Numerical Modeling of Ocular Dysfunction in Space

E.S. Nelson\textsuperscript{1}, L. Mulugeta\textsuperscript{2}, J. Vera\textsuperscript{1}, J.G. Myers\textsuperscript{1}, J. Raykin\textsuperscript{3}, A.J. Feola\textsuperscript{3}, R. Gleason\textsuperscript{3}, B. Samuels\textsuperscript{4}, and C.R. Ethier\textsuperscript{3}

\textsuperscript{1}NASA Glenn Research Center, Cleveland, OH
\textsuperscript{2}Universities Space Research Association, Houston, Texas
\textsuperscript{3}Georgia Institute of Technology, Atlanta, GA
\textsuperscript{4}University of Alabama at Birmingham, AL

30\textsuperscript{th} Annual Meeting of the American Society for Gravitational and Space Research
Pasadena, CA, October 26, 2014
Astronauts in both short- and long-duration spaceflight have reported visual impairment in microgravity (29%\(^1\) / 42.7%\(^2\)) but relatively recently, severe cases of post-flight ocular pathology have been seen.

- No definitive explanation as to why such ophthalmic changes might occur in microgravity (\(\mu g\))
- The Digital Astronaut Project is seeking answers via integrated modeling

---

\(^1\)Mader et al. (2011)
\(^2\)Tarver and Otto (2012). Examinations are still in process.
Post-flight ophthalmic pathophysiology

Some features of this pathophysiology resemble terrestrial Idiopathic Intracranial Hypertension, which is characterized by high Intracranial Pressure (ICP).

Astronauts exhibit:
• Optic disk edema
• ONS distension
• Globe flattening
• Choroidal folds
• Increased CSF pressure
• Wool spots
• Decreased Intraocular Pressure (IOP) post-flight
• ON kinking

In cases found to date, changes to visual acuity began to emerge after 3 weeks to 3 months in μg.
Fluid redistribution in space

- The equilibrium shape for a blob of liquid water in μg is spherical (surface tension dominates in reduced gravity).
- When contained in a uniformly elastic sac, like a balloon, it is also spherical.

Now consider a human being...
Cephalic fluid shift

- Facial tissues swell\(^2\); jugular, temple and forehead veins are full & distended \(^1, 3\)
- Dramatic changes to leg volume occur *within the first 4-6h* after entry to \(\mu g\); leg volume \(\downarrow\) by \(~6-12\% ~\text{(}1 \text{ L per leg}\text{)}\) within the first week (green arrow) \(^1,4,5\); reaches a new homeostatic value within \(~1-2 \text{ weeks}\) \(^1\)
- Upper body expands, waistline \(\downarrow\); Center of Mass shifts \(\uparrow\); spine \(\uparrow\) 4-6 cm \(^1\)
- Smaller changes in arm volume (blue arrow) \(^1-2\)
- Inference of fluid volume from circumferential measurements probably conflates with *muscle atrophy* (even seen in a 5-day Apollo flight \(^6\))
Numerical approach

A sequence of stand-alone models at varying length scales and spatial fidelity:

- **Cardiovascular system (CVS):** fluid shift, cranial blood flow
- **Central nervous system (CNS):** Intracranial Pressure (ICP), ocular blood flow
- **Eye model (lumped):** globe volume, Intraocular Pressure (IOP)
- **Eye model (finite element):** biomechanical stress/strain, tissue remodeling
The goal of the CVS model is to predict the modified homeostatic state in \( \mu g \) (fluid distributions, mean fluid flows, pressures).

Some lumped CVS models exist, but none have the capabilities to properly simulate *chronic* \( \mu g \). The CVS model must properly incorporate:

- Hydrostatic forces
- Adequate spatial resolution
- Relevant regulatory functions
- Astronaut-specific data

Code is being verified/validated against Lakin et al. (2003) and others.

Revision includes:

- physiological ranges relevant to astronauts (e.g., height, total blood volume, age)
- \( \mu g \) and head-down tilt (HDT) data on plasma volume loss, spinal elongation, changes to osmotic pressure, etc.
Central Nervous System (CNS) model

- Some lumped parameter CNS models exist; most use Monro-Kellie doctrine (rigid cranium)
- Initial implementation based on Stevens et al. (2005). Code is being validated
- Cranial blood flow provides the link between CVS and CNS models
- Revision to include better compliance models and $\mu$g/HDT data

Verification test: Filtration properties at the blood/brain barrier

Stevens et al. (2005), Lakin et al. (2007)
• Very few LP models of the eye exist; none incorporate the human choroid and retrobulbar subarachnoid space (rSAS)

• Almost all of the hydrodynamic data on ocular blood flow (volume, pressure, net flowrate) is qualitative, even in 1g

• Measured permeability of dura mater, the tissue surrounding the rSAS (previously assumed impermeable)

• Developed a means of estimating blood flow from choroidal thickness and pulsatility during a cardiac cycle

• Derived compliance models for the globe/rSAS and globe/blood compartment
Compliance

- Living eyes regulate blood flow in, e.g., saline injection tests
- Pressure/volume relations for the globe have been well-studied
- We attribute the net impact of ocular blood flow dynamics as the difference between P/V curves of living vs. enucleated eyes. Compliance = dV/dP
- Compliance of posterior globe tissue derived from surgical intervention which reduced IOP
Conclusions

- Established a suite of numerical models that could link the biomechanical effects of whole-body fluid shift to the stress/strain in tissues of the eye posterior.

- Comprehensively explored literature to inform model development and credibility assessments at 1g and μg.

- Used theoretical and experimental techniques to fill in the gaps for defining the choroid and retrobulbar space.
Ongoing development

• Following NASA-STD-7009 standard for the development of credible, well-documented simulations with rigorous verification, validation and uncertainty analysis

• Coordinating with NASA’s medical databases and current research to make smart choices on relevant physiological ranges and material properties

• Minimal quantitative data ➔ extensive sensitivity analysis
The VIIP Modeling Team

**NASA DAP**
- Emily S Nelson, PhD (GRC)*
- Jerry Vera, BS (JSC)
- Lealem Mulugeta, MS (JSC)
- Jerry Myers, PhD (GRC)*

**NASA Academy**
- Rachel Price
- Sarah Gady
- Katherine Heinemann

**Ga Tech/UAB**
- Ross Ethier, PhD (Ga Tech), PI
- Andrew Feola (Ga Tech)
- Julia Raykin (Ga Tech)
- Brian Samuels, MD, PhD (UAB)*
- Rudy Gleason, PhD (Ga Tech)*

---

*Co-Investigators on NRA proposal **“Microgravity-driven Optic Nerve/Sheath Remodeling Simulator (MONSTR Sim)”**
Backups
Choroidal blood flow

Vortex veins (~3-8 of them)

One (of 2) long posterior ciliary arteries

Short posterior ciliary arteries (~10-20 of them at the sclera)
Verification and Validation

- All models and simulations (M&S) will be verified and validated in accordance to NASA-STD-7009
- Obtain data from LSAH/LSDA to develop and validate M&S
- Establish collaborative data sharing agreement with current and future NASA and NSBRI funded VIIP investigators
- Work closely with VIIP Project Scientist and subject matter experts for technical review of M&S
The optic nerve and its sheath

In clinical applications on earth, Optic Nerve Sheath Diameter (ONSD) has become a surrogate for Intracranial Pressure (ICP) in the diagnosis of Idiopathic Intracranial Hypertension (IIH). By convention, measurements are made 3mm behind globe.

OND = Optic Nerve Diameter
ONSD = Optic Nerve Sheath Diameter

Zoomed to 300X

- Geeraerts et al. (2008)
What we could do with the models?

- Integrated LP model of CVS/CNS/LS
  - Mean ICP after weeks in \( \mu g \)
  - Peak ICP during exercise/valsalva in \( \mu g \)

- LP model of globe/choroid/aqueous space
  - IOP as a function of ICP, blood/aqueous humor flow
  - Effect of venous congestion on IOP

- FE model of globe/choroid/RB-SAS
  - Visual acuity change
  - Ocular hypotony/hypertony
  - Reversible ON/ONS distension, globe deformation
  - Biomechanical effects of venous congestion, choroidal engorgement
  - Potential for compartment syndrome

- Tissue remodeling algorithm
  - Persistent anatomical changes (globe flattening, ON/ONS distension)
  - Effect of mission duration