A Framework for Modelling Connective Tissue Changes in VIIP Syndrome

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BACKGROUND AND HYPOTHESIS

Visual Impairment and Intracranial Pressure (VIIP) syndrome:
- A spectrum of ophthalmic changes including posterior globe flattening, choroidal folds, distension of the optic nerve sheath, kinking of the optic nerve and potentially permanent degradation of visual function.
- Slow onset and chronic condition.
- Similarities to certain ophthalmic findings in patients with raised intracranial pressure.

Hypothesis: (i) biomechanical factors play a role in VIIP, and (ii) connective tissue remodeling must be accounted for if we wish to understand the pathology of VIIP.

This work addresses 2 knowledge gaps: **VIIP1**: We do not know the etiological mechanisms and contributing risk factors for ocular structural and functional changes seen in-flight and postflight, and **CV7**: How are fluids redistributed in flight?
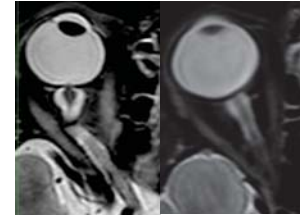

Figure 1. MRI images showing tortuous optic nerve sheath in VIIP syndrome (left) vs. a control eye (right). From: Kramer et al. "Orbital and intracranial effects of microgravity: findings at 3-T MR imaging", *Radiology*, 2012.

METHODS AND APPROACH

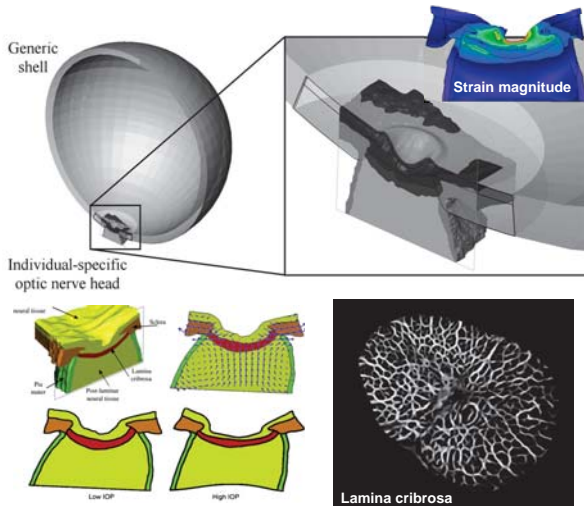### Modeling/Characterization of Ocular Biomechanics

Figure 2. Finite element modeling of ocular biomechanics. Top & bottom left: A patient-specific human optic nerve head, reconstructed from serial histologic sections, is embedded in a generic corneo-scleral shell, which is pressurized to different levels of IOP. Color inset at top right shows computed local tissue mechanical strains. Bottom right: Segmented porcine lamina cribrosa based on enhanced micro-CT imaging, used to drive local models of lamina cribrosa biomechanics.

Top: From Sigal et al., Tech & Health Care, 13:313-329, 2005. Bottom left: Sigal et al., Invest Ophth Vis Sci, 45:4378-4387, 2004. Bottom right: Courtesy of Dr Ian Campbell, Georgia Tech.
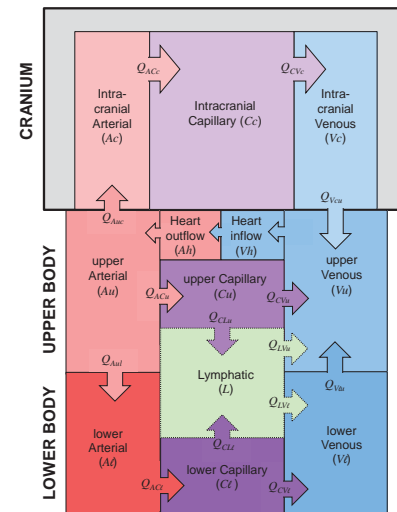
Fluids Transport Models

Figure 3. Compartmental model for computation of arterial, venous, intracranial and lymphatic pressures acting on the eye. This model will be coupled to models for intracranial dynamics and ocular transport based on Lakin (Av Sp & Env Med, 2007) and Kiel et al. (Prog Retin Eye Res, 2011) to compute IOP and intraocular blood volumes.
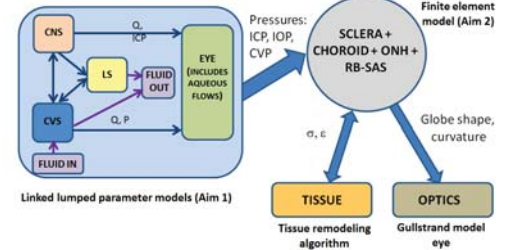
Linkage/Tissue Remodeling Models

Figure 4. High-level overview of our proposed computational studies of VIIP, showing information flow among finite-element, tissue and lumped-parameter sub-models.

Aim 1: Create lumped parameter models of fluid transport
Aim 2: Create finite element models of ocular tissue remodeling
Aim 3: Couple models

CNS = central nervous system; CVP = cardiovascular pressure; CVS = cardiovascular system; LS = lymphatic system; ICP = intracranial pressure; IOP = intraocular pressure; ON = optic nerve; ONH = optic nerve head; P = pressure; Q = flowrate; RB-SAS = retrobulbar sub-arachnoidal space; ε = strain; σ = stress.
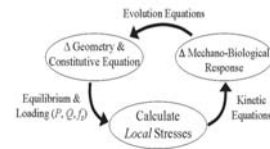

Figure 5: Conceptual framework for growth and remodeling simulations, in which the local stress environment drives tissue adaptation and growth, which in turn leads to changes in tissue microarchitecture and geometry. P = pressure, Q = flow, f_z = external forces.

NEXT STEPS

- Validate our implementation of the Kiel et al. equations for ocular fluid transport; Make measurements of optic nerve sheath physical parameters (see poster by Raykin et al.); Implement remodeling algorithm in FEBio (www.febio.org) ; Couple compartment model with ocular finite element model.

ACKNOWLEDGEMENTS