KTH SOLID MECHANICS SEMINAR; Tuesday, November 14th, 13.10; KTH Solid Mechanics Seminar room

Sandra Loerakker "Growth and remodeling of native and tissue-engineered heart valves"

Sandra Loerakker is assistant professor in Modeling in Mechanobiology at the Department of Biomedical Engineering, Eindhoven University of Technology (TU/e), The Netherlands. She obtained her MSc degree in Biomedical Engineering in the field of computational fluid dynamics in 2007 (cum laude), and defended her PhD thesis in the field of pressure ulcer etiology in 2011, both at TU/e. Her PhD work was awarded with the Best Doctoral Thesis in Biomechanics Awards of the European Society of Biomechanics and the Novice Investigator Award of the European Pressure Ulcer Advisory Panel. From 2011 till 2014, she worked as postdoctoral researcher in the field of heart valve mechanobiology at TU/e, after which she was promoted to her current position of assistant professor. From 2016 till 2017, she spent one year as visiting assistant professor at Stanford University, supported by a Marie Curie Individual Fellowship. The aim of her research is to integrate computational and experimental methods to understand the biological mechanisms responsible for soft tissue development, adaptation, and disease, and ultimately translate those findings into novel therapies in the field of regenerative medicine.

Heart valves ensure uni-directional blood flow in the human body by opening and closing about 3 billion times in a lifetime. In case of valvular disease or congenital malformations, heart valves are often replaced by either mechanical or bioprosthetic valves. Although these are life-saving devices, their main limitation is that they consist of non-living materials, and hence cannot remodel in response to changing demands or grow in line with the somatic growth of the individual. Tissue-engineered heart valves (TEHVs) are a promising alternative to current treatment options, as these living, autologous tissues have the intrinsic capacity to grow and remodel. The major challenges are to (1) understand the underlying growth and remodeling mechanisms, and (2) design TEHVs such that these mechanisms lead to physiological development and adaptation. Computational modeling plays an important role in addressing both challenges. In our group at TU/e, we have developed a computational framework of soft tissue remodeling, incorporating the effects of cellular (re)orientation and traction forces, cell-mediated collagen crimp, and mechanically-induced collagen remodeling, inspired by experimental data on the individual mechanisms. With this framework, we predicted that cellular contractility is crucial for obtaining a successful outcome with TEHVs implanted in the pulmonary position, whereas hemodynamic factors appeared to dominate valve remodeling in case of implantations in the aortic position. Via a one-year pre-clinical follow-up, we recently confirmed that the long-term functionality and remodeling of TEHVs can indeed be predicted and, importantly, also guided towards a successful outcome via design optimization. Besides focusing on TEHVs, we also aim to improve our understanding of the development of human native heart valves, as these present the benchmark for TEHVs. Using a computational-experimental analysis, we demonstrated that aortic and pulmonary valves appear to maintain a stretch homeostasis throughout life. Interestingly, our computational models also suggested that growth and remodeling play opposing roles in maintaining this homeostasis. Finally, in a recent computational study we observed that the development of the native collagen architecture in human valves is not only determined by mechanical factors, but also depends considerably on the presence of topographical features.

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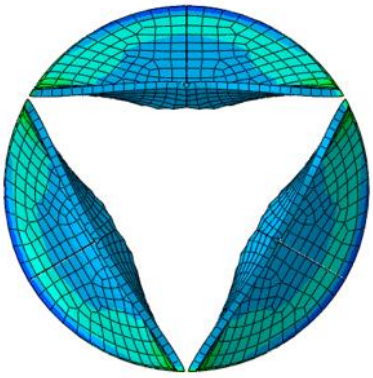

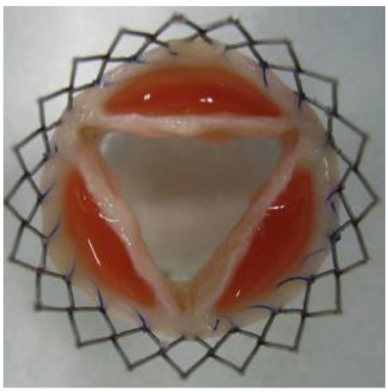

Figure 1: FEM model (left) and tissue-engineered (right) heart valve.