Cell Migration Within Porous Electrospun Nanofibrous Scaffolds in a Mouse Subcuticular Implantation Mode

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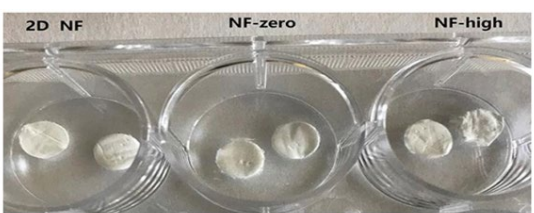
Purpose: Bone has a complex structure and composition. An ideal bone substitute must recreate the bone extracellular matrix (ECM) environment and facilitate osteointegration of bone and implant materials as well as repair of bone or soft-tissue defects. One promising scaffold fabrication technique to mimic bone ECM structure is electrospinning. Historically, cellular infiltration into electrospun nanofibers (NFs) was limited due to their dense structure and small pore sizes. To address these issues, we developed a programmed NF collector that can fabricate porous NFs with desired pore sizes and thickness. Previously, we demonstrated improved cellular proliferation and differentiation of osteoblasts, osteoclasts and fibroblasts with polycaprolactone (PCL) NFs with increased pore sizes in vitro. This study investigated in vivo host cell migration and vascular ingrowth within porous NF sheets implanted subcutaneously in a mouse model. We hypothesized that increased cellular migration would occur within the NF sheets with larger pore sizes.

Methods: Two types of PCL NFs with well-defined pore sizes were created using varying speeds of the NF collector: NF-zero (no movement, pore size 14.4 ± 8.9 μm^2) and NF-high (0.232 μm/min, pore size 286.7 ± 381.9 μm^2). NFs obtained from a classical flat NF collector (2D NF, pore size 1.09 ± 1.7 μm^2) was included as a control. The 3 formulae of NFs were implanted subcutaneously in 18 BALB/cJ mice. Sacrifice occurred at 7 and 28 days (n = 3 per group per time point). The subcutaneous tissue with the implanted NFs were collected for histologic analysis.

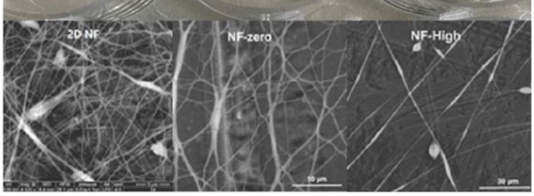
Results: The 7-day samples showed little inflammatory response. At 28 days, the efficiency of tissue penetration of PCL NF sheet matrices was directly linked to pore size and area. NFs with the largest pore area had more efficient tissue migration and new blood vessel formation compared to those with smaller pore sizes. No newly formed blood vessels were observed in the control 2D NF group.

Conclusion: An NF scaffold with controllable pore size has potential for tissue repair/regeneration in situ. This creates the potential for many applications in orthopaedics including repair of bone and/or soft-tissue defects in a posttraumatic setting.

(A)



(B)



(C)

Group	NF-2D	NF-Zero	NF High
Pore Size (μm²)	1.09 ± 1.07	14.43 ± 8.93	286.74 ± 381.97