Integrated Model of the Eye/Optic Nerve Head Biomechanical Environment

C. R. ETHIER\(^1\), A. FEOLA\(^1\), J.G. MYERS\(^2\), E. NELSON\(^2\), J. RAYKIN\(^1\) AND B. SAMUELS\(^3\)

\(^1\)DEPARTMENT OF BIOMEDICAL ENGINEERING, GEORGIA INSTITUTE OF TECHNOLOGY/EMORY UNIVERSITY, ATLANTA, GA
\(^2\)NASA GLENN RESEARCH CENTER, CLEVELAND, OH
\(^3\)DEPARTMENT OF OPHTHALMOLOGY, U. ALABAMA AT BIRMINGHAM, BIRMINGHAM, AL
Structural Changes in the Posterior Eye


Normal

Astronaut with VIIP
Hypothesis

Increased CSF pressure, transmitted to the RB-SAS, drives remodeling of connective tissues in the posterior eye and optic nerve sheath

Eventually leads to the vision disturbances characteristic of VIIP
Goal

Develop an integrated model approach to understand how environmental conditions impact deformation of tissues of the posterior eye and optic nerve sheath

Key tools: Numerical and finite element modeling
Numerical Model
Lumped Parameter Eye Model

Model features:
- Four-compartment model
  - Anterior Chamber
  - Blood compartment (cardiovascular model)
  - Globe
  - Retrobulbar subarachnoid space (rSAS)

Simulating Head Down Tilt (HDT)

\[15^\circ\]
Finite Element Model
Finite Element Geometry


Adopted from Ekington et al. 1990.
Model Overview
Finite element model

Diagram showing:
- Axis of Rotation
- Prelaminar Tissue
- Annular Ring
- Peripapillary Sclera
- Lamina Cribrosa
- Central Retinal Vessel
- Optic Nerve
- Pia Mater
- Dura Mater
Tissue Constitutive Models

- Mooney-Rivlin plus von Mises Distributed Fibers
  - Proposed by Girard and Ethier for the sclera
  - Implemented into FEBio V2 by Gouget and Girard for thin tissues

\[ \Psi = F_1(\vec{I}_1, \vec{I}_2) + \int_{\theta_p - \frac{\pi}{2}}^{\theta_p + \frac{\pi}{2}} P(\theta) F_2(\tilde{\lambda}[\theta])d\theta + \frac{K}{2}[\ln(J)]^2 \]

- F_1 represents ground substance (neo-Hookean): \( F_1 = C_1(\vec{I}_1 - 3) \)
- F_2 represents collagen fibers
  - Collagen fibers are loaded within their non-linear region

\[ \dot{\lambda} \frac{\partial F_2}{\partial \dot{\lambda}} = 0, \dot{\lambda} \leq 1 \]

\[ \dot{\lambda} \frac{\partial F_2}{\partial \dot{\lambda}} = C_3(e^{c_4(\lambda - 1)} - 1), 1 < \dot{\lambda} \leq \lambda_m \]
Collagen Orientation in the Sclera

- Sclera: collagen fibers treated as transversely isotropic
- Peripapillary sclera: moderately aligned collagen fibers
- Annular ring: highly aligned collagen fibers

- Pijanka et al. 2012 & Zhang et al. 2015
Collagen Orientation in the ONS

Pia mater and dura mater: fibers were modeled as transversely isotropic

~Raspanti et al. 1992 Noort et al. 1980 & Raykin et al. 2015

Dura Mater
# Tissue Material Properties

<table>
<thead>
<tr>
<th>Material Inputs</th>
<th>Mooney-Rivlin solid with embedded collagen fibers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ground Stiffness ($c_1$)</td>
<td>Collagen Stiffness ($c_3$ &amp; $c_4$)</td>
</tr>
<tr>
<td>Tissue Properties</td>
<td>Distribution of embedded collagen fibers</td>
</tr>
</tbody>
</table>

- Sclera
- Peripapillary sclera
- Annular ring
- Pia mater
- Dura mater
- Prelaminar neural tissue
- Lamina cribrosa
- Optic Nerve
- Central retinal vessel
Integration Overview

Lumped-Parameter Model

Ocular Model
- Aqueous Humor
- Globe
- Blood

Initial Condition
- IOP₀
- MAP₀
- ICP₀

Simulated HDT
- IOP
- MAP
- ICP

Finite Element Model
Outcome measures

- Strain (fractional tissue elongation) in all tissue regions
  - Strain is a tensor and can be decomposed into 3 primary components
    - First principal strain (stretch)
    - Second principal strain
    - Third principal strain (compression)

- Why do we care about strain?
  - Cells are mechanosensitive and alter their phenotype in response to mechanical strain
Primary outcome measures: peak tensile and compressive strains in the prelaminar tissue, lamina cribrosa and retrolaminar optic nerve
Results
Pressures from Eye Model

Intraocular Pressure

Blood Pressure

- Arterial P
- Venous P

HDT

15°
Principal Strain Magnitudes

1\textsuperscript{st} Principal Strain (Tension)

3\textsuperscript{rd} Principal Strain (Compression)

Supine

HDT

3\%

-3\%
### HDT on ONH Deformation

<table>
<thead>
<tr>
<th>Area</th>
<th>Supine</th>
<th>HDT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lamina Cribrosa</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tension</td>
<td>0.60%</td>
<td>0.93%</td>
</tr>
<tr>
<td>Compression</td>
<td>-0.98%</td>
<td>-1.51%</td>
</tr>
<tr>
<td>Retrolaminar Optic Nerve</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tension</td>
<td>1.16%</td>
<td>1.39%</td>
</tr>
<tr>
<td>Compression</td>
<td>-1.64%</td>
<td>-2.44%</td>
</tr>
<tr>
<td>Prelaminar Neural Tissue</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tension</td>
<td>0.77%</td>
<td>1.25%</td>
</tr>
<tr>
<td>Compression</td>
<td>-1.75%</td>
<td>-2.69%</td>
</tr>
</tbody>
</table>
Summary

- Our integrated model approach predicts an increase in strains at the ONH after HDT.
- These strains, if persistent, may induce a phenotypical change in ONH cells.
- Future experimental work should examine how strains initiate a remodeling response in the optic nerve and optic nerve sheath.
Experimental Effects of ICP on the Optic Nerve
Experiment Objective

- Measure strain in the optic nerve due to elevations in ICP
- Refraction of the X-ray by the sample
- Tissues can be intact and untreated (no contrast agent required)

- However, for resolution of our small complex tissues requires X-rays with high spatial coherence
Experimental Design

- 3 porcine eyes
  - Micro-CT scans were acquired at an ICP = 4, 10, 20 & 30 mmHg
  - IOP was kept constant at 15 mmHg
Phase-contrast micro-CT

Non-uniform expansion of the dura mater

CSFp = 4 mmHg

CSFp = 30 mmHg
Optic Nerve Deformation

ICP

CSFp: 10 mmHg  20 mmHg  30 mmHg

1st Principal Strain

3rd Principal Strain

10%  -10%
Experimental Work Summary

- Increased ICP directly elevated strains in the optic nerve
- Our experimental results agree with earlier finite element model work
  - The magnitude of strain was higher in experimental results
Ongoing Work
Additional FE Work

- Prelaminar Tissue
- Annular Ring
- Peripapillary Sclera
- Axis of Rotation
- Lamina Cribrosa
- Central Retinal Vessel
- Optic Nerve
- Pia Mater
- Dura Mater
- Bruch’s Membrane
- Choroid
Simulate Choroidal Swelling

- Choroid modeled as a solid mixture to allow swelling
  - Linear-Elastic material (E = 0.3 MPa)
  - Apply uniform swelling (5 uL) to simulate volume change during cardiac cycle
Impact of Choroidal Swelling

IOP = 15 mmHg
Choroid Swelling = 0 uL

IOP = 15 mmHg
Choroid Swelling = 5 uL

1st Principal Strain

3rd Principal Strain
### Latin Hypercube Sampling Inputs

<table>
<thead>
<tr>
<th></th>
<th>Cardiovascular</th>
<th>Central Nervous</th>
<th>Eye Model</th>
<th>FEM</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Run 1</strong></td>
<td>$w_1 \ldots w_{42}$</td>
<td>$x_1 \ldots x_{17}$</td>
<td>$y_1 \ldots y_3$</td>
<td>$z_1 \ldots z_{20}$</td>
</tr>
<tr>
<td><strong>Run 2</strong></td>
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<td>$y_1 \ldots y_3$</td>
<td>$z_1 \ldots z_{20}$</td>
</tr>
<tr>
<td><strong>Run N</strong></td>
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<td>$y_1 \ldots y_3$</td>
<td>$z_1 \ldots z_{20}$</td>
</tr>
</tbody>
</table>

16 Compartment Cardiovascular System

6 Compartment Central Nervous System

Blood Pressure

4 Compartment Eye

ICP

Aqueous Humor

Globe

Blood

IOP
Acknowledgements

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