

Micro-mechanical Analysis of PLLA scaffolds for Bone Tissue Engineering

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INTRODUCTION: Many tissue engineering strategies rely on using combined cells and scaffold approaches. Bone is thought to use local mechanical strain as a cue for bone production, thus ensuring bone is laid down where it is needed most. It is reported that an agonist to strain-operated membrane channels, Bay K8466, enhances the sensitivity of bone cells to strain and increases matrix production [1]. Encapsulating this agonist into the scaffold may make bone cells more responsive to local mechanical strains in the scaffold. If so, mechanically loading the scaffold will lead to increased bone production at locations of apposite strain.

To test this strategy of enhancing bone regeneration in vitro, the relation between strain at the cellular level and micro-level bone matrix formation must be investigated. Because the scaffolds consist of random pores, we propose to derive the inhomogeneous surface strain distribution numerically by combining micro-compression experiments with micro-Finite Element (FE) models, both based on micro-Computed Tomography (μ CT) reconstructions. A linear FE model is applied to estimate the local micro-level surface strains in wet poly (L-lactic acid) scaffolds. Bone regeneration is measured by the local degree of mineralization using μ CT and related to the local surface strain environment at different locations throughout the scaffold.

METHODS: In an initial experiment six PLLA scaffolds, of which three enhanced with Bay, are scanned with μ CT before seeding and culture of MG63 cells in a perfusion-compression bioreactor. The $15 \times 15 \times 15 \mu\text{m}$ voxels of the reconstruction of each scaffold are directly converted to 8-node brick element meshes. The linear FE model is applied using Scanco Medical FE software on a Pentium 4 - 3.2 GHz platform with 4GB RAM.

After fixation the samples are dried chemically prior to the second μ CT scan. The mineralised bone is segmented from the scaffold and soft tissue. The reconstructions are realigned with the first scan, to locate the corresponding positions in pores in both reconstructions where mineralised bone is found. This is performed manually on 2D cross-sections, based on the calculated centre of mass of each mineralised bone segment.

RESULTS: Each scaffold retained its morphology during the whole experiment (*fig.1*), allowing correlation of the positions of all formed mineralised bone segments (35-85 per sample) to the pore in the original scaffold (*fig.2*).

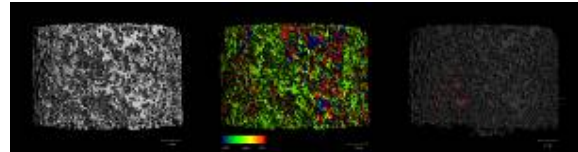


Fig. 1: Side views of a 3D reconstruction of a sample: the blank scaffold (left); FE-derived principal strain values in scaffold (middle); the tissue-scaffold construct (mineralised tissue is highlighted red)(right).

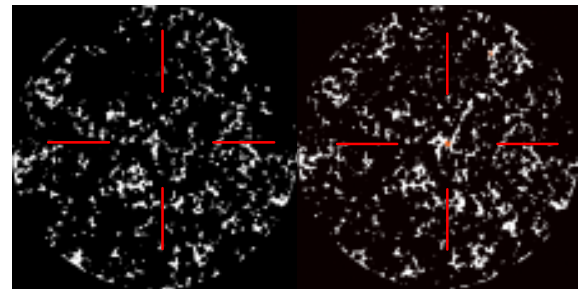


Fig. 2: Two corresponding cross-sections of a sample scanned before (left) and after (right) cell culture (mineralized bone is orange).

DISCUSSION & CONCLUSIONS: The model successfully generates local and sample specific strain values at locations of mineralised tissue formation. This allows investigation of the relevance of a number of parameters, like local strain distribution characteristics, how local the effect of apposite strain is and the effects of Bay enhancement. Also the effect of compressive strain well within the scaffold can be compared to fluid flow shear effects at the scaffold periphery with respect to bone mineralization.

REFERENCES: ¹ L.M. Walker, S.J. Publicover, M.R. Preston, M.A. Said Ahmed & A.J. El Haj (2000) *J Cell Biochem*, **79**, pp 648-661.

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