Optimisation of fluid distribution inside a porous construct

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Orthopaedic disease or trauma can lead to substantial loss of tissue significantly affecting the patient's quality of life. Tissues such as bone and cartilage can be grown outside the body. To do this, the cartilage cells (chondrocytes) or bone cells (osteoblasts) are taken from a small piece of cartilage or bone tissue from the patient and grown up in a dish in the laboratory. These cells are then placed onto a porous biodegradable scaffold. This cell/scaffold sample can then be cultivated in an environment called a 'bioreactor'. The bioreactor is designed to overcome the limitations in static cultures by improving mass transfer of nutrients and removal of waste products by continuous perfusion of culture media through the 3-D sample. Perfusion of culture media also delivers flow mediated shear stresses to cells seeded within the construct. Shear stress is known to be a potent regulator of osteoblast function. Shear stresses in the range of 0.5–1.5 Pa (5-15 dynes/cm2) affect osteoblasts proliferation, production of alkaline phosphatase, nitric oxide (NO) and prostaglandin
(PGE2). A variety of perfusion systems have recently been developed to enhance the development of bone cell seeded 3-D constructs. These studies have reported the beneficial effects of various media flow rates on cell behaviour and extra-cellular matrix synthesis. The flow rate is considered an independent variable in these studies; but the resulting shear stress is a function of both flow rate and scaffold microarchitecture (porosity, pore size, and pore distribution). There is considerable variation in the scaffolds and geometries reported in these studies and so the local shear stresses experienced by the cells differ greatly in these studies even for the same input flow rate. There is also heterogeneity in the matrix synthesis in these constructs due to non uniformity in the distribution of nutrients and oxygen from the culture media. In vivo cells are no more than 100μm from the blood supply (capillaries) and this permits efficient diffusion of species from and to the tissue. Oxygen is one of the most important nutrients for cells but is often the limiting nutrient for successful tissue growth in vitro. This is due to the low solubility of oxygen in the culture media and the reduction in diffusion permeability in proportion to the quantity of matrix deposited on the construct by the cells.

A method to overcome this problem is to incorporate hollow, porous biodegradable tubes within the construct and allow media perfusion through them. This will potentially increase the availability of oxygen at closer proximity to the cells and overcome some of the limits to oxygen diffusion.

A bioreactor design for osteochondral tissue engineering is being developed at Keele University in collaboration with Dr Nikki Goodstone. The bioreactor will be divided into chambers optimized for either cartilage or bone. The bone chamber will contain an osteoblast seeded 3-D porous ceramic scaffold with 2 incorporated biodegradable tubes. The tubes have pore size of 5microns. Cells are over 10microns in size and therefore cannot infiltrate the tube but culture media will be able to flow through these pores. Culture media will be perfused through the chamber and through the individual tubes. We propose this study to simulate the perfusion conditions in this chamber and obtain velocity, pressure, and shear stress field throughout the scaffold. Additionally we would like to obtain an oxygen profile through the construct generated by the tube flow.

REFERERENCES

1. B. Porter, R. Zauel, H. Stockman, R. Guldberg, and D. Fyhrie. 3-D computational modeling of media flow through scaffolds in a perfusion bioreactor. *J Biomech.* 38 (3):543-549, 2005

    - Using microcomputed tomography to reconstruct scaffold microarchitecture
    - Computational fluid dynamic modelling code based on Lattice-Boltzmann method

2. F. Boschetti, M. T. Raimondi, F. Migliavacca, and G. Dubini. Prediction of the micro-fluid dynamic environment imposed to three-dimensional engineered cell systems in bioreactors. *J Biomech.* 39 (3):418-425, 2006

    - Modelling of flow through a 3D scaffold of homogenous geometry
    - 3D model and mesh built using GAMBIT (Fluent Inc)
    - Commercial code FIDAP (Fluent Inc.) used for flow modelling