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Elimination of Induced Hypoxic Regions in Depth of 3D Porous Silk Scaffolds by the Introduction of Channel Configuration

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Abstract:

Development of large, clinically sized tissue constructs with efficient mass transport is a tremendous need in tissue engineering. One major challenge in large tissue-engineered constructs is to support homogeneous delivery of oxygen and nutrients throughout the tissue scaffold while eliminating induced hypoxic regions in depth. To address this goal, we introduced an especial channeled architecture on porous silk-based tissue scaffolds to improve supplying of oxygen to the cells in central regions of the scaffolds. Oxygen gradients were measured and evaluated in three scaffold prototypes, namely, one unchanneled and two channeled scaffolds with different channel diameters (500 μm and 1000 μm). The channels were introduced into the constructs using stainless-steel rods arranged uniformly in stainless-steel mold, a fabrication method that enables precise control over channel diameter and the distance between channels. During 2-week culture of G292 cells, the 1000 μm channeled scaffolds demonstrated higher oxygen concentration at the center compared to 500 μm channeled prototype; however, the oxygen concentration approached the same level around the last days of culture. Nevertheless, homogenous oxygen distribution throughout the 1000 μm channeled constructs and the consequence of higher cell proliferation at day 14 postseeding corroborate the efficient elimination of induced hypoxic regions; and therefore, it holds promise for clinically relevant sized scaffold especially in bone tissue engineering.

Keywords: tissue engineering, homogeneous oxygen delivery, silk-based tissue scaffold, channel constructs, hypoxic regions, cell proliferation