MECHANOBIOLOGICAL REGULATION OF LARGE BONE DEFECT REGENERATION WITHIN MEW AND FDM SCAFFOLDS

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Introduction

The treatment of large bone defects is an unmet clinical need. 3D printed scaffolds represent a promising strategy to support large bone defect regeneration.
Scaffolds fabricated with melt electrowriting (MEW) were shown to perform better in terms of new bone formation in a critically sized rat femoral defect over fused deposition modelling (FDM) scaffolds [1]. However, how those specific scaffold microarchitectures influence the mechanical environment within the defect, the cellular behaviour within the scaffold pores and thus the bone formation pattern is not fully understood.
Here, we aim to investigate the influence of FDM and MEW scaffold microarchitecture on the bone healing process during scaffold-supported bone regeneration, using a computer modelling approach.

Methods

A multiscale in silico model for scaffold-guided bone regeneration [2] was adapted to replicate a previously published experimental set-up [1]: a large rat femoral osteotomy (5 mm) stabilized with an internal PEEK fixator and either (1) left empty or augmented with PCL scaffolds coated with hydroxyapatite (HA) fabricated by (2) FDM (Fig.1 A) or (3) MEW (Fig.1 B).
The computer model couples finite element analysis at the tissue level, to determine the mechanical environment within the scaffold, and agent-based models at the cell level describing the biological processes occurring throughout the healing.

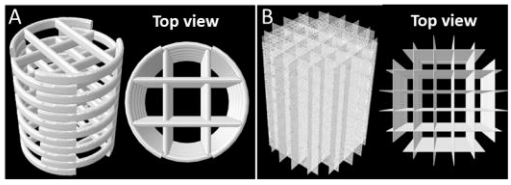

Figure 1: A) FDM and B) MEW scaffold geometries.

Results

In the FDM scaffold, high mechanical stimuli favourable for fibrous tissue formation were determined within the scaffold pores, both after 6 and 12 weeks (Fig. 2A). In addition, a small amount of bone formation was predicted (Fig.2 A). In the MEW scaffold, mechanical stimuli more beneficial for bone formation were predicted close to the bone ends which, together with the higher specific surface available for tissue deposition, led to the observed enhanced newly formed bone, in agreement with experimental results (Fig.2 B). For the empty case, very limited bone formation was predicted, in agreement with the experimental data (Fig.2 C).
Furthermore, the predicted shapes of the new bone ends resembled the ones observed experimentally, with spicules through the FDM scaffold pores and more rounded bone ends in the MEW scaffold.

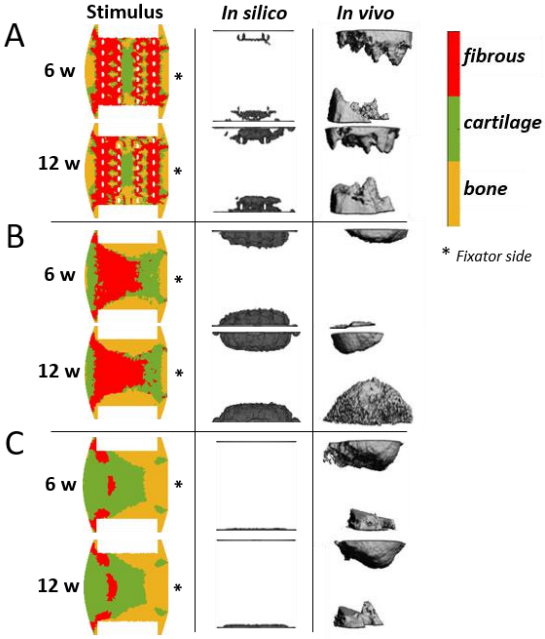

Figure 2: From the left, computed mechanical stimulus, in silico µCT, in vivo µCT [1] for A) FDM scaffold, B) MEW scaffold and C) empty case after 6 and 12 weeks.

Discussion

Our results show that not only the inherent scaffolds microarchitecture but also the induced mechanical environment can explain the experimentally observed enhanced bone formation within MEW as compared to FDM scaffolds.
In the future, we plan to include angiogenesis to better understand how micro-architectural features modulate vessel formation and the associated effects on the healing process.

References

1. Eichholz et al, Biofabrication, 14:045013, 2022.
2. Perier-Metz et al, Acta Biomater, 145:329-341, 2022.

Acknowledgements

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