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A PHYSICALLY MOTIVATED CONSTITUTIVE MODEL FOR CELL-MEDIATED COMPACTION AND COLLAGEN REMODELING IN ENGINEERED TISSUES

Sandra Loerakker[1,*], Christine Obbink-Huizer[1] and Frank P.T. Baaijens[1]

[1] Department of Biomedical Engineering, Eindhoven University of Technology, P.O. Box 513, 5600 MB Eindhoven, The Netherlands, s.loerakker@tue.nl

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Collagen is the main load-bearing component of many soft tissues and has a large influence on the mechanical behavior of tissues when exposed to mechanical loading. It is important to increase our understanding of collagen remodeling in soft tissues to understand the mechanisms behind pathologies and to control the development of the collagen network in engineered tissues.

The goal of the present study was to develop a theoretical and computational framework to describe tissue compaction and collagen remodeling in engineered cardiovascular tissues. The engineered tissue was modeled as a mixture of cells, collagen fibers, and isotropic tissue components. The contractile stresses exerted by the cells in response to mechanical stimuli were included using the recently published model of Obbink-Huizer *et al.* [1]. Collagen remodeling consisted of strain-dependent degradation and oriented production. Tissue compaction was modeled by including cell-mediated contraction of the collagen fibers, where the reference length of the fibers was changed as a function of the cell stress.

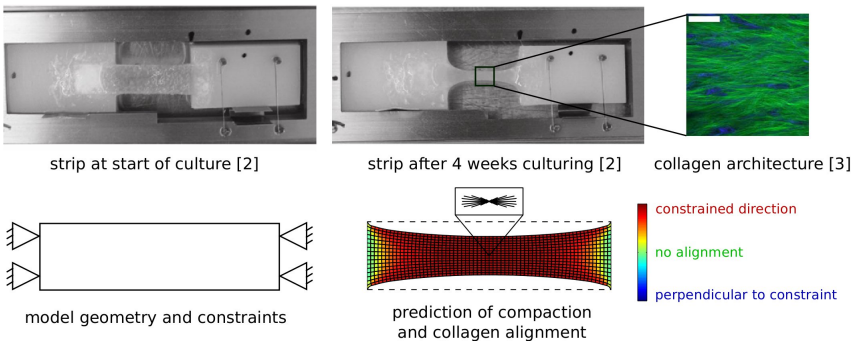

Figure 1: Tissue compaction and collagen alignment in engineered tissue strips observed in experiments (top) and predicted by the model (bottom).

Rectangular tissue-engineered strips usually compact half in width and show a strong collagen alignment in the constrained direction [2, 3]. Application of the model to simulate this process resulted in 43% compaction in the middle of the strip and also a clear collagen alignment in the constrained direction (Fig. 1). Collagen fibers in engineered vascular grafts are circumferentially aligned near the inner wall and axially aligned near the outer wall [4]. This was also predicted by the computational model (Fig. 2).

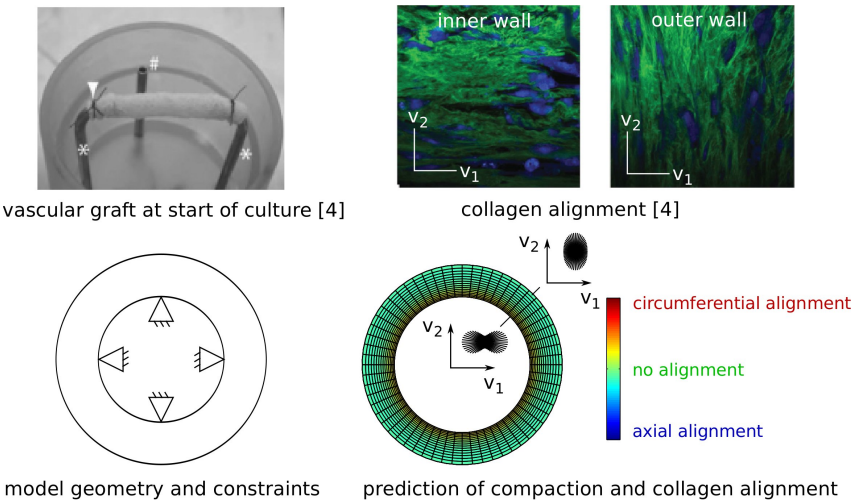

Figure 2: Tissue compaction and collagen alignment in engineered vascular grafts observed in experiments (top) and predicted by the model (bottom). Directions $\vec{v}_1$ and $\vec{v}_2$ represent the circumferential and axial direction, respectively.

The model predictions generally correspond with reported experimental observations. Therefore, the model can help to increase our understanding of tissue compaction and collagen remodeling, and it may ultimately provide a tool for determining the optimal experimental conditions for obtaining native-like collagen architectures in engineered cardiovascular tissues.

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