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Injectable Microfibers for Minimally Invasive in Situ Vascularization

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ABSTRACT (NO MORE THAN 500 WORDS:)

Despite the significant advancements in fabricating various scaffolding systems over the past decade, generation of functional vascularized tissues remains challenging for the currently available biofabrication approaches. On the other hand, the applicability of traditional surgical transplantation of vascularized tissue constructs is limited due to the sophisticated surgical procedures, which are invasive, leading to increased risks of scar formation and infection. Here, we demonstrate a convenient strategy capable of directly fabricating highly controllable and injectable vascularized microarchitectures using a microfluidic technology. The specially designed double T-junction microfluidic chip with an expansion chamber was used for the generation of microvessels composed of SA and Gel. Initially, a 2⁴ full-factorial design was employed to optimize different formulation parameters. Then, human umbilical vein endothelial cells (HUVECs)-laden microvessels were generated by dispersing them in the SA/Gel solution and subsequently crosslinked with calcium chloride (CaCl₂) to homogeneously encapsulate the cells inside the microrods. Then, the samples were soaked in genipin for different times to control the crosslinking densities in the periphery and center portions of the microrods, which would regulate cell growth as well as their migration towards the periphery of the microrods. Finally, in vivo performance of the fabricated microvessels was explored by injecting the HUVECs-laden microrods in the severe combined immunodeficiency (SCID) mice. The vessel-like microarchitectures could be derived through controlled penetration of the crosslinker genipin for the gelatin phase, ensuing differential degrees in crosslinking of peripheral and central portions of the microstructures, leading to the formation of vascular lumen-like hollow cavities via endothelial cell migration and proliferation during culture in vitro. Furthermore, in vivo performance confirmed successful neovascularization in a rodent model. We believe that the development of these modular microvessels for minimally invasive delivery is of great interest and thus offer a convenient approach for vascularization in situ.