Numerical Modeling of Ocular Dysfunction in Space

E.S. Nelson¹, L. Mulugeta², J. Vera¹, J.G. Myers¹, J. Raykin³, A.J. Feola³, R. Gleason³, B. Samuels⁴, and C.R. Ethier³

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

30th 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
Some features of this pathophysiology resemble terrestrial Idiopathic Intracranial Hypertension, which is characterized by high Intracranial Pressure (ICP).

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

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

\[ \Delta V \text{ vs. time on Skylab 4} \]

- 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 ↓ by \(\sim 6-12\%\) (\(\sim 1 \text{ L per leg}\)) within the first week (green arrow)\(^1,4,5\); reaches a new homeostatic value within \(\sim 1-2 \text{ weeks}\)\(^1\)
- Upper body expands, waistline ↓; Center of Mass shifts ↑; spine ↑ 4-6 cm\(^1\)
- Smaller changes in arm volume (blue arrow)\(^1-2\)
- Inference of fluid volume from circumferential measurements probably conflates with \textit{muscle atrophy} (even seen in a 5-day Apollo flight\(^6\))
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 μg (fluid distributions, mean fluid flows, pressures).

Some lumped CVS models exist, but none have the capabilities to properly simulate chronic μg. 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)
- μg and head-down tilt (HDT) data on plasma volume loss, spinal elongation, changes to osmotic pressure, etc.
Central Nervous System (CNS) model

9 COMPARTMENT MODEL

- Stevens et al. (2005), Lakin et al. (2007)

Verification test: Filtration properties at the blood/brain barrier

- 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
Eye model

- 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)*

---

*Lumped Parameter Models*

- Cardiovascular System
- Central Nervous System

*Finite Element and Tissue Models*

- Eye + Retrolubular Subarachnoid Space
- Tissue

*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 μg
- Peak ICP during exercise/valsalva in μg

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