Mathematical and Computational Applications, Vol. 12, No. 3, pp. 173-179, 2007.

MATHEMATICAL SOLUTION OF THE FLOW FIELD OVER GLYCOCALYX INSIDE VASCULAR SYSTEM

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Abstract-Mathematical analysis of the the flow field over the glycocalyx located on the endothelial cells (EC) inside cardiovascular system was investigated. Two flow regions were considered. A core flow region which is located in the lumen of the vessel. The flow in this region is similar to Poiseuille flow seen inside the straight pipes. Flow region through the glycocalyx is located near the lumen wall. The flow in this region is considered as a flow through the porous media. Solutions are found in both regions and wall shear stresses (WSS) and drag force are calculated.

Keywords- Mathematical modeling, Glycocalyx, Blood Flow, Wall Shear Stress

1. INTRODUCTION

Cardiovascular disease is the leading cause of death in the world. Cardiovascular system consist of blood vessels. Endothelial cells line inside the blood vessels. The relation between the blood flow inside blood vessels and endothelial cells have been investigated for two decades. The problem is the formation of the atherosclerosis which will cause the blockage of the blood vessels which can be the cause of the death for patients, [1]. Figure 1 shows the flow regions schematically. Upper part shows the core flow region and lower part shows the porous flow region.

Many applied problems in fluid mechanics, other areas of physics and mathematical biology were formulated as the mathematical models of partial differential equations [2 - 4]. Moreover, fluid flow studies and the effect of the shear stress on the EC's were calculated [5 - 8], oncotic forces inside the vessels are calculated [9, 10]and also theoretical calculations of the flow inside microvessels were done, [11]. A model for transport across microvessel endothelium was developed to determine the forces and bending moments acting on the structure of the flow over EC [12].

In this paper specific modeling of the fluid flow over the EC inside the arteries was performed. Two regions were assumed, the flow which is close to EC was taken as flow through porous media and core flow region which is far from EC. General formulation for the calculation of the velocities in both regions are solved. The result of the solution will lead us to calculate the WSS which is assumed one of the most important factor causing the atherosclerosis formation.

2. PROBLEM DEFINITION

Figure 1 shows the structure of the EC inside the vessels. There is a layer of glycocalyx on top of the structure. Proteins and extracellular matrix is located under it. There are protein channels on the cell membrane. Figure 2 shows the schematic of the capillary vessel. Region which is close to the wall is called porous medium and the region which is in the center of the vessel is called as core flow. Endothelial surface layer or glycocalyx has several roles: as a transport barrier, as a porous hydrodynamic interface in the motion of red and white cells in microvessel and as a mechanotransducer of fluid shearing stresses to the actin cortical cytoskeleton of the endothelial cell. Critical flow regions such as turbulent region, low WSS regions were hypothesized on the formation of the fatty structure, atherosclerosis inside the vessel. There is a biochemical signaling due to the flow over the glycocalyx inside the vessel.

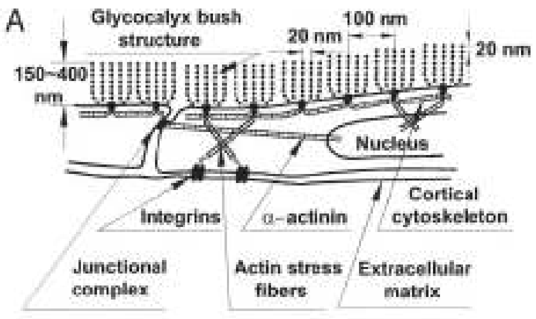

Figure 1. Sketch of endothelial surface level showing core protein arrangement and spacing of scattering centers along core proteins and their relationship to actin cortical cytoskeleton [1].

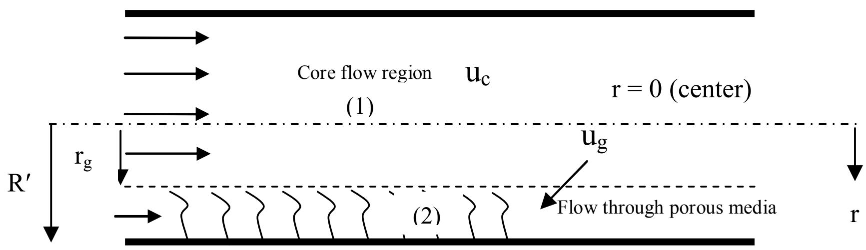

Figure 2. Schematic of the flow regions inside capillary vessels for modeling.

3. ANALYTICAL SOLUTION OF THE FLOW FIELD INSIDE THE BLOOD VESSEL

We can start the solution for the flow field inside the microvessel with the Navier Stokes equations in cyclindrical coordinates, Velocity is given as follows;

$$U = U(R, Z, \theta)$$

Assume fully developed, unidirectional flow in rigid tube

$$\frac{\partial U}{\partial t} = \frac{\partial U}{\partial Z} = \frac{\partial U}{\partial \theta} = 0$$

Equations inside the core region (1) and porous region (2) are given as follows;

$$\frac{\partial P}{\partial Z} = \mu \frac{1}{R}\frac{\partial}{\partial R}\left(R\frac{\partial U_c}{\partial R}\right) \tag{1}$$

$$\frac{\partial P}{\partial Z} = \mu \frac{1}{R}\frac{\partial}{\partial R}\left(R\frac{\partial U_g}{\partial R}\right) - F_z \tag{2}$$

where U_c is the velocity of the core flow and U_g is the velocity of the flow inside porous media. Equation (2) is also known as the Brinkman equation. Drag force is given by equation (3)

$$F_z = \frac{\mu U_g}{K_p} \tag{3}$$

Where K_p is Darcy permeabiality, describes how densely the proteoglycans are packed inside the porous medium. To simplify the equations we can nondimensionalize the equations using the following variables:

$$U=U'u,\ \ R=R'r,\ \ Z= R'z,\ \ P=P'p = (\mu\, U')/ R'$$

Where U', R' and P' are the characteristic velocity, length and pressure
Then the equations (1) and (2) become:

$$\frac{\partial p}{\partial z} = \frac{1}{r}\frac{\partial}{\partial r}\left(r\frac{\partial u_c}{\partial r}\right) \tag{4}$$

$$\frac{\partial p}{\partial z} = \frac{1}{r}\frac{\partial}{\partial r}\left(r\frac{\partial u_g}{\partial r}\right) - \alpha^2 u_g \tag{5}$$

where

$$\alpha^2 = \frac{R'}{\sqrt{K_p}}$$

Boundary and matching conditions need the velocities and shear stress to match at the edge of the glycocalyx, no-slip condition at the endothelial cell membrane, ($r=l$) and symmetry in the center

$$u_c(r_g) = u_g(r_g)$$
$$\frac{\partial u_c(r_g)}{\partial r} = \frac{\partial u_g(r_g)}{\partial r}$$
$$u_g(1) = 0$$
$$\frac{\partial u_c(0)}{\partial r} = 0$$

solving for u_c

$$\frac{\partial}{\partial z}\frac{\partial p}{\partial z} = \frac{\partial}{\partial z}\left(\frac{1}{r}\frac{\partial}{\partial r}\left(r\frac{\partial U_c}{\partial r}\right)\right) \Rightarrow \frac{\partial^2 p}{\partial z^2} = 0 \Rightarrow$$
$$\frac{\partial p}{\partial z} = consant$$

The pressure gradient is constant throughout the tube and integrating up twice and using a matching condition and a boundary condition we get:

$$u_c = -\frac{1}{4}\frac{\partial p}{\partial z}(r_g^2 - r^2) + u_g(r_g)$$

solving for u_g we can rewrite the Brinkman equation in the form:

$$r^2(u_g)_{rr} + r(u_g)_r - r^2\alpha^2 u_g = \frac{\partial p}{\partial z}r^2$$

looks like an inhomogeneous Bessel equation and normal Bessel equation takes the form

$$x^2 y'' + xy' + (\lambda x^2 - r^2)y = 0$$

it has a particular solution

$$(u_g)_p = -\frac{1}{\alpha^2}\frac{\partial p}{\partial z}$$

still solving for u_g, a glimpse into the solution process, we make a few approximations

$$\widetilde{A}=\frac{\frac{-\partial p}{\alpha^2\partial z}(\frac{\alpha r_g}{2}-\frac{K_1(\alpha r_g)}{K_0(\alpha)})}{\frac{K_1(\alpha r_g)}{K_0(\alpha)}+\frac{I_1(\alpha r_g)}{I_0(\alpha)}}\approx\frac{-\partial p}{\alpha^2\partial z}(-1)=\frac{-\partial p}{\alpha^2\partial z}C_1$$

$$\widetilde{B}=\frac{\frac{-\partial p}{\alpha^2\partial z}(\frac{\alpha r_g}{2}-\frac{I_1(\alpha r_g)}{I_0(\alpha)})}{\frac{K_1(\alpha r_g)}{K_0(\alpha)}+\frac{I_1(\alpha r_g)}{I_0(\alpha)}}\approx\frac{-\partial p}{\alpha^2\partial z}(\frac{\frac{\alpha r_g}{2}}{\frac{K_1(\alpha r_g)}{K_0(\alpha)}})=\frac{-\partial p}{\alpha^2\partial z}C_2$$

$$\Rightarrow u_c(r)=-\frac{1}{4}\frac{\partial p}{\partial z}(r_g^2-r^2)+u_g(r_g)=-\frac{1}{4}\frac{\partial p}{\partial z}(r_g^2-r^2)+\frac{-\partial p}{\alpha^2\partial z}C_3$$

Final solution equation ***for*** u_g**,** using the boundary conditions, matching conditions, and the final solutions are given with equations (5) and (6);

$$u_c(r)=-\frac{1}{4}\frac{\partial p}{\partial z}(r_g^2-r^2)+\frac{1}{\alpha^2}\frac{-\partial p}{\partial z}(\frac{r_g\alpha}{2}+1) \tag{6}$$

$$u_g(r)=-\frac{1}{\alpha^2}\frac{\partial p}{\partial z}(-\frac{I_0(r\alpha)}{I_o(\alpha)}+\frac{r_g\alpha}{2}\frac{K_0(r\alpha)}{K_1(r_g\alpha)}+1) \tag{7}$$

We calculate the drag force over the glycocalyx inside the porous medium. F_z force per volume, need force per length. Darcy permeability and the volume fraction of the proteoglycans (c) are given by [9]:

$$K_p=\frac{\ln(c^{-1/2})-0.745+c-\frac{c^2}{4}+O(c^4)}{4\pi}$$

$$\text{where } c=\frac{\pi a_p^2}{(2a_p+\Delta)^2\frac{\sqrt{3}}{2}}$$

For a regular group of glycocalyx, Δ is the distance among the proteoglycans, a is the protein radius. Drag force is calculated from equation (7)

$$F_{drag}=\frac{\pi\mu u_g(r)a_p^2}{cK_p} \tag{8}$$

We can also calculate the WSS using equation (9).

$$\tau_w=\mu\frac{\partial u_g(r)}{\partial r} \tag{9}$$

$$\tau_w=\mu(-\frac{1}{\alpha^2}\frac{\partial p}{\partial z}(-\frac{\alpha I_1(r\alpha)}{I_o(\alpha)}-\frac{r_g\alpha}{2}\frac{\alpha K_1(r\alpha)}{K_1(r_g\alpha)})$$

$$\tau_w = \mu(\frac{1}{\alpha^2}\frac{\partial p}{\partial z}(\frac{\alpha I_1(r\alpha)}{I_o(\alpha)} + \frac{r_g\alpha}{2}\frac{\alpha K_1(r\alpha)}{K_1(r_g\alpha)})) \tag{10}$$

Drag force coming onto the glycocalyx and the shear stress over the wall will give us how much stress is applied to the wall and the effect of it on the biochemical signaling through the cells. Computational code is being written to understand the effect of different flow rates on the endothelial cells with different magnitudes of the WSS and drag forces.

4. CONCLUSIONS

The effect of the flow over the glycocalyx were investigated. The flow equations inside the core flow and porous flow regions were established. Boundary conditions in the center of the microvessel, at the edge of the glycocalyx and at the wall were applied and the solutions of the velocities were found for both core and porous regions under the steady flow conditions. Drag forces and WSS were also calculated. Low WSS can be considered one of the causes of the atherosclerosis formation and biochemical signal activation. A new computer code regarding the flow analysis over the endothelial cells has been written. In vivo studies together with the modeling studies will give more detailed understanding of the flow phenomena inside both regions.

Acknowledgement-I would like to thank to Professor C. Forbes Dewey from Mechanical Engineering and Biological Sciences department of the Massacchusetts Institute of Technology (MIT) for their valuable discussion regarding the effect of the flow over endothelial cells and the mechanotransduction during my visit to MIT in the year of Summer 2005.

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