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Mechanobiology of low-density lipoprotein transport within an arterial wall—Impact of hyperthermia and coupling effects

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ABSTRACT

The effects of hyperthermia, coupling attributes and property variations on Low-density lipoprotein (LDL) transport within a multi-layered wall while accounting for the fluid structure interaction (FSI) is analyzed in this work. To understand the potential impact of the hyperthermia process, thermo-induced attributes are incorporated, accounting for the plasma flow, mass transfer, as well as the elastic wall structure. The coupling effect of osmotic pressure, Soret and Dufour diffusion is discussed and their influence on LDL transport is examined, demonstrating that only the Soret effect needs to be accounted for. The effect of thermal expansion on changing the behavior of flow, mass transport, and elastic structure is illustrated and analyzed while incorporating the variations in the effective LDL diffusivity and consumption rate, as well as other dominating parameters. It is shown that hyperthermia results in an enhancement in LDL transport by increasing the concentration levels within the arterial wall.

1. Introduction

Cardiovascular diseases have received considerable attention due to their impact on health issues within the society and 80 million adults patients in America alone (American Heart Association, 2007; Khakpour and Vafai, 2008) with half a trillion dollars in expenses (American Heart Association, 2008; Hossain et al., 2011). Atherosclerosis usually occurs in larger arteries and can lead to other kinds of cardiovascular diseases. This aortic disease is not only associated with 1/5 of deaths in the United States by its complications (American Heart Association, 2008; Hossain et al., 2011) but also the 14th cause of death in America by itself (Gillum, 1995; Khanafer et al., 2009). Studying atherosclerosis is important for a better diagnosis and treatment of this disease.

Low-density lipoprotein (LDL), is considered to be one of the main factors in causing atherosclerosis as it accumulates in an arterial wall. Oxidization of LDL damages the cells and the wall function of an artery, resulting in the plaque formation and lumen stenosis. An accurate and comprehensive model of LDL molecule accumulation in the wall, can demonstrate the involved processes leading to atherosclerosis. Wall-free and lumen-wall models were introduced earlier and have been used by other researchers (Rappitsch and Perktold, 1996; Wada and Karino, 2000; Moore and Ethier, 1997; Stangeby and Ethier, 2002a, b; Prosi et al., 2005). However, the structure and phenomena within the arterial wall is complex as shown in Fig. 1a, and a detailed multi-layered model with different consideration in each of the layers of an artery is far more appropriate. Transport phenomena through porous media has been studied for numerous different fields of research (Tien and Vafai, 1989; Vafai and Hadim, 2000; Razi et al., 2005; Li and Stoliarov, 2013). Darcy and extended Darcy models have been applied in earlier works (Chung and Vafai, 2010; Shi and Vafai, 2010).

Yang and Vafai (2006, 2008) and Ai and Vafai (2006) developed a multi-layered model in an artery to accurately represent different transport behavior within each of the layers. Four arterial layers, endothelium, intima, IEL, and media, were considered. The Staverman–Kedem–Katchalsky membrane equation (Kedem and Katchalsky, 1958) and osmotic pressure were invoked to describe the transport through a thin porous membrane with low permeability. Based on this model, the impact of macro-structure such as stenosis (Ai and Vafai, 2006; Khanafer et al., 2009) or bifurcation (Khakpour and Vafai, 2008) has also been studied. Furthermore, Chung and Vafai (2012, 2013) coupled the model with extended physics to represent the effect by fluid-structure interactions and atherosclerotic plaque.

Characteristics and properties of transport within these layers have been studied, both from macro-scale view point (Huang et al., 1994; Tada and Tarbell, 2004; Prosi et al., 2005; Ai and Vafai, 2006) as well as a micro-scale point of view (Curry, 1984a, b; Fry, 1985; Huang et al., 1992; Hunag et al., 1997; Huang and Tarbell, 1997; Yuan et al., 1991; Weinbaum et al., 1992; Karner et al., 2001; Liu et al., 2011; Chung and Vafai, 2012, 2013). Several theorems have been developed to calculate the properties by the parameters that describe the microstructure in each of the different arterial layers,

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Nomenclature

c	LDL concentration
c_T	thermal capacity
D	LDL diffusivity
f_s	solid domain body force
k	reaction coefficient
k_T	thermal-diffusion coefficient
k_D	diffusivity effective rate
K	hydraulic permeability
L	length of the artery
M	molecular weight
p	hydraulic pressure
r	radial location from the centerline
r_m	molecular radius
R	universal gas constant
R_0	radius of lumen domain
T	temperature
T_H	hyperthermia temperature applied at the Lunmen-wall interface
T_{ref}	reference temperature chosen as core body temperature (310 K)
u	axial velocity of blood flow
$\overrightarrow{u}$	velocity vector
U_0	maximum velocity at entrance
v	filtration (radial) velocity
x	axial location from the inlet
α	thermal diffusivity
α_{lj}	ratio of LDL molecule radius to half-width of the leaky junction
β_{lj}	leaky-bulk expansion ratio
β_T	thermal expansion coefficient
ε	elastic strain
ε_T	thermal strain
μ	viscosity
σ	reflection coefficient
σ_s	Cauchy stress tensor
ΔT	temperature drop from inner to outer surface of the wall

Subscripts

0	refers to entrance condition
70 mmHg	refers to property under 70 mmHg pressure drop across the wall without hyperthermia
eff	refers to effective property
end	refers to endothelium property
f	refers to plasma property
lj	refers to leaky junction property

such as pore theorem and fiber matrix model which have been utilized by Huang et al. (1994), Karner et al. (2001), Liu et al. (2011) and Chung and Vafai (2012, 2013).

Hyperthermia is involved as an important factor or solution in several health issues, such as cancer treatment (Jain, 1987) or vascular stent delivery (Stoeckel et al., 2004), and the application can possibly be extended to treatment of atherosclerosis or other cardiovascular diseases. Therefore, for transport within an artery, since thermal impact is an important issue, the consideration of heat-induced effect is also important. Mass flux driven by temperature gradient (Soret effect) and its counter part Dufour effect need to be analyzed particularly for hyperthermia applications. Furthermore, based on Einstein- Stoke model, the molecular diffusivity is dominated by temperature. The thermal expansion behavior of an artery has been studied by a number of researchers (Rabin and Plitz, 2005; Jimenez Rios and Rabin, 2006), and hyperthermia can change the of transport properties, based on Chung and Vafai (2012) FSI work. Another aspect which can be affected by temperature is the reaction rate of LDL in the media layer.

In summary, the current work aims at investigating the impact of coupling effect between hydraulic, mass, and heat transport, by examining influence of osmotic, Soret, and Dufour effects. Further, to study the impact of the hyperthermia effect on molecular transport in an artery, thermal expansion, as well as temperature-dependent effective diffusivity and reaction rate of LDL, is analyzed. This study provides, for the first time, a detailed understanding of the physics that can potentially be induced by hyperthermia treatment for cardiovascular issue.

2. Formulation

2.1. Multi-layer model

Fig. 1a shows the layered structure of an arterial wall with, from inner to the outer side, lumen, glycocalyx, endothelium, intima, IEL, media, and adventitia layers. Glycocalyx in this study is neglected (Yang and Vafai, 2006, 2008; Ai and Vafai, 2006) due to its negligible resistance (Michel and Curry, 1999; Tarbell, 2003), while adventitia is incorporated as part of the outer boundary condition for flow, heat and mass transfer. A cylindrical geometry is adopted to represent the computational domain with lumen radius of R_0 (310 μm), axial length L (0.2232 m). Detailed information of the other layers surrounding the lumen are given in Table 1a (Karner et al., 2001; Prosi et al., 2005; Yang and Vafai, 2006, 2008; Ai and Vafai, 2006; Khanafer and Berguer, 2009; Chung and Vafai, 2012, 2013). The transport properties of arterial layers are obtained using either pore theorem or fiber matrix model using the micro-structure information (Karner et al., 2001; Chung and Vafai, 2012). The properties in this table are only given by their original value, and can be affected under the impact of thermal or elastic effects.

2.2. Governing equations—Original and uncoupled

Assuming steady state based on the negligible effect of blood pulsation (Yang and Vafai, 2006; Chung and Vafai, 2012), the conservation of mass, momentum and species inside the lumen are expressed as

$$\nabla \cdot \overrightarrow{u} = 0 \quad (1)$$

$$-\nabla p + \mu_f \nabla^2 \overrightarrow{u} = 0 \quad (2)$$

$$\overrightarrow{u} \cdot \nabla c = D_f \nabla^2 c \quad (3)$$

where $\overrightarrow{u}$ is the velocity vector, c LDL concentration, p hydraulic pressure, and μ_f and D_f are the plasma viscosity and diffusivity coefficient, respectively.

The Darcy–Brinkman equation is used to describe the flow, while diffusion–convection–reaction equation incorporating the Staverman–Kedem–Katchalsky membrane equation (Kedem and Katchalsky, 1958) is applied to describe molecular transport of LDL