DESIGN OF A HIGH-THROUGHPUT PERFUSION BIOREACTOR FOR ON-LINE µCT MONITORING OF MINERALIZED MATRIX DEVELOPMENT

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Introduction

Bioreactors are defined as devices enabling a closely monitored, tightly controlled environment and providing a high degree of reproducibility, control and automation [Martin et al., 2004]. Some bioreactors are able to apply physical stimuli such as compression or shear stresses to cultured constructs. Perfusion bioreactors stimulate constructs by fluid flow, similar to the flow of interstitial fluid through the lacuno-canalicular system of bone induced by habitual loading [Burger and Klein-Nulend, 1999]. Several studies used computational fluid dynamic (CFD) models to simulate the mechanical environment in perfused constructs [Cioffi et al., 2006; Porter et al., 2005; Yao et al., 2010]. However, most studies only simulated shear stresses and fluid velocities in the construct not including the effect of the bioreactor geometry itself.
Additionally, an important limitation of many perfusion bioreactor designs is the low-throughput of these systems due to space limitations [Dahlin et al., 2012]. The aim of this study was to design a novel high-throughput perfusion bioreactor with the help of CFD modelling meeting the following requirements: (1) uniform flow field for all constructs; (2) housing of multiple constructs; and (3) possibility for on-line µCT monitoring.

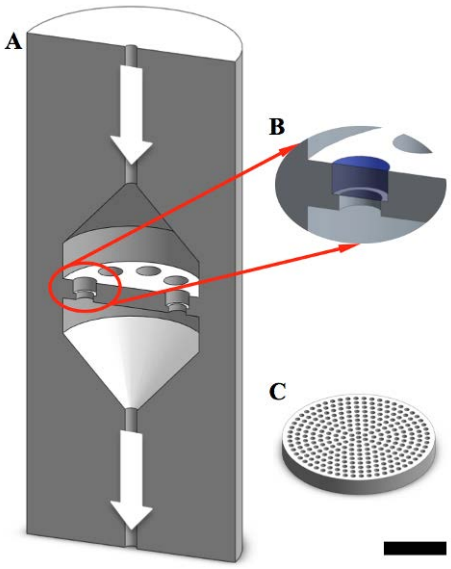

Figure 1: CAD drawings of the bioreactor design. (A) Bioreactor body cut in z-direction. White arrows indicate fluid flow. (B) Section of inlay. A scaffold is indicated in blue. (C) Flow conditioner with cylindrical pores (scale bar A, C = 1cm).

Methods

Various bioreactor geometries have been designed with the help of computer-aided-design (CAD, Fig 1A, B). CAD models were then imported into COMSOL Multiphysics and flow velocities in the constructs were simulated at different flow rates, with different flow conditioner geometries and different bioreactor and flow conditioner heights.

Results

Simulations without a flow conditioner showed a non-uniform flow field in scaffold constructs (Fig 2A). The implementation of flow conditioners improved the uniformity of the flow field significantly. The best results have been observed using a flow conditioner with circularly aligned cylindrical pores (Fig 1C, 2B).

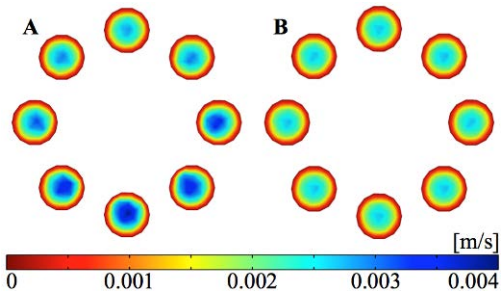

Figure 2: Fluid flow velocity profiles showing the top of the constructs. (A) Simulation without flow conditioner. (B) Simulation with flow conditioner.

Discussion

It was possible to design a bioreactor housing eight scaffold constructs all subjected to a uniform flow field. Additionally, the bioreactor was designed to match the requirements for µCT scanning. This novel bioreactor design enables to perform high-throughput perfusion studies over several weeks and simultaneously perform on-line µCT monitoring of mineralized matrix production.
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