

SBC2008-192833

**AGE-RELATED CHANGES IN SCLERAL MATERIAL PROPERTIES
OF THE MONKEY EYE**

**Michaël J.A. Girard (1,2), Jun-Kyo F. Suh (1), Michael Bottlang (3),
Claude F. Burgoyne (4), and J. Crawford Downs (2)**

(1) Department of Biomedical Engineering
Tulane University
New Orleans, Louisiana

(2) Ocular Biomechanics Laboratory
Devers Eye Institute
Legacy Health System
Portland, Oregon

(3) Biomechanics Laboratory
Legacy Research & Technology Center
Legacy Health System
Portland, Oregon

(4) Optic Nerve Head Research Laboratory
Devers Eye Institute
Legacy Health System
Portland, Oregon

INTRODUCTION

The sclera is the outer shell and principal load-bearing tissue of the eye, which 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 sustain intraocular pressure (IOP). In the posterior sclera, there is a fenestrated canal, called the optic nerve head (ONH), through which the retinal ganglion cell axons pass transmitting visual signals from the retina to the brain. The opening of the ONH is structurally supported by a fenestrated connective tissue called the lamina cribrosa.

Glaucomatous optic neuropathy (one of the three leading causes of blindness in the U.S) manifests as damage to the neural and connective tissues of the ONH at normal and elevated levels of IOP. It has been shown that age-related cross-linking of collagen manifests as higher tissue stiffness. In this study, we test hypotheses regarding the effects of aging on monkey posterior sclera so as to understand the effect of scleral aging on glaucomatous damage within the ONH.

To our knowledge, aging effects on the material properties of monkey posterior sclera have not been investigated. In humans, it has been shown that older patients are at higher risk for developing glaucoma [1] but at present it is unclear how scleral mechanics contribute to ONH susceptibility to glaucomatous damage. By providing a constitutive model to predict the 3-D mechanical behavior of the posterior scleral shell from young and old monkeys (and eventually humans), we hope to elucidate the mechanisms underlying aging as a risk factor for the development and progression of glaucoma at all levels of IOP.

MATERIAL AND METHODS

Experimental Set Up and Testing Protocol

Immediately following enucleation, the posterior scleral shells from both eyes of 8 monkeys (4 younger than 2 years old and 4 older than 18 years old) were individually mounted at the equator on a custom-built pressurization device (Figure 1). Each scleral sample was blotted, covered with white titanium powder, and immersed in saline. IOP was slowly increased by incremental steps of 0.2 mm Hg from 5 to 45 mm Hg, and the 3-D displacement field of each posterior sclera was measured at equilibrium using an electronic speckle pattern interferometry (ESPI) sensor (Ettmeyer AG, Q100).

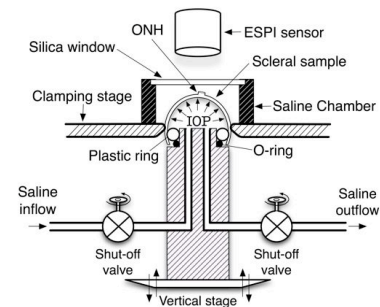


Figure 1. Schematic of the pressurization apparatus.

The ESPI sensor (resolution: ~0.1 μm; field of view: 35 mm × 25 mm × 13 mm) captured laser speckle images from 4 independent illumination directions for each IOP step [2]. Speckle image subtraction and fringes analysis algorithms (Ettmeyer AG, ISTR A Q100 V2.7) were employed to extract the 3 components of the displacement field for the following IOP changes: 5 to 7, 5 to 10, 5 to 20, 5 to 30 and 5 to 45 mm Hg. Finally, The outer surface geometry of the scleral shell was digitized using with a 3-D digitizer arm

(MicroScribe, G2X), and the scleral thickness was measured at predetermined locations throughout the entire shell with a 20 MHz ultrasound transducer (Sonomed, Inc., PacScan 300P). Geometrical data were used to reconstruct the anatomical geometry of the posterior half of each eye (Figure 2).

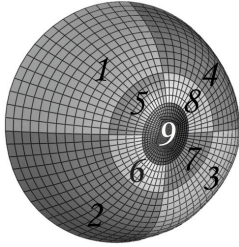


Figure 2. Mesh of one monkey posterior scleral shell. Regions 1-4 are the peripheral sclera, Regions 5-8 are the peripapillary sclera and Region 9 is the ONH.

Constitutive modeling

Scleral collagen fiber alignment was assumed to be confined within a plane tangent to the shell surface at each material point, with a probability distribution P , known as semi-circular Von Mises distribution:

$$P(\theta, k) = \frac{1}{\pi I_0(k)} \exp(k \cos(2(\theta - \theta_p))) \quad (1)$$

where I_0 is the modified Bessel function of the first kind (order 0), θ_p is the preferred orientation of the collagen fibers and k is defined as the fiber concentration factor. The probability distribution P was incorporated into the scleral strain energy function W_{sclera} defined as:

$$W_{sclera} = W_{matrix} + \int_{\theta_p - \pi/2}^{\theta_p + \pi/2} P(\theta, k) W_{fiber}(\theta) d\theta \quad (2)$$

where W_{matrix} is an isotropic contribution from the proteoglycan-based ground matrix (Neo-Hookean material). W_{fiber} is an anisotropic contribution from the collagen fiber family in the orientation of θ [3] such that

$$\lambda(\theta) \frac{\partial W_{fiber}(\theta)}{\partial \lambda(\theta)} = c_3 (\exp(c_4 (\lambda(\theta) - 1)) - 1) \quad (3)$$

where c_3 is exponential fiber stress coefficient, c_4 is the fiber uncrimping coefficient and $\lambda(\theta)$ is the fiber stretch in the orientation of θ . Using our proposed constitutive model, model displacements were fitted to the experimental displacements simultaneously at 7, 10, 20, 30 and 45 mm Hg using a genetic optimization algorithm, which estimated a unique set of material parameters.

Two deformation parameters (SCE: the scleral canal expansion, PLD: the posterior laminar deformation) were calculated for each eye at 10, 30 and 45 mm Hg as defined on Figure 2.

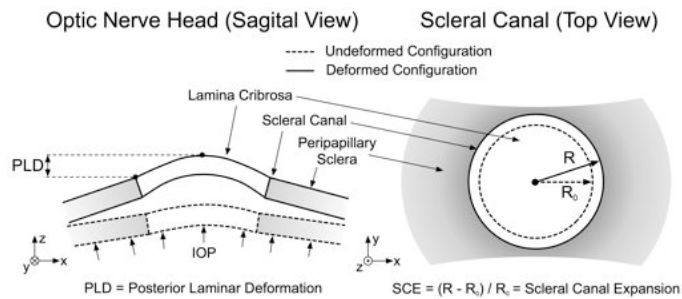


Figure 3. Definition of the two deformation parameters.

Finally, Peak maximum principal strains and maximum principal stresses were monitored in the peripapillary sclera region (Regions 5-8) of each eye.

RESULTS

On average, eyes from old monkeys exhibited lower scleral strains and scleral canal expansion, but higher scleral stresses and posterior laminar deformation than eyes from young monkeys (Table 1). For each eye, scleral canal expansion and scleral strains were nonlinear functions of IOP, showing a large increase of scleral stiffness with IOP.

Young Group

IOP range [mm Hg]	SCE [%]	PLD [μm]	Peak Max. Prin. Strain [×100]	Peak Max. Prin. Stress [×IOP]
5-10	0.31±0.05	4.33±2.51	0.52±0.26	28.0±7.38
5-30	1.03±0.29	22.8±8.91	1.29±0.60	35.9±11.0
5-45	1.31±0.42	36.0±13.1	1.50±0.69	38.7±10.6

Old Group

IOP range [mm Hg]	SCE [%]	PLD [μm]	Peak Max. Prin. Strain [×100]	Peak Max. Prin. Stress [×IOP]
5-10	0.25±0.05	8.89±3.50	0.23±0.14	38.9±5.60
5-30	0.64±0.14	44.8±13.1	0.59±0.22	51.3±9.95
5-45	0.74±0.21	69.8±19.4	0.71±0.28	54.6±9.84

Table 1. Scleral Strains, scleral stresses and deformation parameters (mean ± standard deviation) for 3 IOP ranges.

DISCUSSION

Scleral shells from older monkeys were considerably stiffer than those from young monkeys as they experienced lower strains but higher stresses. In eyes from old monkeys, the sclera acted minimally on the ONH in terms of scleral canal expansion, and as a consequence, higher posterior laminar deformations were observed. Conversely, sclera from young monkeys exhibited larger scleral canal expansion, which served to pull the lamina taut and reduce posterior laminar deformation. In aged eyes, damage to the ONH could be triggered by either high posterior laminar deformation or high stresses in the peripapillary sclera at high IOP, but this remains to be seen. Scleral canal expansion is a parameter that could eventually be measured clinically and could provide a marker for connective tissue damage in glaucoma patients. In this study, the ONH was assumed to be isotropic and linear with a modulus of 1 MPa for both the young and old eyes. Therefore the posterior laminar deformation data should be taken with caution, as the ONH may also exhibit stiffening with aging. Further work is needed to investigate the aging effects on the ONH and this is currently under investigation in our laboratory [4].

REFERENCES

- Hernandez, M. R., Xing Luo, X., Andrzejewska, W., Neufeld, A. H., 1989, "Age-related changes in the extracellular matrix of the human optic nerve head," Am J Ophthalmol, 107, pp. 476-484.
- Erne, O. K., Reid, J. B., Ehmke, L. W., Sommers, M. B., Madey, S. M., and Bottlang, M., 2005, "Depth-dependent strain of patellofemoral articular cartilage in unconfined compression," J Biomechanics, 38, pp. 667-672.
- Weiss, J. A., Maker, B. N., and Govindjee, S., 1996, "Finite element implementation of incompressible, transversely isotropic hyperelasticity," Comput Methods Appl Engr, 135, pp. 107-128.
- Downs, J. C., Roberts, M. D., Burgoyne, C. F., Hart, R. T., 2007, "Finite element modeling of the lamina cribrosa", ASME proceedings.