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Influence of hydration on fiber geometry in electrospun scaffolds

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ABSTRACT

Finite element models of tissue engineering scaffolds are powerful tools to understand scaffold function, including how external mechanical signals deform the scaffold at the meso- and microscales. Fiber geometry is needed to inform finite element models of fiber-based tissue engineering scaffolds; however, the accuracy and utility of these models may be limited if they are informed by non-hydrated geometries. Scanning electron microscopy and confocal microscopy, coupled with Fourier analysis of the resulting images, were used to quantify how hydration alters fiber geometry in electrospun collagen and polycaprolactone (PCL) scaffolds. The results also quantify how image size affects fiber geometry. Hydration is demonstrated to increase fiber tortuosity, defined as the ratio of actual fiber length:end-to-end fiber length. For collagen scaffolds, hydration increased the mean tortuosity from 1.05 to 1.21, primarily from large ~2- to 10-fold) increases in smaller (<40 μm) wavelength amplitudes. For PCL fibers, the mean tortuosity increased from 1.01 to only 1.04, primarily from modest ~2-fold) increases in larger (>100 μm) wavelength amplitudes. The results demonstrate that mechanical simulations of electrospun scaffolds should be informed with hydrated scaffold geometries of at least 200 μm scale, in order to capture geometrical effects associated with fiber straightening.

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1. Introduction

The development of functional engineered tissues is a critical step in reducing the number of patients (around 18) who die in the U.S. every day while waiting for an organ transplant [1]. Unfortunately, the current generation of engineered tissues often fails to match the biological function and mechanical properties of native tissue. For example, engineered skin, although successful at closing large full-thickness burn wounds, does not recapitulate the full anatomy or strength of the native dermis [2] and remains several orders of magnitude weaker than normal full-thickness human skin [3,4]. As the body is a chemically and mechanically dynamic environment, it has been proposed that the static environment in which many tissues are cultured may not be sufficient to deliver the appropriate signals for more natural tissue development. This has motivated studies to better mimic in vivo conditions, with a particular focus on applying mechanical forces to the tissue during development [5–9].

In extracellular-matrix-rich engineered tissues, such as engineered dermis and tendon, mechanical signals are transferred from the external environment to cells via scaffold–cell interactions. To gain the most benefit from mechanical stimulations, it is critical to first understand and predict how a scaffold deforms under an applied load/extension and subsequently to understand how scaffold deformation controls cell deformation. For example, the type of scaffold material has been shown to play a large role in the cellular response of the same engineered tissue system. When mesenchymal stem cells were cultured in a collagen gel vs. collagen sponge and exposed to the same 2.4% strain profile for 12 days, only those within the collagen sponge produced a stronger, more organized engineered tendon [10]. Due to the virtually unlimited number of scaffold chemistry/architecture and mechanical stimulation profile combinations, the development of an in silico model of scaffold deformation would help to establish the role of initial scaffold geometry and material mechanics on the macro- and microscale scaffold response to external mechanical stimuli.

Finite element models of fiber-based tissue engineering scaffolds require fiber geometry and local fiber mechanical properties as input parameters. Several different geometric features and characterization methods have been used to furnish this information. Fiber diameter, angle, density and tortuosity are commonly quantified manually and with the aid of computer software [11–13]. Fiber orientation and anisotropy have been quantified using fully automated procedures such as mean intercept length, line fraction deviation, and the fast Fourier transform method [14–20]. This

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