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AN INTEGRATED IN-VITRO AND IN-SILICO WORKFLOW TO STUDY THE PULMONARY BIFURCATION HEMODYNAMICS

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Summary. In the context of cardiovascular diseases (CVDs), there is a lack of knowledge in the patient-specific modeling of pulmonary artery (PA) hemodynamics using in-vitro and in-silico tools. In this work, the PA, including its main branch with right (RPA) and left (LPA) arteries, was investigated. A specific Genetic Algorithm (GA) was developed to estimate the three-elements Windkessel (RCR) model based on patient-specific Phase Contrast Magnetic Resonance Imaging (PCMRI) data. This code took into account not only for the physiological pressure range, but also for the replica of the patient-specific right-left (R/L) flow split, thus providing specific RCR values for RPA and LPA.

1 INTRODUCTION

Cardiovascular diseases (CVDs) are the number one cause of the death globally, taking about 17.9 million lives each year [1]. Among these disorders, the Tetralogy of Fallot (TOF) represents a rare and severe congenital condition caused by a combination of several defects. This disease can lead to circulation problems affecting the pulmonary artery (PA).

Nowadays engineering tools, such as numerical simulations and mock circulatory loops (MCLs), can be used to support the medical approach in both diagnosis and treatment of CVDs, clinical approach personalization, intervention prediction and disease knowledge improvement [2-3]. Numerical models and MCLs were successfully developed for the investigation of the pathological aortic fluid dynamics [2-4]. On the contrary, there is still lack

of research works concerning the PA district. Both in numerical and experimental simulations, it is necessary to quantify the resistive action of the capillaries and the compliant nature of the vessels surrounding the anatomy of interest, to replicate physiological conditions in terms of pressures and flows. For this purpose, three-element Windkessel models are usually adopted [5], consisting by two resistances and one capacitor, namely RCR. The RCR values of the model were widely discussed for the aorta structures but a correct characterization for the PA district is still lacking.

The aim of this work was to study a cohort of TOF cases through image processing techniques to allow the development of experimental and numerical setups for a high-fidelity replica of a patient-specific pathologic PA hemodynamics. More precisely, the main goal was to replicate the patient-specific physiological RCR parameters of the PA, including the right (RPA) the left (LPA) pulmonary arteries, taking into account not only for the pressure range in the main PA branch (MPA) but also for the replica of the right/left (R/L) flow split. The presented rationale permitted the validation of the in-silico and in-vitro setup through in-vivo patient-specific measurements.

3 MATERIAL AND METHODS

The workflow followed in this work was divided into four main parts: image processing of a cohort of PA cases affected by TOF (i); genetic algorithm (GA) code development for PA district impedance estimation (ii); development of a high-fidelity patient-specific in-vitro setup (iii); development of a patient-specific Computational Fluid Dynamic (CFD) simulation (iv).

3.1 Image processing

Image processing techniques were applied to a dataset consisting of magnetic resonance imaging (MRI) and phase contrast magnetic resonance imaging (PCMRI) data of 21 patients affected by TOF, to extract geometrical and functional data. The structural MRI images were processed using a semiautomatic segmentation approach. Given the great morphological heterogeneity, a representative TOF case of study was selected based on characteristic shape parameters, including PA branches cross-sections, lengths, and tortuosity. Statistical indices of position and variability were extracted for each shape parameter distribution. The flow curves were successfully extracted, and an average flow curve was generated.

3.2 Genetic algorithm

A custom GA code was developed to determine the RCR model parameters by using patient-specific pressure range and flow profiles as inputs. The code was structured in two main phases. The first phase was given by the minimization of a cost function defined based on the pressures resulting from the electrical equivalent of the fluid dynamic problem. The second part exploited the results of the first by introducing a specific scale factor for the flow profile matching in both the LPA and RPA branches, maintaining the same hydraulic load and physiological pressure regime.

3.3 In-vitro setup

The in-vitro simulation was set according to the schematic circuit (Figure 1a). The TOF representative PA model was 3D printed using stereolithographic technique (Figure 1b) and inserted in the MCL mimicking the pulmonary circulation of the selected patient [3]. Pinch valves and air-filled chambers were used as resistive and capacitive components for the replica of the Windkessel models in the MCL. Pressure and flow sensors were used for measurements at LPA and RPA branches. The overall system is controlled by a custom LabView application including a real time controller.

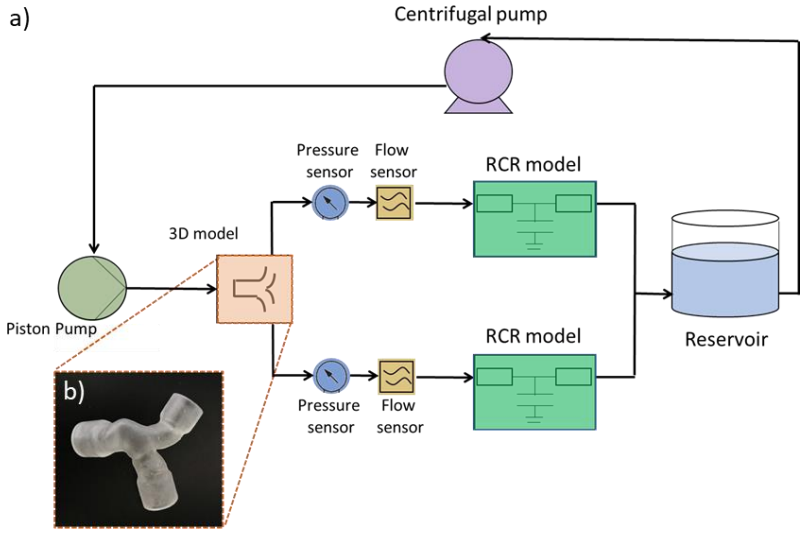

Figure 1 – Schematic representation of MCL system (a) with details of the 3D printed PA phantom (b).

3.4 In-silico setup

A computational replica of the same experiment was developed via a CFD tool. The three-dimensional Navier-Stokes equations for incompressible flows are thus considered as governing equations and the LS-Dyna software was adopted for the simulations. The domain was discretized with a mesh of 13,666 tetrahedral elements. At the inlet section of the computational domain we imposed plug flow with the measured flow-rate waveform of the experiment. The RPA and LPA outlets were set according to the RCR model, with parameters defined based on the GA results. Blood was considered as Newtonian and incompressible fluid with density and dynamic viscosity respectively equal to 1.06 g cm^{-3} and 0.05 g cm^{-1} s^{-1}.

4 RESULTS AND DISCUSSION

The GA code was successfully implemented. The reported parameters were demonstrated to be effective in replicating the desired physiological conditions in both the in-vitro and in-silico context, even if a finer tuning was required to compensate the MCL parasite leakages.

Figures 2a and 2c depict the flow comparison between in-vitro, in-silico waveforms and GA code predictions, respectively at RPA (Figure 2a) and LPA (Figure 2c). Figure 2b shows

results of CFD simulation at systolic peak, where the R/L flow split is clearly noticeable.

The patient-specific physiological pressure values were correctly covered in-silico within the MPA section with a relative error of 9.3%, considering a range of 10.3-34.8 mmHg (average pressure range of the population). The flow curves also showed an average relative error equal to 6% for the RPA and to 18% for the LPA. The experimental and computational results revealed a remarkable agreement. The proposed methodologies demonstrated to be effective for the evaluation of the patient-specific hemodynamics PA models.

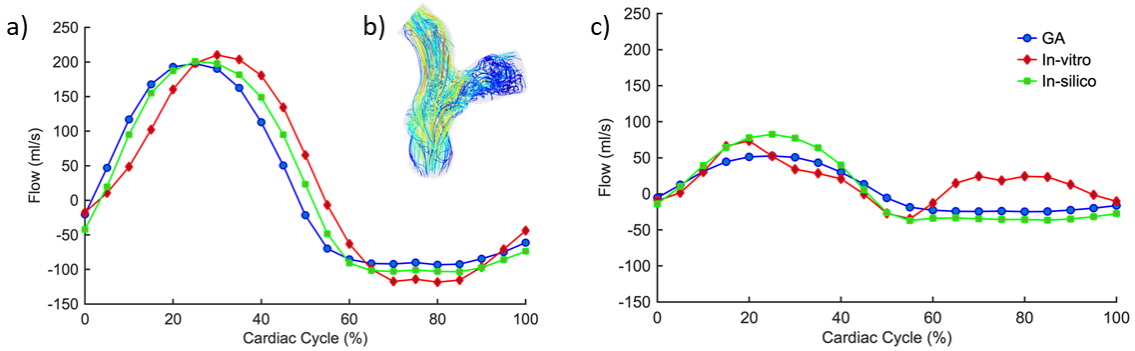

Figure 2 – Comparison of flow curves from GA prediction, in-vitro experiment and in-silico simulation, respectively for RPA (a) and LPA (c), with detail of CFD simulation results at systolic peak (b).

5 CONCLUSIONS

In this study a novel method based on a custom GA script for the estimation of patient-specific RCR parameters for the PA bifurcation, considering the flow split of the subject, was presented. The effectiveness of the computed RCR values, from solely imaging data, was demonstrated in-vitro and in-silico. Further investigations, involving more case studies, may increase the confidence of experimental setups and CFD simulations for the investigation of PA pathologies, thus facilitating the translation of engineering tools in clinics for individualized healthcare.

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