

## A combined computational-clinical framework to investigate the impact of lower body negative pressure on the cardiovascular system

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The application of negative pressure to the lower extremities induces a fluid shift towards the caudal region, decreasing venous return to the heart and leading to a cardiovascular compensatory response triggered by short-term regulation mechanisms<sup>1</sup>. Due to its physiological effects, lower body negative pressure (LBNP) has been investigated as a potential countermeasure against cardiovascular deconditioning, which occurs during long-term spaceflights.

In recent years, mathematical modeling has proven to be an effective tool for understanding cardiovascular functioning under various conditions<sup>2,3</sup>. In this context, we propose a combined in silico-in vivo framework (see Figure 1) to investigate the impact of varying levels of LBNP on the cardiovascular system and to assess its effectiveness as a spaceflight countermeasure. The cardiovascular model consists of a 1D description of the main arteries and a 0D representation of the peripheral circulation, the venae cavae compartments, the coronary, the cardiopulmonary and the ocular-cerebrovascular circulations<sup>4</sup>. In particular, the peripheral and venous circulations are described by using several three-element Windkessel models and are organized into five body regions: head, arms, upper abdomen, lower abdomen and legs. To model the LBNP, a negative external pressure is applied to all the compartments of the legs region by introducing a negative pressure term in the constitutive relation. In addition, the model accounts for gravity changes and is equipped with short-term regulation mechanisms (baro- and cardiopulmonary reflexes) capable of replicating the changes in heart rate and vascular tone typically induced by LBNP application.

The multiscale model is validated considering a cohort of 30 young male and female healthy volunteers and performing central and cerebral measures. The present approach can provide valuable insights into the effectiveness of LBNP under varying levels of magnitude and different gravity conditions (0g and 1g).

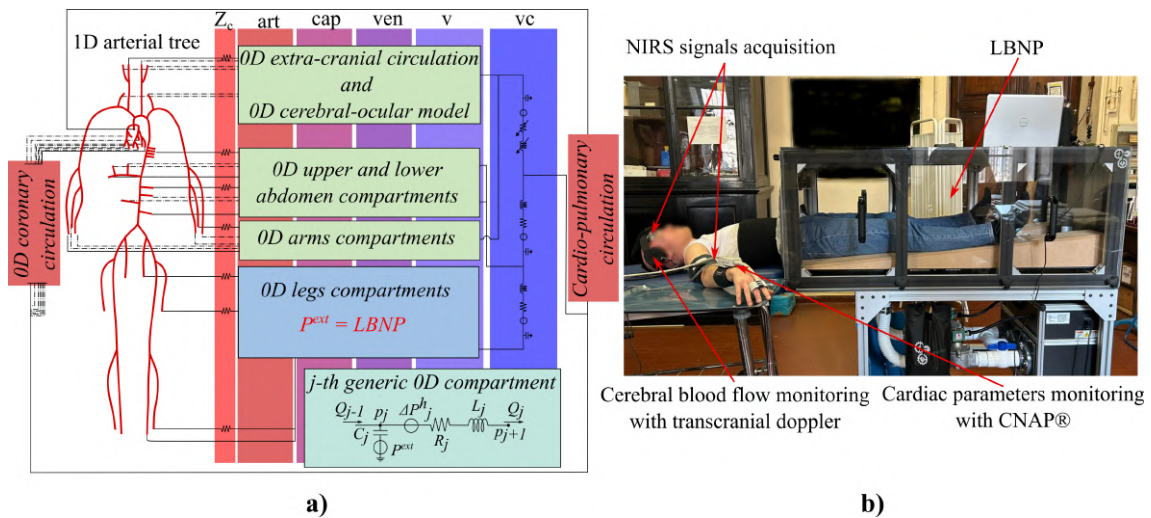


Figure 1: a) Scheme of the entire 0D-1D cardiovascular model: the 1D arterial tree is illustrated in red. Each terminal 1D artery is linked to the downstream 0D compartments (art: arteriolar, cap: capillar, ven: venular, v: venous, vc: vena cava). b) LBNP experimental setup.

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<sup>1</sup>Goswami et al., *Physiological reviews* **99.1**, 807-851 (2019)

<sup>2</sup>Fois et al., *Acta Astronautica* **200**, 435-447 (2022)

<sup>3</sup>Fois et al., *Frontiers in Physiology* **13** (2022)

<sup>4</sup>Fois et al., *npj Microgravity* **10**, 22 (2024)