Biomechanics in Glaucoma: Insights from Computational Studies

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ABSTRACT

Glaucoma is a common ocular disease in which mechanics plays a central role. Due to the difficulty of making experimental measurements, computational modeling is ideally suited to help understand the link between mechanics and the disease process. We describe the results of simulations on idealized and patient-specific models that highlight the importance of scleral properties on the biomechanics of the eye.

INTRODUCTION

Glaucoma describes a group of potentially blinding ocular disorders. Approximately 60.5 million people worldwide will have glaucoma in 2010, increasing to 79.6 million by 2020 [1]; of these, 8.4 million will be bilaterally blind by 2010, increasing to 11.2 million by 2020. The central event in glaucoma is slow and irreversible damage of retinal ganglion cells, responsible for carrying visual information from the retina to the brain (see Figure 1). As these cells become damaged and eventually die, vision is lost.

The eye is internally pressurized, with the level of pressure within the eye being known as the intraocular pressure (IOP). Although glaucoma can occur at any level of IOP, we know elevated IOP is a risk factor for glaucoma [2-5], and that significant, sustained IOP reduction benefits most patients [3, 4, 6, 7], although some patients continue to progress even with treatment [3, 6]. Unfortunately, we do not understand the mechanism by which elevated IOP leads to the loss of retinal ganglion cells.

There are two theories to explain how elevated IOP damages retinal ganglion cells: vasogenic and biomechanical. These theories are not mutually exclusive; here we focus on the biomechanical theory, which is the subject of much recent research, see e.g. the review [8]. This theory hypothesizes that IOP deforms the optic nerve head (ONH) tissues, and in particular, the lamina cribrosa (LC; Figure 1). This deformation causes a change in lamina cribrosa astrocytes, leading to gliosis and retinal ganglion cell damage. This theory is supported by much circumstantial evidence, e.g. retinal ganglion cell damage occurs at the level of the LC; certain features of vision loss in glaucoma are consistent with the physical structure of the LC [9]; astrocytes are sensitive to mechanical stretch (e.g. [10]); and the LC is a very biomechanically active tissue [11].

To evaluate this theory, it is essential to understand the biomechanical environment in the optic nerve head in the normal and glaucomatous eye. This is challenging, since the optic nerve is small and relatively inaccessible. We have therefore adopted a computational modeling approach, informed by available experimental data.

METHODS

Finite element models of the whole eye have been constructed. Initially these were based on a generic ocular geometry [12], but more recently they have incorporated key features of scleral geometry as measured by high-resolution MR scans [13] and of optic nerve head anatomy as measured by 3D histologic reconstructions [14] (Figure 2).

In addition to specifying the geometry of the problem, we must specify material properties for the constituent tissues. In general this is challenging, since most soft connective tissues show nonlinearity and anisotropy [15]; in the case of the eye, it is particularly challenging since experimental measurements have not been carried out on several of the tissues of the optic nerve head. In the absence of suitable data, we have assumed linear and isotropic material properties based on experiments carried out on similar tissue types, as discussed in more detail elsewhere [12, 16, 17]. More recent work has used nonlinear material properties for sclera, as measured in biaxial tests [18, 19].

All simulations have been carried out using commercial software (ANSYS). The exterior surface of the eye has a pressure of zero imposed on it, while the interior surface of the ocular shell is pressurized to IOP levels from 5 to 50 mmHg. Zero displacement is imposed on a small region of the anterior cornea to prevent translation while leaving the optic nerve head tissues free to deform.

RESULTS

Models based on both idealized and generic ocular geometries give generally similar results, the main features of which are:

- Computed strains in the lamina cribrosa and pre-laminar neural tissue, which are believed to be centrally involved in the glaucomatous disease process, reach levels of 12-15% at highly elevated IOPs. These strains exceed measured threshold values at which ONH cells are affected by mechanical stimulations [10, 20].
- Compressive strains (third principal strain) have larger magnitude than extensile strains (first principal strain) in the optic nerve head region [11].
- The mechanical properties and thickness of the sclera have a very substantial effect on ONH biomechanics. In fact, of all the factors considered in several sensitivity analyses [16, 17], they were the most influential factors determining strains and stresses in the lamina cribrosa and prelaminar neural tissues.

In view of the apparent importance of scleral properties in glaucoma, our ongoing work seeks to better determine the mechanical properties of human sclera. Results of biaxial mechanical testing of sclera will be presented, as well as further modeling studies based on these measured data.

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REFERENCES


Figure 1: Important tissues in glaucomatous optic neuropathy. Left: cross-sectional overview of a human eye. The boxed region is the optic nerve head area, where the optic nerve exits the eye posteriorly via the scleral canal. Middle (after Hayreh): Overview of the major anatomical features of the optic nerve head. LC – Lamina Cribrrosa; PCA – Posterior ciliary arteries; C – choroid; R – retina; S – sclera. Right: en face view of the human lamina cribrosa, showing connective tissue elements only and pores, through which the retinal ganglion cell axons pass.
Figure 2: Models used for finite element modeling of optic nerve head biomechanics. *Left:* Generic human ocular model, showing an overall view of the eye with the optic nerve head region at the bottom. *Centre:* Magnified views of the optic nerve head region and corresponding finite element mesh, with different tissue regions labelled. *Right:* Cross-sectional view through a reconstructed human optic nerve head, based on serial histologic sections. Legend: S = Superior; I = Inferior; N = Nasal; T = Temporal. Show generic eye model, scleral geometry and ONH geometry. From Sigal et al. [12] (left and centre) and [11] (right).

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![Strain plots](image)

Figure 3: Contour plots of computed strain magnitudes in an individual-specific optic nerve head model (cross-sectional view), at an IOP of 50 mmHg. From Sigal et al. [11].