Toward Digital Twins of Arterial Biomechanics: Patient-Specific Computational Modeling for the Comprehensive Assessment of Hemodynamic and Structural Stimuli

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Summary

Cardiovascular pathologies remain the leading cause of morbidity and mortality worldwide, primarily driven by complex pathophysiological processes. Among these, atherosclerosis stands out as the predominant pathology, often culminating in ischemic events such as myocardial ischemia, myocardial infarction, or stroke. Despite advances in diagnostics and therapy, a comprehensive understanding of the biomechanical forces contributing to disease initiation, progression, and plaque destabilization remains incomplete. Local hemodynamic disturbances and stress concentrations in the arterial wall are known to modulate endothelial dysfunction and vascular remodeling. However, their non-invasive quantification remains unreliable and lacks accuracy. Computational modelling offers a powerful solution to these issues, enabling patient-specific *in silico* investigation of blood flow and vascular wall mechanics. This doctoral dissertation presents the novel development and implementation of patient-specific computational modelling frameworks that advance the simulation of arterial biomechanics, offering enhanced precision and clinical relevance in the assessment of hemodynamic and structural stimuli. The overarching goal is to contribute to the advancement of digital twin technologies for cardiovascular pathophysiology assessment by developing of *in silico* medicine tools. The research leverages numerical techniques such as fluid–structure interaction (FSI), moving-wall computational fluid dynamics (CFD), and nonlinear structural mechanics to simulate and analyze the dynamic interplay between blood flow and vascular tissue mechanics in both physiological and pathological conditions. Particular attention is given to the evaluation of wall shear stress (WSS) and mechanical wall stress (MWS) fields, two critical biomechanical stimuli implicated in the initiation, progression, and destabilization of atherosclerotic plaques.

In the first part of the dissertation, the carotid artery is considered, based on its critical role in cerebral blood flow and its susceptibility to atherogenesis. The carotid bifurcation is a well-known site of disturbed flow patterns, strongly associated with the initiation and progression of atherosclerotic plaques.

Consequently, the first central part of this work involves the implementation of a fully coupled two-way FSI framework applied to patient-specific carotid bifurcations with the implementation of fiber-reinforced arterial wall models, where collagen fibers are embedded in an isotropic continuum to represent its anisotropic behavior, and external tissue support. Ten subject-specific carotid models were analyzed using an open-source environment, and FSI simulation results were compared against traditional rigid-wall CFD models in terms of WSS-based descriptors as well as bulk flow features, including helicity and flow recirculation. Findings revealed that while FSI simulations offer enhanced physiological realism, CFD-based rigid-wall models still adequately capture key hemodynamic markers in carotids as a consequence of limited wall deformation, supporting their use for time-efficient and clinically scalable analyses.

The second part of the dissertation focuses on the structural analysis of atherosclerotic coronary arteries using multimodal intravascular imaging data from patients with acute coronary syndrome. Three-dimensional finite element (FE) vessel models were obtained after a co-registration of the imaging modalities and compared in terms of MWS against the corresponding two-dimensional cross-sections, using hyperelastic, multi-material formulations for representing coronary wall and plaque components. The comparative analysis highlights that 2D simulations, although representing computationally efficient tools, largely systematically overestimate peak MWS compared to 3D models, particularly in non-lipidic regions, yet retain good spatial concordance for peak stress localization.

Building upon these methodological foundations, the final section of the thesis outlines two ongoing research activities. The first relies on the FE models of atherosclerotic coronary arteries to implement multicomponent FSI models, incorporating heterogeneous arterial layers and plaque constituents. The second addresses the role of cardiac motion and displacement in coronary hemodynamics, a main source of uncertainty in current CFD and FSI models. To do so, a moving-boundary CFD approach was implemented to simulate dynamic coronary artery motion. Such approach is applied in patients affected by myocardial bridging, by virtue of the clinical relevance of the coronary motion in this pathology. Initial assessments on a representative case demonstrated persistent luminal narrowing in the bridged segment, even during diastole, with locally elevated WSS—findings that support the hypothesized association of myocardial bridge with proximal flow perturbations, atherosclerotic plaque presence, and intimal injury or dissection.

More broadly, the thesis contributes to a more detailed mechanistic understanding of cardiovascular disease by investigating the interplay between hemodynamic forces and arterial wall mechanics. The results presented here also provide insights

into which aspects of modeling should be included or can reasonably be excluded in view of a future clinical translation of computational models into practical tools for personalized cardiovascular diagnostics, treatment planning, and disease monitoring, thereby contributing to the broader vision of *in silico* medicine and digital twin technologies in healthcare.