

LUMPED PARAMETER MODELS OF THE CENTRAL NERVOUS SYSTEM FOR VIIP RESEARCH

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INTRODUCTION: Current long-duration missions to the International Space Station and future exploration-class missions beyond low-Earth orbit, such as to Mars and asteroids, expose astronauts to increased risk of Visual Impairment and Intracranial Pressure (VIIP) syndrome [1]. It has been hypothesized that the headward shift of cerebral spinal fluid (CSF) and blood in microgravity may cause significant elevation of intracranial pressure (ICP), which in turn induces VIIP syndrome through biomechanical pathways [1, 2]. However, there is insufficient evidence to confirm this hypothesis. In this light, we are developing lumped-parameter models of fluid transport in the central nervous system (CNS) as a means to simulate the influence of microgravity on ICP. The CNS models will also be used in concert with the lumped parameter and finite element models of the eye described in the related IWS abstracts submitted by Nelson et al., Feola et al. and Ethier et al.

METHODS: We have developed a nine compartment CNS model (Figure 1) capable of both time-dependent and steady state fluid transport simulations, based on the works of Stevens et al. [3]. The breakdown of compartments within the model includes: vascular (3), CSF (2), brain (1) and extracranial (3). The boundary pressure in the Central Arteries [A] node is prescribed using an oscillating pressure function $PA(t)$ simulating the carotid pulsatile pressure wave as developed by Linninger et al. [4]. For each time step, pressures are integrated through time using an adaptive-timestep 4th and 5th order Runge-Kutta solver. Once pressures are found, constitutive equations are used to solve for flowrates (Q) between each compartment. In addition to fluid flow between the different compartments, compliance (C) interactions between neighboring compartments are represented.

We are also developing a second CNS model based on the works of Linninger et al. [4] which takes a more granular approach to represent the interactions of the intracranial and spinal compartments with the inclusion of arteries, arterioles, capillaries, venules, veins, venous sinus, and ventricles. The flow through the arteries, veins and CSF compartments are governed by continuity, momentum and distensibility balance equations. Furthermore, unlike the Stevens et al. approach, the Monro-Kellie doctrine of constant cranial volume and the bi-phasic nature of the brain parenchyma are implemented. These features appear to be more consistent with the physiologic and anatomical behavior of the CNS, and follow a modeling philosophy similar to the lumped parameter eye model that is intended to be integrated with the CNS model. However, Linninger's approach has never been implemented to include hydrostatic gradient and microgravity simulation capabilities. Therefore, we aim to implement this modeling approach for spaceflight simulations and assess its overall applicability to VIIP research.

OBJECTIVES: We will present verification and validation test results for both models, as well as head-to-head comparison to explore their strengths and limitations with respect to mathematical implementation and physiological significance for VIIP research. In doing so, we hope to provide some guidance to the HRP research community on how to appropriately leverage lumped parameter models for space biomedical research.

REFERENCES

- [1] Alexander, D.J., et al., *Evidence Report: Risk of spaceflight-induced intracranial hypertension and vision alterations*. 2012, NASA. [2] Mader, T.H., et al. *Ophthalmology*, 2011. **118**(10): p. 2058-2069. [3] Stevens, S., et al. *Aviation, Space, and Environmental Medicine*, 2005. **76**: p. 329-338. [4] Linninger, A. A., et al. *Journal of Mathematical Biology*, 2009. **59**: p. 729-759.

