INTER-SPECIES DIFFERENCES IN PULMONARY ARTERY MORPHOMETRY AND HEMODYNAMICS

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Introduction

Large animal models, such as pigs or sheep, are commonly used in pre-clinical studies for evaluation of efficacy and safety of cardiovascular implantable devices such as heart valve prostheses. In-silico models for device evaluation, as for example finite element simulation of implantation procedures, might allow to omit animal experiments altogether in the future. However, these models might already provide valuable information regarding differences in mechanical and hemodynamic properties between human and animals, enhancing the information gathered from pre-clinical trials as well as the translation from animal models towards clinical application. In this study, the pulmonary artery of sheep, pigs, and humans were compared with respect to their anatomical and hemodynamic similarity focusing on parameters relevant for assessment of devices to be implanted in the pulmonary artery. The aim of this analysis was to understand whether these animal models adequately mimic the parameter ranges observed in human patients.

Methods

For this study, the subject-specific anatomy was reconstructed from CT image data, whereas the hemodynamic information was calculated using computational fluid dynamics.

The anatomy reconstruction was performed mostly manually using diastolic image data of 14 ovine, 41 porcine as well 48 human pulmonary arteries. For subsequent hemodynamic simulations, the reconstructed surface geometries had to be smoothed and truncated at all vessel in- and outlets. Anatomical parameters, such as the lengths of the main (MPA), left (LPA) and right pulmonary artery (RPA), their diameters, curvatures as well as the bifurcation angle between the LPA and RPA were calculated automatically, using a centerline-based approach.

To collect information on the subject-specific hemodynamics within the pulmonary artery, simulations were conducted using a finite volume solver STAR-CCM+ (v. 17.04, Siemens PLM). For some data sets also in-vivo measurements of the volume flow waveform in the MPA were available and were used as boundary condition. For subjects where this information was not available, average waveforms that were matched to the subject's stroke volume and heart rate were used. Due to lack of information regarding the subject-specific pulmonary resistance, zero pressure boundary conditions were used for all outlets. The parameters to be evaluated were velocities, wall shear stresses and the oscillating shear index.

Results and Discussion

The anatomy of the pulmonary artery featured distinct differences between the three species. While lengths and diameters were roughly comparable, especially the diameter changes observed in humans were more rapid than that in both animals. This was most pronounced in the first bifurcation were the MPA splits into LPA and RPA. Furthermore, relevant differences in the curvatures of the LPA and RPA as well as the bifurcation angle between these two vessels were observed for the three species (see Figure 1).

Evaluation of the hemodynamic parameters is still ongoing. Especially due to the changes in curvatures and the bifurcation angle, inter-species differences in the hemodynamic parameter distributions are to be expected.

Quantification of those differences might allow to better understand the intricate differences between large animal models and human application and therefore lead to better designed animal experiments in the future. However, ideally computational simulations will provide an outright alternative to animal testing, if feasibility of assessing device effect and efficacy using these models can be demonstrated.

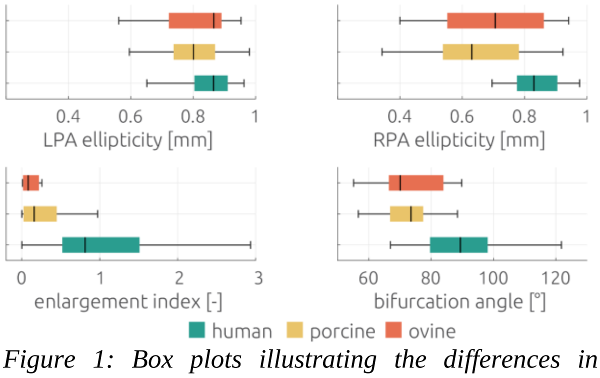

Figure 1: Box plots illustrating the differences in distributions of exemplary anatomic parameters between the three species.

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