Computational-experimental characterization of cell behaviour for skeletal tissue regeneration

B.G. Sengers (1), C.P. Please (2), M. Taylor (3), R.O.C. Oreffo (1)

1. Bone & Joint Research Group, University of Southampton, UK; 2. School of Mathematics, University of Southampton, UK; 3. School of Engineering Sciences, University of Southampton, UK

Regeneration strategies for skeletal tissues such as bone and cartilage aim at the restoration of critical size defects using cell seeded constructs cultured in bioreactors. However, currently the functionality of these constructs is insufficient for clinical application. One of the main factors involved is the effect of limitations in nutrient transport, which result in a reduction in cell viability or non-optimal conditions for the synthesis of functional tissue components. In addition, it is unclear how this process of extracellular matrix formation by individual cells translates into the overall mechanical properties which eventually determine construct functionality and thus clinical applicability.

The main focus of the talk will be on cell migration, since insufficient cell ingrowth is a key problem in the application of porous biomaterials (scaffolds) for bone reconstruction. To address this issue, migration and proliferation of an interacting cell population can be studied in vitro, using wound healing type assays. To derive intrinsic parameters that can be used for predictions, it is essential to generalise the results of these experiments by means of mathematical modelling. However, limited experimental observations impede a precise assessment of such theoretical models and insight into the underlying mechanisms. The objective of the current study was therefore, to combine experiments with computational modelling to characterise cell population spreading in 2D, and evaluate the applicability of these methods to predict 3D scaffold colonization.

Based on the parameters estimated from the 2D studies, a computational (Finite Element) model was developed to predict the progression of cell colonization on the surface of 3D scaffolds. To provide experimental validation, measurements of Human Bone Marrow Stromal Cell population migration on trabecular bone slices were compared with dedicated micro CT-based Finite Element models. This type of mathematical model will prove useful in understanding and predicting cell ingrowth and improving strategies for the control of skeletal tissue regeneration.