5) Oxygen mass transfer in a human tissue-engineered trachea

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Abstract

On June 2008, the first human tissue-engineered trachea replacement was performed using decellularized (de-antigenised) cadaveric donor trachea, seeded with recipient epithelial cells on the internal surface of the graft and mesenchymal stem-cell-derived chondrocytes on the external. During the follow-up, cytological analysis at 4 postoperative days showed a migration of the stem-cells derived chondrocytes from the outer to the inner surface of the first 2 cm of the graft length. With the aim to rationalize these clinical findings, and under the hypothesis that cellular migration is driven by the oxygen gradients developing from the external part of the construct (exposed to O_2 deficiency) towards the better oxygenated epithelial region, an accurate computational model of oxygen transport in the trachea engineered construct was developed and solved using finite element method (FEM). Results confirm that critical limitation to oxygen transport prevalently occurs from proximal to middle section, within the first 2.8 cm of longitudinal length, in good agreement with experimental observation. In the proximal section, recognized as the most critical part of the engineered construct, the severe O_2 mass transfer limitation causes a drastic reduction of the diffusive flux within a distance of 650 μm. At cell density of 1×10^7 cells/cm^3, the 30% c.a of the total section area is under oxygen deficiency (O_2 partial pressure below the critical threshold of 38 mmHg). Along the whole tracheal construct, the Thiele modulus ranges within 2.3 and 3.7 in the external chondrocyte compartment, confirming thus the importance of the mass transfer limitation to oxygen diffusion rate. In general, the efficiency of the O_2 transport reduces considerably in the region close to proximal section.