PROBABILISTIC MODELING OF OCULAR BIOMECHANICS IN VIIP: RISK STRATIFICATION

A. Feola¹, J.G. Myers², J. Raykin¹, E.S. Nelson², L. Mulugeta³, B. Samuels⁴, C.R. Ethier¹

¹Department of Biomedical Engineering, Georgia Institute of Technology/Emory University, Atlanta, GA; ²NASA Glenn Research Center, Cleveland, OH; ³Universities Space Research Association, Houston, TX; ⁴Department of Ophthalmology, U. Alabama at Birmingham, Birmingham, AL
The Eye in Microgravity

Edema

Posterior Globe Flattening
Optic Nerve ‘kinking’

Choroidal folds

-Mader et al. 2011; Kramer et al. 2012
Hypothesis

- Cephalad fluid shifts in microgravity affect intracranial and intraocular pressures, leading to altered biomechanical loads on the connective tissues of the posterior globe and optic nerve sheath.

- Leads to connective tissue remodeling that persists upon return to 1G, which is an important contributing factor to vision changes seen in the VIBP syndrome.

-humanresearchroadmap.nasa.gov
Goal & Approach

• **Goal:** To build a computational framework to understand the response at the optic nerve head (ONH) to elevations in intracranial pressure (ICP)
  – Examine how inter-individual variations alter deformations

• **Finite Element Analysis (FEA)**
  – Simulates effects of loads (pressures) on tissues with complex anatomy/material properties
  – Previously used to understand how intraocular pressure (IOP) alters the strains in the lamina cribrosa

-Sigal et al. 2004; Sigal et al. 2005
Geometric Model

• Overall Geometry

Taken from Liu and Kahn 1993
Geometric Model

• Optic Nerve Head

Taken from Elkington et al. 1990
Model Considerations

• Incorporate collagen fiber orientation and material properties
  – **Tissues:** sclera, peripapillary sclera, annular ring, pia mater and dura mater
    o Allow for us to incorporate more complex, nonlinear behavior and collagen fiber orientation and stiffness
  – 3 inputs describing tissue mechanical behavior: stiffness of the ground substance (c₁) and of the collagen fibers (c₃ and c₄)

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- Pijanka et al. 2012 & Zhang et al. 2015
Model Considerations

• Incorporate collagen fiber orientation and material properties
  – **Tissues:** sclera, peripapillary sclera, annular ring, pia mater and dura mater
    o Allow for us to incorporate more complex, nonlinear behavior and collagen fiber orientation and stiffness
  – 3 inputs describing tissue mechanical behavior: stiffness of the ground substance ($c_1$) and of the collagen fibers ($c_3$ and $c_4$)

• Linear-elastic, homogenous and isotropic
  – **Tissues:** lamina cribrosa, optic nerve, retina and retinal vessel
    o Simplifications of complex tissue behavior, but chosen due to limited information on the biomechanical properties
  – 2 input parameters: stiffness (E) and tissue compressibility ($\nu$)
• Peak tensile and compressive strains in the prelaminar neural tissue, lamina cribrosa (LC) and optic nerve
Latin Hypercube Sampling (LHS)

- Examine how variation in the pressures and tissue mechanical properties altered the strains in the optic nerve head (ONH)
Peak Strain Distributions in the ONH

- Examined the histograms and cumulative distribution functions (CDFs) of the peak strains of the lamina cribrosa, optic nerve and retina from each set of input parameters
  - Represents the distribution of peak strains over a population of individuals with our eye geometry
Lamina Cribrosa

- Decrease in strains as ICP increased

Graphs showing cumulative probability against peak strain for Peak Compression and Peak Tension, with different ICP conditions: Upright, Supine, and Elevated ICP.
Optic Nerve

- Strains outside the predicted physiological range with elevated ICP
Prelaminar Tissue

• Decrease in strains as ICP increased
LHS/PRCC

• Determines how the uncertainty in each input parameter influenced the peak tensile and compressive strains
  – Results in a correlation coefficient (±1) for each input parameter to each outcome measure
  – We ranked the magnitude of the correlation coefficient and summed them across each tissue region
  – Normalized this ranking to the highest possible ranking (i.e. 138) to determine the “cumulative influence factor”
Cumulative Influence Factor

- Cumulative influence factor for all 23 model inputs

- Considered input parameters with an average cumulative influence factor for all three ICPs > 0.5 as the most relevant for influencing peak strains in the ONH
Cumulative Influence Factor

- IOP and ICP had a large influence on the peak strains
- Stiffness of the optic nerve (ON), lamina cribrosa (LC), nerve compressibility (Poisson’s), and retina (Ret)
- Collagen fiber stiffness of the pia mater (pia c₃), peripapillay sclera (ppSC c₃) and annular ring (AR c₃ & AR c₄) had a large influence on peak strains
Conclusions

• Examined how ICP affects the peak strains in the ONH
• Identified pressures and tissue properties that had the largest influence on the peak strains in the ONH
• From our CDF’s we found that c. 47% of individuals would experience “extreme strains” in the optic nerve
  – These strains may induce connective tissue remodeling
    o Note: This simulated population with extreme strains is coincidently similar to the 41% of astronauts suffering from VIIP syndrome
  – These CDF’s also identified specific factors that are associated with these extreme strains
    o ICP and a weak pia mater stiffness
Future Work

- Examine the influence of geometry on the peak strains in the ONH

- Compare strains in the lamina cribrosa and optic nerve predicted from the computational model to those strains measured from elevated ICP in an experimental model

- Investigate how strains initiate a remodeling response in the optic nerve and optic nerve sheath
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