TRANSLATION OF IN-SILICO ANIMAL TRIAL TO HUMAN CONDITIONS: PULMONARY ARTERY PRESSURE SENSOR HEMODYNAMICS

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Introduction

Heart failure (HF) is a leading cause of death and hospitalization with high prevalence of 1-2% [1]. Recently pulmonary artery pressure sensors (PAPS) were proposed to detect earlier acute decompensation that can ideally be mitigated by pharmaceutical treatment. A novel PAPS designed to be implanted in the left or right PA is currently under development. Preclinical evaluation of safety and efficacy in frames of bench tests and animal trials is necessary for any novel medical device. However, animal trials are still limited with respect to the information that can be assessed and their translation towards use in humans is challenging. The aim of the study presented here was to investigate a translation of in silico animal trial [2] towards humans. This is required since conditions differs among different species [3]. Respective, intra-arterial hemodynamics before and after virtual device implantation in human PAs was simulated using CFD and hemodynamic parameters in animal and human PA were compared.

Materials and Methods

The study based initially on the chronic animal trial: 20 PAPS (one in the left and one in the right PA) were implanted in 10 pigs (app. weight of 60 kg). CT acquisition, which was done before and after implantation was used for in silico image-based CFD analysis of the porcine PA hemodynamics with and without PAPS [2]. To compare hemodynamics in porcine and human PA, human PA geometries were selected from a retrospective cohort using similarity of geometric parameters (lengths and diameters of all three major PA segments, LPA-RPA bifurcation angle, and number of side branches) as measured by L1 norm. Finally, 20 PAPS were virtually implanted into the human PA aiming to mimic pairwise implantation sites in porcine PA of the animal trial (see figure 1).

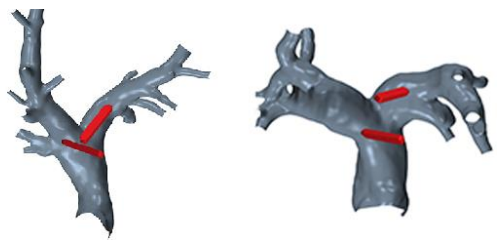

Figure 1: Left: porcine PA with two implanted PAPS. Right: human PA with similar implanted sensors.

PA hemodynamics with and without PAPS was analyzed based on transient blood flow simulations performed using STAR-CCM+ flow solver (15.04, Siemens PLM, USA). Blood was modelled as an incompressible fluid with a shear-rate dependent viscosity following a Carreau-Yasuda model. A k-omega SST turbulence model is used to account for turbulent effects. Flow rate curves at the main PA of pigs and humans were generated synthetically using a hybrid approach considering weights for definition of heart rates (HR) and cardiac outputs (CO), whereas patient-specific HR and CO were used in humans. Three parameters were evaluated: time-averaged wall shear stress (TAWSS) and oscillating shear index (OSI), which are parameters associated with a risk of thrombus formation as well as pressure drop caused by the PAPS.

Results

We found significantly larger diameters (left Pa: 18±1.3 mm vs. 14±1.7 mm; right PA: 20±1.2 mm vs. 15±2.0 mm) and larger bifurcation angle (89±8° vs. 80±7°) in humans. Comparing boundary conditions, we found significantly lower HR in humans with 65±6.0 bpm vs. 100±2.9 bpm, whereas no significant differences in CO (4.3±1.2 L/min vs. 4.7±0.2 L/min).

We found significantly higher TAWSS in human PA after implantation (pre: 1.38[1.11] Pa; post: 1.44[1.15] Pa), which is clinically neglectable. No significant difference was found for the OSI (pre: 0.16[0.07]; post: 0.15[0.07]). In the human PA TAWSS was significantly lower as in the porcine, whereas OSI significantly higher. PAPS implanted in the human PA causes relatively low averaged pressure drop of 0.8±0.8 mmHg, which non-significantly differs from the pressure drop calculated in porcine PA with 0.7±1.1 mmHg.

Summarizing, we found significant difference in hemodynamics between porcine and human PA that is probably associated with lower protection against thrombosis risk under human conditions. Despite these differences both in silico studies (porcine and human) found no higher thrombosis risk due to PAPS.

References

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Acknowledgements

This work has been funded under the European Union's Horizon 2020 programme under Grant No. 101017578