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Effects of artificial gravity on the cardiovascular system: Computational approach

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ABSTRACT

Artificial gravity has been suggested as a multisystem countermeasure against the negative effects of weightlessness. However, many questions regarding the appropriate configuration are still unanswered, including optimal g-level, angular velocity, gravity gradient, and exercise protocol. Mathematical models can provide unique insight into these questions, particularly when experimental data is very expensive or difficult to obtain. In this research effort, a cardiovascular lumped-parameter model is developed to simulate the short-term transient hemodynamic response to artificial gravity exposure combined with ergometer exercise, using a bicycle mounted on a short-radius centrifuge. The model is thoroughly described and preliminary simulations are conducted to show the model capabilities and potential applications. The model consists of 21 compartments (including systemic circulation, pulmonary circulation, and a cardiac model), and it also includes the rapid cardiovascular control systems (arterial baroreflex and cardiopulmonary reflex). In addition, the pressure gradient resulting from short-radius centrifugation is captured in the model using hydrostatic pressure sources located at each compartment. The model also includes the cardiovascular effects resulting from exercise such as the muscle pump effect. An initial set of artificial gravity simulations were implemented using the Massachusetts Institute of Technology (MIT) Compact-Radius Centrifuge (CRC) configuration. Three centripetal acceleration (artificial gravity) levels were chosen: 1 g, 1.2 g, and 1.4 g, referenced to the subject's feet. Each simulation lasted 15.5 minutes and included a baseline period, the spin-up process, the ergometer exercise period (5 minutes of ergometer exercise at 30 W with a simulated pedal cadence of 60 RPM), and the spin-down process. Results showed that the cardiovascular model is able to predict the cardiovascular dynamics during gravity changes, as well as the expected steady-state cardiovascular behavior during sustained artificial gravity and exercise. Further validation of the model was performed using experimental data from the combined exercise and artificial gravity experiments conducted on the MIT CRC, and these results will be presented separately in future publications. This unique computational framework can be used to simulate a variety of centrifuge configuration and exercise intensities to improve understanding and inform decisions about future implementation of artificial gravity in space.

1. Introduction

The cardiovascular system experiences important changes during spaceflight in response to a weightlessness environment. These changes include the central fluid shift phenomenon, the reduction in total circulation blood volume, and a decrease in heart size, venous compliance, and baroreflex sensitivity [1–5]. In general, this adaptation is successful. However, the re-adaptation process when crewmembers return to a gravity environment is more problematic, and orthostatic intolerance may occur [6–8].

Several countermeasures are currently in place [1,9]. In general, they are system specific, focusing on one aspect of human deconditioning in space. In particular, cardiovascular countermeasures include aerobic exercise, fluid loading, the use of leg cuffs to reduce the amount of fluid shift from the lower extremities to the upper extremities, and the use of Lower Body

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Negative Pressure (LBNP) that induces a cardiovascular stress [1]. However, despite the variety of countermeasures, their effectiveness in terms of maintaining preflight levels has not been demonstrated, and their specificity and difficult application to several physiological systems at the same time makes their use difficult and time consuming [9–11]. Artificial gravity is seen as an integrated countermeasure capable of challenging several physiological systems at the same time [10]. In particular, short-radius centrifugation combined with exercise may be effective against cardiovascular deconditioning in space [12]. However, the centrifuge configuration still needs to be selected in order to maximize its effectiveness. These critical design questions include g-level, radius, gravity gradient, angular velocity, and exercise protocol [6,7].

Some of these questions can be resolved using ground analogs, like bed-rest [13–19]. However, others can be approached using mathematical simulations. An important advantage of computational modeling is that it allows the exploration of many different configurations with a large flexibility at a low computational cost. Guyton was the “pioneer' of the quantitative physiological system analysis of circulation regulation. He developed a large circulatory model with hundreds of equations used to quantify the different subsystems of the circulation and their control [20]. His main contributions include (but are not limited to) the understanding of the interaction between venous return and cardiac function, the whole body autoregulation, renal body-fluid feedback mechanism in long-term blood pressure control, graphical analysis of physiological regulation, and quantitative computer modeling of physiological systems [21–23]. Although Guyton's work was focused on long-term steady-state cardiovascular responses, the principles he developed are still applicable, and are widely used in the field [24].

The cardiovascular system can be modeled using different approaches depending on the modeling objective and the assumptions on the spatial degrees of freedom. Three-dimensional (3D) models are used when detailed information about the blood flow in a particular region is needed. In these models, the fluid behavior is usually described by the Navier–Stokes equations for incompressible fluids. Despite the progress of current numerical methods, the computational cost of these models is very high, limiting their application to small localized regions. One-dimensional (1D) models assume axial symmetry and only have one degree of freedom, namely translation along the axial direction. These models are useful to analyze arterial wave propagation, and they are described by hyperbolic partial differential equations. Finally, zero-dimensional models (0D), or lumped-parameter models, represent the spatial variation in a highly aggregated manner, as they compartmentalize the cardiovascular system into discrete functional units. They describe the time evolution of the pressure and flow in each compartment using ordinary differential equations [25]. The objective of our modeling effort is to capture the beat-to-beat, short-term hemodynamic response to artificial gravity generated by a compact-radius centrifuge. Thus, a lumped-parameter model is the logical choice, since it provides beat-to-beat average variables (including pressures, flows, and volumes) at a low computational cost.

1.1. *Modeling orthostatic stress*

With regard to the cardiovascular adaptation to gravitational stress, many computational models have been developed with a large variety of temporal and spatial resolutions, depending on the representation and the objective of the model [25,26]. Various mathematical models investigate the physiological responses to postural changes, such as active standing [27], head-up tilt [28–31], or lower body negative pressure [28,32]. Some models were designed to explain observations seen during human spaceflight [31,33,34], including the recent Visual Impairment and elevated Intracranial Pressure (VIIP) syndrome [35].

For our purpose, the cardiovascular model to be developed needs to have enough compartments to capture the strong hydrostatic gradient generated by a compact-radius centrifuge. Heldt developed a lumped-parameter model using 21 compartments in order to simulate the short-term ($\approx$ 5 minutes), transient, beat-to beat hemodynamic response to gravitational stress, such as head-up tilt and lower body negative pressure [36]. The hemodynamic model included the systemic circulation (arterial system, microcirculation, and the venous system), the cardiac chambers, and the pulmonary circulation. The cardiovascular system was represented by seventeen vascular and four cardiac compartments grouped into four main sections: head and arms, thorax, abdomen, and legs. The full 21-compartment model is shown in Fig. 1 and is currently incorporated in the expanded research version of CVSim, a computational platform developed at the Harvard-MIT Division of Health Science and Technology [37]. Parameters such as compliance, volume, resistance, or vascular length (to determine the hydrostatic pressure) were estimated from the literature [36]. The model also incorporated the arterial baroreflex and the cardiopulmonary reflex to maintain blood pressure homeostasis during orthostatic stress. Based on the 21-compartment model developed by Heldt, Zamanian built a lumped-parameter hemodynamic model for the cardiovascular response to centrifugation [38]. This new model introduced the simulation of the hydrostatic pressure resulting from centrifugation as well as a model for the collapsibility of blood vessels under high orthostatic stress (negative transmural pressure). Simulations at 11.6 rpm, 22.9 rpm, and 29.4 rpm were validated with experimental measurements conducted in the Man Vehicle Laboratory using the MIT short-radius centrifuge.

Despite the broad range of applications, to our knowledge, no previous computational models have been applicable to exercise in altered gravity environments. In the current modeling effort, Heldt's and Zamanian's approaches are combined and upgraded with a new exercise module to develop a unique cardiovascular model capable of capturing the short-term, beat-to-beat hemodynamic responses to artificial gravity generated by a compact-radius centrifuge combined with lower-body ergometer (i.e. cycling) exercise. In the following sections, the mathematical details of the model are described so it can be reproduced by the reader. Additionally, a series of preliminary simulations are presented and discussed to show the model capabilities and potential applications.

2. Modeling approach

The cardiovascular system can be represented as a fluid vessel network with regulatory control systems. This fluid network can also be represented by electric circuit analogs [36,38,39]. Thus, the cardiovascular system can be represented by a series of vascular segments modeled by electric circuit blocks or compartments. The model developed by Heldt [36] and used in this work consists of fifteen compartments representing the systemic circulation, four compartments representing the cardiac chambers, and two compartments representing the pulmonary circulation. In addition, the model includes the two major reflex mechanisms concerning the short-term hemodynamic response to orthostatic stress, namely the arterial baroreflex and the cardiopulmonary reflex.

Centrifugation using a short-radius centrifuge induces a significant orthostatic stress in the cardiovascular system. The artificial gravity induces both a primary rapid fluid shift from the upper body to the lower extremities, and a secondary slower fluid shift from the intravascular to the interstitial fluid compartment.