Modeling the Effects of Spaceflight on the Posterior Eye in VIIP


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Commercial Relationships Disclosure

No relationships to disclose for any co-author

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VIIP Syndrome

Permanent changes in visual function/ocular anatomy after long-duration space flight

- 41.7% incidence in U.S. astronauts
- Choroidal folds, papilledema, globe flattening, optic nerve dura distention/kinking

Hypothesis

Increased intracranial pressure (ICP) due to cephalad fluid shift leads to:

- Connective tissue remodeling in the posterior eye/optic nerve sheath
- Mechanical loading/insult to ONH cells and tissues, and eventual vision loss
Goal

Study the biomechanical response of the optic nerve sheath and posterior eye to changes in ICP

- Account for different ICP “cases”
  - Terrestrial supine
  - Terrestrial standing
  - Microgravity (presumed elevated ICP)
- Account for variations of ICP within these cases
- Account for variations in tissue properties
Methods

COMPUTATIONAL (FINITE ELEMENT) MODEL
Model Geometry

- Axis of Rotation
- Retina
- Peripapillary Sclera
- Sclera
- Lamina Cribrosa
- Central Retinal Vessel
- Optic Nerve
- Pia Mater
- Dura Mater

- Model Geometry
## Model Inputs

### Pressures

<table>
<thead>
<tr>
<th>Name</th>
<th>Abbreviation</th>
<th>Units</th>
<th>Baseline</th>
<th>Standard Deviation</th>
<th>Low</th>
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<tr>
<td>Intraocular Pressure</td>
<td>IOP</td>
<td>mmHg</td>
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<td>1.85</td>
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<td>19</td>
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<td>Intracranial Pressure</td>
<td>ICP</td>
<td>mmHg</td>
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<td></td>
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<tr>
<td>Upright</td>
<td></td>
<td></td>
<td>0</td>
<td>2.0</td>
<td>-4</td>
<td>4</td>
</tr>
<tr>
<td>Supine</td>
<td></td>
<td></td>
<td>10</td>
<td>2.0</td>
<td>6</td>
<td>14</td>
</tr>
<tr>
<td>Elevated</td>
<td></td>
<td></td>
<td>20</td>
<td>2.5</td>
<td>15</td>
<td>25</td>
</tr>
<tr>
<td>Mean Arterial Pressure</td>
<td>MAP</td>
<td>mmHg</td>
<td>86</td>
<td>7.96</td>
<td>60</td>
<td>112</td>
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</table>

### Biomechanical Properties

<table>
<thead>
<tr>
<th>Name</th>
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<th>Units</th>
<th>Baseline</th>
<th>Standard Deviation</th>
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<th>High</th>
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<tr>
<td>Sclera Young’s modulus</td>
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<td>MPa</td>
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<td>MPa</td>
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<td>0.1</td>
<td>0.9</td>
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</tr>
<tr>
<td>Pia Mater Young’s modulus</td>
<td>Pia</td>
<td>MPa</td>
<td>5</td>
<td>1</td>
<td>9</td>
<td></td>
</tr>
<tr>
<td>Dura Mater Young’s modulus</td>
<td>Dura</td>
<td>MPa</td>
<td>1</td>
<td>0.2</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Optic Nerve Young’s modulus</td>
<td>ON</td>
<td>MPa</td>
<td>0.05</td>
<td>0.01</td>
<td>0.09</td>
<td></td>
</tr>
<tr>
<td>Retina Young’s modulus</td>
<td>Ret</td>
<td>MPa</td>
<td>0.05</td>
<td>0.01</td>
<td>0.09</td>
<td></td>
</tr>
<tr>
<td>Retinal Vessel Young’s modulus</td>
<td>RV</td>
<td>MPa</td>
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<td>0.2</td>
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<td>Neural Poisson’s ratio</td>
<td>Poisson’s</td>
<td>-</td>
<td>0.45</td>
<td>0.4</td>
<td>0.49</td>
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</table>
Latin hypercube sampling

Efficiently simulates variation in input parameters (Monte Carlo)
Outcome measure

Strain in ONH tissues

- Physical quantity that represents stretching of cells and tissues
- Local cells are mechanoresponsive
- Strain drives connective tissue remodeling in many other tissues, e.g. artery walls
Results

COMPUTATIONAL (FINITE ELEMENT) MODEL
Effect of ICP: Baseline case

1st Principal Strain (Stretch)

ICP: 0 mmHg

ICP: 10 mmHg

ICP: 20 mmHg

3rd Principal Strain (Compression)
### Average strains: Baseline case

<table>
<thead>
<tr>
<th>Tissue Region:</th>
<th>Lamina Cribrosa</th>
<th>Optic Nerve</th>
<th>Retina</th>
</tr>
</thead>
<tbody>
<tr>
<td>Strain Type:</td>
<td>Tension</td>
<td>Compression</td>
<td>Tension</td>
</tr>
<tr>
<td>ICP = 0 mmHg</td>
<td>0.57%</td>
<td>-0.86%</td>
<td>0.61%</td>
</tr>
<tr>
<td>ICP = 10 mmHg</td>
<td>0.78%</td>
<td>-1.11%</td>
<td>0.78%</td>
</tr>
<tr>
<td>ICP = 20 mmHg</td>
<td>0.97%</td>
<td>-1.35%</td>
<td>0.96%</td>
</tr>
</tbody>
</table>

**Regions of Interest:**

![Diagram of tissue regions](image)
Lamina Cribrosa Strain Histograms

Denote 5th and 95th percentile values as “Peak strains”
Distribution within population

Use Latin Hypercube Sampling

Cumulative Distribution

Histogram

Peak strain in LC

0% 1% 2% 3% 4% 5%
“Peak” Strains in Lamina Cribrosa

Cumulative Probability

Compression

Tension

Upright ICP
Supine ICP
Elevated ICP
“Peak” Strains in Retina

Cumulative Probability

- Compression
- Tension

- Upright ICP
- Supine ICP
- Elevated ICP
“Peak” Strains in Optic Nerve

Cumulative Probability

Upright ICP
Supine ICP
Elevated ICP

5% 20%
“Out of this World Strains”

<table>
<thead>
<tr>
<th>Tissue Region:</th>
<th>Lamina Cribrosa</th>
<th>Optic Nerve</th>
<th>Retina</th>
</tr>
</thead>
<tbody>
<tr>
<td>Strain Type:</td>
<td>Tension</td>
<td>Tension</td>
<td>Tension</td>
</tr>
<tr>
<td></td>
<td>Compression</td>
<td>Compression</td>
<td>Compression</td>
</tr>
<tr>
<td>Supine</td>
<td>8%</td>
<td>20%</td>
<td>10%</td>
</tr>
<tr>
<td></td>
<td>5%</td>
<td>6%</td>
<td>13%</td>
</tr>
</tbody>
</table>

Percentage of individuals with elevated ICP experiencing strains larger than those experienced under terrestrial conditions (standing or supine)
Optic Nerve Sheath

EXPERIMENTAL MEASUREMENTS
Collagen orientation in dura

SHG microscopy images of dura

0 mm Hg

Nerve Axis

10 mm Hg

Nerve Axis
Optic nerve has slack

Liu et al., BJO, 1992
What is state of ON stretch?

Expose optic nerve, transect, observe retraction (or not)

Perform craniotomy

Expose orbit

Remove periorbital tissue covering the optic nerve

Place markers on the optic nerve

Transect nerve and record axial retraction

Optic nerve retraction
Summary

ICP affects strains in ONH tissues:

- Average strain values are low
- Simulation of “population” shows that 5-20% of individuals will experience ICP-induced strains in space that are more extreme than those on earth

Uncertainties/Limitations

- Optic nerve appears to be under tension (?!)
- Some tissue properties still not well understood
- Pathophysiology of vision loss and connection with strain not established
BME at Georgia Tech/Emory