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Simulation of Direct Perfusion through 3D Cellular Scaffolds with Different Porosity

Sahba Sadir, Andreas öchsner, M.R.A Kadir, Muhamad Noor Harun
Faculty of Mechanical Engineering
Medical Implant Technology Group, Faculty of Biomedical Engineering and Health Sciences
Universiti Teknologi Malaysia
Skudai, 81310, Johor, Malaysia
andreas.oechsner@gmail.com
rafiq@fkm.utm.my

[*]***Abstract*—The perfusion bioreactor has become an ideal environment for cultivating tissues such as cardiac muscle, liver and cartilage. In this study, a perfusion process was modeled using computational fluid dynamics (CFD). The CFD model is based on simplification of the geometry of porous scaffolds, and is designed to predict functions that relate fluid's characteristics, namely wall shear stress level and distribution, pressure drop and permeability, to the porosity of scaffolds. Three group models, corresponding to three different porosities were built. A commercial finite volume code is used to simulate the model. This simulation showed the influence of the geometrical scaffold parameter porosity on the distribution and level of shear stress, pressure drop and mass flow rate. Based on these investigations, the dynamic conditions of a micro fluid passing through the scaffold were characterized for tissue engineering applications.**

Keywords-component; Computational fluid dynamic, micro-fluid dynamic, porosity, permeability, scaffold, tissue engineering.

I. INTRODUCTION

A scaffold is a structure that consists of a porous microstructure containing a fluid phase, a solid matrix and cells. The fluid phase moves through the pores to transport biological or biochemical endogenous and exogenous organs. One of the vital criteria of tissue-engineered constructs is its efficiency to deliver oxygen and nutrient to the site as well as its mechanical properties [1, 2, 3]. Bioreactors allow perfusion of the culture medium to overcome diffusion limitations associated with static culturing by enhancing oxygen and nutrient delivery and catabolite removal from the constructs. These systems also provide flow-mediated mechanical stimuli, which have been successfully used to increase matrix collagen-GAG deposition in tissue engineered cartilage [4, 5, 6, 7, 8, 9]. Bioreactors reproduce the physiological environment of native tissue. Perfusion bioreactors pomp culture media directly into scaffolds through interconnected pores to improve mass transfer inside the three dimensional cellular structures. The perfusion bioreactor has become the ideal environment for cultivating tissues such as cardiac muscle [10, 11], liver [12], and cartilage [13, 14]. In addition, such bioreactors expose the cells to shear stress, which has been accepted to provide essential mechanical stimulus for the development of various tissues, such as cartilage [14], bone [15], and blood vessels [16, 17]. Computational fluid dynamics were employed to simulate the fluid flow through the interconnected pores [18]. A lattice-Boltzmann method has been used before to simulate the fluid dynamics within the bone microstructure [19]. In this work, CFD models were developed to examine the effects of media perfusion on the cell-scaffold constructs with different porosities. The cell-scaffold constructs with a more homogenous distribution of pores have been suggested to provide a more precise control over the shear stresses imposed on cells [20, 21]. The hydrodynamic stress imposed to cells will depend not only on the culture medium flow rate, but also on the three dimensional (3D) micro structures of the scaffold. The result from the computational fluid dynamics simulations are analyzed in terms of direct perfusion for tissue engineering applications.

II. MATERIAL AND METHODS

The dimensional (3D) computational fluid dynamics (CFD) simulations were applied within this study. The CFD simulation were performed with the CFD solver software; ANSYS FLUENT version 6.3. A domain of the 3D matrix structure is arrayed by 27 solid spheres connected with 27 tubes; the fluid domain is obtained by subtracting the spheres and tubes from a cube (with 1 mm edge length according to the model size). Therefore, the final pattern is designed as a honey-comb shape (Figure 1). Three groups of models corresponding to different porosities 59%, 77%, 89% were created. The porosity was defined as the ratio of the void volume to the total volume.

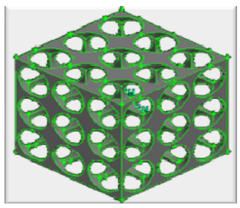

Figure 1. Model of the scaffold.

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The commercial solid modeler Gambit was used to build the 3D model and the mesh. A 4-node tetrahedral mesh was used; the meshes presented a number of elements up to 200,000 depending on the porosity, with a corresponding number of nodes up to 50,000. A velocity inflow at the bottom of the model is imposed at the inlet. The lateral fluid walls are treated as closed walls with a no slip condition and the outlet is modeled as a constant static pressure outlet. The flow of the scaffold medium was modeled as an incompressible, laminar and homogeneous Newtonian fluid with $\rho = 1000\, Kg/m^3$ and a viscosity of $\vartheta = 0.001 kgm^{-1}s^{-1}$. The inlet velocity was calculated as the ratio of the flow rate, Q, and the area of the inlet section effective to the flow (the surface area of the inlet section multiplied by the surface porosity). An average flow rate of $0.5 ml/\text{min}$ was considered. The Reynolds number was estimated using the hydraulic diameter definition:

$$\mathrm{Re} = \frac{u d_h}{\vartheta}. \tag{1}$$

where u is the velocity, ϑ is the kinematic viscosity of water $0.01 m^2/s$ and d_h is the hydraulic diameter defined by:

$$d_h = \frac{4V}{A}. \tag{2}$$

The incompressible steady-state Navier-Stokes equations were solved by Fluent:

$$\rho(\mathrm{v}.\nabla\mathrm{v}) = -\nabla p + \mu\nabla^2\mathrm{v}. \tag{3}$$

where p and v are the pressure and velocity field, respectively. Velocity and wall shear stress distribution as well as their average values and overall pressure drop were calculated for each model.

The intrinsic permeability can be calculated using an empirical relationship known as Darcy's law. It relates the volumetric flow rate and induced pressure difference in a flow channel. Darcy's law for a viscous flow can be expressed as [22]:

$$K = \frac{\mu v}{\frac{\Delta \mathrm{p}}{\mathrm{L}}}. \tag{4}$$

where K is the permeability coefficient, μ is the dynamic viscosity of the medium, L is the thickness, v is the fluid velocity and Δp is the pressure drop. The Kozeney- Carman equation is a relation used in fluid dynamics in order to calculate the pressure drop of a fluid flowing through a packed bed of solids which is only valid for laminar flow [23].

$$\frac{\Delta \mathrm{p}}{l} = \frac{150\bar{\mathrm{v}}\mu}{\Phi_s^2 D_p^2}\frac{(1-\varepsilon)^2}{\varepsilon^3}. \tag{5}$$

where Δp is the pressure-drop $\bar{\mathrm{v}}$ is the fluid velocity, μ is the dynamic viscosity, l is the thickness, ε is the porosity, Φ_s is the sphericity of the particles in the packed bed, D_p is the diameter of the related spherical particle. The permeability coefficient can be function of the porosity, based on the Darcy (4) and Kazeny – Carman (5). To this end, if the right sides of these two equations are equal, the following equation can be acquired for a spherical hollow structure $(\Phi_s = 1)$:

$$k = \frac{D_p^2}{150}\frac{(1-\varepsilon)^2}{\varepsilon^3}. \tag{6}$$

III. Result and Discussion

Before Here, the microstructure was modeled in 3D, hopefully giving more realistic predictions of the flow dynamics inside the perfused scaffold. Substantial simplifications were, however, introduced in order to reduce the computational resources needed to model the actual scaffold microstructure. Furthermore, the real inlet velocity profile being unknown, we imposed a developed laminar flow at the inlet, the inlet velocities, calculated as the ratio of the average flow rate to the area effective to the flow, were 0.0295, 0.018, and 0.013 m/s for the model porosities 59%, 77%, 89%. Figure 2 shows respective maps of cross-sectional contour of velocity for all the models. Clearly delineated 6 openings interlinking each pore to its neighboring pores. The openings included those which were positioned perpendicular to the flow direction as well as pores distributed in parallel to the flow direction. The former included two openings at the bottom and top side of the pore, where very high velocity gradients occurred (Figure 2, red areas).

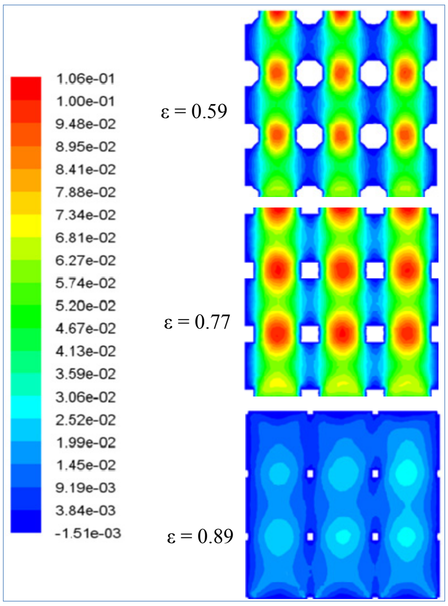

Figure 2. Contours of velocity magnitude (m/s) at a Scaffold cross-section calculated for the porous scaffold provided with an inlet flow velocity of 0.5cm/s

As it can be seen from figure 3, pressure drops are affected by the porosity: for decreasing porosity, the pressure drop increases.

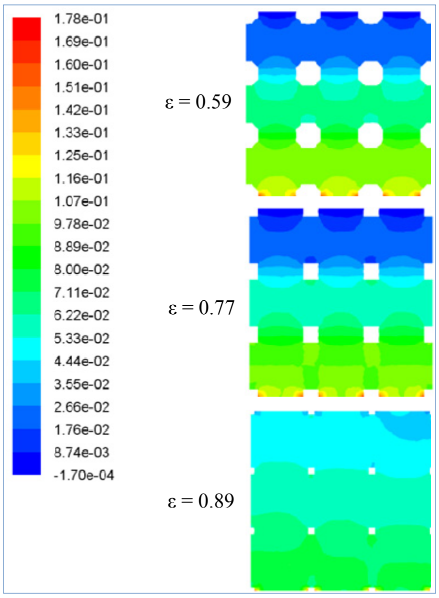

Figure 3. Contour of pressure (Pascal) at a scaffold cross-section calculated for the porous scaffold

Figure 4 outlines the calculated wall shear-stress distribution of the shear stress measured for all models. It can be seen that the porosity affects the shear stress level and distribution.

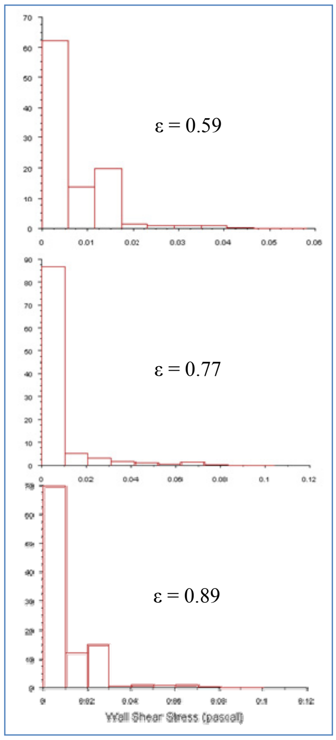

Figure 4. Wall shera stress distrubation

One of the major criticisms of the present models can be easily identified in the lack of experimental validation of the estimated shear stress distribution. Although any experimental data would add value to this modeling study, in fact, it is nearly impossible to measure the shear stress distribution inside such microstructures in an experimental set-up.

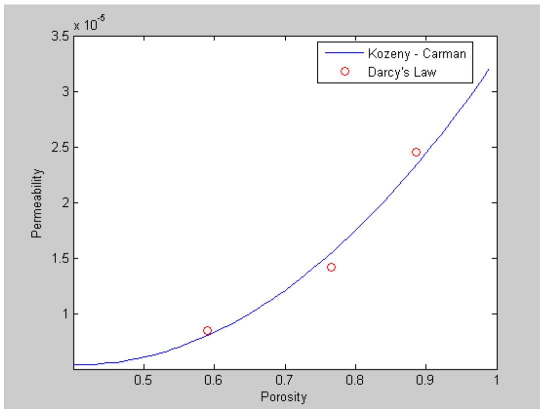

Figure 5. Porosities and permeability values for a radius R = 1.5 of the last model based on the Darcy and Kazeny – Carman equation.

In figure 5, the acquired permeability values from the obtained pressure and Darcy's law (4) are compared with the permeability values of (6), as it is obvious there is a excellent agreement for these two types of values which can validate the carried out simulation in this work.

IV. CONCOLUSION

In the present study, a considerably different fluid dynamic behavior is estimated by using of microscopic cellular structures. The usage of a simplified geometry with a regular and homogeneous distribution of pores allowed us to study the effect of the porosity as a typical geometrical parameter on the magnitude of velocity, drop pressure and shear stress distribution; to this end the effect of 3D cellular scaffold with different porosities on fluid flow was simulated and investigated by considering the laminar flow of the scaffold medium through the structures then the combination of Darcy as well as Kozeney- Carman equations were applied in order to validate the simulation which caused excellent agreement among the required and mentioned equations' results. The presented results can be extrapolated to more complex architectures, although this assertion requires further work on more complex and realistic geometries to be studied.

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