Microgravity-driven Optic Nerve/Sheath Biomechanics Simulations

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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

Study the biomechanical response of the optic nerve sheath and posterior eye to elevated CSF pressures

Key tool: Finite element modeling
Methods
Basic Modeled Geometry


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

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

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

- \( F_1 \) represents ground substance (neo-Hookean): \( F_1 = C_1(\tilde{I}_1 - 3) \)

- \( F_2 \) represents collagen fibers
  - Collagen fibers are loaded within their non-linear region

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

\[
\dot{\lambda} \frac{\partial F_2}{\partial \dot{\lambda}} = C_3 (e^{C_4(\lambda-1)} - 1), \quad 1 < \dot{\lambda} \leq \lambda_m
\]
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
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
Latin Hypercube Sampling (LHS)

How do variations in pressures and tissue mechanical properties affect tissue strains?
Latin Hypercube Sampling (LHS)

Primary outcome measures: peak tensile and compressive strains in the retina, lamina cribrosa and retrolaminar optic nerve

Regions of Interest:

- Retina
- Lamina Cribrosa
- Optic Nerve
Tissue Material Properties

1. Linear-elastic, homogenous and isotropic
   ◦ **Tissues**: lamina cribrosa, optic nerve, retina and retinal vessel
     ◦ Simplification chosen due to limited information & low impact
   ◦ 2 input parameters: stiffness (E) and tissue compressibility (v)

2. Mooney-Rivlin solid with embedded collagen fibers
   ◦ **Tissues**: sclera, peripapillary sclera, annular ring, pia mater and dura mater
     ◦ Allows more complex, nonlinear behavior and collagen fiber orientation and stiffness
Principal Strain Magnitudes

1\textsuperscript{st} Principal Strain (Tension)

3\textsuperscript{rd} Principal Strain (Compression)

ICP: 0 mmHg

ICP: 20 mmHg
Principal Strain Directions

1\textsuperscript{st} Principal Strain

3\textsuperscript{rd} Principal Strain
Is LHS Sampling Unbiased?

Use sign test to identify possible sampling bias
- Do input parameters generated by LHS have a median value significantly different than our baseline value?
- Answer: no (p>0.48 for all input parameters)

Confirmed by scatter plots
Lamina Cribrosa

Peak Compression

Peak Tension

Cumulative Probability

Peak Strain (%)
Optic Nerve

Peak Compression

Peak Tension

Cumulative Probability

Peak Strain (%)

-5%  -3%  -1%  1%  3%  5%

5.6%
47.3%

Upright ICP
Supine ICP
Elevated ICP
Prelaminar Tissue

Peak Compression

Cumulative Probability

Peak Strain (%)

Peak Tension

-6% -2% 2% 6%

0 0.2 0.4 0.6 0.8 1

Upright ICP
Supine ICP
Elevated ICP
What creates “extreme strains”? 

- ICP significantly higher in G2
- Lower pia mater ground substance and fiber stiffness in G2
- Lower MAP and higher optic nerve compressibility in G2

![Graph showing cumulative probability vs. peak strain for G1 and G2 groups.](image-url)
Summary

- 47% of individuals experience “extreme strains” in the optic nerve (c.f. 41% of astronauts suffering from VIIP syndrome)
- Identified specific factors that are associated with these extreme strains
  - Elevated ICP, weak pia mater
- Future experimental work should examine how strains initiate a remodeling response in the optic nerve and optic nerve sheath
Ongoing Work
## Integration

### LHS Inputs

<table>
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<th></th>
<th>Cardiovascular</th>
<th>Central Nervous</th>
<th>Eye FE</th>
</tr>
</thead>
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<tr>
<td>Run 1</td>
<td>$x_1 \ldots x_{42}$</td>
<td>$y_1 \ldots y_{17}$</td>
<td>$z_1 \ldots z_{20}$</td>
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<td>$z_1 \ldots z_{20}$</td>
</tr>
</tbody>
</table>

16 Compartment Cardiovascular System

6 Compartment Central Nervous System

Blood Pressure

Intracranial Pressure (ICP)
Model Integration

Eye

IOP

MAP

ICP

CNS

CVS

Material Properties

Retina Strain

LC Strain

Optic Nerve Strain

Material Properties
Acknowledgements

- NASA support, grant NNX13AP91G
- Drs. DeVon Griffin and Beth Lewandowski