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Executive Summary of the Thesis

Coupling between 3D hemodynamics and reduced immersed valve dynamics for the pulmonary circulation

Laurea Magistrale in Mathematical Engineering - Ingegneria Matematica

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1. Introduction

In this work we detail an innovative computational framework to study and to numerically simulate the hemodynamics in the pulmonary artery, including the pulmonary valve leaflets, which is based on a 3D-0D fluid-structure interaction (FSI) model.

The pulmonary valve is located between the main pulmonary artery and the right ventricle. It is composed by three leaflets that open when the ventricle pressure is higher than the artery one and close when the flow rate changes sign. The pulmonary valve can be affected by different pathologies. Our study, patient-specific, analyzes two patients, affected by the congenital anomaly tetralogy of Fallot. Years after the Ross procedure in pediatric age, in which the diseased aortic valve was replaced with the patient's own pulmonary valve, they have undergone the implant of a prosthetic pulmonary valve. The tomographic images are provided by the Niguarda Hospital, Milan.

The pulmonary circulation is not much studied in literature, and this is the first time that a 3D-0D fluid-valve interaction model is applied to the right heart. The choice of a 0D valve model, instead of a 3D one, allows to provide reliable information on the valve dynamics with reduced computational cost, without neglecting its interaction with the blood flow.

2. Mathematical models and numerical methods

The blood flow, modeled as an incompressible, homogeneous and Newtonian fluid, is described by the Navier-Stokes equations, where the valve is represented by the Resitive Immersed Implicit Surface (RIIS) method. This approach, already employed in [2] in a clinical context for the mitral valve, is inspired by on the Resistive Immersed Surface (RIS) approach, originally proposed in [1].

The 3D hemodynamics is coupled with a lumped-parameters model, derived from a local force balance at the leaflets, which reproduces the valve dynamics, introduced in [3], for the aortic valve.

2.1. Fluid model and Resistive Immersed Implicit Surface method

The presence of the valve is taken into account in the momentum equation of the Navier–Stokes system by adding a localized penalty term,

specifically a resistive term, which weakly enforces the blood to adhere to the leaflets.
The geometry of the moving valve Γ_t is represented as a surface immersed in the fluid domain Ω (Figure 1). It is implicitly described at each time t by a level-set function $\varphi_t : \Omega \to \mathbb{R}$, as

$$\Gamma_t = \{\mathbf{x} \in \Omega : \varphi_t(\mathbf{x}) = \mathbf{0}\}. \tag{1}$$

The velocity $\mathbf{u}$ and pressure p of the blood satisfy the following formulation of the Navier-Stokes equations:

$$\begin{cases} \rho\partial_t\mathbf{u} + \rho(\mathbf{u}\cdot\nabla)\mathbf{u} - \nabla\cdot\boldsymbol{\sigma} + \\ \quad +\frac{R}{\epsilon}(\mathbf{u}-\mathbf{u}_\Gamma)\delta_{\Gamma,\epsilon} = \mathbf{0} & \text{in } \Omega,\ t\in(0,T], \\ \nabla\cdot\mathbf{u} = 0 & \text{in } \Omega,\ t\in(0,T], \\ \mathbf{u} = \mathbf{0} & \text{on } \Sigma_{wall},\ t\in(0,T], \\ \boldsymbol{\sigma}\mathbf{n} = p_{in}\mathbf{n} & \text{on } \Sigma_{in},\ t\in(0,T], \\ \boldsymbol{\sigma}\mathbf{n} = p_{out}\mathbf{n} & \text{on } \Sigma_{out},\ t\in(0,T], \\ \mathbf{u} = \mathbf{0} & \text{in } \Omega,\ t=0, \end{cases} \tag{2}$$

where $\boldsymbol{\sigma}(\mathbf{u},p) = -p\mathbf{I} + \mu(\nabla\mathbf{u} + (\nabla\mathbf{u})^T)$ and $\mathbf{u}_\Gamma$ is the velocity of the valve, which constitutes a datum for the fluid problem.
The resistive penalty coefficient is the ratio between the resistance coefficient R and the half-thickness ϵ of the leaflets, and the resistive term enforces with the condition $\mathbf{u} = \mathbf{u}_\Gamma$ as $\epsilon \to 0$. It has support in a narrow layer around Γ_t, represented by a smeared Dirac delta function $\delta_{\Gamma,\epsilon} : \Omega \to [0,+\infty)$, as follows:

$$\delta_{\Gamma,\epsilon}(\mathbf{x}) = \begin{cases} \dfrac{1+\cos(\pi\varphi_t(\mathbf{x})/\epsilon)}{2\epsilon} & \text{if } |\varphi_t(\mathbf{x})| \le \epsilon, \\ 0 & \text{if } |\varphi_t(\mathbf{x})| > \epsilon. \end{cases} \tag{3}$$

With regard to the boundary conditions, Σ_{in} is the inlet, where blood enters, from the ventricle, $\Sigma_{out} = \Sigma^1_{out} \cup \Sigma^2_{out}$ consists in two outlets, the left and right pulmonary artery, while Σ_{wall} represents the artery wall (Figure 1). Moreover p_{in} and p_{out} represent the physiological values of pressure in the right ventricle and in the pulmonary artery, respectively, and they are extracted from a simulation of the 0D model of the whole cardiovascular system, where the systemic and pulmonary circulations are modeled with resistance-inductance-capacitance (RLC) circuits exploiting the hydraulic/electric analogy.

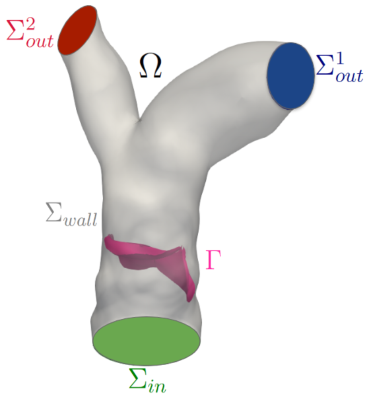

Figure 1: Computational domain.

2.2. Lumped-parameters structure model

Aiming at providing the configuration and the velocity of the valve, represented by $\delta_{\Gamma,\epsilon}$ and $\mathbf{u}_\Gamma$ in the fluid problem (2), we describe a reduced, lumped-parameters model which is able to describe the main features of cardiac valve dynamics, between its closed and open configurations, in a realistic manner.
Denoting by $\mathbf{d}_\Gamma : [0,T] \times \widehat{\Gamma} \to \mathbb{R}^3$ the displacement of the leaflet with respect to its reference configuration $\Gamma_0 = \widehat{\Gamma}$, we can represent the current configuration Γ_t as

$$\Gamma_t = \{\mathbf{x} \in \mathbb{R}^3 : \mathbf{x} = \mathbf{T}_t(\widehat{\mathbf{x}}) = \widehat{\mathbf{x}} + \mathbf{d}_\Gamma(t,\widehat{\mathbf{x}}) \\ \text{for some } \widehat{\mathbf{x}} \in \widehat{\Gamma}\}.$$

We assume that every point $\mathbf{x} \in \Gamma_t$ of the leaflet is subject, at each time t, both to an external force $\mathbf{f}(t,\mathbf{x})$ due to the surrounding fluid, and to an elastic force, that is related to the leaflet curvature $H(t,\mathbf{x})$. Both these contributions depend on the current configuration of Γ_t described by $\mathbf{d}_\Gamma(t,\widehat{\mathbf{x}})$. The curvature-induced elastic force is assumed to act only normally to the surface and is imposed to vanish on $\widehat{\Gamma}$. Finally we assume that the valve motion can be affected by some damping effect. In accordance to these assumptions we can formulate a local force balance as follows:

$$\rho_\Gamma\ddot{\mathbf{x}} + \beta\rho_\Gamma\dot{\mathbf{x}} = \\ = \mathbf{f}(t,\mathbf{x}) - \gamma[H(t,\mathbf{x}) - \widehat{H}(\widehat{\mathbf{x}})]\mathbf{n}_\Gamma(t,\mathbf{x}), \tag{4}$$

where ρ_Γ is the surface density of the valve, β is a damping coefficient, γ is an elasticity coefficient, and $\mathbf{n}_\Gamma$ is the normal to the surface Γ_t. The function $\widehat{H}(\widehat{\mathbf{x}})$ represents the total curvature of the surface $\widehat{\Gamma}$ in the position $\widehat{\mathbf{x}} = \mathbf{T}_t^{-1}(\mathbf{x})$ corresponding to $\mathbf{x}$.
In order to reduce equation (4) to a 0D model, we assume that $\mathbf{d}_\Gamma$ can be decomposed as

$$\mathbf{d}_\Gamma(t, \widehat{\mathbf{x}}) = c(t)\mathbf{g}(\widehat{\mathbf{x}}), \tag{5}$$

where $\mathbf{g} : \widehat{\Gamma} \to \mathbb{R}^3$ is known and takes into account the spatial dependence of the displacement, while $c : [0, T] \to [0, 1]$ has to be modeled. In particular, $\mathbf{g}$ represents the valve opening field, and it has to be provided. Indeed it reproduces the displacement of the valve between its closed and open positions, and it depends on the patient-specific model. On the other hand, c represents the valve opening coefficient and expresses the fraction of the valve opening: $c = 0$ corresponds to the valve in closed position, while $c = 1$ denotes the open valve.
Therefore the local balance (4), re-written considering (5), taking the component along $\mathbf{n}_\Gamma$ and integrating over Γ_t, reduces to an ordinary differential equation for c:

$$\ddot{c} + \beta\dot{c} = \frac{\int_{\Gamma_t} \mathbf{f} \cdot \mathbf{n}_\Gamma d\mathbf{x} - \gamma \int_{\Gamma_t} [H - \widehat{H}] d\mathbf{x}}{\int_{\Gamma_t} \rho_\Gamma \mathbf{g} \cdot \mathbf{n}_\Gamma d\mathbf{x}}. \tag{6}$$

We consider the closed, fixed valve as initial configuration:

$$c(0) = 0, \quad \dot{c}(0) = 0.$$

2.3. Coupling of the fluid and structure models

The 3D fluid model and the 0D valve model can be coupled in a reduced FSI model. The fluid-to-valve stress $\mathbf{f}$, appearing in equation (6), is computed from the 3D fluid model in terms of $\mathbf{u}$, p and the RIIS-related quantities, while the valve position and velocity are provided by the 0D valve model.
The valve position allows to compute the signed distance function φ_t and successively the function $\delta_{\Gamma,\epsilon}$ according to (1), (3), while, looking at definition (5), the surface velocity can be expressed as:

$$\mathbf{u}_\Gamma(t, \mathbf{x}) = \dot{c}(t)\widetilde{\mathbf{g}}(\mathbf{x}), \tag{7}$$

where $\widetilde{\mathbf{g}} : \Omega \to \mathbb{R}^3$ is the closest-point extension of $\mathbf{g} : \widehat{\Gamma} \to \mathbb{R}^3$.
In order to express the forces $\mathbf{f}$ exerted by the fluid on the valve which are related to the stress jump across Γ_t, we introduce some additional notation related to the representation of the immersed surface Γ_t. Being φ_t a signed distance function, the domain Ω can be partitioned into two regions:
$\Omega_t^+ = \{\mathbf{x} \in \Omega : \varphi_t(\mathbf{x}) > 0\}$,
$\Omega_t^- = \{\mathbf{x} \in \Omega : \varphi_t(\mathbf{x}) < 0\}$.
Any function f defined over Ω can be decomposed as $f = f^+ + f^-$, where $f^\pm = f|_{\Omega^\pm}$.
Thus,

$$\mathbf{f} = [\boldsymbol{\sigma}\mathbf{n}_\Gamma]|_{\Gamma_t} = \boldsymbol{\sigma}^+|_{\Gamma_t}\mathbf{n}_\Gamma - \boldsymbol{\sigma}^-|_{\Gamma_t}\mathbf{n}_\Gamma.$$

Moreover, the function φ_t allows to define $\widetilde{\mathbf{n}}_\Gamma$ and $\widetilde{H}$:

$$\widetilde{\mathbf{n}}_\Gamma = \frac{\nabla\varphi_t}{|\nabla\varphi_t|}, \qquad \widetilde{H} = -\mathrm{div}\widetilde{\mathbf{n}}_\Gamma.$$

These quantities are actual extensions of the normal vector and curvature, since $\widetilde{\mathbf{n}}_\Gamma|_\Gamma = \mathbf{n}_\Gamma$, $\widetilde{H}|_\Gamma = H$.
Considering the surface smearing introduced by the smooth Dirac delta $\delta_{\Gamma,\epsilon}$ and the above mentioned definitions, the integral terms that appear in (6) can be approximated as follows:

$$\int_{\Gamma_t} \mathbf{f} \cdot \mathbf{n}_\Gamma \simeq \int_\Omega \Big(\boldsymbol{\sigma}\widetilde{\mathbf{n}}_\Gamma \cdot \widetilde{\mathbf{n}}_\Gamma \delta^+_{\Gamma,\epsilon} - \boldsymbol{\sigma}\widetilde{\mathbf{n}}_\Gamma \cdot \widetilde{\mathbf{n}}_\Gamma \delta^-_{\Gamma,\epsilon} \Big),$$
$$\int_{\Gamma_t} \rho_\Gamma (\mathbf{g} \circ \mathbf{T}_t^{-1}) \cdot \mathbf{n}_\Gamma \simeq \int_\Omega \rho_\Gamma (\mathbf{g} \circ \mathbf{T}_t^{-1}) \cdot \widetilde{\mathbf{n}}_\Gamma \delta_{\Gamma,\epsilon},$$
$$-\gamma \int_{\Gamma_t} \Big(H - \widehat{H} \circ \mathbf{T}_t^{-1} \Big) \simeq -\gamma \int_\Omega \Big(\widetilde{H} - \widetilde{\widehat{H}} \Big) \delta_{\Gamma,\epsilon}.$$

2.4. Numerical approximation

The fluid model is discretized in space through a Finite Element (FE) formulation with the Streamline Upwind Petrov-Galerkin along and the Pressure-Stabilizing Petrov-Galerkin (SUPG-PSPG) stabilization and in time by means of backward differentiation formula (BDF) of order 1 and by adopting a semi-implicit treatment for the nonlinear term.
The 0D structure problem, instead, is discretized with the explicit, fourth-order Runge-Kutta method.
The fluid and structure models are then weakly coupled at each time-step:

Given $\mathbf{u}_h^n$, p_h^n, c^n for $n = 0$, and computed the functions φ^n, $\widetilde{\mathbf{n}}_\Gamma^n$, $\widetilde{H}^n$ corresponding to the surface Γ^n for $n = 0$

for $n = 1$ *to* $N = \frac{T}{\Delta t}$ **do**

1. Compute the integrals of the valve model, in terms of $\mathbf{u}_h^{n-1}$, p_h^{n-1}, Γ^{n-1}, φ^{n-1};
2. Find c^n by advancing the 0D valve model with a step of an explicit fourth-order Runge-Kutta method;
3. Move the immersed surface to its new configuration Γ^ndescribed by $\mathbf{d}_\Gamma^n = c^n \mathbf{g}$ and compute $\mathbf{u}_\Gamma^n = \dfrac{c^n - c^{n-1}}{\Delta t} \widetilde{\mathbf{g}}$;
4. Compute the new signed distance function φ^n w.r.t. Γ^n and assemble the normal and curvature fields $\widetilde{\mathbf{n}}_\Gamma^n$ and $\widetilde{H}^n$;
5. Find $(\mathbf{u}_h^n, p_h^n) \in V_h^r \times Q_h^r$ by solving the discretized fluid problem.

end

3. Pre-processing and mesh generation

The computational domain for the numerical simulations is obtained starting from computed tomography (CT) scans of two patients provided by the Niguarda Hospital, Milan. The correct reconstruction of the pulmonary artery and the proper positioning of the valve, in its closed and open positions, are of utmost importance in reproducing the patient-specific hemodynamics.

3.1. Pulmonary artery

The first step consists in the segmentation process which has the goal of extracting the region of interest, in our case the pulmonary artery. Successively, since the segmented surface appears rough and irregular, principally due to the presence of noise in the clinical images, the quality of the surface and of the boundaries is improved.

In order to simplify the imposition of the boundary conditions, we do not consider the secondary branches of the pulmonary artery, but we consider two outlets only, the right and the left pulmonary arteries, of almost the same length.

We generate a hexahedral non-uniform mesh, with low characteristic length in correspondence of the valve, our region of interest, to ensure higher accuracy.

3.2. Pulmonary valve

Since the flow field strongly depends on the pulmonary valve function and geometrical configuration, it should be necessarily included in the model. The valve has to be first reconstructed and then correctly positioned in the artery. We are interested in both the open and closed configurations of the valve. All the steps have to be performed for both patients due to the patient-specificity of the model.

3.2.1 Reconstruction

Since the valve leaflets are not recognizable from the CT, due to its low resolution, a generic valve model has been employed. In particular the one provided by MOX Laboratory of Politecnico di Milano in the iHEART project, starting from a model developed by Zygote [www.zygote.com].

3.2.2 Positioning

The valve has to be first correctly oriented and then properly rotated in its orifice plane. The correct orientation is achieved by considering the positions of the valve sinuses and of the hexagonal stent, extracted from the CT, on which the prosthetic valve is mounted. Successively it undergoes a planar rotation to make the commissures (the area where the valve leaflets abut one another) conforming to those extracted from the CT.

Finally the valve is resized to correctly match the artery dimensions.

3.2.3 Open and closed configurations

The open configuration is geometrically reconstructed from the closed one. In particular, each point of the valve in the closed position has to be translated in order to obtain the open one. The open configuration is obtained by considering the distance from a circumference on the artery wall.

The displacement array joining the closed with the open configuration is provided to the 0D valve model, in order to define the valve opening field, together with the closed position.

4. Numerical results

The first step consists in proving the validity of the values of the parameters describing the pulmonary valve in the lumped-parameters model of the whole cardiovascular system, from which the boundary conditions are extracted, through a sensitivity analysis.
Successively we perform simulations focusing on the systolic phase, starting just before the valve opening, when the valve is still closed, and on the first part of the diastole, when the valve comes back to its closed configuration. To describe the open valve a proper opening field $\mathbf{g}$ has been introduced on the leaflets, i.e. the displacement array, joining the two valve configurations, previously reconstructed, so that the surface $\Gamma_{open} = \{\mathbf{x} = \widehat{\mathbf{x}} + \mathbf{g}(\widehat{\mathbf{x}}),\ \widehat{\mathbf{x}} \in \widehat{\Gamma}\}$, corresponds to an opening coefficient $c = 1$. As a preliminary test, a simulation with prescribed valve dynamics and instantaneous opening and closing was run to verify the pre-processing and mesh generation steps. Then, we address the 3D-0D coupled model through the results discussed in the following.

4.1. Calibration of the parameters

The aim is to tune the parameters in order for the model to be able to reproduce the physiological behavior of the pulmonary circulation, in terms of the overall trend of valve motion, the opening and closing times and the duration of the systole.
Beyond the valve modeling parameters showing up in equation (6), we introduce two more parameters: the first one takes into account the inertial properties of the leaflet and represents the scaling between the valve leaflets density and the blood density; the second term is summed up to $\widehat{H}$ in order for the elastic force to always act in the same verse. Thus the parameters to calibrate, both the value and the sign which is related to the geometrical visualization of the leaflets, are:

- damping β;
- elasticity γ.
- density scaling factor;
- initial curvature term.

The correct trend of leaflets motion is achieved by the identification of the correct sign of the parameters. On the other hand to obtain the correct times for the duration of the systole and the opening and closing stages we have to modify their values.
The opening stage is influenced by the parameter as follows : it is slowed down due to the presence of the damping term and due to an increase of the density scaling factor, while it is delayed if the elasticity parameter increases. We underline that the density scaling factor has to be taken sufficiently large in order to maintain the valve open after the opening phase, providing a sufficient inertia to the leaflets, and the elasticity parameter must not be excessively large otherwise the valve is not able to open during systole. Finally the initial curvature term is chosen in order for the elastic term to always have the same sign, physically meaning that the elastic force always acts in the same verse, that is pulling the leaflets to their closed configuration.
The opening phase shows some oscillations for any value of the parameters and the closing phase does not reproduce the physiological behavior, occurring when backflow is generated. An idea to cure these oscillations in the system is to modulate the intensity of the leaflets velocity $\mathbf{u}_\Gamma$, up to the quasi-static case $\mathbf{u}_\Gamma = \mathbf{0}$. In particular, we consider a factor $\eta \in [0, 1]$ multiplying $\mathbf{u}_\Gamma$ in the fluid momentum equation. This approximation allows to restore the correct trend of valve motion (Figure 2). It can be interpreted as an extra parameter in the Navier-Stokes equations and a re-calibration of the orifice size. Indeed, increasing the factor η, the orifice area increases, being the immersed surface perceived by the fluid as a smaller obstacle. Due to the patient-specificity of the model, the fraction of $\mathbf{u}_\Gamma$ which better allows to reproduce the physiological behavior is different for the two patients. The approximation physically violates the adherence of the blood to the moving valve, but only in a limited time and space.

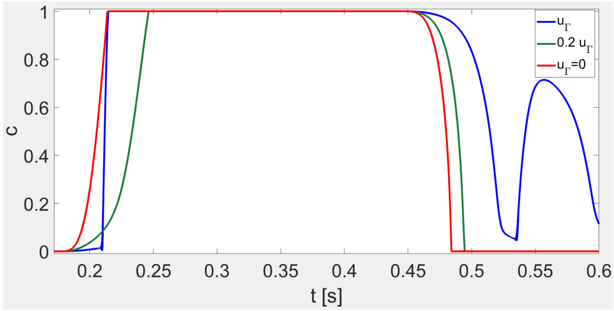

Figure 2: Valve opening coefficient.

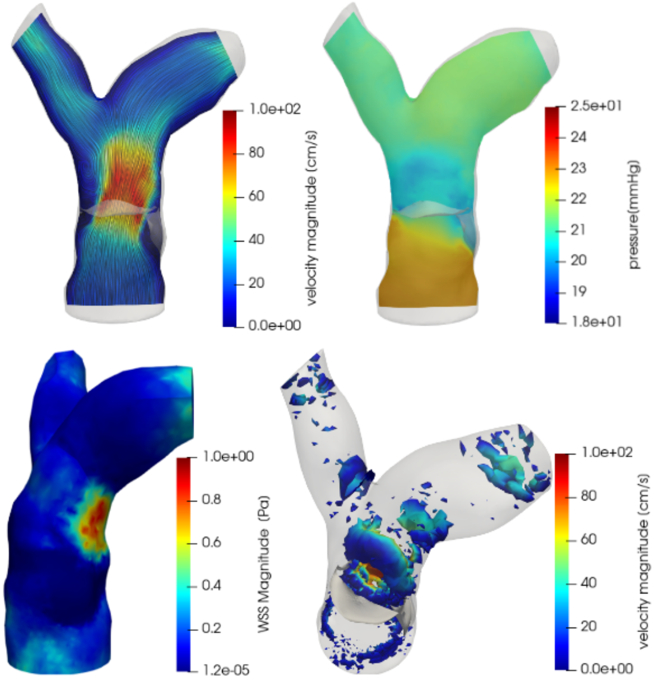

Figure 3: Flow quantities at systolic peak.

4.2. Results of the computational hemodynamic simulations

The results of the computational hemodynamic simulations concern the model parameters and the approximation of the leaflets velocity that better reproduce the physiological behavior.
The flow direction is influenced by the patient-specific valve geometry that leads to an asymmetric jet impinging on the pulmonary artery wall (Figure 3, *top left*).
When the valve is closed the whole pressure gradient develops within the 2ϵ valve thickness, showing the capacity of the method to reproduce the presence of the valve and its effectiveness in providing an obstacle to the flow, without the necessity of meshing the valve. We highlight that, in order to obtain this behavior, the parameter ϵ has to be chosen relying on the mesh size in the region of the valve, as a general guideline at least 1.5 times larger. When the valve is open the highest pressure gradient is localized among the leaflets, while, downstream to the valve the deviation of the flow induces a corresponding pressure peak near the wall and, as a result, a depression zone in the central part of the main pulmonary artery (Figure 3, *top right*).
The visualization of the wall shear stress (WSS) confirms the asymmetry of the velocity field (Figure 3, *bottom left*) and the Q-criterion isosurfaces highlight the presence of coherent structures, which enhance the efficiency of the blood supply (Figure 3, *bottom right*) .

5. Conclusions

We review the principal results:

- the pre-processing procedure succeeds in the reconstruction of the patient-specific pulmonary valve leaflets in both open and closed positions;
- the calibration procedure of the 0D valve model succeeds in reproducing the valve motion and the associated hemodynamics;
- the RIIS method is able to provide an effective obstacle to the blood flow and to capture the sharp pressure jump across the valve without meshing the leaflets;
- the patient specificity of the model is of utmost importance since the variability among different patients can be captured only considering the patient-specific pulmonary artery geometry and the patient-specific leaflets in the correct position.

Different directions can be undertaken in order to enhance this work: first the adoption of an implicit coupling between the blood and valve dynamics, instead of the explicit one; second, a further investigation on the leaflets velocity approximation or alternative strategies; third, the comparison with other 3D-0D FSI models; finally, the application of this model to other cardiac valves.

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