A PATIENT-SPECIFIC REDUCED-ORDER MODEL FOR CORONARY CIRCULATION

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ABSTRACT

We introduce a patient-specific model for coronary circulation, by combining anatomical, hemodynamic and functional information from medical images and other clinical observations. The main components of the coupled model are: a lumped heart model, a reduced-order model for hemodynamics in the arterial vessel tree (both healthy and stenosed), and a physiological model for the microvascular bed. The anatomy of the vessel tree is extracted from Coronary Computed Tomography Angiography (CTA) images, followed by an estimation of the impedance of the distal microvascular network. For the blood flow simulations, three states are modeled: rest, drug-induced hyperemia and intense exercise. The results show an excellent agreement with the literature and provide a model for virtual assessment of the flow and underlying functional measures in healthy and stenosed coronary arteries.

Index Terms - reduced-order model, coronary circulation, Coronary Computed Tomography, pressure drop, stenosis

1. INTRODUCTION

Coronary Artery Disease (CAD) is one of the leading causes of deaths worldwide, with an estimated 7.2 million deaths each year. In spite of the significant improvements in medical imaging and other diagnostic modalities, the incidence of premature morbidity and mortality for CAD patients is still very high, the main reason being the lack of accurate in-vivo and in-vitro patient-specific estimates for accurate diagnosis and decision support.

The main task of the coronary circulation is to supply adequate perfusion to the myocardium. As opposed to other organs, the coronary flow is high during diastole and low during systole. This is caused by the interaction between the coronary vessels and the myocardial contraction, which limits the flow during the systolic phase. In recent years, Computational Fluid Dynamics (CFD) based models have been proposed for analyzing the coronary circulation [1, 2, 3, 4], with promising results. The main challenges for such methods are the lack of patient-specific data including anatomy and boundary conditions, inefficient multi-scale coupling and the large-scale computational resources required for the complex simulations (often requiring several hours of simulations on large clusters). These challenges limit the scope of such methods in a routine clinical setting.

In this paper, we propose a coupled reduced-order model for analyzing the blood flow in patient-specific coronary vessel trees (both for healthy and stenotic vessels). The flow is computed under three conditions - normal resting, intracoronary drug-induced hyperemia and intense exercise to obtain functional parameters associated with the circulation. The proposed model is composed of axi-symmetric one-dimensional and lumped models of the coronary and systemic circulation, coupled with a heart model to include the effects of the myocardial contraction on the coronary flow (and provide the inflow). Patient-specific data is extracted from Coronary CTA scans by image segmentation, centerline extraction and lumen extraction.

The paper is organized as follows. In Section 2, we provide an overview of the proposed methodology. The results for three different scenarios are presented in Section 3, followed by a brief discussion on the future work.

2. METHODS

2.1. Anatomical model from Coronary CTA data

Image segmentation and centerline extraction is performed on CTA data, to extract the anatomy. It is transformed into a surface model, and a corresponding centerline tree with cross-section contours (and thus the cross-sectional area) at each point on the centerline tree (Figure 1).

2.2. Reduced-order coronary flow model at hyperemia

We model the aorta, the large arteries which are supplied by it (subclavian, brachiocephalic, common carotid) and the coronary epicardial vessels by axi-symmetric 1D vessel segments (see Figure 2), where the flow satisfies the following properties: conservation of mass, conservation of momentum, and a state equation for wall deformation (Equations 1-3). The vessel wall is modeled as a purely elastic material, with its properties determined through an empirical relationship fit to the measured data [5].
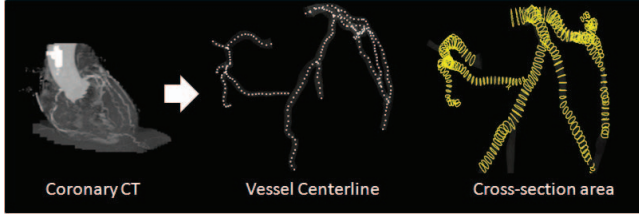
Figure 1: Anatomical Modeling

The inflow boundary condition is specified by an implicit coupling with the heart model, the outflow boundary condition is given by the implicit coupling with the lumped models of the vascular beds, while the junctions are solved by considering the continuity of total pressure and flow.

$$\frac{\partial A(t)}{\partial t} + \frac{\partial q(t)}{\partial x} = 0 \qquad (1)$$

$$\frac{\partial q(t)}{\partial t} + \frac{\partial}{\partial t}\left(\alpha \frac{q^2(t)}{A(t)}\right) + \frac{A(t)}{\rho}\frac{\partial p(t)}{\partial x} = K_R \frac{q(t)}{A(t)} \qquad (2)$$

$$p(t) = \frac{4}{3}\frac{Eh}{r_0}\left(1 - \sqrt{\frac{A_0}{A(t)}}\right) \qquad (3)$$

where q is the flow rate, A is the cross-sectional area, p is the pressure, α is the momentum-flux correction coefficient, K_R is a friction parameters, ρ is the density, E is the Young modulus, h is the wall thickness and r_0 is the initial radius.

The coronary microvascular beds are modeled through lumped or 0D models: the systemic beds are represented by regular windkessel elements, while coronary beds are represented by special models which account for the influence of the myocardial contraction on the flow waveform [6]. Figure 2 displays the detailed elements of this type of boundary condition.

An important aspect for the clinical decision making is the modeling of the hyperemic state. Hyperemia is obtained either through intense exercise or by drugs that are administered either intravenously or intracoronary. Since
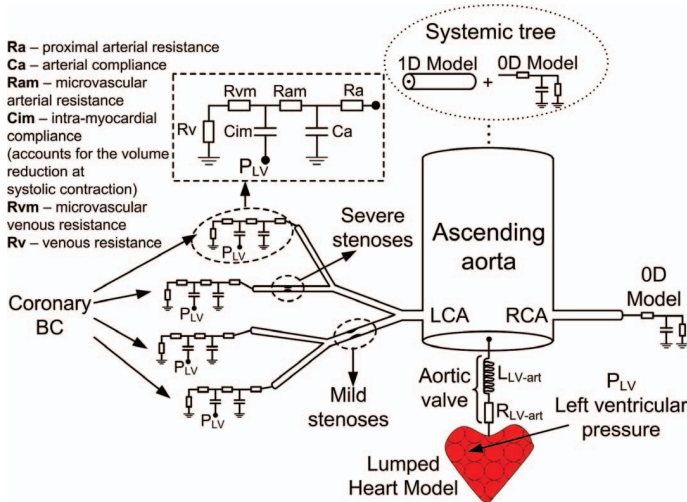

Figure 2: Proposed reduced-order model of the coronary circulation

measurements can not be taken reliably during intense exercise, drug-induced hyperemia is preferred. Intravenous administration of vasodilators leads to a slight increase of heart rate and decrease in blood pressure [7]. For simulations, the effect of an intracoronary vasodilator can be extended infinitely and this alternative to obtain hyperemia does not influence heart rate and blood pressure [7]. The resistance and compliance of the systemic or coronary lumped models (for the normal rest state) is obtained by imposing a structured-tree outflow boundary condition [5]. These impedance values are then adapted for the patient-specific model by a parameter estimation process. The hyperemic state is modeled through a corresponding decrease in the microvascular resistances, as caused by the administration of intracoronary adenosine [8] (epicardial arteries are not influenced by vasodilators [9]) and leads to a 3 to 5 fold increase in the coronary flow.

The third major component of the blood flow model is a lumped heart model. Several models have been proposed that can determine the pressure and the flow in the different heart chambers. Several parameters like contractility, stroke volume, time-to-maximum, dead volume (V_0) or heart rate can be adapted in order to account for different states of the body and to personalize the model. For the current study, a varying elastance model (Equation 4) has been used, which is coupled to the aortic input through a lumped aortic valve model (Figure 2) and indirectly coupled to the specialized microvascular models of the coronary arterial tree through the left ventricular pressure.

$$E(t) = \frac{P_{LV}(t)}{V_{LV}(t) - V_0}. \qquad (4)$$

For the intense exercise state, the hyperemic coronary resistances are used; the systemic resistances are decreased correspondingly, while the heart rate and the contractility are increased correspondingly. Several considerations have led to the modeling of all major arteries of the systemic tree and not only of the coronary arterial tree. This way the heart is directly coupled to the aorta and the flow is determined by the interaction between the left ventricle and the systemic impedance. The overall pressure is mainly determined by the large arteries, while the coronary resistances (microvascular and stenosis-based) have a negligible influence and hence the trans-stenotic pressure drops can be modeled more precisely.

2.3. Stenosis model

The patient-specific coronary tree is coupled with stenosis segments. One of the assumptions made during the derivation of the reduced-order model is that the axial velocity is dominant and the radial components are negligible. This assumption holds well for normal, healthy vessels, but in case of sudden changes in lumen diameter, e.g. for a stenosis, the radial components can no longer be

excluded. Much attention has been directed towards the local velocity fields, but for the overall functional assessment the trans-stenotic pressure drop is the most important. Previous works have included semi-empirical stenosis models in 1D blood flow models [10, 11] and have obtained good results compared to full-scale models. The pressure drop is expressed as a sum of three terms (viscous term, turbulent or Bernoulli term and inertance term):

$$\Delta P_s = \frac{\mu K_v}{2\pi r_0^3} q + \frac{\rho K_t}{2 A_0^2}\left(\frac{A_0}{A_s}-1\right)^2 |q|q + \frac{\rho K_u L_s}{A_0}\frac{\partial q}{\partial t} \quad (5)$$

where μ is the blood viscosity, L_s is the stenosis length, K_v, K_t and K_u are the viscous, turbulent and inertance coefficient respectively (quantities indexed with 0 refer to the normal vessel while s refers to the stenosis). The segments treated as stenosis segments are coupled to the regular segments by considering continuity of total pressure and of flow rate.

3. RESULTS

The system of equations in the reduced-order arterial model are solved using a finite-difference approach and the two-step Lax-Wendroff method, with a grid-spacing of 0.1 cm and a time step of 2.5e-5s. The average computation time for each cardiac cycle was 54.3 seconds. The patient-specific coronary geometry is displayed in Figure 3a. The coronary arterial tree has been simulated during rest, at hyperemia and during intense exercise. As specified, the coronary geometry has been coupled to a general model of the systemic circulation comprising 9 segments (the coronary model contains 15 segments). There are two locations with significant narrowing of the vessel, hence two stenosis segments are included inside the model in the left coronary tree: a mild stenosis (Figure 3b) with 48% area reduction, and a mild to moderate stenosis (Figure 3c) with a 67% area reduction).

Figure 4 displays a flow waveform comparison with waveforms reported in literature for the rest state (the waveforms are normalized since they were recorded at different locations and on different models). All three waveforms display the typical low systole and high diastole flow; diastolic decays are similar while the minor differences at systole can be explained through the different coronary models adopted. The simulation parameters and the results are tabulated in Table 1. There are several other parameters, which are adopted and which are independent of the state: dead volume of the heart (V_0=10ml), stroke volume (V=120ml), minimum elastance value (E_{min}=0.08 mmHg/ml), aortic valve resistance (R_{LV-art}=10.0 g/cm^{4}s), aortic valve inertance (L_{LV-art}=0.69 g/cm^4). The results obtained for the rest state are within normal average values, coronary flow represents 4.28% of the total flow (4 - 5% is the average value).

For simulating drug-induced intracoronary hyperemia, only the lumped parameters of the left coronary tree are adapted. Average pressure was found to be almost identical, as reported by invasive measurements [7]. The slight decrease is caused by the decrease of the left coronary resistance. Cardiac output and right coronary flow are almost unchanged. Left coronary flow experiences a three-to-fourfold increase which is again within measured ranges of three-to-five. For the intense exercise state, the left coronary microvascular parameters are identical to the ones used during hyperemia while the other lumped models, namely the right coronary and systemic, are adapted correspondingly. Average aortic pressures increases by around 10mmHg, while the cardiac output triples. The simulation corresponds to a heart rate of around 171 bpm. Coronary flow represents 5.62% of total flow. This increase compared to the rest value can be explained as follows: since oxygen extraction in the coronary capillaries is close to maximum levels even at rest state, the increased metabolic need can be satisfied only through an increased flow. On the other side, skeletal muscles can increase oxygen extraction and thus compensate the increased metabolic need not only through a rise in flow rate.
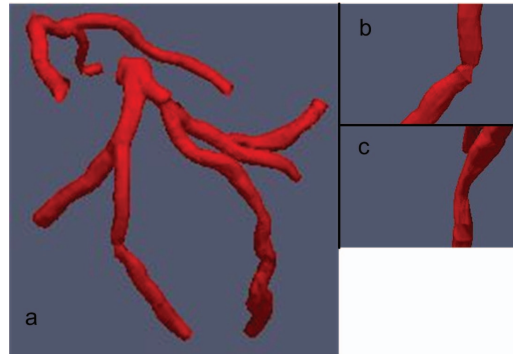

Figure 3: (a) Patient-specific coronary tree, (b) stenosis 1 (48% area reduction), (c) stenosis 2 (67% area reduction)
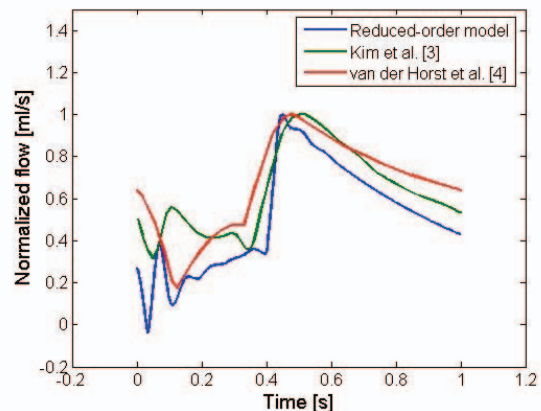

Figure 4: Coronary flow waveform comparison

State	E_{max} [mmHg/ml]	t_{max} [s]	T [s]	Pa [mmHg]	Cardiac output [ml/min]	Left coronary flow [ml/min]	Right coronary flow [ml/min]
Normal (Rest)	2.1	0.35	1	85.73	3754.6	102.44 (2.73%)	58.32 (1.55%)
Hyperemia	2.1	0.35	1	84.23	3788.9	350.13 (9.24%)	54.91 (1.45%)
Intense exercise	2.3	0.17	0.35	95.98	11395.8	437.23 (3.84%)	203.54 (1.78%)

Table 1: Simulation parameters and results

The average pressures distal and proximal to the stenosis at normal and hyperemia state are listed in Table 2. In order to investigate the effect of a more pronounced occlusion, the severity of the second stenosis has been virtually increased and the results are displayed in the last two columns. Average proximal pressures (Pa) are close to the aortic average pressure (Table 1) since the pressure loss along the large epicardial arteries is very small. Distal average pressures are close to the proximal pressures during rest state, even for the virtual severe stenosis. At hyperemia, the trans-stenotic pressure drop along the two stenosis of the patient-specific model is functionally insignificant. On the other side, the virtual severe stenosis introduces a functionally significant pressure drop. Figures 5 a, b show the time-varying pressures for the second stenosis (67% area reduction).

4. CONCLUSIONS

We have introduced a reduced-order model for patient-specific coronary circulation which determines the distribution of time-varying and average flow and pressure in the coronary tree extracted from CTA images. Three different patient-states are simulated. In terms of clinical diagnosis and decision-making the most important one is the drug-induced intracoronary hyperemia, since values of different indices such as FFR (Fractional Flow Reserve) may be estimated. In terms of computation time, the proposed reduced-order model is significantly faster (at least two orders of magnitude) when compared to the full-order models reported in the literature, thereby making it amenable in a clinical setting.

State	Stenoses 1 (48% AR)		Stenoses 2 (67% AR)		Stenoses 2' (84% AR)	
	Pa	Pd	Pa	Pd	Pa	Pd
At Rest	85.39	84.98	85.16	84.23	85.12	78.13
Hyperemia	83.31	81.37	83.09	78.57	82.93	58.16

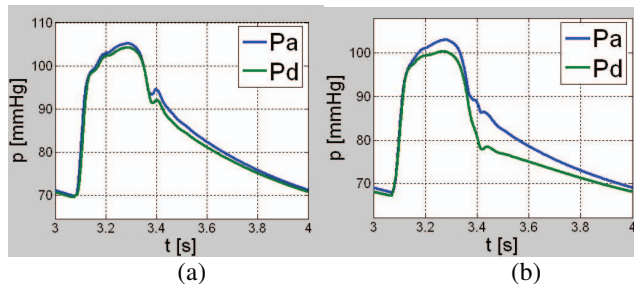Table 2: Stenosis distal and proximal average pressures [mmHg]

Figure 5: Proximal and distal time-varying pressures for stenoses 2, (a) - at rest, (b) – at hyperemia

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