AN AGENT-BASED MODEL FOR SIMULATING THE ARTERIAL STENOSIS INVOLVED IN THE VIBRATION-INDUCED RAYNAUD'S SYNDROME

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Introduction

We hypothesized that chronic exposure to Hand-Arm transmitted Vibration (HAV) may result in growing and remodeling the digital arteries walls leading possibly to stenosis. Indeed, our previous works have shown that acute exposure to HAV can decrease the Wall Shear Stress (WSS) exerted by blood on the arterial endothelium [1]. Furthermore, as established in a host of studies [2], low WSS can promote the secretion of the Platelet-derived growth factor BB (PDGF-BB) by endothelial cells (EC). This secreted PDGF-BB is assumed to alter the behavior of the smooth muscles cells (SMCs). Then, on the long term these changes of SMCs' phenotype may lead to the onset of intimal hyperplasia (IH) giving rise to stenosis. Moreover, this thickening of the artery layer due to IH may potentially disturb the circumferential stress field (σ_θ) inside the arterial wall, which can also modulate the SMCs secretion of PDGF-BB [3] by other pathways than those involved with the WSS. In this present study, we proposed an agent-based model (ABM) that described the SMCs dynamics altered by both WSS and mechanical stress. This ABM was coupled to a finite element model (FEM) providing the circumferential stress field inside the arterial wall. Our model simulated the chronic cells behavior during physiological state and for a low WSS resulting from vibration exposure.

Methods

The ABM was implemented in NetLogo© and based on biological laws derived from the literature describing ECs behaviors when exposed to low WSS. The initial geometry was a cylindrical muscular artery of 1-mm-diameter including the endothelium (ECs) and media layer (SMCs and Extracellular Matrix (ECMs)). The SMCs dynamics were modelled using probabilistic equations that describe biological mechanisms such as proliferation, apoptosis and migration. A regularization method was also implemented in the ABM in order to overcome the non-uniformity in cells movement due to the lattice symmetry [4]. Starting from an equilibrium state (WSS of 3 Pa), the model was then disturbed by a WSS value resulting from a vibration exposure (1 Pa). At each time step, the ABM communicated the change in geometry to the FEM through a Python© script (Figure 1). The FEM was implemented in the FEniCS modeling platform. The arterial tissue was modeled as an anisotropic hyperelastic material. The computed circumferential stress field was then retrieved from the FEM and communicated back to the ABM. Experimental data of the PDGF-BB concentrations secreted by HUVECs (Human

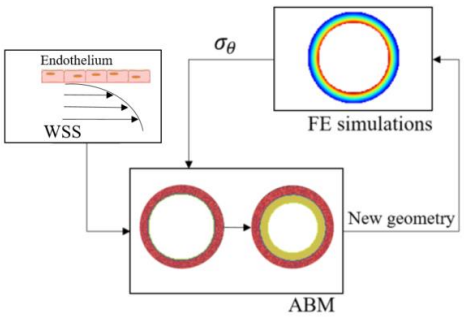

Figure 1. The ABM-FEM computational framework.

Umbilical Vein Endothelial Cells) when exposed to a low WSS were used as input parameters for our biological model.

Results

Results of the cellular tests on HUVECs showed that the ECs secreted almost 50% more PDGF-BB for WSS = 1 Pa (27.93 ± 5.14 pg/ml) than for WSS = 3 Pa (18.50 ± 7.97 pg/ml) ($p < 0.05$, $n = 7$). In addition, our model succeeded in simulating: i) the physiological equilibrium state in the absence of vibration, and ii) the arterial lumen narrowing resulting from vibration exposure. Indeed, Figure 2 shows a constant lumen area during physiological state, and a 50% decrease in lumen area if exposed to vibration 4 hours a day for 5 years.

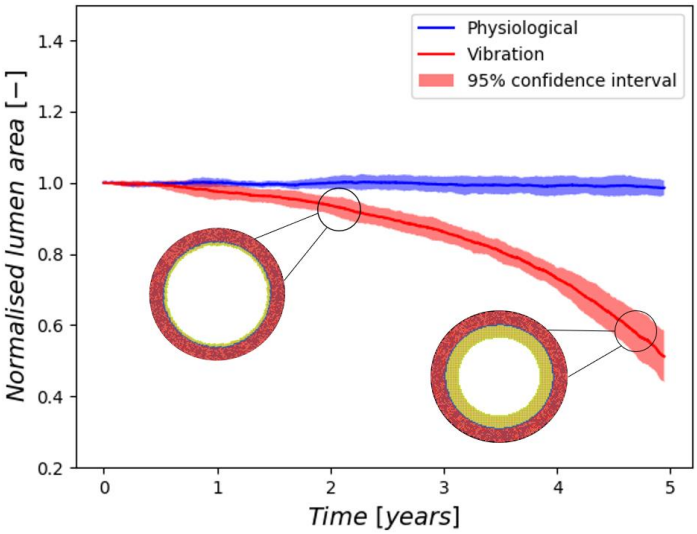

Figure 2. Change in lumen area for physiological and vibration exposure states (average of 5 simulations).

Discussion

In this study, we presented a coupled ABM-FEM that simulated the arterial stenosis involved in the vibration-induced Raynaud's syndrome. The model took into account the change in the secretion of PDGF-BB when the arterial wall was exposed to a low WSS. The PDGF-BB plays a crucial role in proliferation and migration of SMCs. Our model offers the possibility to include additional cellular mechanisms, simulate other mechanical behaviors and study more work conditions with different exposure times.

References

[1] Noel, C., Settembre, N. (2021) Assessing mechanical vibration-altered wall shear stress in digital arteries, Submitted to *Journal of Biomechanics*.

[2] Hsieh, H. J., Li, N. Q. and Frangos, J. A. (1991) Shear stress increases endothelial platelet-derived growth factor mRNA levels, *American Journal of Physiology - Heart and Circulatory Physiology*, 260(2 29-2), pp. 1–5. doi: 10.1152/ajpheart.1991.260.2.h642.

[3] Li, Z., Moore, S. and Alavi , M.Z. (1995) Mitogenic factors released from smooth muscle cells are responsible for neointimal cell proliferation after balloon catheter deendothelialization, *Experimental and Molecular Pathology*, 63(2), pp. 77-86. doi: 10.1006/exmp.1995.1032. PMID: 8941042.

[4] Reda, M., Noel, C., *et al.* (2020) Agent-based modelling of the smooth muscle cells migration induced by mechanical vibration : a preliminary study, *Computer Methods in Biomechanics and Biomedical Engineering*, 23(S1), pp. S255–S256. doi: 10.1080/10255842.2020.1815326.