Agent Based with Finite Element Method for Plaque Progression in the Carotid Artery

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***Abstract*—Atherosclerosis is condition characterized by arterial lumen stenosis through the formation of a plaque (atheroma). Plaques can be comprised of foam cells, fatty substances, lipids, cholesterol, cellular waste products, elastin, collagen, fibrin, calcium and many other constituents. A new computational model for plaque progression in the carotid artery using coupled Agent Based Method (ABM) and Finite Element Method (FEM) was developed. The ABM was coupled with an initial Wall Shear Stress (WSS) profile, which triggers a pathologic vascular remodeling by perturbing the baseline cellular activity and favoring lipid infiltration and accumulation within the arterial wall. The ABM model takes shear stress and LDL initial distribution from the lumen and starts iterative calculation inside the wall for lipid infiltration and accumulation using a random number generator for each time step. After ABM iterations, both wall lipid distribution and wall geometry are changed. Fluid-structure solver is running and lumen domain is calculated again. First results show good agreement between proposed method and clinical measurements in the follow up 3D Ultrasound image reconstruction. The integrated model ABM and FEM can help to predict the evolution of atherosclerotic plaque which is very significant for appropriate diagnostics and vascular treatment planning.**

Keywords—Atherosclerosis; Agent Base Method; Finite Element Method; Ultrasound images; plaque growth; carotid artery;

I. INTRODUCTION

Atherosclerosis is characterized by dysfunction of endothelium, vasculitis and accumulation of lipid, cholesterol and cell elements inside the blood vessel wall. This process allows discrete modeling technique to be implemented. One of the discrete modeling techniques is Agent Based Method (ABM). Atherosclerosis develops from oxidized Low-Density Lipoprotein (LDL) molecules. When oxidized LDL evolves in plaque formations within an artery wall, a series of reactions occur to repair the damage to the artery wall caused by oxidized LDL.

ABM allows the single decision components' perspective for simulation of the atherosclerosis process. The whole process is relied on the interactions over time of a collection of agents responding to local environmental conditions and neighboring agent results. The network of agents is collecting information, learning and acting in parallel in an environment produced by the nonlinear spatial-temporal interactions to simulate complex process [1]. Garbey et al. [2] analyse vascular adaptation and make cross-validation of the two models by creating an accurate matching procedure. They added the degree of accuracy given by the ABM to a simplified model dynamic system that can serve as powerful predictive tool for the clinic. Doran et al. [3] described the role of smooth muscle cells in the initiation and early progression of atherosclerosis. Corti et al. [4] analysed a fully coupled computational fluid dynamics--agent-based model of atherosclerotic plaque development.

In this paper we make fully integrated model of ABM and FEM for carotid artery and predict the evolution of atherosclerotic plaque.

II. MATERIALS AND METHODS

A. ABM atherosclerosis modeling

While cell agents are responsible for cell mitosis and apoptosis and Extracellular Matrix (ECM) production, ECM agents are involved in ECM degradation, meaning that the code scans the grid looking for cells or ECM, respectively. Considering the work of Garbey et al. [2], coefficient β for the intima, media and adventitia layers were set in order to guarantee stable trends of ECM in each layer under baseline conditions. The probability of cell mitosis and ECM production in the intima increases with the inflammation level, the number of neighboring lipids and the closeness to the lumen [3], leading to the following:

$$p_{mit} = \begin{cases} \alpha_1 \cdot (1 + \alpha_2 I^k) \; if \; n_{lip} = 0 \\ \alpha_1 \cdot (1 + \alpha_2 I^k)\left(1 + \alpha_3 n_{lip}\right)\{1 + \exp(-d^k_{lumen})\} \; if \; n_{lip} \neq 0, \end{cases} \quad (1)$$

$$p_{prod} = \begin{cases} \alpha_4 \cdot (1 + \alpha_2 I^k) \; if \; n_{lip} = 0 \\ \alpha_4 \cdot (1 + \alpha_2 I^k)\left(1 + \alpha_3 n_{lip}\right)\{1 + \exp(-d^k_{lumen})\} \; if \; n_{lip} \neq 0. \end{cases} \quad (2)$$

where α_2 and α_3 weight the effect of the inflammation state I^k and the influence of the neighboring lipids n_{lip}, while d^k_{lumen} is the distance between the site k and the lumen wall. The coefficients were set following the framework proposed by Corti et al. [4], with the additional requisites of obtaining probability values of the agent dynamics and an accelerated plaque formation under atherogenic condition.

Under atherogenic conditions, the ABM also implements the process of lipid infiltration in the intima. In order to simulate an earlier adaptive intimal thickening [5], lipid dynamics is activated once the intima thickens over a given threshold. Since circulating low density lipoproteins were not explicitly modeled, the probability of lipid infiltration is computed as the probability of a site k at the lumen wall to allow lipids to invade the intima, expressed by:

$$p_{lipid} = \alpha_5(1 + I^k)\{1 + \alpha_6 \cdot \exp(-d^k_{lip})\}\left(1 + \frac{n_{lip}}{\alpha_7}\right), \quad (3)$$

where α_5 sets the event probability in the interval (0, 1). The terms $\alpha_6 \cdot \exp(-d^k_{lip})$ and $\left(1 + \frac{n_{lip}}{\alpha_7}\right)$ promote lipid clustering, by increasing the probability of a lipid to occupy a site k close to another lipid, whose distance is d^k_{lip}. The terms and coefficients of equation (3) are set so to obtain a lipid nucleus resembling histological characteristics [6].

B. Coupling ABM and FEM

The ABM was coupled with an initial Wall Shear Stress (WSS) profile, which triggers a pathologic vascular remodeling by perturbing the baseline cellular activity and favoring lipid infiltration and accumulation within the arterial wall. Finite element mesh was generated for fluid and solid domains. Governing equations for the fluid domain and numerical procedures are used. Fluid-structure interaction and mesh motion was implemented. All algorithms are incorporated in program PAK - Athero [6].

During each step we calculated with FEM the velocity distribution, LDL transport distribution, pressure distribution, and shear stress distribution inside the lumen area. The ABM model takes shear stress and LDL initial distribution from the lumen and starts iterative calculation inside the wall for lipid infiltration and accumulation using a random number generator for each time step. After ABM iterations, both wall lipid distribution and wall geometry are changed. This directly influences the wall artery geometry which is also modeled with finite element, including ABM elements inside these large finite elements. Then, fluid-structure solver is running and lumen domain is calculated again [7,8].

C. Image processing and 3D reconstruction

The scheme of the entire methodology within the Ultrasound image processing module, employed within the TAXINOMISIS project [9] is shown in Fig. 1. Ultrasound images used as the basis for the whole reconstruction module are shown in Fig. 1A. These images are annotated and preprocessed and shown in Fig. 1B. These pairs of original and annotated images are used for the training of the CNNs. Then, a specific set of Ultrasound images (shown in Fig. 1C) is used to extract the segments of the carotid artery by using the trained models, as shown in Fig. 1D. Then, the information obtained in the deep learning module is further directed to the reconstruction module, where the relevant shapes of the carotid bifurcation are created, like shown in Fig. 1E, in order to obtain the finite element mesh of the reconstructed geometry, shown in Fig. 1F. Finally, the finite element mesh is ready to be used within the Computer Fluid Dynamics (CFD) module for the simulations of blood flow and plaque progression. Dataset from patients and validation were done in project TAXINOMISIS [9].

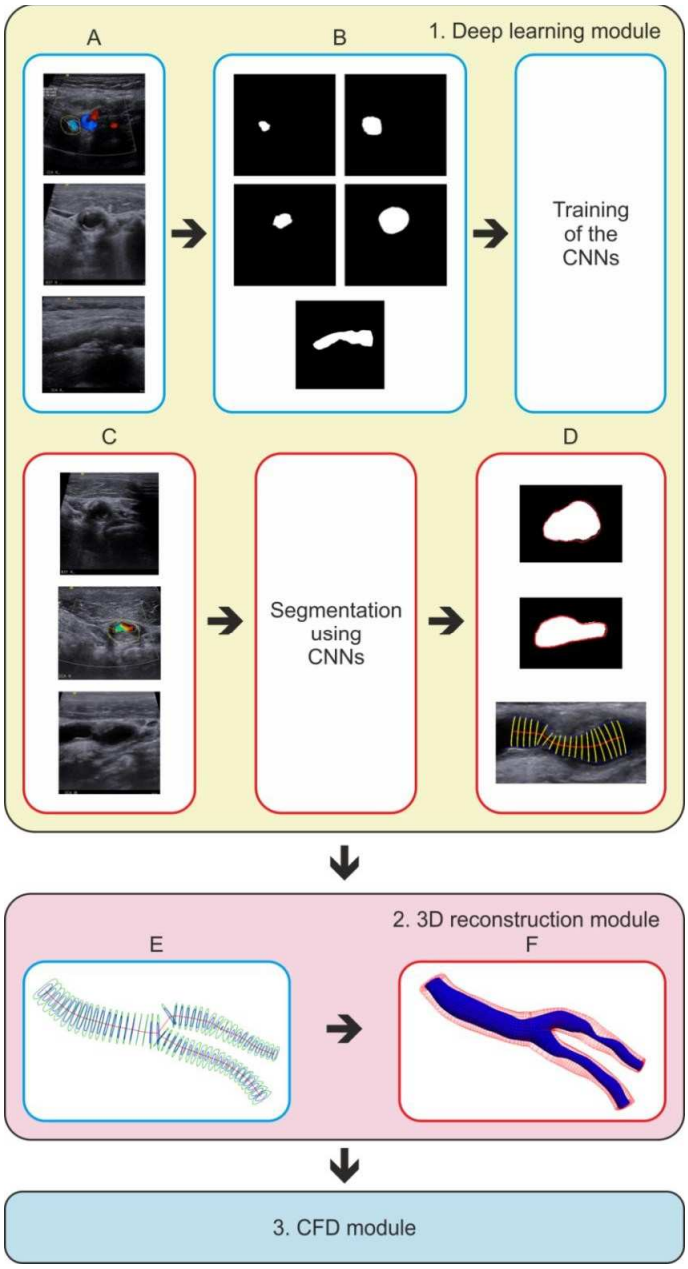

Fig. 1. Developed methodology for the reconstruction of carotid bifurcations using Ultrasound imaging. Deep learning module is using training of CNNs for segmentation. 3D reconstruction module makes 3D finite element mesh. CFD module calculated blood velocity, pressure and WSS distribution.

III. Results

We used one specific patient for carotid artery model of plaque progression. It can be used for verification and validation of the proposed coupled methodology of ABM and FEM. We analysed patient-specific plaque location, size and structure at baseline and follow-up after 6 months.

The results of the 3D reconstruction and model of the plaque including the separation of plaque components are shown in Fig.2 for chosen patient-specific carotid bifurcation from the patient dataset from TAXINOMISIS project [9]. In order to keep the results in accordance with the annotated Ultrasound images from clinical partner, in the following image the fibrous plaque is colored in yellow, the lipid plaque is colored in blue and the calcified plaque is colored in green.

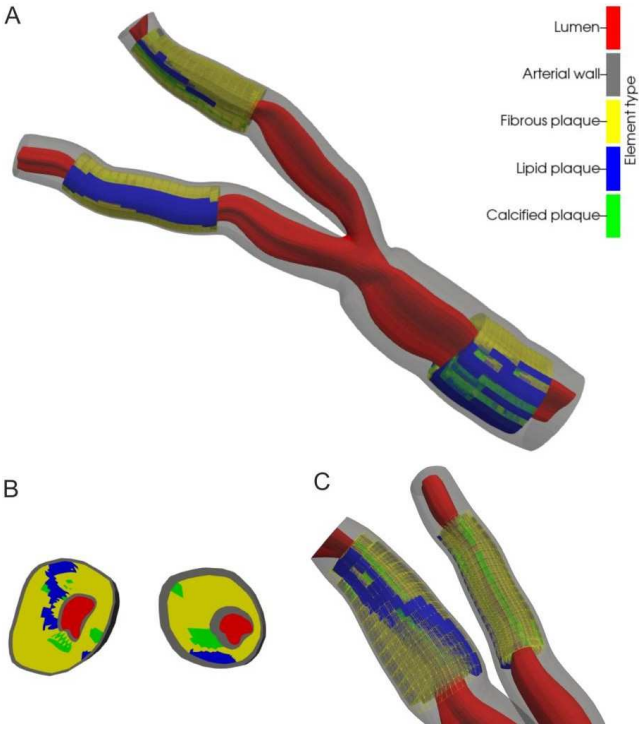

Fig. 2. Reconstructed geometry for the patient #044 from NKUA dataset with separated plaque components; A – Whole reconstructed mesh shown with transparent wall; B – transversal cross-section; C – augmented part of the mesh containing FE elements defined as plaque.

This is first study where fully coupling of ABM and FEM was performed on the carotid artery from Ultrasound images. Also, plaque progression model was developed for patient specific prediction.

IV. Conclusions

We have developed simulation of plaque progression in the carotid artery with ABM which is coupled with FEM. Specific patient was reconstructed from Ultrasound images and 3D model was running with coupled solver based on FEM and ABM. First results show good agreement between proposed method and clinical measurements in the follow up. Our approach can help to predict the evolution of atherosclerotic plaque in the carotid artery which is very useful for diagnostics and vascular treatment planning [9].

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