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AGENT-BASED MODEL AND SIMULATION OF ATHEROSCLEROTIC PLAQUE PROGRESSION

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Summary: Atherosclerosis is a local inflammatory disease characterized initially by the recruitment of leukocytes into the arterial wall. Arterial walls can develop plaques comprising of lipids, fatty substances, cholesterol, cellular waste products, elastin, fibrin, calcium and other constituents. The rate of production of these constituents are different in the disease progression stages. The described numerous components contribute to plaque creation and progression, each one with proper characteristics, behaviour and rulesets. The interaction between these components and the environment they evolve determines plaque progression. Agent-based modelling (ABM) is selected as a proper approach to reproduce the evolution of plaque progression and artery reshaping by simulating the behaviour of autonomous cellular agents (components). The dynamic system allows for complex phenomena to emerge from the interaction of simple rule-based behaviour of agents, living in a dynamically reshaping environment. We hypothesize that ABM model represents a reliable prediction model that is able to describe adequately history of atherosclerosis development. As a result, we created a multiscale atherosclerosis modeling framework based on ABM 2D modelling that simulates the hemodynamic-driven artery wall and plaque development. The model included behaviour of cells, Extracellular Matrix (ECM), and lipid dynamics in a variety of vessel cross-sections. A sensitivity study was also carried out to assess the oscillation of the ABM output in response to changes in the inputs and identify the ABM parameters that have the highest influence. The ABM results were mostly influenced by cell and ECM dynamics, which had a substantial impact on the lumen area. A group of factors was discovered that influence the ultimate lipid core size while having no effect on cell/ECM or lumen area trends. A full coupling of computational fluid dynamics (CFD) and agent-based modelling (ABM) framework would include simulation computed hemodynamics in a 3D artery model, coupled with ABM 2D modelling in order to characterize atherosclerotic morphological and compositional alterations in the arteries.