MULTISCALE MODELING TO SIMULATE VASCULAR ADAPTATION PROCESSES

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Introduction

The thorough understanding of vascular adaptation processes in atherosclerosis and restenosis is lacking. Multiscale agent-based modeling frameworks, integrating both continuum and discrete approaches, have recently emerged as promising mechanobiological models to capture the multiscale and multifactorial network of events underlying those diseases, which are characterized by the interplay between biomechanical forces, cellular behavior, and molecular pathways [1].
Our research group has recently developed a multiscale agent-based modeling framework, which has been used to study atherosclerosis [2], restenosis after percutaneous transluminal angioplasty (PTA) and in-stent restenosis [3,4]. Herein, a novel patient-specific framework of restenosis after PTA is proposed to capture the remodeling process in response to the PTA-induced damage and perturbed hemodynamics.

Methods

Figure 1 shows the main steps of the developed multiscale framework of restenosis following PTA, applied to a patient-specific diseased femoral artery for a follow-up time of 2 months.

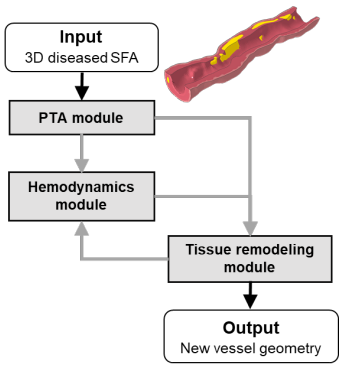

Figure 1: Multiscale framework

The framework consists of a PTA, a hemodynamics, and a tissue remodeling module. Within the PTA module, a finite element analysis of balloon expansion was performed and the post-PTA arterial configuration and damage were determined. Hyperelasticity was considered to model the arterial wall tissues [5] and a damage model with element deletion strategy was implemented to simulate the damage and arterial wall laceration experienced during the intervention. Within the hemodynamics module, steady-state computational fluid dynamics simulations were performed and the wall shear stress (WSS) was computed. Within the tissue remodeling module, (i) a 2D agent-based model (ABM) of 11 evenly-spaced cross-sections simulated cellular dynamics driving the arterial wall remodeling in response to the PTA-induced wall damage and post-operative WSS, and (ii) the 3D arterial lumen geometry was reconstructed from the ABM outputs. After 1 month, the hemodynamics and tissue remodeling modules were coupled to update the WSS input to the cellular activities.

Results

Figure 2 shows details of the damage and WSS maps at day 0, driving the 2-month ABM evolution of 3 explanatory vessel planes. The ABM at day 0 embedded the damage-induced laceration. At month 2, the intimal growth was mainly observed at regions with elevated damage levels and low WSS: the lacerations were filled and a median restenosis of 25% was obtained at 2 months, with the greatest reduction in lumen area occurring during the first post-operative month.

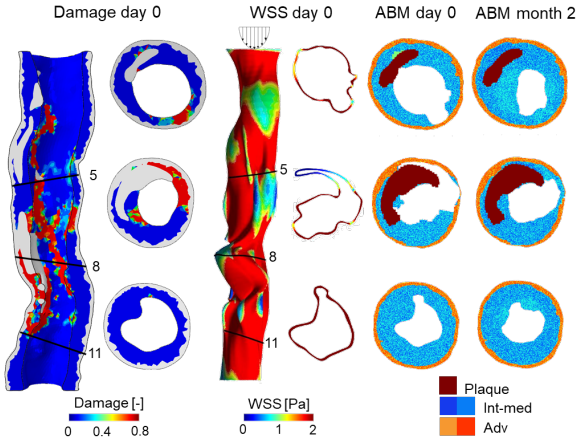

Figure 2: Arterial wall remodeling following PTA

Conclusions

By showing the application of the framework to the study restenosis following PTA in a patient-specific scenario, this work demonstrates the potentiality of this hybrid, multiscale, multifactorial and systems biology approach to capture the mechanobiological mechanisms underlying vascular adaptation.

References

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