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Femtosecond laser ablation enhances cell infiltration into three-dimensional electrospun scaffolds

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ABSTRACT

Electrospun scaffolds are used extensively in tissue-engineering applications as they offer a cell-friendly microenvironment. However, one major limitation is the dense fibers, small pore size and consequently poor cell infiltration. Here, we employ a femtosecond (FS) laser system to ablate and create microscale features on electrospun poly(L-lactide) (PLLA) nanofibrous scaffolds. Upon determining the ablation parameters, we pattern structured holes with diameters of 50, 100 and 200 μm and spacings of 50 and 200 μm between adjacent holes on the scaffolds. The elastic moduli of ablated scaffolds decrease with the decrease in spacing and the increase in hole size. Cells seeded on the laser-ablated scaffolds exhibit different morphology but similar proliferation rate when compared with control (non-ablated) scaffold. Furthermore, animal studies indicate that ablated scaffolds facilitate endothelial cell ingrowth as well as drastically increase M2 macrophage and overall cell infiltration. These findings demonstrate that FS laser ablation can be used to increase cell infiltration into nanofibrous scaffolds. Laser ablation not only can create desired features in micrometer length scale but also presents a new approach in the fabrication of three-dimensional porous constructs for tissue engineering.

1. Introduction

Biocompatible three-dimensional scaffolds play a pivotal role in tissue engineering. These scaffolds are fabricated with controlled mechanical and biological properties so that they are able to support new tissue formation while providing physical and chemical cues that promote various cellular processes, including proliferation, migration and differentiation [1]. Specifically, the architecture of tissue-engineered scaffolds is designed to mimic closely the organized structure and biological function of native extracellular matrix (ECM). Thus, a favorable ECM-like microenvironment for cells is crucial to achieve the desirable scaffold integration as well as cell–material interactions and tissue ingrowth.

Electrospinning is a popular technique used to fabricate tissue-engineered scaffolds [2–5]. It is a consistent, versatile method that produces nonwoven, three-dimensional fiber structures with controllable fiber diameters [6–8]. Electrospun scaffolds have great potential in that their structures, especially in nanoscale networks, not only closely resemble natural ECM but also exhibit high surface-area-to-volume ratios favorable for attachment of cells and bioactive molecules to fiber surfaces [9]. However, one main issue that limits their utilization is their small pore size. The small pore size of electrospun scaffolds results from the dense network of fibers, which hinders cell infiltration and ultimately reduces their use in replacing large tissues that require ample vascularization and nutrient diffusion. Various techniques to overcome this shortcoming have been investigated, including the incorporation of sacrificial fibers and porogens [10,11], modification of fiber diameter [12], and post-processing by photopatterning [13] or ultraviolet radiation treatment [14] to increase pore size and overall porosity.

Although laser machining is an attractive approach for many biomedical applications, a major concern with using this method to process biomaterial scaffolds is the potential for thermal effects, such as those induced by nanosecond lasers. However, ultrafast lasers are considered promising tools to rapidly process and create complex structures on electrospun scaffolds. For example, although a few studies have investigated the use of femtosecond (FS) lasers to

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