Enhanced human bone marrow mesenchymal stem cell function on 3D printed nanobone scaffolds with microvascular network

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ABSTRACT

Critical sized bone defects resulting from traumatic injury, cancer, degenerative diseases, or birth defects present a crucial clinical problem. The area of such defects is typically large and is often debilitating to those afflicted. As a multifunctional tissue comprised of both a porous nanobone extracellular matrix and an interconnected microstructure of blood vessels, it is hard to repair due to the need for an adequate vascular network. Although various biomaterials and 3D fabrication approaches to address critical sized bone defects have been investigated, it is still very challenging to replicate the complex integration of vasculature within a bone structure. In addition, it is difficult to create large engineered bone constructs that replicate macroscopic patient specific injuries, although also adequately incorporating biomimetic nano and micro architecture. In this study, we will integrate 3D bioprinting and nanomaterials to create a novel vascularized bone scaffold. A series of microstructured scaffolds containing both a bone matrix and a microvascular network were designed and 3D printed. The size of the bone microstructure was kept constant (i.e., 350 μm hexagonally shaped pores alternating with dense linear patterns, layer by layer, to adequately restrict fluid perfusion through the bone network itself). The sizes of the microvascular network were 500 μm (large vascular) and 350 μm (small vascular). Printed scaffolds were then conjugated with nanocrystalline hydroxyapatite (nHA, bone minerals), using an acetylation chemical functionalization process. Young's modulus compiled from mechanical compression data showed the scaffold with a smaller microvascular network has higher mechanical stiffness and more bone-like properties. Human bone marrow derived mesenchymal stem cell (hMSC) 4 h adhesion and 1, 3, and 5 day proliferation were investigated in vitro. The 4-h cell adhesion result demonstrated that 3D printed scaffolds with a smaller microvascular network and nHA had the greatest cell adhesion. In addition, 5-day hMSC proliferation result also showed an excellent cell growth on all scaffolds, with the greatest increase on small microvascular nHA scaffolds, at 1 and 5 days. Further study will focus on co-culturing hMSCs and endothelial cells in the bone scaffold for improved osteogenesis and bone formation.