechanical properties of the peripapillary sclera are altered in early experimental glaucoma using uniaxial testing and linear viscoelastic theory [1]. From this study, we described an increase in the equilibrium modulus of the peripapillary sclera from glaucomatous monkey eyes but no changes in the time-dependent viscoelastic parameters between contralateral normal and glaucomatous monkey eyes. These results, as well as those from several computational studies, suggest that the sclera plays an important role in the development and progression of glaucoma, which is also supported by other investigators [2].

In this study, we model the posterior sclera as a nonlinear, anisotropic, inhomogeneous soft tissue using a fiber-reinforced constitutive theory that includes stretch-induced stiffening and multi-directional collagen fiber distributions [3]. We then derived shell-specific sets of biomechanical properties (based on the experimental observations) using an inverse finite element (FE) method [4] in both eyes of 8 adult monkeys in which one eye had been given experimental glaucoma by inducing chronic IOP elevations of modest magnitude and duration.

MATERIAL AND METHODS

Experiments

Experimental glaucoma was induced in one eye of 8 rhesus monkeys without initial ocular abnormality. Briefly, the trabecular meshwork was photocoagulated using laser in one eye of each monkey in order to elevate IOP. After the initial photocoagulation, IOP was monitored with a TonoPen (Reichert, Depew, NY) over time in both eyes of each monkey. After the first IOP elevation was confirmed, all 8 monkeys were maintained for different time periods in order to create different stages of scleral biomechanical changes due to elevated IOP. Here, we defined cumulative IOP insult as the difference in area under the IOP-time curve between the glaucomatous and the normal eye. Monkey specimen were arranged in the order of increasing cumulative IOP insult, where monkey 1 received the lowest cumulative IOP insult and monkey 8, the highest.

After sacrifice, the posterior scleral shells from both eyes of each monkey were cleaned from intra- and extra-orbital tissues and individually mounted on a custom-built pressurization apparatus. After mounting, each shell was blotted dry, covered with a contrast medium, and immediately immersed in isotonic saline at room temperature. IOP was incrementally increased from 5 to 45 mm Hg and an electronic speckle pattern interferometry sensor (Q100, Ettemeyer AG, Germany) was used to record the full-field 3-D displacements of each shell surface at a resolution of 0.1 μm. IOP was then reset to 5 mm Hg and scleral topography was manually measured with a 3-D digitizer arm (MicroScribe G2X, Immersion, San Jose, CA). Scleral thickness

was also measured at twenty predetermined locations with a 20 MHz ultrasound transducer (PacScan 300P, Sonomed, Inc., Lake Success, NY). The topography and thickness data were combined to create a FE mesh for each posterior scleral shell.

Modeling

We modeled the posterior sclera as a nonlinear, anisotropic, inhomogeneous soft tissue using fiber-reinforced composite theory [3]. For each posterior scleral shell, we estimated a set of thirteen model parameters from the experimental data using an inverse FE method [4], which was driven by the differential evolution algorithm [4]. Local tangent moduli were computed and mapped for each shell in both the peripapillary sclera (sclera close to the ONH) and peripheral sclera (sclera close to the equator). Data for each glaucomatous eye was compared to its contralateral normal and only differences exceeding inter-eye differences from 8 bilaterally normal monkeys were considered significant.

RESULTS

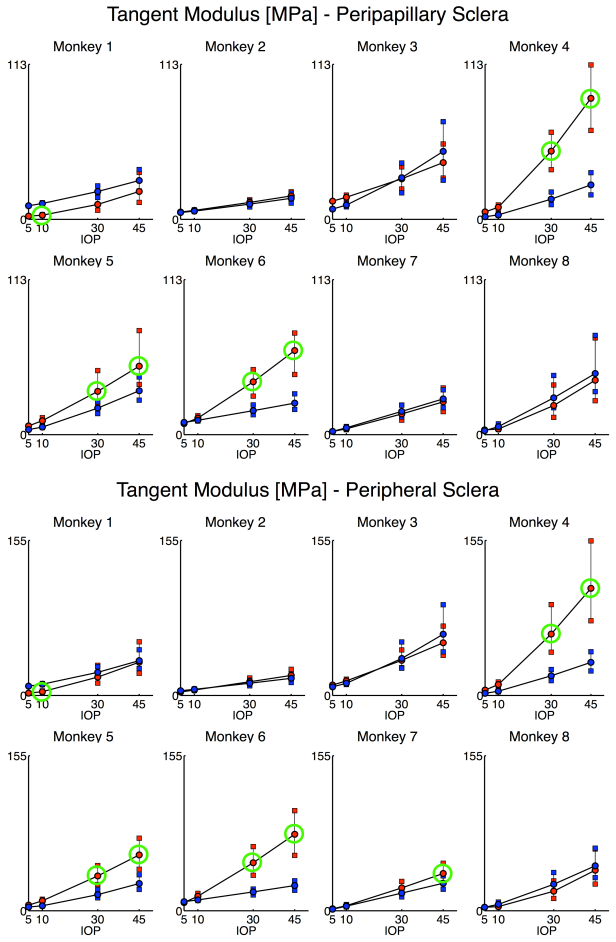

Figure 1. Tangent modulus in contralateral eyes (blue: normal, red: glaucomatous) for both the peripapillary (top) and peripheral (bottom) scleral regions of each monkey as a function of IOP. A green circle represents a significant difference between the normal and glaucomatous eye that exceeds the inter-eye differences from 8 normal monkeys.

Overall and regional changes in scleral thickness between glaucomatous and normal eyes was insignificant when compared to the physiologic inter-eye difference from 8 normal monkey eyes ($p > 0.05$). However, a trend toward scleral thinning was observed in the glaucomatous monkey eyes compared to their contralateral normal controls.

We observed no significant changes (exceeding the physiologic inter-eye difference of normal monkeys) in tangent modulus (Figure 1) between the normal and glaucomatous eyes of monkeys 2, 3, and 8.

We observed significant changes in tangent modulus between the normal and glaucomatous eyes of monkeys 1, 4, 5, 6 and 7 (Figure 1). The glaucomatous eye in monkey 1 exhibited a significant decrease in tangent modulus (at 10 mmHg). The glaucomatous eyes in monkeys 4, 5 and 6 exhibited a significant increase in tangent modulus (30 and 45 mm Hg). Monkey 7 exhibited a significant increase in tangent modulus (45 mm Hg) in the peripheral sclera only.

Finally, we did not detect changes in scleral anisotropy parameters ($p > 0.05$) between normal and glaucomatous eyes in either the peripapillary or peripheral regions.

DISCUSSION

Overall, our results suggest that significant changes in the biomechanical behavior of the sclera are associated with chronic IOP elevations. These changes are complex, individual-specific, and likely the result of scleral extracellular matrix remodeling. Our findings suggest that scleral thinning occurs in the peripapillary sclera of glaucomatous eyes, that sclera with initially large thickness (monkey 2; data not shown) or tangent modulus (monkeys 3 and 8) are less prone to biomechanical changes, that a decrease in tangent modulus (possibly due to elastin damage) occurs at the earliest stage of glaucoma, that an increase in tangent modulus (possibly associated with collagen) occurs at moderate stages of glaucoma, and that fiber reorientation does not occur in glaucomatous eyes. Since the sclera is a significant determining factor in the levels of stress and strain transmitted to the ONH, a change in the biomechanical environment of the posterior sclera through remodeling will inevitably perturb the biomechanics of the ONH. Scleral remodeling may provide a protective mechanism and act to keep stress and strain levels within a normal range. Our future work will study the complex biomechanical interactions between the posterior sclera and ONH in both normal and glaucomatous eyes.

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