Multiscale Biomechanical Modeling of the Human Eye

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ABSTRACT

A multiscale modeling approach is presented for advancing understanding of the biomechanical behavior of the human eye under various physiological conditions. The approach involves the development of large and small scale numerical models to predict stress and strain throughout the eye and its constituent anatomical structures that span length scales ranging from centimeters to microns. The numerical models are based on computational fluid dynamic (CFD) analysis combined with a fully-coupled fluid-structure interaction (FSI) capability as well finite element-based structural analysis. Preliminary modeling results of pressure-induced tissue deformation are demonstrated via application to an idealized eye geometry. A physical cadaveric eye model that will be used for model validation is also presented. A discussion is given of challenges and opportunities of using this approach to advance understanding of biomechanical behavior of the human eye.

Keywords: Eye Biomechanics, intraocular pressure, IOP, intracranial pressure, ICP, optic nerve sheath diameter, ONSD, intracranial fluid structure interactions, optic nerve stress, stress and strain of eye tissue.

1 INTRODUCTION

The human eye is a highly specialized organ consisting of various tissues with different physical properties and functionality and pressurized fluid-filled compartments in balance with an intricate neurovasculature system. Owing to this complexity, there are many aspects of the biomechanical behavior of the eye that are not fully understood, yet critical to proper function. Among these are the relationships between intraocular (IOP) and intracranial (ICP) pressures and the structurally sensitive constituents such as the ocular globe, retina and optic nerve. These pressures can have a significant and detrimental impact on vision, both short and long term. For example, elevated IOP is known to be a major risk factor for glaucoma, the second leading cause of blindness worldwide [1]. Moreover, pressure related ocular effects have drawn international attention recently due to reported observations of significant ocular abnormalities in astronauts that are subjected to prolonged exposure to low gravity environments. The anatomical changes and subsequent visual sequelae include choroidal folds, retinal nerve fiber layer thickening, cotton wool spots, optic disc edema, optic nerve protrusion, hyperopic shifts and visual deficits among others [2, 3]. The etiology of these effects is not well understood and is hypothesized to be primarily related to the observed cephalad fluid shift observed during space flight, but they need to be resolved to enable longer term space exploration.

To date, various mathematical models have been developed in an attempt to elucidate the impact of pressure...
on the eye and its constituent tissues. However, these models tend to be limited in scope to biomechanical deformation of portions of the eye under specific mechanical loadings. Moreover, the majority of these models have been purely structural in nature, i.e. neglecting fluidic analysis. A multiscale modeling approach is essential for analyzing critical physiological effects of the eye as these occur in anatomical features that span length scales ranging from centimeters to microns. Our modeling effort involves the use of computational fluid dynamics with fully coupled fluid structure interactions (CFD-FSI) for predicting flow, pressure and tissue deformation, and the coupled impact that deformed compliant ocular tissues have on fluid pressure. We demonstrate the analysis via application to an idealized model of the eye that includes its basic constituents: iris, lens, corneo-sclera shell and a portion of the optic nerve structure as shown in Fig. 1a. We used this model to compute the level of stress and strain throughout the eye as shown in Fig. 2. In addition, we use numerical finite element-based structural analysis to predict the deformation of ocular tissues, such as the optic nerve sheath, under variations in ICP/IOP loading. We discuss the application of the models and the challenges and opportunities of using computational modeling to advance understanding of biomechanics of the human eye discuss model validation using a human cadaveric eye model and head-down bed rest studies.

2 THEORY AND MODELING

The vast majority of biomechanical models used to study the human eye have been purely structural in nature (i.e. no fluidic analysis) [4-7,9,10]. Many of these have been developed to study the behavior of the cornea. Similar models have been developed to study IOP-induced stress at the optical nerve head (ONH). Fewer models have been developed to study the entire corneo-scleral shell to analyze its response to IOP or to indentation or applanation tonometry. Very few models have been reported that take into account coupled fluid-structure interactions in the eye as presented here, and these tend to be focused on understanding vibration in the eye. The material properties incorporated into these models varied in complexity, with most being isotropic and a few being anisotropic. However, most researchers have considered small deformations and have made the simplifying assumption that the tissues elastic behavior is linear.

The outer (corneo-sclera) shell of the eye is surrounded by fatty tissue and encased by the bony orbit. There are also six extraocular muscles attached to the eye. The bony orbit, muscles and fatty tissue can be included in the model explicitly, which adds considerable complexity, or as an approximation, they can be accounted for in terms of boundary conditions, either via pressure prescribed on the outer boundary of the corneo-sclera shell, or physical constraints at points on its exterior surface.

In our initial work we have studied an idealized model of the eye as shown in Fig. 1. A stereolithography (STL) file was produced from CAD generated eye geometry. This file was then imported into the computational domain of a numerical model. Fig. 1b shows the progression from the CAD geometry to its computational mesh. We have used a CFD-based program FLOW3D (www.flow3d.com) for the analysis. This program takes into account fully-coupled fluid-structure interaction. Different equation sets and numerical schemes are used for the fluid and stress analysis, respectively. The fluid is modeled using the continuity and Navier-Stokes equations for incompressible Newtonian flow,

\[ \nabla \cdot \mathbf{v} = 0 \]  
\[ \rho \left( \frac{\partial \mathbf{v}}{\partial t} + \mathbf{v} \nabla \mathbf{v} \right) = -\nabla p + \nabla \cdot (\eta \nabla \mathbf{v}) \]

where \( v, \rho \) and \( \eta \) are the velocity, pressure and viscosity of the fluid, respectively. The fluid equations are solved using the Volume-Of-Fluid (VOF) method [8], which is implemented using a finite-differencing numerical scheme that employs a structured finite-difference mesh throughout the fluid regions. Tissue deformation is modeled using the Galerkin finite element method (FEM). The equation governing tissue deformation is

\[ \rho \frac{d^2 \mathbf{x}}{dt^2} = \nabla \cdot \mathbf{\tau} + \rho \mathbf{b} \]

where \( \rho \) is the tissue density, \( \mathbf{x} \) is the coordinate of a point in the tissue, \( \mathbf{\tau} \) is the Cauchy stress tensor and \( \mathbf{b} \) is the body force vector. The Cauchy stress tensor is a measure of the stress in the tissue and is computed using:

\[ \mathbf{\tau}^{n+1} = \mathbf{\tau}^n + \left( \mathbf{K} + \frac{2}{3} \mathbf{G} \right) \text{tr}(\mathbf{E}') + 2\mathbf{GE}' \]

where \( n \) and \( n+1 \) refer to successive time-steps and \( \mathbf{K} \) and \( \mathbf{G} \) are the bulk and shear moduli of the tissue, respectively. The term \( \text{tr}(\mathbf{E}') \) is the trace of the incremental strain tensor,

\[ \mathbf{E}' = \frac{1}{2} \left[ (\nabla \mathbf{u})^T + \nabla \mathbf{u} \right] \]

where \( \mathbf{u} = \mathbf{x}^{n+1} - \mathbf{x}^n \) is the incremental displacement and \( \mathbf{x}^n \) and \( \mathbf{x}^{n+1} \) are the positions of a point in the tissue at time steps \( n \), and \( n+1 \), respectively. To track fluid-structure interaction, the fluid pressure is applied to the boundary faces of the finite element mesh during each time step of the computation. Pressure is extracted for each boundary face of the FE mesh from the fluid mesh by interpolation. The changing conformation of the tissue affects the fluid flow, i.e. as the tissue surface moves inward or outward, it
causes a corresponding inward or outward motion of the tissue layers.

For our initial analysis, we assume that the interior of the eye is filled with a liquid having the same properties as H$_2$O. Standard atmospheric pressure is applied outside the eye. In order to pressurize the interior of the eye in a self-consistent way, fluid is injected into its interior compartments until a nominal IOP of 22 mmHg is achieved, as indicated in Fig. 2a. As the incompressible fluid flows into the interior of the eye, the surrounding tissues deforms to accommodate the additional volume of fluid. The principle strain (deformation) profiles in the x and y directions throughout the eye tissue at the target pressure are shown in Figs. 2b and 2c. The modeling indicates that the maximum x-directed strain occurs along the back edge of the corneo-sclera shell, just above the region at which the optic nerve attaches to the posterior eye. The maximum y-directed strain occurs at the top and bottom edges of the corneo-sclera shell, midway along the ocular cavity.

Furthermore, we have developed several small-scale, 2-D axisymmetric, FE-based structural models of the posterior eye that take into account tissues that include a portion of the corneo-scleral shell attached to the optic nerve head, the scleral canal, laminar cribrosa, prelaminar neural tissue, and the optic nerve (pia mater, subarachnoid space (SAS), trabeculae, and optic nerve sheath (ONS)). We have utilized the COMSOL (www.comsol.com) structural analysis solver for this investigation. For this model, we used properties (thickness and Young’s modulus) provided in the literature [9] for all tissues except for the trabeculae and ONS, which to the best of our knowledge are unknown. We fit these latter properties to measured optic nerve sheath diameter (ONSD) vs. ICP data as described below. Under conditions of elevated ICP, the SAS can become engorged with cerebrospinal fluid and balloon substantially. This, in turn, can deform the posterior portion of the ocular shell and induce undesired pressure on the optic nerve and deformation of the posterior orbital layers. Fig. 3a shows the posterior eye geometry with IOP = 15.5 mmHg and with ICP = 0. It should be noted that this figure shows the un-deformed geometry (white interior) superimposed with the deformed geometry (colored interior), wherein the deformation is greatly magnified for visual purposes. The deformation is radially outward in all directions in response to IOP. This level of deformation is consistent with previous work by Sigal et al [10]. The model predicts a circumferential stress in the shell of \( \sigma_{\text{shell}}=1.46 \times 10^3 \text{N/m}^2 \) at its upper boundary as shown in Fig. 3a, which is consistent with the estimation of hoop stress for a compliant shell with the dimensions used in the model: \( R = 12 \text{mm}, \) thickness \( t=0.8 \text{ mm}, \) i.e. \( \sigma_{\text{shell}}=\text{IOP} \times \frac{R}{2t} = 1.6 \times 10^3 \text{N/m}^2. \) Fig. 3b shows ONS diameter when ICP = 65 mmHg. The white regions between the ON and the deformed ONS represent the trabeculae. We used an effective Young’s modulus for this tissue that was fit to measured data. In the case shown, the ONSD reaches a maximum of 50% greater than in its undeformed state, located 3mm from the globe, which is consistent with data taken from cadaveric eyes by Hansen et al [11]. (Fig. 3c). The difference in slopes in Fig. 3c might be due to the fact that the trabeculae and ONS need to be modeled using nonlinear elastic properties, which we will investigate in future projects.

In addition to the computational modeling, we are developing experimental models to validate and calibrate the numerical predictions. One such model, shown in Fig. 4, consists of post-mortem non-fixated human (cadaveric) eyes with isolated human optic nerve preparations obtained from autopsies. This model will reproduce acute changes in ICP and IOP to be correlated with ocular structural changes, which will be evaluated using ultrasound techniques and optical coherence tomography. For the ICP
measurements, two blunt injection cannulae will be inserted into the perineural SAS. The cannulae will be fixated and the SAS sealed using silicone plastic material. One of the cannulae will be connected with a pressure sensor and the other one with a height adjustable water tank. The water tank will contain isotonic sodium chloride solution and will be height adjustable to apply controlled pressures within the SAS to mimic variations in ICP. The physical models will be used to validate the numerical predictions. The physical models will be used to validate the numerical predictions.

3 CONCLUSIONS

The human eye is a highly complex organ, and much remains to be known about its biomechanical response to elevated intraocular and intracranial pressure (IOP and ICP). The interest in these effects has grown dramatically recently due to new observations of myriad pressure related ocular abnormalities in astronauts exposed to microgravity environments [2-3]. In this presentation we have described a method to advance understanding in this field. Our approach involves a coupled modeling and experimental effort in which numerical models are used to predict the biomechanical response of eye under pressure loading, and a physical model combined with appropriate imaging modalities are used to validate the model predictions of tissue deformation within the eye. This approach could provide a much better understanding of causal effects responsible for the observed changes seen in terrestrial disease states such as Glaucoma and Idiopathic Intracranial Hypertension. The models and experiments may also assist in developing predictive paradigms for humans working in a microgravity environment for extended periods.

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4 REFERENCES