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Effect of Packing Density and Diameter of Fibers in 3-D Electrospun Scaffolds on Spreading, Proliferation, and Migration of Human Umbilical Vein Endothelial Cells

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Abstract – Electrospun scaffolds offer an attractive ECM-mimicking approach for 3D tissue engineering. For better performance of these scaffolds, porosity should be high enough to allow cell infiltration and mass transfer inside the scaffolds. We report a method of modulating porosity in 3D scaffolds by simultaneously tuning fiber diameter and the fiber packing density. PCL fibers were electrospun in the form of random nonwoven mats and characterized for physico-chemical and biological properties. It was demonstrated that microfibers with low packing density resulted in better cell viability, proliferation and infiltration in 3D scaffolds.

Electrospinning is recognized as an efficient technique for manufacturing polymeric fibers that are of interest for applications in tissue engineering, due to the tuneability of the fiber material and morphology. The efficacy of this approach is likely to depend on the interaction between cells and the physico-chemical composition of the scaffold. In this respect, a high porosity is required in the electrospun scaffolds to allow the cellular infiltration and ensure the delivery of nutrients and oxygen to the seeded cells. A major problem in electrospinning consists of the fiber tendency to accumulate densely, which results in poor porosity hindering cells to infiltrate inside the scaffolds and, thus, limiting their potential for 3D tissue engineering applications. The porosity and pore size in the electrospun scaffolds are mainly dependant on the fiber diameter and their packing density. Thus, the objective of this study was to optimize diameter and packing density of fibers together to tune the pore size and porosity for improved cell spreading, proliferation, and infiltration into the scaffolds.

Electrospun poly(ε-caprolactone) (PCL) scaffolds with different fiber diameter and packing density were obtained by optimizing both solution properties and processing parameters. Results are presented for four electrospun scaffolds made of (a) microfibers with low fiber density (M-LD), (b) microfibers with high fiber density (M-HD) (c) nanofibers with low fiber density (N-LD), and (d) nanofibers with high fiber density (N-HD). Fibrous scaffolds were characterized for diameter and morphology by scanning electron microscopy (SEM). Tensile tests were performed to investigate their mechanical properties. The scaffold porosity was measured using liquid intrusion method while the pore size distributions were estimated via approximate statistical models.

It was found that fiber diameter and packing density played an important role in regulating cell proliferation into nonwoven fibrous scaffolds as evident by Alamar Blue assay (Fig.1). Microfibers showed a higher adhesion and proliferation rates as compared with the nanofibers. Also, low density (LD) fibrous scaffolds showed significantly higher rate of proliferation than those with high fiber density (HD). The distribution of cells inside the scaffolds was studied by confocal laser scanning microscopy. Both M-LD and N-LD clearly showed densely packed cells inside the scaffolds while M-HD and N-HD showed cells only in the top layer of the scaffolds. Also, M-LD exhibited maximum cell adhesion and proliferation compared with the other scaffolds under consideration ($p < 0.05$). These results clearly underline the synergistic effect of large fiber diameter and low fiber density in the electrospun nonwoven mats.

Table 1: Characterization of fibrous scaffolds

Scaffold type	Fiber diameter (ω) , mean ± RMS (μm)	Porosity (ε %)	Pore size $\langle 2r \rangle$ (μm)	Average Young's Modulus ± RMS (MPa)
M-HD	2.72 ± 0.65	73	8.7	7.13±1.75
M-LD	2.68 ± 0.55	89	64.3	4.3±0.32
N-HD	0.31 ± 0.37	77	0.15	1.4±0.3
N-LD	0.33 ± 0.35	83	0.75	0.8±0.2

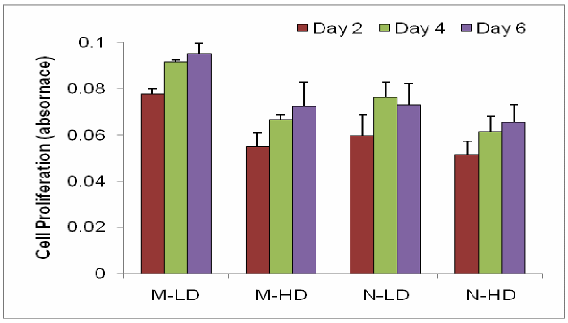

Figure1. Cell Proliferation on different scaffolds