Measuring fluid transport through scaffolds for engineered tissue

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Micro x-ray imaging tracks nutrients pumped though porous synthetic tissue scaffolds by rhythmic squeezing.

Synthetic scaffolds can provide structure for large pieces of artificial tissue, but nutrients must penetrate the deepest layers in order for cells to colonize the implant. Diffusion alone is insufficient for prostheses more than 300µm thick. I am exploring whether repetitive distortion will move nutrients and waste products through porous scaffolds. Ingrowth of surrounding native tissues needed to anchor implanted prostheses will depend on this transport. Ideally, blood vessels will do the job, but their initial invasion into the scaffold also depends on effective flow of fluids.

Because the scaffolds are made of opaque polymers, tracking the movement of nutrients through them is difficult. Previous work has measured the concentration of solutes outside such scaffolds to estimate how well nutritional solutes might penetrate the structure. However, such methods provide no quantitative information about the distribution of solutes inside the scaffold, which ultimately determines where cells will or will not survive. To overcome these limitations, I developed an x-ray imaging technique to measure the movement of solutes though pores in the polymer while the scaffold is repeatedly wrung or squeezed.

Deformable scaffolds with specific mechanical properties were made by blending flexible, biodegradable polymers. Labyrinths of pores with specific shapes and interconnectivity were formed into cube-shaped samples using injection molding and 3D printing. These prototypes were then cyclically distorted to varying degrees and in several ways: compressed or twisted, for instance. Micro x-ray imaging followed the movement of a contrast dye through the scaffolds as they were manipulated.

Figure 1. A tissue scaffold loaded with contrast agent rests in a fluid reservoir beneath a compression device. A molybdenum x-ray source creates 2D projection images of the scaffold after cycles of distortion.

X-rays produce images with micrometer resolutions without destroying the sample scaffold. Because the physics of x-rays is well understood, precise quantitative information about the local concentration of a radiation-absorbing contrast agent can be obtained. As illustrated in Figure 1, the scaffolds were loaded with the contrast agent and placed in a fluid reservoir mounted underneath a compression device. The entire apparatus fit within a micro x-ray scanner used to create images of the scaffold after each cycle of distortion.

Mechanical manipulation sped the contrast dye—a surrogate for nutrients—through the scaffolds. After 300 cycles (5min) of compression, the average concentration of the contrast agent in the pores decreased by 80%. In comparison, only 40% of the dye was removed after 60min of diffusion. Figure 2 shows a typical scaffold imaged after loading the indicator and after 5min of passive diffusion or cyclic compression at 1Hz. Repetitive deformation also allows solutes to penetrate farther into the scaffold.

In the future, I will use this novel technology to find the optimal deformation parameters (e.g., amplitude and frequency) Continued on next page
and pore geometry for transporting solutes uniformly into deep layers of the scaffold. Achieving this is essential to engineering functional artificial tissues.

This work was completed in Erik L. Ritman’s laboratory and will be presented at SPIE Medical Imaging, 16–21 February 2008 in San Diego, CA.

Figure 2. X-ray projection images of a 560µm-diameter pore within a 3.1mm³ scaffold before and after 5min of passive diffusion or removal by squeezing.

References