Physical and Numerical Design of a Fluidised Bed Bioreactor for Stem Cell Expansion

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Introduction

Bone substitutes with enhanced biological activity are required for the replacement, repair and regeneration of skeletal tissue. This project aims to design a bioreactor for stem cell expansion on novel calcium phosphate based (HA/TCP) bone substitute materials designed for accelerated osseointegration of implants. The substitute material will be porous to allow cell expansion throughout. Mathematical modelling has been used alongside physical and biological experiments to define the bioreactor environment.

Bone Substitute Material

Porous bone substitute material has been produced from hydroxyapatite and tricalcium phosphate (HA/TCP). Figure 1 shows a photograph of a porous particle made from HA/TCP and some adjacent powdered material, medical grade calcium phosphate based granules. The aim of this project is to seed this material with bone cells and then grow them in a fluidised bed bioreactor; a method which allows both good mixing and transport of nutrients and also causes some controllable shear on the cells. Figures 2 and 3 show SEM images of the porous particles. The surface comprises individual grains of HA/TCP which can also be seen in Figure 4, an SEM image of a flat disk of the same HA/TCP material, produced in a press. These will be used as static controls and to evaluate cell-surface interactions. Figure 5 shows an SEM image of MG63 cells grown on a flat disk of HA/TCP.

Modelling of Distributor and Fluidisation

A CFD model of the distributor and fluidisation is being developed to enable aspects of the design to be optimised outside of the laboratory. Figures 6 - 8 show a model of liquid flow through a distributor in a 25 mm diameter column. The 6 mm thick distributor is placed 10 mm above the narrow inlet nozzle to improve the distribution of the liquid across the column. Initial tests have been performed to fluidise the dense bone substitute material shown on the right hand side of Figure 1. Figure 10 shows images of the particles being fluidised in a 25 mm diameter column. The distributor comprised 1 mm holes in a non-optimised pattern. In the first image, the flow rate is insufficient to fluidise the particles. In the second image the flow rate has been increased and the bed has slightly expanded, the gaps between the particles can be seen to have increased in size. In the third image the flow rate has been increased again and has resulted in greater mixing of the particles. In the final image the flow rate has been increased to achieve full fluidisation, with a greatly expanded bed and significant mixing.

Fluidisation of Calcium Phosphate Granules

Initial tests have been performed to fluidise the dense bone substitute material shown on the right hand side of Figure 1. Figure 10 shows images of the particles being fluidised in a 25 mm diameter column. The distributor comprised 1 mm holes in a non-optimised pattern. In the first image, the flow rate is insufficient to fluidise the particles. In the second image the flow rate has been increased and the bed has slightly expanded, the gaps between the particles can be seen to have increased in size. In the third image the flow rate has been increased again and has resulted in greater mixing of the particles. In the final image the flow rate has been increased to achieve full fluidisation, with a greatly expanded bed and significant mixing.

Conclusions

- The SEM images show that cell expansion on this material is possible. Cell expansion on the particles and granules, as opposed to the flat disks, will also be dependent on the cells’ interaction with the surface which shows greater undulation, but similar physico-chemical properties to the flat disks.
- Fluidisation of the granules was achieved, but fluidisation of the porous particles suffered problems due to their interlocking nature. This could be overcome with a larger diameter column, an optimised distributor or by applying mechanical force to the particles to cause any large protuberances to be removed, thus reducing interlocking.
- The modelling has shown that the velocity required to fluidise spherical particles of similar size and density to the granules underestimated the velocity required. The next stage of the modelling process will be to adapt the model to account for this difference.

References