Determining optimal scaffold stiffness for in vivo models: a novel in silico method

Determining scaffold optimal scaffold stiffness for *in vivo* models: a novel *in sillico* method

D C Betts[1], E Wehrle[1], G Kuhn[1], S Hofmann[2,3], R Müller[1]

[1]Institute for Biomechanics, ETH Zurich, Zurich, Switzerland, [2]Department of Biomedical Engineering and [3]Institute for Complex Molecular Systems, Eindhoven University of Technology, Eindhoven, The Netherlands.

INTRODUCTION: It has long been known that deformation of the soft tissue/haematoma is a driving force for tissue differentiation as bone regenerates in vivo. An optimal amount of deformation promotes bone formation, while overloading or under loading lead to increased levels of cartilaginous tissue formation or reduced levels of bone formation respectively, both can potentially lead to non-unions in extreme cases. Previously through using time-lapsed *in vivo* micro-computed tomography (microCT) in combination with micro finite element analysis (microFE), we have demonstrated that up to 88% of bone formation during the reparative stage of fracture healing occurs in tissue with a certain amount of strain energy density (SED) (Betts et al. 2015). We hypothesised that the material properties of a scaffold inserted into a healing bone defect will influence the amount of deformation in the tissue and consequently the size of the viable volume in which bone can regenerate. In this study we virtually implant scaffolds and perform a parameter study assessing the effect scaffold stiffness on potential bone formation.

METHODS:

A femoral defect of 1.24 [SD=0.13] mm was created in five female mice (C57BL/6) by first stabilizing the femur with an external fixator (MouseExFix, RISystem, Switzerland). Mice were scanned weekly using micro-CT imaging (vivaCT 40, Scanco Medical, Switzerland) over a period of 6 weeks, resulting in a series of time-lapsed images. The osteogenic strain range for bone formation in this empty defect was determined in a previous study (Betts et al. 2015). A scaffold of porosity 0.75 was virtually implanted (fig 1.) into the defect; the scaffold was 100 µm shorter than the osteotomy and matched the profile of the periosteal surface extending 50 µm radially further away from the surface. Material properties were assigned to the scaffold leading to elastic moduli between 2.5 MPa and 65 MPa of the bulk scaffold in the wet state. These models were then solved using ParOsol and the strain energy density (SED) calculated, the ratio of soft tissue voxels within the osteogenic SED range in the scaffold model compared to the empty defect was calculated, we term this the "viable volume fraction" (VVF).

RESULTS:

We found that a range of material properties exist (3-6 MPa) which increased the VVF above 100%, however that values both higher and lower result in decreased VVF as seen in fig. 1B.

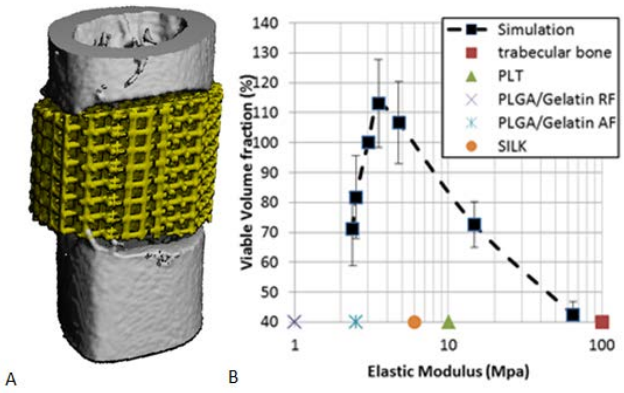

Fig. 1:A) Visualisation of the virtually implanted scaffold (yellow) in microCT scan of defect. B) The viable volume fraction of the different scaffold materials, as well as several materials commonly used for scaffold production.

DISCUSSION & CONCLUSIONS: This study neglects the (bio)chemical influence from the material instead focusing purely on mechanic effect. We have demonstrated the role scaffold material properties play in influence the local mechanical environment.

REFERENCES: D. C. Betts, E. Wehrle, G. A. Kuhn, S. Hofmann and R. Müller. Abstracts 4th TERMIS World Congress, Boston, USA, September 8-11, Tissue Eng. Part A, 21(S1):56, 2015

ACKNOWLEDGEMENTS: The authors acknowledge support from the EU (BIODESIGN FP7-NMP-2012-262948) and the Swiss National Supercomputing Centre (CSCS).