

Scientific Paper:

Journal of Biomechanics 41, 2918 – 2925, 2008

Computational evaluation of oxygen and shear stress distributions in 3D perfusion culture systems: Macro-scale and micro-structured models

M. Cioffi^{a,b,c,*}, J. Küffer^d, S. Ströbel^b, G. Dubini^a, I. Martin^b, D. Wendt^b

^aLaboratory of Biological Structure Mechanics, Department of Structural Engineering, Politecnico di Milano, Italy

^bDepartment of Surgery and Research, University Hospital Basel, Switzerland

^cIRCCS Istituto Ortopedico Galeazzi, Milano, Italy

^dInstitute for Product and Production-Engineering, University of Applied Sciences Northwestern Switzerland, Switzerland

Abstract:

We present a combined macro-scale/micro-scale computational approach to quantify oxygen transport and flow-mediated shear stress to human chondrocytes cultured in three-dimensional scaffolds in a perfusion bioreactor system. A macro-scale model was developed to assess the influence of the bioreactor design and to identify the proper boundary conditions for the micro-scale model. The micro-scale model based on a micro-computed tomography (μ CT) reconstruction of a poly (ethylene glycol terephthalate)/poly (butylenes terephthalate) [PEGT/PBT] foam scaffold, was developed to assess the influence of the scaffold micro-architecture on local shear stress and oxygen levels within the scaffold pores. Experiments were performed to derive specific oxygen consumption rates of constructs perfused under flow rates of 0.3 and 0.03 ml min⁻¹. While macro-scale and micro-scale models predicted similar average oxygen levels at different depths within the scaffold, μ CT models revealed small local oxygen variations within the scaffold micro-architecture. The combined macro-scale/micro-scale approach indicated that 0.3 ml min⁻¹, which subjected 95 % of the cells to less than 6.3 mPa shear, would maintain the oxygen supply throughout the scaffold above anoxic levels (> 1 %), with 99,5 % of the scaffold supplied with 8-2 % O₂. Alternatively, at 0.03 ml min⁻¹, the macro-scale model predicted 6 % of the cells would be supplied with 0.5 – 1 % O₂, although this region of cells was confined to the periphery of the scaffold. Together with local variations predicted by the micro-scale model, the simulations underline that in the current model system, reducing the flow below 0.03 ml min⁻¹ would likely have dire consequences on cell viability to pronounced regions within the engineered construct. The presented approach provides a sensitive tool to aid efficient bioreactor optimization and scaffold design.

Key-words: Tissue engineering, Micro-CT, Scaffold, Bioreactor, Computational fluid dynamics