15th International Symposium on Computer Methods in Biomechanics and Biomedical Engineering
and
3rd Conference on Imaging and Visualization
CMBBE 2018
P. R. Fernandes and J. M. Tavares (Editors)

Abstract ID-119

COMPUTATIONAL MODELLING OF HUMAN MESENCHYMAL STEM CELL PROLIFERATION AND EXTRA CELLULAR MATRIX PRODUCTION IN 3D POROUS SCAFFOLDS IN A PERFUSION BIOREACTOR

Mohammad Mehrian[(1)], Ioannis Papantoniou[(2)], Toon Lambrechts[(3)], Liesbet Geris[(1)]

[(1)]**Biomechanics Research Unit, GIGA In silico Medicine, University of Liège, Belgium**
m_mehrian@yahoo.com, liesbet.geris@uliege.be

[(2)]**Skeletal Biology and Engineering Research Center, KU Leuven, Belgium**
ioannis.papantoniou@med.kuleuven.be

[(3)]**M3-BIORES, KU Leuven, Belgium**
toon.lambrechts@kuleuven.be

Keywords: Computational modelling, Tissue engineering, Human mesenchymal stem cell, Matrix production, Perfusion bioreactor, 3D porous scaffolds

Summary: Introduction
3D porous scaffolds are frequently used in tissue engineering (TE) applications in combination with bioreactor systems because of their ability to induce reproducible culture conditions that can control specific cell behavior such as proliferation and extracellular matrix (ECM) production. A computational model describing neotissue growth inside 3D scaffolds in a perfusion bioreactor was developed [1], with neotissue being considered the combination of cells and their extra cellular matrix. In the model, the speed of neotissue growth depends on the flow-induced shear stress, curvature and the local concentrations of oxygen, glucose and lactate. The goal of this study is to make a distinction between the cell and the ECM fraction within the neotissue in the model [2] to allow for a more detailed validation and optimization of the process.
Methods
The neotissue variable (and corresponding equation) was separated into two variables – one for the cell compartment and one for the ECM compartment. The density of the cells is modelled to be affected by the presence of ECM and the total available space. The final model was composed of five model variables and implemented in MATLAB®. The model was calibrated using previously obtained experimental results [3] where human mesenchymal stem cells seeded on 3D printed titanium scaffolds were cultured for 28 days. The combined ECM and cell volume was measured using contrast-enhanced nanofocus computed tomography imaging of the scaffold filling and the cell fraction was quantified through DNA measurements.
Results and Discussion
The simulation results showed a good correspondence for cell and ECM compartments, as well as the total filling percentage between the model predictions and the experimental data. Applying the previously implemented optimization routines [1] to this extended model now allows to design culture strategies that will favor cell expansion over matrix production whilst limiting the overall cost of culture. This modeling endeavor will assist in the transition from flask-based expansion to cost efficient culture in perfusion bioreactors.

References

[1] Mehrian , et al., Biotech & Bioeng, revised version submitted, 2017.
[2] Lemon, et al., J Theoretical Biol, 2007.
[3] Sonnaert, et al., J Tis Eng Reg Med, 2017.