

A Multiphysics Continuum Model for In-Stent Restenosis

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Healing in soft biological tissues is a chain of events on different time and length scales. A nonlinear continuum model to capture and couple important mechanical, chemical and biological aspects of healing has been recently published, cf. [1]. The model considers interstrand delamination in collagen as most important damage mechanism that initiates a biochemical response to damage and starts the chain of healing. On micro-scale, the evolution of growth factors and matrix metalloproteinases is modeled. These in turn degrade and produce collagen. Due to the collagen turnover, the volume as well as the mechanical properties of the tissue change. Furthermore, prestretch of the extracellular matrix is considered and remodeling occurs to reobtain homeostasis. The model is formulated in the context of the homogenized constrained mixture theory, which is designed for the modeling of growth and remodeling in soft tissues.

In the present work, an extension of the model is proposed that captures damage in several collagen fiber families and takes cell activities into account. While growth factors and matrix metalloproteinases have negligibly small masses, the mass of cells have to be considered in the balance of mass. Accordingly, the balance equation is extended to capture cell diffusion, chemotaxis, cell removal and production as well as phenotypic differentiation. Thus, beside the displacements, the concentrations are additional primary unknowns of the problem. Focusing on the case of restenosis occurring in arteries after angioplasty or stenting, smooth muscle cells, fibroblasts and myofibroblasts are modeled. These species react to damage, interact with matrix metalloproteinases and growth factors, and play a key role in the mass turnover of the extracellular matrix.

The model capabilities are assessed by means of a finite element simulation of a three dimensional, stenotic artery segment. The model is a further step towards a predictive tool for healing processes in soft tissues, and specifically for restenosis, it can help to better understand the formation of restenosis.

REFERENCES

[1] M. Gierig, P. Wriggers, M. Marino, Computational model of damage-induced growth in soft biological tissues considering the mechanobiology of healing. *Biomech. Model. Mechanobiol.*, Vol. **20**, pp. 1297–1315, 2021.