MECHANO-BIOLOGY OF TISSUE REGENERATION WITHIN SCAFFOLDS IN LARGE BONE DEFECTS COMORBID WITH TYPE 2 DIABETES

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Introduction

Bone has the ability to regenerate itself. However, the treatment of large bone defects remains a clinical challenge which gets even more challenging when comorbid with Type 2 Diabetes (T2D). T2D is a chronic metabolic disease known by the presence of elevated blood glucose levels that is associated with reduced bone regeneration, high fracture risk and non-union [1]. Scaffolds have a high potential in the treatment of large bone defects, acting as a guiding structure during bone regeneration [2]; however, their application in T2D is highly challenging. Moreover, the mechanobiological mechanisms behind bone regeneration within scaffolds in T2D remains largely unknown. This study aims to investigate the mechanobiological regulation of tissue regeneration within scaffolds in a large bone defect comorbid with T2D, using a combined in silico/in vivo approach.

Materials and Methods

An in silico approach [3] that combines finite element (FE) analysis, to determine the mechanical environment, and agent-based models (ABM), describing the biological processes, was used to investigate bone regeneration within scaffolds in healthy and T2D rats. Gyroid scaffolds were virtually inserted into a large bone defect in a rat femoral osteotomy model (Fig. 1), replicating an experimental setup. Scaffold pores were initially filled with granulation tissue, while PCL, PEEK and titanium material properties were assigned to the scaffold, plate and screws, respectively. Bone regeneration was simulated both in healthy and T2DM animals and compared with in vivo microCT after 6 weeks. In the FE models, differences in bone properties and animal body weight between healthy and T2D were taken into account. In the ABM, to simulate the effect of T2D on cellular behaviour, cellular activity rates (e.g. migration, proliferation) were adapted based on experimental values reported in the literature.

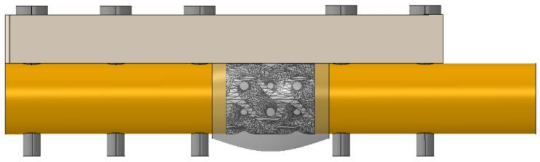

Figure 1: CAD model of the rat femur large bone defect filled with a gyroid scaffold and stabilized with a plate.

Results

Mechanical strains were higher in the T2D model compared with the healthy model, immediately post-surgery (Fig. 2). Specially, in the region close to the cortices, higher strains where predicted within the scaffold in the T2D animals. The predicted healing outcome was substantially different between the healthy and T2D. In the healthy case, the bone formed at the walls of the scaffold, similar to in vivo observations. The T2D model showed reduced bone formation, in agreement with in vivo data (Fig. 2).

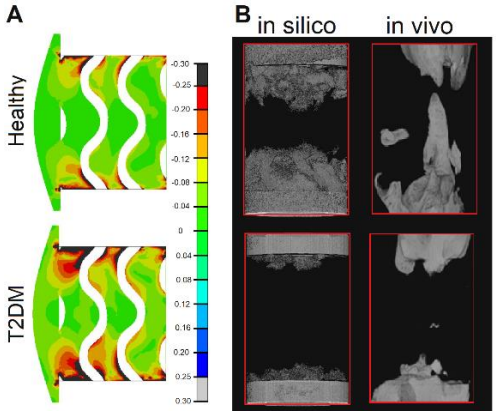

Figure 2: Healthy vs T2D: A) Minimum Principal strains within scaffold pores. B) MicroCT images of regenerated bone 6 weeks post-surgery.

Discussion and Conclusions

In this study, we developed a computational model to investigate the mechanobiological regulation of bone regeneration within scaffolds in large bone defects with T2D. The model was able to describe experimental observations of reduced healing potential in T2D defects. Future studies will focus on identifying the main cellular activities leading to this reduced healing outcome and the optimization of the scaffold design with the aim to enhance bone regeneration in T2D.

References

1. Hamman et al., Am J Physiol Endocrinol Metab, 2011
2. Werner, M et al., Advanced science, 2017
3. Perier-Metz et al, Front. Bioeng. Biotechnol 2020

Acknowledgements

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