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Numerical modelling of mass transport in an arterial wall with anisotropic transport properties

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ABSTRACT

Coronary artery disease results in blockages or narrowing of the artery lumen. Drug eluting stents (DES) were developed to replace bare metal stents in an effort to combat re-blocking of the diseased artery following treatment. The numerical models developed within this study focus on representing the changing trends of drug delivery from an idealised DES in an arterial wall with an anisotropic ultra-structure. To reduce the computational burden of solving coupled physics problems, a model reduction strategy was adopted. Particular focus has been placed upon adequately modelling the influence of strut compression as there is a paucity of numerical studies that account for changes in transport properties in compressed regions of the arterial wall due to stent deployment. This study developed an idealised numerical modelling framework to account for the changes in the directionally dependent porosity and tortuosities of the arterial wall as a result of radial strut compression. The results show that depending on the degree of strut compression, trends in therapeutic drug delivery within the arterial wall can be either increased or decreased. The study highlights the importance of incorporating compression into numerical models to better represent transport within the arterial wall and suggests an appropriate numerical modelling framework that could be utilised in more realistic patient specific arterial geometries.

1. Introduction

Coronary artery disease (CAD) that results in inadequate blood flow to the heart is responsible for 2150 deaths in the US each day, an average of 1 death every 40 s (Go et al., 2013). A key advancement in the treatment of coronary artery disease in recent years has been the introduction of drug eluting stents (DES). It is hence important that a therapeutic amount of drug is delivered to this region to alleviate the initiation of smooth muscle cell (SMC) proliferation to the site of injury after stent implantation (O'Connell et al., 2010). In a study by Axel et al. (1997) it was found that Paclitaxel can have a therapeutic effect in the medial layer after 20 min of exposure and therefore this study assesses therapeutic levels of drug in the vasculature in these early time periods. Many numerical studies have assumed that the transport properties of the arterial wall are isotropic in nature. However, this is an ideal assumption which is generally used in order to gain an initial understanding of how various physical processes affect therapeutic drug delivery in the arterial wall (D'Angelo et al., (2011); Mongrain et al., 2007; Pontrelli and DE Monte, 2007, 2010; Zunino et al., 2009). However experimental studies have shown that the ultra-structure of the arterial wall is anisotropic in nature (Creel et al., 2000; Hwang and Edelman, 2002; Hwang et al., 2001; Levin et al., 2004; Lovich et al., 2001; Tada and Tarbell, 2001). Some authors have chosen to include anisotropic transport properties in their numerical studies where the main findings here are that there is greater spatial distribution of drugs in the longitudinal/planar direction where the diffusion coefficient can be up to one order of magnitude greater than that of the radial/transmural direction depending on the molecular size of the drug (Balakrishnan et al., 2008; Green et al., 2005; Horner et al., 2010; Yang and Burt, 2006). However, few of these studies address the issue of stent strut compression and there is a complete paucity of numerical studies that focus on representing a bi-directional change in the transport physics of the arterial wall as a result of applied stent strut compression. Many authors approach this topic from the perspective of analysing the influence of drug binding by accounting for the drug's hydrophobic or hydrophilic nature. However, while accounting for partitioning coefficients in the effective diffusion coefficient equation other mechanical factors such as the tortuosity and porosity are neglected even though their effect does influence transport in a porous media like the arterial wall (Creel et al., 2000; Horner et al., 2010; Hwang and Edelman, 2002; Hwang et al., 2001; Wan et al., 1999). This study

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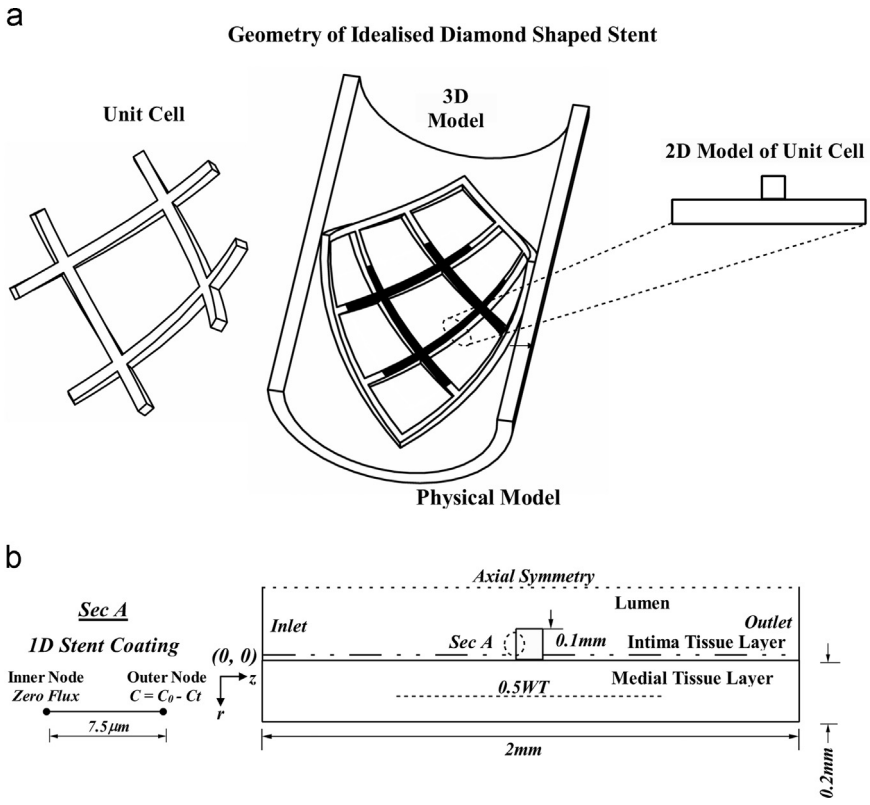

Fig. 1. (a) Model reduction of the unit cell of an idealised diamond shaped stent. (b) Schematic side view diagram of the physical model including a 1D model representing the stent's polymer coating.

uses an experimentally estimated porosity value taken from literature and arbitrary calculated tortuosity values, on an idealised 2D stent model to develop a numerical modelling framework to better represent drug transport in compressed arterial walls, which can then be applied to more patient specific diseased models.

2. Geometry used in numerical models

Fig. 1(a) shows a 2D model that was used to represent the unit cell of the 3D curved model. The geometries created are representative of the intimal and medial layers where a single stent strut is interfaced with the arterial wall. Fig. 1(b) shows a side view of the arterial wall and luminal domains in direct contact with a single square stent strut. Also shown in Fig. 1(b) is a 1D schematic that is representative of the polymer coating domain. The models explored in this study are a variation of the 2D schematic presented in Fig. 1(b).

3. Mathematical model

Drug transport within the stent coating and arterial wall were modelled using the transient diffusion equation (Eq. (1))

$$\frac{\partial C}{\partial t} = D_r \frac{1}{r}\frac{\partial}{\partial r}\left(r\frac{\partial C}{\partial r}\right) + D_z \frac{\partial^2 C}{\partial z^2} \tag{1}$$

D_r and D_z are the effective diffusivities in the radial and longitudinal directions of the medial layer respectively, C represents the species concentration, r and z indicate position and t represents time. Mass transport within the arterial wall can be referred to as wall side mass transport (WSMT) and Eq. (1) describes the governing equation for diffusion dominated mass transport where this is assumed in the arterial wall (Mongrain et al., 2007; 2005). However, when considering a luminal contribution i.e. blood side mass transport (BSMT), convective forces need to be accounted for. Blood was assumed to be Newtonian incompressible and its fluid mechanics were described with the continuity and steady state Navier–Stokes equations in the case of axisymmetric flow (Eqs. (2) and (3)).

$$\frac{1}{r}\frac{\partial}{\partial r}(ru_r) + \frac{\partial}{\partial z}(u_z) = 0 \tag{2}$$

$$\rho\left(\frac{\partial u_r}{\partial t} + u_r\frac{\partial u_r}{\partial r} + u_z\frac{\partial u_r}{\partial z}\right) = -\frac{\partial p}{\partial r} + \mu\left[\frac{\partial}{\partial r}\left(\frac{1}{r}\frac{\partial}{\partial r}(ru_r)\right) + \frac{\partial^2 u_r}{\partial z^2}\right] + \rho g_r$$
$$\rho\left(\frac{\partial u_z}{\partial t} + u_r\frac{\partial u_z}{\partial r} + u_z\frac{\partial u_z}{\partial z}\right) = -\frac{\partial p}{\partial z} + \mu\left[\frac{1}{r}\frac{\partial}{\partial r}\left(r\frac{\partial u_z}{\partial r}\right) + \frac{\partial^2 u_z}{\partial z^2}\right] + \rho g_z \tag{3}$$

where u_r, u_z, p, μ, ρ, g_r, g_z and t represent the r–z components of velocity, pressure, dynamic viscosity, density, r–z components of gravitational force and time respectively. In summary to this, coupled drug transport analysis in a 2D cylindrical coordinate system can be described by the species convection diffusion equation (Eq. (4)) (Salama, 2011).

$$\frac{\partial C}{\partial t} + \left(u_r\frac{\partial C}{\partial r} + u_z\frac{\partial C}{\partial z}\right) = D_r\frac{1}{r}\frac{\partial}{\partial r}\left(r\frac{\partial C}{\partial r}\right) + D_z\frac{\partial^2 C}{\partial z^2} \tag{4}$$

3.1. Blood flow boundary conditions

The use of a steady flow inlet condition has been shown to adequately approximately the effects of BSMT (Kolachalama et al., 2009). A zero pressure, zero viscous stress boundary condition was applied at the outlet (Borghi et al., 2008; Zunino et al., 2009). A velocity of zero is applied at stent strut and lumen wall interface boundaries to satisfy the no slip condition