Numerical Modeling of Ocular Dysfunction in Space

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30\textsuperscript{th} Annual Meeting of the American Society for Gravitational and Space Research
Pasadena, CA, October 26, 2014
Background

Astronauts in both short- and long-duration spaceflight have reported visual impairment in microgravity (29%\textsuperscript{1} / 42.7%\textsuperscript{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 (μg)
- The Digital Astronaut Project is seeking answers via integrated modeling

\textsuperscript{1}Mader et al. (2011)
\textsuperscript{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 μg; leg volume ↓ by ~6-12% (~1 L per leg) within the first week (green arrow) \(^1,4,5\); reaches a new homeostatic value within ~1-2 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 muscle atrophy (even seen in a 5-day Apollo flight \(^6\)).

\(\Delta V\) vs. time

on Skylab 4 \(^1\)

\(^1\) Thornton et al. (1986) Skylab 4
\(^2\) Kirsch et al. (1993)
\(^3\) Herault et al. (2000) 6 mo on Mir
\(^4\) Moore and Thornton (1987) Shuttle
\(^5\) Kas’ian et al. (1980)
\(^6\) Hoffler et al. (1975) Apollo
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

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 μg/HDT data

[Diagram with labels and flow arrows indicating the relationship between different compartments: Intracranial Arteries (I), Central Arteries (A), Brain (B), Intracranial Blood (C), Venous Sinus (S), Ventricular CSF (F), Extraventricular CSF (T), Central Veins (V), Thoracic Space (Y)]

**ICP isobars, Lakin et al. (2007)**

- 13 mmHg
- 15 mmHg
- 17 mmHg
- 19 mmHg

**Graph**

- Test1
- Test2
- Test3
- Test4

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<th>Sigma_CB</th>
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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
• 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 = \(\frac{dV}{dP}\)
• 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 $\mu$g

• 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

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**LUMPED PARAMETER MODELS**
CARDIOVASCULAR SYSTEM
CENTRAL NERVOUS SYSTEM
EYE

**FINITE ELEMENT AND TISSUE MODELS**
EYE + RETROBULBAR SUBARACHNOID SPACE
TISSUE
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

- Geeraerts et al. (2008)

OND = Optic Nerve Diameter
ONSD = Optic Nerve Sheath Diameter

Zoomed to 300X

- Geeraerts et al. (2008)

Optic nerve sheath diameter (mm)

ICP (mm Hg)

45 measures

r=0.71

p<0.0001
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