Influence of Fluid Flow on Porous Scaffold Structural Deformation

Jagdeep Podichetty, Dhananjay Dhane, Sundararajan V. Madihally
Oklahoma State University, Stillwater, Ok

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 dimensional changes in the scaffold is not understood. Fluid flow could compress the scaffold which could alter the pore architecture and the nutrient distribution. This study focused on the influence of fluid flow on the integrity of scaffolds and changes in structural dimension.

Methods: First scaffolds were formed using controlled rate freezing and lyophilization using different compositions of chitosan and gelatin: 1%- 1%, 2% and 2%. Since, pore size is affected by freezing temperature, scaffolds were formed at -20°C and -80°C. An experimental setup was developed to determine poison's ratio under hydrated conditions using Phosphate buffered saline solution at a temperature of 37°C. Experiments were performed using 1cm ×7 cm scaffolds. The samples were stretched along the length, length was measured using a scale attached to 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. Further, scaffold pore size and pore numbers were determined using scanning electron micrographs. These values were used in computational simulation. The results from the experiments were used in simulating the 10-cm diameter bioreactor containing porous structures in the path of the fluid flow (**Figure 1A**), optimized for uniform nutrient distribution for various cell types. COMSOL multiphysics software was used to simulate the conditions 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. Reactors were generated to validate the simulation results.

Results. Calculated Poisson ratio values ranged from 0.8 to 1.2 for chitosan-gelatin scaffolds, similar to cartilage samples. No significant effect of pore size was observed at the measured conditions. Simulations were performed by varying the fluid flow rates from 0.1 mL/min up to 1.5 mL/min indicated an increase in compressive stress on the scaffold structure with increase in flow rate (**Table 1**). It was found that maximum stress experienced by the scaffold is greater than the fluid shear stress for higher flow rates. Also the total displacement of the scaffold increased significantly with higher stresses. 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. Total displacement of the scaffold also followed the same pattern.

Table 1. Effect of flow rate on shear stress, Max stress and displacement

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

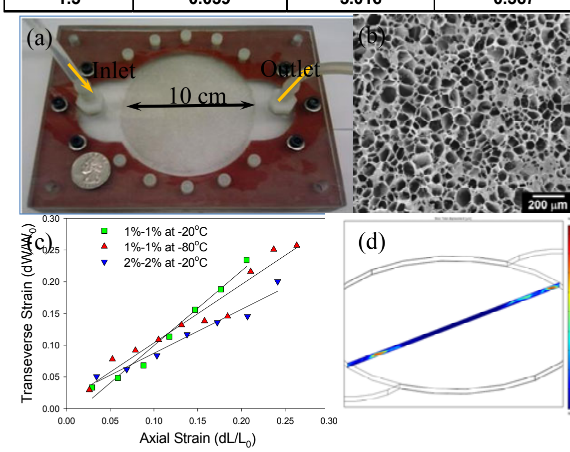

Figure 1. (a) bioreactor configuration. (b) Scanning electron micrograph. (c) Poisson ratio calculations. (d) displacement profile.

Conclusion: Poisson ratio of porous structures were measured and found to be higher than typically range of materials. Structural displacement increases with flow rate. Mechanical stresses are significantly higher than fluid shear stresses at the same flow rate (rigid scaffold).

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.