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Uniform tissues engineered by seeding and culturing cells in 3D scaffolds under perfusion at defined oxygen tensions

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Abstract:

In this work, we assessed whether culture of uniformly seeded chondrocytes under direct perfusion, which supplies the cells with normoxic oxygen levels, can maintain a uniform distribution of viable cells throughout porous scaffolds several milimeters in thickness, and support the development of uniform tissue grafts. An integrated bioreactor system was first developed to streamline the steps of perfusion cell seeding of porous scaffolds and perfusion culture of the cell-seeded scaffolds. Oxygen tensions in perfused constructs were monitored by in-line oxygen sensors incorporated at the construct inlet and outlet. Adult human articular chondrocytes were perfusion-seeded into 4.5 mm thick foam scaffolds at a rate of 1 mm/s. Cell-seeded foams were then either cultured statically in dishes or further cultured under perfusion at a rate of 100 μm/s for 2 weeks. Following perfusion seeding, viable cells were uniformly distributed throughout the foams. Constructs subsequently cultured statically were highly heterogeneous, with cells and matrix concentrated at the construct periphery. In contrast, constructs cultured under perfusion were highly homogeneous, with uniform distributions of cells and matrix. Oxygen tensions of the perfused medium were maintained near normoxic levels (inlet ≈ 20%, outlet > 15%) at all times of culture. We have demonstrated that perfusion culture of cells seeded uniformly within porous scaffolds, at a flow rate maintaining a homogeneous oxygen supply, supports the development of uniform engineering tissue grafts of clinically relevant thicknesses.

Key-words: Bioreactor, fluid flow, chondrocyte, mass transport, functional tissue engineering