HUMAN & BIOTECHNOLOGY

Fields of Expertise TU Graz

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Gabriele Berg, Gernot Müller-Putz, Human & Biotechnology
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In this issue we can report two things: on the one hand we were again successful at receiving awards, on the other hand, this is a very busy period for writing proposals. To go into details, Theresa Rienmüller (Institute of Health Care Engineering) received a Paper Award, Anna Pukaluk and Gerhard Sommer (Institute of Biomechanics) received the Best Collaborative BioTechMed-Graz Paper Award, Michael Wimmer (Institute of Neural Engineering) received an award for his Master's thesis, and Oliver Maier (Institute of Medical Imaging) gained an award for his PhD thesis from the Styrian Brain Research Initiative (Initiative Gehirnforschung Steiermark). Furthermore, on 24 March 2023, Bernd Nidetzky, one of the leaders of our FoE, received an honorary doctorate from Ghent University in Belgium. To mark the occasion, the Faculty of Bioscience Engineering at Ghent University organized a symposium on biotechnology, and we are delighted about its successful outcome. Congratulations to all of the winners – and now a reminder: whenever you want to report successful projects, publications or awards – please let us know.

In fact, each award starts years before with a written proposal. And this is indeed a very important task for all PIs in the FoE. Currently, there is an open call for TU Graz multidisciplinary Lead Projects. In addition, our oldest and largest COMET K2 Center, the Austrian Centre of Industrial Biotechnology ACIB, will apply for a new funding round.

Our contribution to this issue of TU Graz research comes from the field of biomechanics – a traditional area of our FoE. Gerhard Sommer successfully completed his tenure track position. He analyses the biomechanical properties of the aorta system in the context of human health issues, and gives an overview of his research here.

Gerhard Sommer

Exploring the Aorta: Multiscale Aorta Project

Arteries have a remarkable ability to remodel in response to altered hemodynamics, disease progression, and injury. Such remodeling is typically manifested at the macroscopic tissue level, but the underlying mechanisms exist at the micro- and nanoscopic levels, where the extracellular matrix, cells, and molecules interact. This project funded by the Austrian Science Fund (FWF) focused on mechanical characterization and imaging techniques of aortic tissues. In particular, such experimental methods were combined to allow the identification of relationships between the mechanical loading at the macroscale and structural alterations at the micro- and nanoscale in human aortas (Figure 1).

BACKGROUND

In general, efficient diagnosis and treatment of vascular diseases, such as atherosclerosis or the formation of an aneurysm or a dissection in arteries, should be grounded on a thorough understanding of the biomechanical properties of the arterial tissues. Over the past decades, advances in imaging techniques have revealed that biology creates intricate hierarchical structures across multiple scales, where molecular details are exhibited in macroscale mechanical responses. In particular, imaging techniques revealed a complicated network of extracellular matrix constituents (i.e., mainly collagen, elastin, and proteoglycans) in the three arterial layers (i.e., intima, media, and adventitia). In the last years, technological advances have provided us with an increased understanding at the macroscopic (tissue) level, the microscopic (fiber) level, and the nanoscopic (fibril and molecule) level. However, there has been little attempt to combine the different material characterization methods across these length scales.

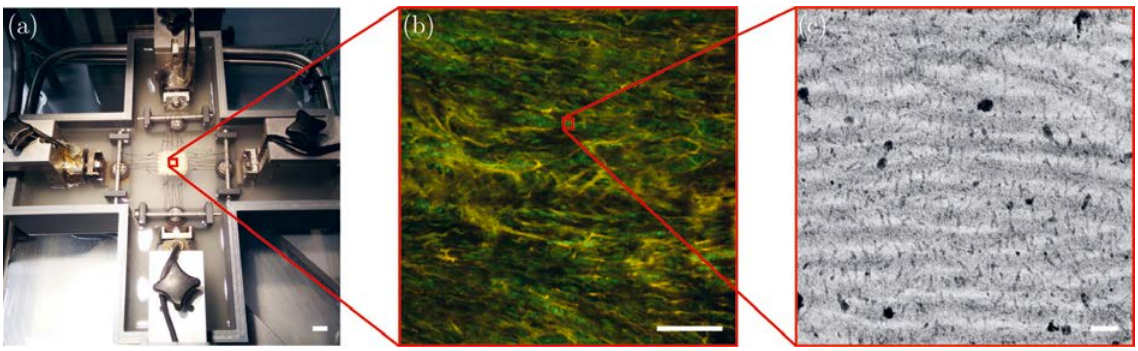

Figure 1: Multiscale experimental approach: (a) biaxial extension test of an aortic wall is accompanied by (b) multi-photon and (c) transmission electron microscopy. Multi-photon microscopy (b) reveals the second-harmonic generation signal of collagen fibers (green) and autofluorescence of elastin fibers (yellow). Transmission electron microscopy (c) shows light gray collagen fibrils connected with spindle-like, dark gray proteoglycans. Scale bars denote (a) 1 cm, (b) 100 µm, (c) 100 nm.

Source: Gerhard Sommer

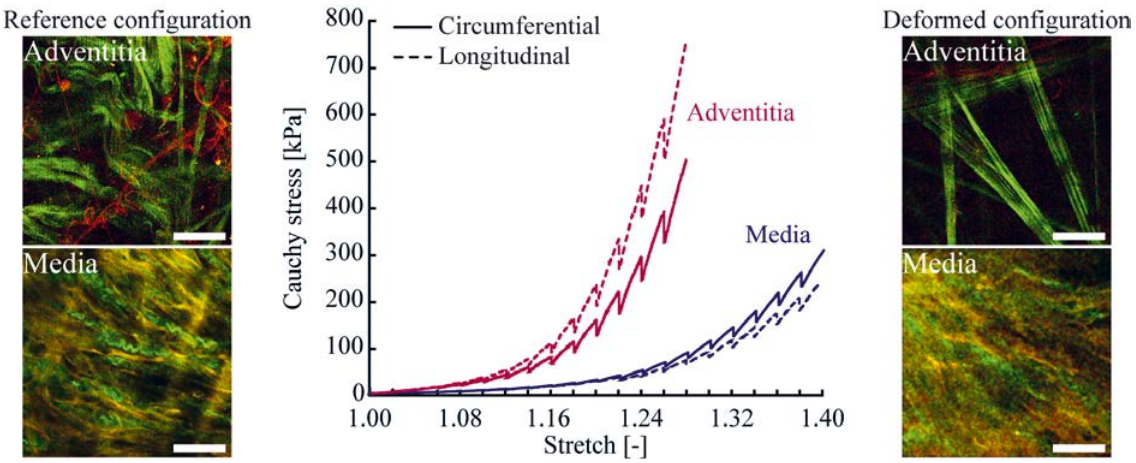

Figure 2: Differences in the mechanical response and the microstructure of the human aortic medial and adventitial layers determined by simultaneous biaxial extension testing and MPM imaging at the reference and deformed (max. stretch achieved) configurations. Collagen is indicated in green and elastin in red/yellow. Scale bars show 50 µm.

Source: Gerhard Sommer

OUR MULTISCALE APPROACH

For the multiscale experiments, pipelines were developed to relate the macro-, micro-, and nanoscales of the human aortic wall. Biaxial extension testing and multi-photon microscopy (MPM) imaging of the mechanically-relevant constituents, collagen and elastin, were simultaneously applied to obtain the aortic properties at macro- and microscales (see Figure 2). At the nanoscale, collagen fibrils and proteoglycans (PGs) were visualized using three-dimensional transmission electron microscopy (3D-TEM) at different biaxial stretches (see Figure 3).

These investigations provided not only qualitative insights into the mutual organization of aortic tissue constituents and their load-induced changes but also allowed the quantification of structural parameters at the micro- and nanoscale. These quantified structural parameters were a primary goal of the project since they are crucial for the development of a novel multiscale material model, which are ultimately important for realistic computer simulations, e.g., for the failure prediction of an aortic aneurysm or dissection. It is important to emphasize that up-to-date material models can reproduce but not predict the mechanical behavior of the human aortic wall. This flaw in material models can be eliminated by experimentally validated knowledge about the multiscale biomechanical properties of arterial tissues, e.g., in the form of mechanical and structural parameters that serve as indicators of the tissue behavior and strength. >

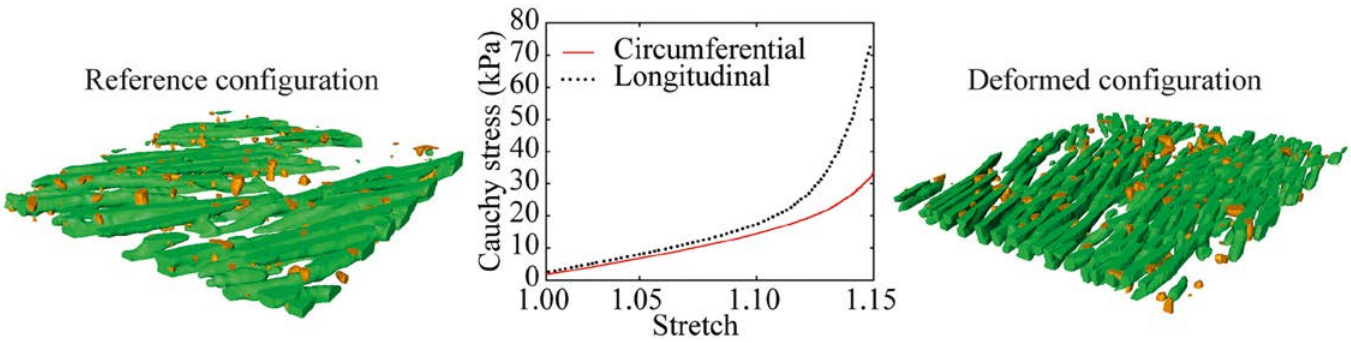

Figure 3: Visualization of the 3D organization of collagen fibrils (green) and PGs (yellow) in the aortic media in the load-free state (left) and at 1.15 stretch (right) recorded with 3D-TEM. Corresponding biaxial mechanical properties of the specimen are given in the middle panel.

Source: Gerhard Sommer

Gerhard Sommer

is associate professor (and laboratory manager of the biomechanics laboratory) at the Institute of Biomechanics. He and his working group focus on multiscale experimental biomechanics and material modeling of biological tissues in health and disease.

Source: Privat

Simultaneous MPM imaging and biaxial extension testing revealed clearly different microstructural changes between the medial and adventitial layers of the aortas (Figure 2). For example, collagen fibers in the adventitia were divided into several fiber families, while the media showed only one fiber family. Moreover, the dispersion of the medial collagen was not affected during biaxial loading, while the dispersion of the adventitial collagen was substantially reduced. The elastin in the adventitia remained also wavier than the elastin in the media during biaxial stretching. Consequently, material models would provide better representation and simulation outcomes when such morphological differences are considered. Organization of collagen fibrils and PGs imaged with 3D-TEM was also shown to be different at the unloaded and loaded configurations (Figure 3). For example, collagen fibrils got closer, i.e., were more packed, at higher stretches, and PGs realign more towards the radial direction, i.e., out-of-plane in reference to the aortic wall.

Most importantly, the results of this project showed that the aortic wall stiffness and the waviness parameters of collagen and elastin fibers should be used as indicators for the mechanical response of the human aorta, e.g., in clinical applications, to estimate the safety margin for strains applied during surgery or to estimate the rupture risk of an aneurysm or the progression of an arterial dissection.

These results could not be obtained without close interdisciplinary cooperation. In particular, this research project brings together specialists not only in biomechanics (G. A. Holzapfel, A. Pukaluk, TU Graz) but also in molecular bioscience (H. Wolinski, Uni Graz), ultrastructure analysis (D. Kolb, G. Leitinger, MedUni Graz), pathology (C. Viertler, P. Regitnig, MedUni Graz), image processing (T. Pock, P. Knöbelreiter, TU Graz), and mathematics (K. Bredies, V. Horak, Uni Graz).