Mean Pore Size and Compressive Strain Effects on the Permeability of Collagen-GAG Scaffolds: Cellular Solids Modeling and Experimental Results

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Statement of Purpose: The permeability of tissue engineering scaffolds controls diffusion-based metabolite and waste transport to and from the scaffold and influences the final solution pressure distribution in the scaffold. Both of these parameters can significantly influence cell behavior and overall scaffold bioactivity. While permeability has been characterized for a variety of biological materials (e.g. cartilage, bone, interstitial tissue) and tissue engineering scaffolds (e.g. ceramics, synthetic polymers), it has not been characterized for a natural polymer scaffold such as the collagen-glycosaminoglycan (CG) scaffold. Appropriate modeling tools that quantitatively describe scaffold permeability in terms of salient microstructural features would be advantageous. Scaffold pore size and compressive strain can vary significantly across different applications, making them important features to study in the context of scaffold permeability. The objective of this study was to characterize the permeability of CG scaffolds as a function of pore size and compressive strain using both experimental and cellular solids modeling techniques.

Methods: *Scaffold:* CG scaffolds were fabricated via lyophilization from a slurry of type I collagen and chondroitin-sulfate in acetic acid. The CG suspension was frozen and the ice content sublimated using a technique developed to produce a homogeneous pore structure with equiaxed pores [1]. The final freezing temperature was varied to produce a series of scaffolds with constant composition and relative density (0.6%), but with four distinct pore sizes (150.5, 121, 109.5, 95.9 μm) [1,2].

Experimental Testing: A device was constructed to measure the permeability of the scaffolds at different compression levels. Permeability (K) was calculated as $K = Q \cdot l / \Delta P \cdot A$. Scaffold samples were hydrated in saline solution for 24 hours prior to testing. The scaffold was then places into the testing apparatus between parallel stainless steel mesh membranes. The mesh supported the scaffold over a brass tube, through which saline solution was actively pumped. Stainless steel spacers of varying thickness (2–5 mm) between the mesh membranes regulated the degree of compression. Scaffold permeability was measured at 0, 14, 29, and 40% compression.

Cellular Solids Modeling: An open-cell foam, cellular solids model utilizing a tetrakaidecahedral unit cell can accurately model physical properties of CG scaffolds [2]. A quantitative model of scaffold permeability (K) in terms of scaffold mean pore size (d), individual strut length (l), percent compression (ε), a system constant (A), and scaffold relative density (ρ^*/ρ_s) was developed:

$$K = A \cdot d^2 \cdot \left(1 - \frac{\rho^*}{\rho_s}\right)^{3/2} \qquad [3]$$

$$d \propto l \cdot (1-\varepsilon) \qquad d = 2.785 \cdot l \qquad [3,4]$$

$$K \propto \left(\frac{d^2}{2.785}\right) \cdot (1-\varepsilon)^2 \cdot \left(1 - \frac{\rho^*}{\rho_s}\right)^{3/2}$$

Results / Discussion:

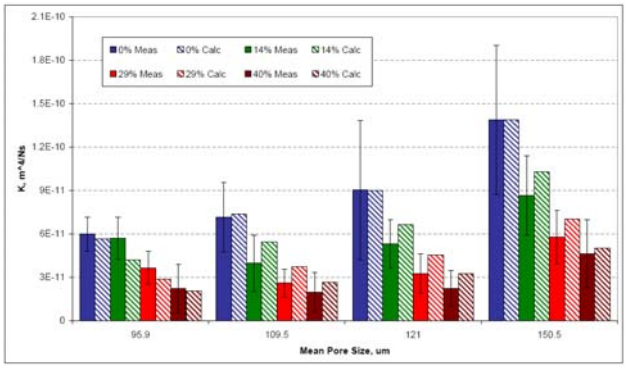

Fig. 1. Experimentally measured vs. cellular solids model predicted permeability as a function of mean pore size and compressive strain.

Fig. 1 shows the results of experimental measurement and cellular solids model prediction of CG scaffold permeability (experimental results: mean ± SD) as a function of pore size and compressive strain. One-way ANOVA tests revealed that scaffold permeability significantly increased with increasing pore size and decreased with increasing compressive strain. Fig. 1 also shows the comparison between experimentally measured results (K_{meas} – solid bar) and cellular solids model predicted values (K_{calc} – striped bar). The cellular solids model gives a good description of the experimentally measured permeability of all four scaffold variants for each level of compressive strain.

Conclusions: Experimental results and the cellular solids model of scaffold permeability indicate that scaffold permeability increases with increasing pore size and decreases with increasing compressive strain. Previously we have shown an inverse relationship between pore size and specific surface area (SA/V) [2]. SA/V is likely a primary factor causing differences in permeability: scaffolds with greater SA/V exhibit increased resistance to fluid flow and therefore reduced permeability. The excellent comparison between experimentally measured and cellular solids model predicted scaffold permeability suggests that cellular solids modeling techniques can be used as a predictive model of scaffold permeability for many different scaffold architectures under a variety of physiological loading conditions.

References: [1] O'Brien FJ, Harley BA, Yannas IV, Gibson LJ. Biomaterials 2004; 25:1077-1086. [2] O'Brien FJ, Harley BA, Yannas IV, Gibson LJ. Biomaterials 2005; 26: 433-441. [3] Gibson LJ, Ashby, MJ. 1992. [4] Gent AN, Rusch KC. J. Cell. Plast. 1966; 2:46-51.