Influence of Fluid Flow on Porous Scaffold Structural Deformation

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Statement of purpose: Tissue engineering provides means to replace, restore tissue functions by growing cells on three-dimensional (3D) matrices. Porous structures are molded into the desired shape of the tissue and are used to support cells to colonize, organize and produce their own extracellular matrix elements. Regenerating the tissue outside the body is necessary when tissue functionality is critical to the survival of a patient. Bioreactors are utilized in tissue regeneration to ensure complete nutrient distribution and apply defined hydrodynamic stresses. Moreover, tissue regeneration is a dynamic process where the porous characteristics of the scaffolds change due to proliferation of cells, de novo deposition of matrix components, degradation of the porous architecture, and flow of nutrients through the reactor. These changes affect the transport characteristics and there is an imminent need to understand the influence of these factors. Previously, our group has evaluated the influence of various factors including reactor shape, inlet location and inlet shape on nutrient distribution, changes in pore size and void fraction in reactors suitable for regenerating large tissues [1, 2]. However, the effect of fluid flow on the dimensionality is not understood. Fluid flow could compress the scaffold which could alter the pore architecture and the nutrient distribution.

Methods: This study focused on the influence of fluid flow on the integrity of scaffolds and changes in structural dimension. For this purpose, evaluating changes in dimensionality under applied stress and the amount of stress experienced by the scaffold is necessary. Poison's ratio was selected as criteria for analysis. Scaffolds made from different compositions viz. 1% chitoson- 1% gelatin frozen at -20°C , 1% chitoson- 1% gelatin frozen at -80°C, and 2% chitoson- 2% gelatin frozen at -20°C were selected for investigating poison's ratio. Experiments were performed under hydrated conditions using Phosphate buffered saline solution at a temperature of 37 degree centigrade. An experimental setup was designed to determine poison's ratio. The samples were stretched along the length, length was measured using a scale attached to the setup, and a digital vernier caliper was used for measuring width. The recorded reading was used for calculating the poisson's ratio of various samples.

Results: The results from the experiments were used in simulating the bioreactor at various flow rates and scaffold compositions. COMSOL multiphysics software was used to simulate the conditions experienced by the scaffold in the bioreactor. Brinkman equation (for estimating pressure drop across a porous structure), moving mesh module and solid stress-strain modules (for estimating displacement and stress experienced by the scaffold) in COMSOL were used for CFD analysis. Simulations performed at different flow rates viz. 0.1 ml/min; 0.5 ml/min; 1ml/min and 1.5ml/min indicated an increase in stress on the scaffold structure with increase in flow rate. Total displacement of the scaffold also followed the same pattern. Table 1 shows the Viscous or fluid shear stress, Maximum stress and total displacement experienced by the scaffold at different flow rates.

Flow rate (ml/min)	viscous or fluid Shear stress (Pa)	Max. Stress Experienced by scaffold (Pa)	Total displacement of scaffold (µm)
0.1	0.00286	0.0013	0.00014
0.5	0.0139	0.0048	0.0045
1	0.0269	0.0763	0.0059
1.5	0.039	3.016	0.367

Table 1. Fluid shear stress, Max. stress and displacement at different flowrates

Maximum stress on scaffold due to flow was compared with the fluid shear stress to evaluate whether stress on scaffold can be neglected. It was found that stress experienced by the scaffold is greater than the fluid shear stress for higher flow rates. Also the total displacement of the scaffold increases significantly with higher stress. Simulation were also performed for much higher flow rates, COMSOL failed to converge due to the fact that scaffold becomes unstable and loses its integrity at such high flow rates. The pattern of scaffold deformation was also examined; the maximum deformation of the scaffold was noticed in the beginning and at the end of the scaffold, as shown in figure 1 below.

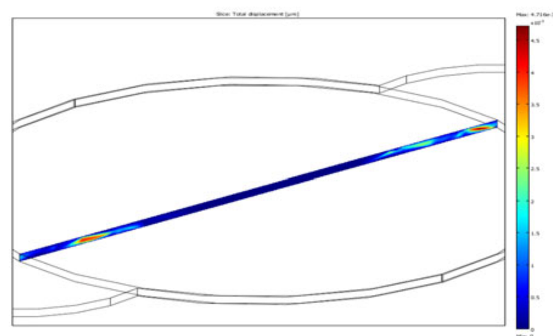

Figure 1. total displacement (µm, 1ml/min)

Conclusion: Accounting for the variation in scaffold structure during reactor operation will help understand its suitability at given conditions, and hence improve tissue quality.

References: [1] Lawrence BJ, Devarapalli M, Madihally SV. Flow Dynamics in Bioreactors Containing Tissue Engineering Scaffolds. Biotechnology/Bioengineering. 102(3): 935-947, 2009. [2] Devarapalli M, Lawrence BJ, Madihally SV. Modeling Nutrient Consumptions in Large Flow-Through Bioreactors for Tissue Engineering. Biotechnology/ Bioengineering. 103(5):1003-1015, 2009.

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