FIRST RESULTS ON A 3D MODEL FOR IN-STENT RESTENOSIS

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Introduction

Coronary artery disease (CAD) is one of the most common causes of death, and is responsible for about 7.3 million deaths per year worldwide [Mendis, 2011]. A common coronary interventional procedure is balloon angioplasty with stenting, which can be followed by in-stent-restenosis (ISR), an excessive regrowth of tissue due to the injury caused by the stent deployment. Although there are a number of different hypotheses [Jukema, 2011], the pathophysiological mechanisms and risk factors of ISR are not yet fully clear as they involve complex nonlinear biological processes. Computational medicine intends to overcome this complexity by developing computational models which can help achieve a qualitative and quantitative understanding of structure and function of these processes in health and disease [Winslow, 2012].

Methods

After evaluating the processes involved in ISR [Evans, 2008], we have developed an off-lattice 3D multiscale model (ISR3D) where a vessel consists of cells that interact, deforming the tissue, grow and divide following the cell cycle. We hypothesize that this cell proliferation drives the restenosis, and that this is affected most heavily by wall shear stress of the blood flow, which regulates endothelium recovery, and by growth inhibiting drugs diffused by a drug-eluting stent. Such a model allows us to simulate the response of the system with different stent designs, injury scores or endothelium recovery rates and then validate the results against available experimental data.

Results

Preliminary results without blood flow in Figure 1 show first results on ISR3D with full stent deployment and a decreased lumen diameter for a higher injury score, in line with porcine data [Gunn, 2002]. Simulations including blood flow are still being computed.

Discussion

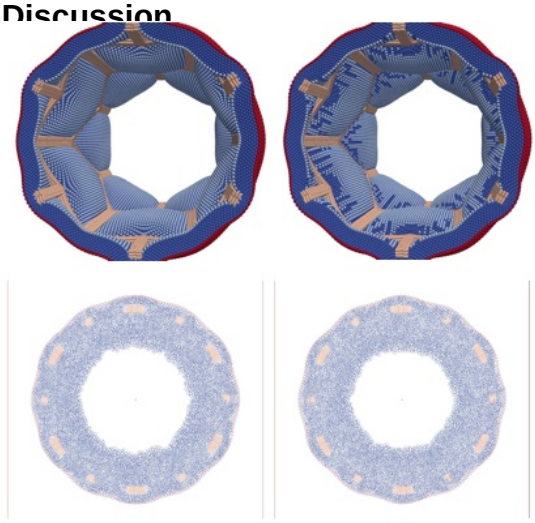

Figure 1: Deployment (3D view, up) and following growth after 10 days (slice, down) for a fenestrated internal elastic lamina (left) and a broken one (right).

ISR3D is based on a longitudinal ISR2D model [Caiazzo, 2011] [Tahir, 2011] although it provides improvements such as hyperelastic cell interaction, full stent design and an extra dimension in which cells can now move providing more accuracy, realism and the possibility to directly compare with the restenotic histological sections available in the literature, which are usually not longitudinal.
The model is limited to porcine simulations, as human simulations would span for a too long timescale and would also require the modeling of atherosclerosis.

References

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