

Numerical Simulation of Functional Tissue Engineering for Articular Cartilage

Markus A. Wimmer¹, Uwe-Jens Görke², Sibylle Grad³, Mauro Alini³, Hubert Günther⁴

¹ Department of Orthopedics, Rush University Medical Center, Chicago, USA

² Institute of Mechanics, Chemnitz University of Technology, Chemnitz, Germany

³ Biochemistry & Cell Biology, AO Research Institute, Davos, Switzerland

⁴ AO Research Institute & TBZ-PARIV GmbH, Chemnitz, Germany

INTRODUCTION: Mechanical pre-conditioning of implantable chondrocyte-seeded constructs for cartilage repair is of increasing clinical and scientific interest. However, the determination of the 'correct' parameter setting is still object of contrary discussion. Therefore, in this study, a coupled experimental-numerical procedure has been performed to correlate the spatial distribution of biological activity with the development of selected mechanical field variables.

MATERIALS & METHODS: To determine the mechanical loading conditions for a single cell, and deducing from the cell response the prediction of local cell stimulation, a multiscale finite element approach (FEA) has been chosen. Starting with a macro-model of the scaffold-cell construct, the local load history of a selected element of the FEA macro-mesh provided the boundary conditions for a micro-model with a single cell and its neighborhood. Using the biphasic, poroelastic features of a commercially available FEA-code, the viscoelastic effects of the porous polyurethane (PU) scaffold were implemented using a newly developed non-linear bimodular hyperelastic function with a special structural tensor modeling the anisotropic behavior of the solid phase¹. Further, an incorporated stochastic "tissue growth function" helped to determine the time course as well as the spatial distribution of matrix development.

Experimentally, the cylindrical PU scaffolds were seeded with bovine chondrocytes². The scaffolds were held in culture for three days under various loading and boundary conditions to study the effects on cell response. Loading was performed with a recently developed bioreactor³. To localize regions with biological activity, the scaffold was cut into different spatial segments. A biochemical analysis of mRNA expressions of important cartilage genes⁴ was then performed for each segment separately.

RESULTS: Boundary conditions and load frequencies affected the results globally and especially locally. The spatial distribution of gene expression of collagen I, II, aggrecan, COMP, HAS, and PRG4 as well as their time dependent development showed partially different, in some cases even contrary trends. Comparing the spatial distribution of cell messages with the numerically detected development of several mechanical field variables, information about possible mechanical stimuli can be provided. It was shown that the fluid flow and the distribution of the pore pressure as well as its gradient essentially depend on the permeability of the construct. The dependency on load velocity in the range of frequencies under consideration is less distinct.

CONCLUSIONS: In summary, the observed variations in mRNA expressions indicate a gene specific metabolic cell response to different mechanical stimuli. A coupled experimental-numerical procedure would allow a time dependent analysis of process parameters during construct conditioning in tissue engineering in future studies.

REFERENCES: ¹U.-J. Görke et al. (2004) *Trans ECCOMAS*, Jyväskylä, pp. 1-20

²K. Gorna et al. (2002) *Polymer Degrad Stabil* **75**:113

³M.A. Wimmer et al. (2004) *Tissue Engineering* **10**:1436-45.

⁴S. Grad et al. (2005) *Tissue Engineering* **11**(1-2): 249-56.

ACKNOWLEDGEMENTS: This work was supported by AO research grant 02-W66 (AO Foundation, Davos, Switzerland)