3D NUMERICAL SIMULATIONS OF STENT-BASED LOCAL DRUG DELIVERY USING REALISTIC STENT AND VASCULAR WALL STRUCTURES

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ABSTRACT

The efficiency of local delivery using a polymer coated stent depends on the homogeneity of the distribution of the molecule in the vascular wall. The distribution should be as uniform as possible radially and longitudinally with minimal loss in the blood stream. Previous numerical models have investigated the problem with simplified 2D stent geometries and have assumed a normal vascular structure [1]. In this work, we present a 3D model taking into account the CAD geometry of a stent as well as realistic pathologic vessel wall.

1. INTRODUCTION

Angioplasty and coronary stenting result in restenosis in 40% of cases within six months following the initial procedure [2, 3]. Local drug delivery using coated stents have been proposed to inhibit neointimal hyperplasia though affecting the cellular growth mechanisms in the tissues surrounding the stent [4, 5]. In order to affect complete success, drug delivery must act to deliver a therapeutic dose evenly through the treatment region, and must be present for the desired therapeutic duration. Clinical studies have characterized the transport of drugs in solution across the vascular wall, giving radial drug distribution information but offering little accompanying geographic information concerning drug distribution [6, 7, 8]. Porcine models using implanted drug-eluting stents concentrate on measuring the degree of restenosis rather than dose concentration information. It is then difficult to identify the shortcomings of current drug-eluting stent designs based on these results. In that context, numerical modeling of local delivery may help to identify some of the sources of these shortcomings.

For that purpose, we have developed a 3D numerical pharmacokinetic model for realistic stent and vascular structure geometries.

2. METHODS

A three-dimensional model including vessel lumen, arterial wall, stent, and stent coating was constructed using computer aided drawing (CAD), meshed with tetrahedral elements and solved using generic CFD software. Coupled Navier-Stokes and Advection-Diffusion equations were applied in the vessel lumen, and the polymer layer and arterial wall were considered purely diffusive regions. The transient simulation extends over a time of one week. Results were evaluated on the basis of a dose homogeneity index (DHI) defined as the coefficient of variation in a set therapeutic region, and remaining mass percentage (RMP) defined as the percentage of total remaining drug mass.

Basic geometry

The stent geometry corresponds to the Symbiotech endovascular prosthesis [Patent Document Number 2201001]. Figure 1 shows the actual stent and its 3D CAD representation (Pro-E). The stent is shown in a 3.1 mm expanded configuration. The length is about 1.5 cm and the strut width is about 63.5 μm and the modeled polymer coating thickness is 5 μm.

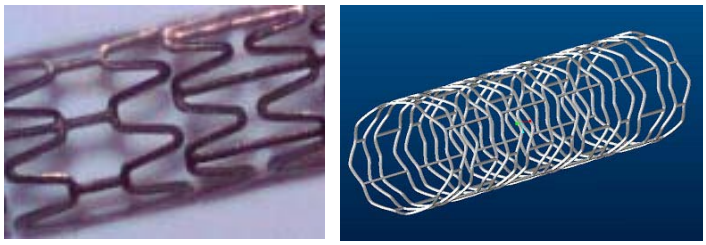

Figure 1. The Symibiotech stent and its CAD representation

Domain discretization

Discretization was carried out using ICEM-CFD with tetrahedral element. Grid independence tests indicated that mesh element side lengths of 2.5 μm surrounding the polymer layer to 25 μm in the outer regions resulted in a favorable computation time/result agreement compromise. Figure 2 illustrates a magnified view near the strut and the resulting local mesh subsequently used in the numerical solver.

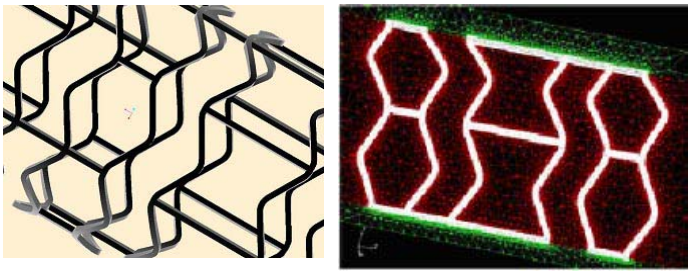

Figure 2. Stent strut and meshing

Numerical model

Coupled 3D Navier-Stokes and Advection-Diffusion equations (1, 3) were applied in the vessel lumen. The polymer coating and arterial wall were considered purely diffusive regions (4). Blood is considered an incompressible Newtonian fluid (2) of density ρ=1.05 g/cm3 and dynamic viscosity μ=0.035 Poise (g/cm.s).

$$\rho(\vec{u}\cdot\nabla)\vec{u} = -\nabla p + \mu\nabla^2\vec{u} \quad (1)$$

$$\nabla\cdot\vec{u} = 0 \quad (2)$$

$$C_t + (\vec{u}\cdot\nabla)C = D_{lumen}\nabla^2 C \quad (3)$$

$$C_t = D_{polymer}\nabla^2 C \qquad C_t = D_{artery}\nabla^2 C \quad (4)$$

For comparison purposes, diffusivities for heparin and taxol in the vessel lumen, arterial wall, polymer coating and pathological tissues were gathered from clinical studies [6, 7, 9].Concentrations at the outer limit of the arterial wall and lumen inlet are set to zero for all time. At the outer wall limit this condition is meant to approximate the effect of dilution resulting from transport of mass from the vasa vasorum. At the inlet concentrations due to dilution in blood will effectively be zero. No-slip velocity conditions are imposed on the polymer coating and arterial wall. Drug loading of the stent is represented as an initial concentration of 1.0 in the polymer.

3. RESULTS

Normal wall modeling

In a first approach the wall is modeled as a cylinder 400 μm thick. Numerical simulations for heparin (hydrophilic) and taxol (hydrophobic) were performed (Figure 3). We also illustrate the RMP over a one week period.

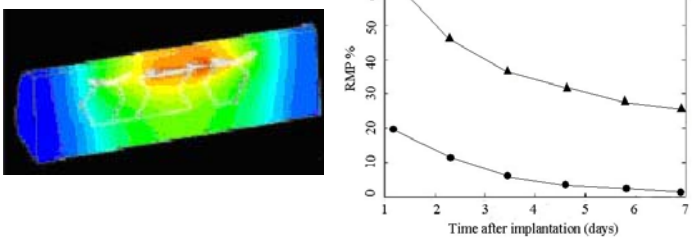

Figure 3. 3D concentration distribution and Remaining Mass Percentage RMP for heparin (▲) and taxol (●)

Pathologic wall modeling

Ongoing work include the extension of the model to simulate the diffusion of the molecule into pathologic vessel structures taking into account the effect of lipid and fibrotic pools. These structures are reconstructed from Intravascular Ultrasound (IVUS) using manual segmentation as illustrated in Figure 4.

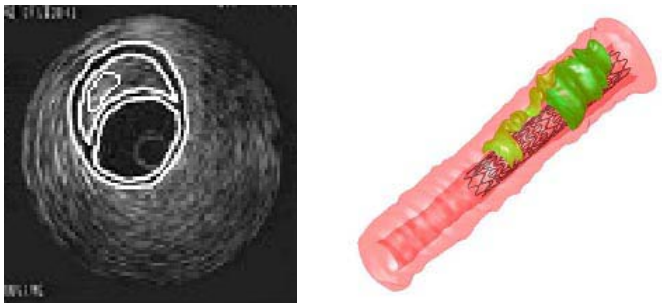

Figure 4. IVUS segmentation and Sent inserted in the 3D reconstructed pathologic wall structure

CONCLUSION

We have presented a method to analyse the 3D distribution of a molecule for local delivery using realistic stent and vessel wall structures. The method allows to visualize the homogeneity of the 3D distribution of the molecule achieved in the vascular wall. The method also allows for quantitative comparison of delivery efficiency in time after stent implantation for various molecules. Such a tool is complementary to current animal investigations in assessing the efficiency of a given coated stent configuration. Finally, the method would also allow to investigate the effect of the stent design itself on the homogeneity of the distribution. With the advent of more sophisticated laser machining and drug deposition techniques, the ultimate goal of producing patient-specific drug loading and stent design characteristics for each stent implantation could be considered.

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