MODELING GRAVITATIONAL DOSE-RESPONSE CURVES DURING TILT, LBNP, AND CENTRIFUGATION

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ABSTRACT

Experimental tests with human subjects are necessary and useful to study the behavior of the human body during space missions. They can provide insights into possible countermeasures to mitigate the negative effects of exposure to altered gravity. However, testing with human subjects is very resource intensive and typically, it requires extensive time and a large number of subjects. In this context, computational models become valuable tools to complement experimental investigations, since they are versatile and can be adjusted quickly to simulate new testing conditions.

In the current research effort, we are using a 21-compartment lumped parameter model of the cardiovascular system (i.e., *full body* model) [1] to generate gravitational dose-response curves during different types of orthostatic stress. The model includes the systemic and cardiac circulation, as well as the two main regulatory mechanisms: the arterial baroreflex and the cardiopulmonary reflex. The orthostatic interventions of interest include a tilt paradigm, lower body negative pressure (LBNP), and centrifugation, and simulations will mimic the same experimental interventions with human subjects that we are also conducting in the lab environment. These simulations will provide new insights into the differences between the three interventions, not only at the global level (i.e., heart rate, cardiac output; these variables are easily collected during experimental testing), but also at the local/compartment level (i.e., differences in blood flow or pressure in a specific compartment; these variables are not easily collected during experimental testing). In addition to these simulations, we are also integrating the current *full body* model (which features a more accurate body representation and a large number of compartments) with other lumped parameter models focused on the upper body/head circulation [2] and the volume/pressure alterations in the eye [3]. This new and comprehensive model will become a more powerful framework to study SANS, the cranial venous system, and the effect of spaceflight countermeasures.

The main limitation of multi-parameter models is the inherent uncertainty in the values selected for each one of the parameters in the model. Differences in parameter selection may significantly change the outcome of the simulations, and more interestingly, they may explain differences in orthostatic response between individuals. To address this limitation, and more generally, to determine which parameters have a stronger impact in model outcomes, we propose to conduct sensitivity analyses during the orthostatic stress simulations of interest. Specifically, we have conducted a comprehensive sensitive analysis in our *full body* numerical model during constant orthostatic stress between 0g and 1g [4]. Results indicated that model parameters related to the length, resistance, and compliance of the large veins and parameters related to right ventricular function have the most influence on model outcomes. These results highlight which model parameters to accurately value in simulations of individual subjects' CV response to gravitational stress, thus improving the accuracy of predictions. In addition, influential parameters remained largely similar across gravity levels, highlighting that accurate model fitting in 1g can increase the accuracy of predictive responses in reduced gravity. Similar sensitivity analyses are currently being conducted during LBNP and in centrifugation conditions.

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