Politecnico di Torino

AEROSPACE ENGINEERING

Optimizing countermeasures against cardiovascular deconditioning and cerebral hemodynamics changes in long-term human spaceflights

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Context of the research activity	The PhD project proposes the development of a multidisciplinary in silico-in vivo framework to investigate the cardiovascular deconditioning and cerebral hemodynamics changes in human spaceflights. The project aims at solidifying the link between cerebral hemodynamics and neurovestibular dysfunctions in microgravity and individuating which are the optimal countermeasures to face long-term human space missions.
	Long-term human spaceflight induces a number of cardiovascular alterations, from blood volume reduction to cardiac atrophy, leading to cardiovascular deconditioning, that is the adaptation of the cardiovascular system to a less demanding environment [1-4]. The main driver of these changes is the fluid shift from lower to upper body, which is as well believed to be the underlying cause of the Spaceflight Associated Neuro-ocular Syndrome (SANS), classified today among the major risks of the human space exploration [5,6]. For none of the countermeasures - currently adopted or investigated to mitigate cardiovascular deconditioning in view of future Moon/Mars missions - definitive findings on the optimal functioning are known [7,8]. In particular, though artificial gravity is one of the most promising countermeasures [9], the current knowledge mainly relies on ground-based analogs [10]. Moreover, being the association between cerebral hemodynamics and SANS a recent frontier for which the underlying mechanisms are barely understood, no ad hoc strategies to contrast cerebral hemodynamic alterations have been so far implemented [8, 11]. We here propose to develop a computational approach, based on our validated multiscale cardiovascular model able to accurately reproduce the hemodynamic response to short- and long-term microgravity exposure [12-14]. Our aims are to: (i) investigate the altered cerebral hemodynamics at broad and then its role on the onset of SANS; and (ii) individuate the optimal countermeasure configuration, among the currently implementable, against cardiovascular deconditioning and neurovestibular dysfunctions induced by hemodynamic alterations (e.g., SANS) for the next manned missions. Results will shed light on the underlying mechanisms altering cerebral

Objectives	hemodynamics and contribute to the design of the most effective cardiovascular countermeasures for long-term missions (including short-term adaptations to each spaceflight phase) to Moon/Mars. The PhD research project is half co-funded by the European Space Agency through the Open Space Innovation Platform (OSIP). [1] Norsk, P. Adaptation of the cardiovascular system to weightlessness: surprises, paradoxes and implications for deep space missions. Acta Physiol. 228, e13434 (2020). doi: 10.1111/apha.13434 [2] Hughson, R. L., Helm, A. & Durante, M. Heart in space: effects of the extraterrestrial environment on the cardiovascular system. Nat. Rev. Cardiol. 15, 167–180 (2018). doi: 10.1038/nrcardio.2017.157 [3] Zhu, H., Wang, H. & Liu, Z. Effects of real and simulated weightlessness on the cardiac and peripheral vascular function on humans: a review. Int. J. Occup. Med. Environ. Health 28, 793–802 (2015). doi: 10.13075/ijomeh.1896.00301 [4] Gunga, H. C., Weller von Ahlefeld, V., Appell Coriolano, H. J., Werner, A. & Hoffmann, U. Cardiovascular system, red blood cells, and oxygen transport in microgravity. Springer (2016). doi: 10.1007/978-3-319-33226-0 [5] Lee, A. G., Mader, T. H., Gibson, C. R., Brunstetter, T. J. & Tarver, W.J. Space flight-associated neuro-ocular syndrome (SANS). Eye 32(7), 1164-1167 (2018). doi: 10.1038/s41433-018-0070-y [6] Lee, A. G., et al. Spaceflight associated neuro-ocular syndrome (SANS) and the neuro-ophthalmologic effects of microgravity: a review and an update. npj Microgravity 6(1), 7 (2020). doi: 10.1038/s41526-020-0097-9 [7] Hargens, A. R. & Richardson, S. Cardiovascular adaptations, fluid shifts, and countermeasures related to space flight. Resp. Physiol. Neurobi. 169, S30-S33 (2009). doi: 10.1016/j.resp.2009.07.005 [8] Jirak, P., et al. How spaceflight challenges human cardiovascular health. Eur. J. Prev. Cardiol. 29(10), 1399-1411 (2022). doi: 10.1093/eurjpc/zwac029 [9] Clément, G. International roadmap for artificial gravity research. npj Microgravity 3(1), 29 (2017). doi: 10.1038/s41526-017-0034-8 [10] Clément, G. R., Bukley, A. P. & Paloski, W.H. Artificial gravity as a countermeasure for mitigating physiological deconditioning during long-duration space missions. Front. Syst. Neurosci. 9, 092 (2015). doi: 10.3389/fnsys.2015.00092 [11] Zhang, L.-F., Hargens, A.R. Spaceflight-induced intracranial hypertension and visual impairment: Pathophysiology and countermeasures. Physiol. Rev. 98(1), 59-87 (2018). doi: 10.1152/physrev.00017.2016 [12] Gallo, C., Ridolfi, L. & Scarsoglio, S. Cardiovascular deconditioning during long-term spaceflight through multiscale modeling. npj Microgravity 6(1),27 (2020). doi: 10.1038/s41526-020-00117-5 [13] Fois, M., Maule, S. V., Giudici, M., Valente, M., Ridolfi, L. & Scarsoglio, S. Cardiovascular Response to Posture Changes: Multiscale Modeling and in vivo Validation During Head-Up Tilt. Front. Physiol. 13,826989 (2022). doi: 10.3389/fphys.2022.826989 [14] Fois, M., Ridolfi, L. & Scarsoglio, S. In silico study of the posture-dependent cardiovascular performance during parabolic flights. Acta Astronaut. 200, pp. 435-447 (2022). doi: 10.1016/j.actaastro.2022.08.018

Skills and competencies for the development of	- Good knowledge of cardiovascular fluid dynamics and related modeling-computational aspects - Good command of advanced numerical methods for ordinary and partial differential equations - Good knowledge of programming languages for computational

development of the activity	hemodynamics - Interest for multidisciplinary research activities related to space physiology and biomedicine