Simulation of Remodelling in Vascular Scaffolds Using Agent Based Models

Houman Zahedmanesh, Caitríona Lally
triona.lally@dcu.ie
Department of Mechanical and Manufacturing Engineering, Dublin City University, Dublin, Ireland

Introduction
Agent based modelling is a robust method that can elucidate the interaction of individual events at the cellular level which combine to produce the complex responses at the tissue level. Remodelling of vascular tissue engineering scaffolds is driven by a complex cascade of chemical, mechanical and biological events at cellular level. The aim of this study was to develop a numerical modelling approach using agent based models which could provide insights into the remodelling process in vascular tissue engineered scaffolds.

Materials and Methods
A mechanobiological model was developed by coupling a finite element model of an artery-scaffold end-to-end anastomosis to an agent based model which controls the behaviour of key cell populations in vascular remodelling, i.e. vascular smooth muscle cells (VSMCs) and endothelial cells (ECs). The model was initialised with VSMCs lining the lumen of the scaffold and the VSMCs could also migrate from the adjacent artery. The value of cyclic stretch that the cells were exposed to due to an applied luminal pressure was calculated using the finite element model and was used to regulate cellular activities such as proliferation, extracellular matrix (ECM) synthesis and cytokine expression by the cells. VSMCs and ECs could move in a random walk manner throughout the scaffold and were biased towards higher concentrations of platelet derived growth factor (PDGF) to model cellular chemotactic migration. VSMCs synthesised ECM, PDGF and transforming growth factor (TGF-β) with their expression upregulated by increases in cyclic stretch. ECs expressed PDGF, TGF-β, and Nitric Oxide (NO), with PDGF expression also upregulated by increases in cyclic stretch [1-3]. The proliferation rate of VSMCs was defined as a function of the local concentration of growth factors, NO, nutrients and the value of cyclic stretch. While PDGF and nutrients increased VSMC proliferation rate, NO, TGF-β and increasing cyclic stretch all had an anti-proliferative effect [1,2,4]. In addition, TGF-β prohibited PDGF driven chemotactic migration [4].

Results
The mechanobiological model predicted ECM synthesis by VSMCs in the scaffold and also the luminal ingrowth of VSMCs leading to the development of intimal hyperplasia. The highest luminal ingrowth and ECM synthesis occurred at the anastomotic site due to migration of VSMCs from the adjacent artery, see Fig 1.

Discussion and Conclusions
Combining agent based and finite element models as a novel mechanobiological modelling approach shows significant potential for vascular tissue engineering applications.

References

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Disclosures
Authors have no conflict of interest to disclose.