

TRIAxIAL COMPRESSION OF THE MATRIX INDUCES CHONDROGENIC DIFFERENTIATION OF HUMAN MESENCHYMAL STEM CELLS IN-VITRO IN A THRESHOLD DEPENDENT MANNER

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Introduction

Application of a multi-axial mechanical loading regime using a sliding contact bioreactor has been shown to induce chondrogenic differentiation of human mesenchymal stem cells (MSCs) within fibrin-polyurethane composite scaffolds even without exogenous TGF- β [Schätti et al, 2011]. In stark contrast, uniaxial compressive loading using the same bioreactor system does not induce chondrogenic differentiation of MSCs [Schätti et al, 2011]. In this context, by studying the differences in the mechanical signals that cells receive within the constructs when they are exposed to uniaxial loading as compared to multiaxial loading, it is possible to identify the optimal mechanical environment for chondrogenic induction of MSCs.

To this end, we employed finite element (FE) modelling to identify the differences in the mechanical stimuli that cells receive within the fibrin-polyurethane composite scaffolds following application of the multi-axial loading regime compared to the uniaxial loading regime in order to better understand the mechanoregulation of chondrogenic differentiation in MSCs.

Methods

Compressive stress-relaxation and permeability experiments were conducted on cylindrical (8 mm diameter \times 4 mm height) fibrin-polyurethane composite scaffold samples. A poroviscoelastic mechanical constitutive model was developed for the scaffolds based on the compressive stress-relaxation and permeability experiments and was used to develop an FE model of the bioreactor system employed in [Schätti et al. 2011], see Figure 1. In the FE model, a multiaxial load comprised of interfacial shear load and cyclic compression was applied and in the case of uniaxial load, dynamic compression alone and also dynamic interfacial shear alone were applied to the constructs according to the loading protocols employed in [Schätti et al, 2011] and the changes in the pore fluid velocity, pressure field and also the strain field within the scaffolds were quantified. In the case of multiaxial loading where chondrogenesis occurred, the mechanical stimuli were examined at the key locations within the scaffolds and the values were

correlated to the level of glycosaminoglycan (GAG) content by histological analysis.

Results

The FE model revealed that combined compression and interfacial shear induced triaxial compression of the matrix at the interfacial contact surface of the scaffolds. At this location where the GAG content was found to be significant, the three principal strains were compressive and had a minimum magnitude of 10% (i.e. minimum compressive principal strain of 10%), see Figure 1. The peak value of the minimum compressive principal strain was found to be 1.86 fold higher using combined compression and interfacial shear compared to compression alone.

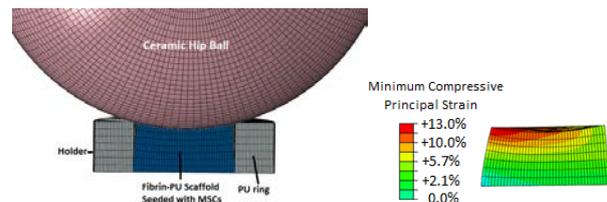


Figure 1: (left) The FE model of the bioreactor system used in [Schätti et al, 2011] (right) the value of the minimum compressive principal strain at the top surface of the scaffolds subject to multiaxial loading.

Discussion

This study revealed that compressive principal strains play a key role in chondrogenic induction of MSCs. Specifically, in Fibrin-polyurethane composite scaffolds dynamic triaxial compressive deformation of the matrix was found to be sufficient to induce chondrogenesis in a threshold dependent manner. In contrast, no direct correlation could be identified between the level of pore fluid velocity and chondrogenesis. Of note, due to the high permeability of the constructs the pore fluid pressures remained negligible and could not contribute to chondrogenesis.

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References

Schätti et al, eCM 22: 214-225, 2011.