Numerical Modeling of Ocular Dysfunction in Space

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Background

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 $\mu$g 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...
Facial tissues swell; jugular, temple and forehead veins are full & distended. 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); reaches a new homeostatic value within ~1-2 weeks. Upper body expands, waistline ↓; Center of Mass shifts ↑; spine ↑ 4-6 cm. Smaller changes in arm volume (blue arrow). Inference of fluid volume from circumferential measurements probably conflates with muscle atrophy (even seen in a 5-day Apollo flight).
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
Cardiovascular (CVS) model

- 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 \textit{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)
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.

- Eisenlohr et al. (1962)
- Silver and Geyer (2000)
- Park et al. (2014)
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

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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)

Zoomed to 300X

OND = Optic Nerve Diameter
ONSD = Optic Nerve Sheath Diameter

- 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