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Developing computational methods for three-dimensional finite element simulations of coronary blood flow

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ABSTRACT

Coronary artery disease contributes to a third of global deaths, afflicting seventeen million individuals in the United States alone. To understand the role of hemodynamics in coronary artery disease and better predict the outcomes of interventions, computational simulations of blood flow can be used to quantify coronary flow and pressure realistically. In this study, we developed a method that predicts coronary flow and pressure of three-dimensional epicardial coronary arteries by representing the cardiovascular system using a hybrid numerical/analytic closed loop system comprising a threedimensional model of the aorta, lumped parameter coronary vascular models to represent the coronary vascular networks, three-element Windkessel models of the rest of the systemic circulation and the pulmonary circulation, and lumped parameter models for the left and right sides of the heart. The computed coronary flow and pressure and the aortic flow and pressure waveforms were realistic as compared to literature data.

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1. Introduction

Computational simulations have become a useful tool in studying blood flow in the cardiovascular system [37], enabling quantification of hemodynamics of healthy and diseased blood vessels [7,22,36], design and evaluation of medical devices [17,34], planning of vascular surgeries, and prediction of the outcomes of interventions [19,31,38]. Much progress has been made in computational simulations of blood flow as the computing capacity and numerical methods have advanced. In particular, more realistic boundary conditions have been developed in an effort to consider the interactions between the computational domain and the absent upstream and downstream vasculatures considering the closed loop nature of the cardiovascular system. These boundary conditions represent the upstream and downstream vasculatures using simple models such as resistance, impedance, lumped parameter models, and onedimensional models and couple to computational models either explicitly or implicitly [9,14,19,24,42].

These boundary conditions can be utilized to quantify flow and pressure fields in the epicardial coronary arteries. However, unlike other parts of the cardiovascular system, prediction of

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coronary blood flow exhibits greater complexity because coronary flow is influenced by the contraction and relaxation of the ventricles in addition to the interactions between the computational domain and the absent upstream and downstream vasculatures. Unlike flow in other parts of the arterial system, coronary flow decreases in systole when the ventricles contract and compress the intramyocardial coronary vascular networks and increases in diastole when the ventricles relax. Thus, to model coronary flow realistically, we need to consider the compressive force of the ventricles, which causes the intramyocardial pressure, acting on the coronary vessels throughout the cardiac cycle.

Most previous studies on coronary flow and pressure using three-dimensional finite element simulations ignored the intramyocardial pressure, and prescribed, not predicted, coronary flow. Further, these studies generally used traction-free outlet boundary conditions [2,3,11,20,21,23,25,27,32,43,47,48] and did not compute realistic pressure fields. Migliavacca et al. [15,19] computed three-dimensional pulsatile coronary flow and pressure in a single coronary artery by considering the intramyocardial pressure but this study was performed with an idealized model and low mesh resolution. Additionally, the analytic models used as boundary conditions were coupled explicitly, necessitating either subiterations within the same time step or a small time step size bounded by the stability of an explicit time integration scheme. To predict physiologically realistic flow rate and pressure in the coronary arterial trees of a patient, computational simulations should be robust and stable enough to handle complex flow

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characteristics, and the coupling should be efficient and versatile with different levels of mesh refinement [13].

In this paper, we describe methods to calculate flow and pressure in three-dimensional coronary vascular beds by considering a hybrid numerical/analytic closed loop system. For each coronary outlet of the three-dimensional finite element model, we coupled a lumped parameter coronary vascular bed model and approximated the impedance of downstream coronary vascular networks not modeled explicitly in the computational domain. Similarly, we assigned Windkessel models to the upper branch vessels and the descending thoracic aorta to represent the rest of the systemic circulation. These outlets feed back to the heart model representing the right side of the heart and travel to the pulmonary circulation, which is approximated with a Windkessel model. For the inlet, we coupled a lumped parameter heart model that completes a closed-loop description of the system. Using the heart model, it is possible to compute the compressive forces acting on the coronary vascular beds throughout the cardiac cycle. Further, we enforced the shape of velocity profiles of the inlet and outlet boundaries with retrograde flow to minimize numerical instabilities [13]. We solved for coronary flow and pressure as well as aortic flow and pressure in subject-specific models by considering the interactions between these model of the heart, the impedance of the systemic arterial system and the pulmonary system, and the impedance of coronary vascular beds.

2. Methods

2.1. Three-dimensional finite element model of blood flow and vessel wall dynamics

Blood flow in the large vessels of the cardiovascular system can be approximated by a Newtonian fluid [22]. In this study, we solved blood flow using the incompressible Navier–Stokes equations and modeled the motion of the vessel wall using the elastodynamics equations [8].

For a fluid domain Ω with boundary Γ and solid domain Ω^s with boundary Γ^s , we solve for velocity $\vec{v}(\vec{x}, t)$, pressure $p(\vec{x}, t)$, and wall displacement $\vec{u}(\vec{x}^s, t)$ [8,4] as follows:

Given $\vec{f}: \Omega \times (0,T) \to \mathbb{R}^3$, $\vec{f}^s: \Omega^s \times (0,T) \to \mathbb{R}^3$, $\vec{g}: \Gamma_g \times (0,T) \to \mathbb{R}^3$, $\vec{g}: \Gamma_g \times (0,T) \to \mathbb{R}^3$, $\vec{g}^s: \Gamma_g^s \times (0,T) \to \mathbb{R}^3$, $\vec{v}_0: \Omega \to \mathbb{R}^3$, $\vec{u}_0: \Omega^s \to \mathbb{R}^3$, and $\vec{u}_{0,t}: \Omega^s \to \mathbb{R}^3$, find $\vec{v}(\vec{x},t)$, $p(\vec{x},t)$, and $\vec{u}(\vec{x}^s,t)$ for $\forall \vec{x} \in \Omega$, $\forall \vec{x}^s \in \Omega^s$, and $\forall t \in (0,T)$, such that the following conditions are satisfied:

$$\rho \vec{v}_{,t} + \rho \vec{v} \cdot \nabla \vec{v} = -\nabla p + div(\tau) + \vec{f} \quad \text{for } (\vec{x}, t) \in \Omega \times (0, T)$$

 $div(\vec{v}) = 0$ for $(\vec{x}, t) \in \Omega \times (0, T)$

$$\rho^{s}\vec{u}_{,tt} = \nabla \cdot \underset{\sim}{\sigma}^{s} + \vec{f}^{s} \quad \text{for}(\vec{x}^{s}, t) \in \Omega^{s} \times (0, T)$$

where

$$\tau = \mu (\nabla \vec{v} + (\nabla \vec{v})^T)$$
 and $\sigma^s = C : \frac{1}{2} (\nabla \vec{u} + (\nabla \vec{u})^T)$ (1)

with the Dirichlet boundary conditions,

 $\vec{v}(\vec{x},t) = \vec{g}(\vec{x},t) \text{ for } (\vec{x},t) \in \Gamma_g \times (0,T)$

 $\vec{u}(\vec{x}^{s}, t) = \vec{g}^{s}(\vec{x}^{s}, t) \text{ for } (\vec{x}^{s}, t) \in \Gamma_{g}^{s} \times (0, T)$ (2)

the Neumann boundary conditions,

$$\vec{t}_{\vec{n}} = [-p \, I + \tau] \vec{n} = \vec{h}(\vec{v}, p, \vec{x}, t) \quad \text{for } \vec{x} \in \Gamma_h$$
(3)

and the initial conditions,

 $\vec{v}(\vec{x}, 0) = \vec{v}_0(\vec{x}) \quad \text{for } \vec{x} \in \Omega$

$$\vec{u}(\vec{x}^{s}, 0) = \vec{u}_{0}(\vec{x}^{s}) \quad \text{for } \vec{x}^{s} \in \Omega^{s}$$
$$\vec{u}_{t}(\vec{x}^{s}, 0) = \vec{u}_{0,t}(\vec{x}^{s}) \quad \text{for } \vec{x}^{s} \in \Omega^{s}$$
(4)

For fluid–solid interface conditions, we use the conditions implemented in the coupled momentum method with a fixed fluid mesh assuming small displacements of the vessel wall [8].

The density ρ and the dynamic viscosity μ of the fluid, and the density ρ^s of the vessel walls are assumed to be constant. The external body force on the fluid domain is represented by \vec{f} . Similarly, \vec{f}^s is the external body force on the solid domain, *C* is a fourth-order tensor of material constants, and σ^s is the vessel wall stress tensor.

We utilized a stabilized semi-discrete finite element method, based on the ideas developed by Brooks and Hughes [4], Franca and Frey [10], Taylor et al. [39], and Whiting et al. [44] to use the same order piecewise polynomial spaces for velocity and pressure variables.

2.2.. Boundary conditions

The boundary Γ of the fluid domain is divided into a Dirichlet boundary portion Γ_g and a Neumann boundary portion Γ_h . Further, we divide the Neumann boundary portion Γ_h into coronary surfaces $\Gamma_{h_{cor}}$, inlet surface Γ_{in} , and the set of other outlet surfaces Γ'_h , such that $\overline{(\Gamma_{h_{cor}} \cup \Gamma_{in} \cup \Gamma'_h)} = \Gamma_h$ and $\Gamma_{h_{cor}} \cap \Gamma_{in} \cap \Gamma'_h = \phi$. Note that for this study, when the aortic valve is open, the inlet surface is included in the Neumann boundary portion Γ_h , not in the Dirichlet boundary portion Γ_g to enable coupling with a lumped parameter heart model. Therefore, the Dirichlet boundary portion Γ_g only consists of the inlet and outlet rings of the computational domain when the aortic valve is open. These rings are fixed in time and space [8].

2.2.1. Boundary conditions for coronary outlets

To represent the coronary vascular beds absent in the computational domain, we used a lumped parameter coronary vascular model developed by Mantero et al. [18] (Fig. 1). The coronary venous microcirculation compliance was eliminated from the original model in order to simplify the numerics without affecting the shape of the flow and pressure waveforms significantly. Each coronary vascular bed model consists of coronary arterial resistance R_a , coronary arterial compliance C_a , coronary arterial microcirculation resistance $R_{a-micro}$, myocardial compliance C_{im} , coronary venous microcirculation resistance $R_{v-micro}$, coronary venous resistance R_v , and intramyocardial pressure $P_{im}(t)$.

For each coronary outlet $\Gamma_{h_{cor_k}}$ of the three-dimensional finite element model where $\Gamma_{h_{cor_k}} \subseteq \Gamma_{h_{cor}}$, we implicitly coupled the lumped parameter coronary vascular model using the continuity of mass and momentum operators of the coupled multidomain method [41] as follows:

$$\begin{split} & [\underbrace{M}_{\sim m}(\vec{v},p) + \underbrace{H}_{\sim m}] \\ &= -\left(R\int_{\Gamma_{h_{cor_{k}}}} \vec{v}(t) \cdot \vec{n} \, d\Gamma + \int_{0}^{t} e^{\lambda_{1}(t-s)} Z_{1} \int_{\Gamma_{h_{cor_{k}}}} \vec{v}(s) \cdot \vec{n} \, d\Gamma \, ds\right) I_{\sim} \\ &\quad + \left(\int_{0}^{t} e^{\lambda_{2}(t-s)} Z_{2} \int_{\Gamma_{h_{cor_{k}}}} \vec{v}(s) \cdot \vec{n} \, d\Gamma \, ds - \vec{n} \cdot \underbrace{\tau}_{\sim} \cdot \vec{n}\right) I_{\sim} + \underbrace{\tau}_{\sim} - (Ae^{\lambda_{1}t} + Be^{\lambda_{2}t}) I_{\sim} \\ &\quad - \left(\int_{0}^{t} e^{\lambda_{1}(t-s)} \cdot Y_{1} P_{im}(s) \, ds + \int_{0}^{t} e^{\lambda_{2}(t-s)} \cdot Y_{2} P_{im}(s) \, ds\right) I_{\sim} \\ & [\vec{M}_{c}(\vec{v},p) + \vec{H}_{c}] = \vec{v} \end{split}$$
(5)



Fig. 1. Schematic of closed loop system including lumped parameter models of the right and left atria and ventricles. The aortic inlet is coupled to the lumped parameter model of the left ventricle at (A). All the outlets of the three-dimensional computational model feed back in the lumped model at (V). The lumped parameter models coupled to the inlet, upper branch vessels, the descending thoracic aorta, and coronary outlets for simulations of blood flow in a normal thoracic aorta model with coronary outlets under rest and exercise conditions are shown on the right. Note that all the outlets of the three-dimensional computational model feed back in the lumped model at (V).

Table 1

Parameter values of the closed loop system at rest and during exercise for the simulations of coronary flow and pressure with normal coronary anatomy.

	Rest	Exercise		Rest	Exercise
Parameter values of the left and right sides of the heart					
R_{LA-V} (dynes s/cm ⁵)	5	5	R _{RA-V} (dynes s/cm ⁵)	5	5
L_{LA-V} (dynes s ² /cm ⁵)	5	5	L_{RA-V} (dynes s ² /cm ⁵)	1	1
R_{LV-art} (dynes s/m ⁵)	10	10	R _{RV-art} (dynes s/m ⁵)	10	10
L_{LV-art} (dynes s ² /cm ⁵)	0.69	0.69	L_{RV-art} (dynes s ² /cm ⁵)	0.55	0.55
$E_{LV,max}$ (mmHg/cc)	2.0	2.0	$E_{RV,max}$ (mmHg/cc)	0.5	0.5
$V_{LV,0}$ (cc)	0	0	$V_{RV,0}$ (cc)	0	0
$V_{LA,0}(cc)$	-60	-60	$V_{RA,0}$ (cc)	-60	-60
E_{LA} (mmHg/cc)	270	350	$E_{\rm RA} (mmHg/cc)$	60	80
Other renews to realize	_				
Other parameter value	5	0.25	Cardian mula (a)	1.0	0.5
$l_{max}(S)$	0.33	0.25	Cardiac cycle (S)	1.0	0.5
R_{pp} (dynes s/m ³)	10	10	C_p (cm ² /dynes)	0.022	0.022
κ_{pd} (dynes s/m ²)	144	144			

where the parameters *R*, *Z*₁, *Z*₂, *A*, *B*, *Y*₁, *Y*₂, λ_1 , λ_2 are derived from the lumped parameter coronary vascular models.

The intramyocardial pressure P_{im} representing the compressive force acting on the coronary vessels due to the contraction and relaxation of the left and right ventricles was modeled with either the left or right ventricular pressure depending on the location of the coronary arteries. Both the left and right ventricular pressures were computed from two lumped parameter heart models of the closed loop system (Fig. 1).

2.2.2. Boundary conditions for the inlet

The left and right sides of the heart were modeled using a lumped parameter heart model developed by Segers et al. [29]. Each heart model consists of a constant atrial elastance E_{A} , atrioventricular valve, atrio-ventricular valvular resistance R_{A-V} , atrio-ventricular inductance L_{A-V} , ventriculo-arterial valve, ventriculo-arterial valvular resistance R_{V-art} , ventriculo-arterial inductance L_{V-art} , and time-varying ventricular elastance E(t).

An atrio-ventricular inductance L_{A-V} and ventriculo-arterial inductance L_{V-art} were added to the model in order to approximate the inertial effects of blood flow.

The time-varying elastance E(t) models the contraction and relaxation of the left and right ventricles. Elastance is the instantaneous ratio of ventricular pressure $P_v(t)$ and ventricular volume $V_v(t)$ according to the following equation:

$$P_{\nu}(t) = E(t) \cdot [V_{\nu}(t) - V_0]$$
(6)

Here, V_0 is a constant correction volume, which is recovered when the ventricle is unloaded.

Each elastance function is derived by scaling a normalized elastance function, which remains unchanged regardless of contractility, vascular loading, heart rate and heart disease, [30,35] to approximate the measured cardiac output, pulse pressure, and contractility of each subject.

The left side of the heart lumped parameter model [29] is coupled to the inlet of the finite element model using the coupled multidomain method [41] when the aortic valve is open [14] as follows:

$$\begin{split} [\underbrace{M}_{\sim m}(\vec{v}, p) + \underbrace{H}_{\sim m}]_{\Gamma_{in}} &= -E(t) \cdot \left\{ V_{LV}(t_{ao,LV}) + \int_{t_{ao,LV}}^{t} \int_{\Gamma_{in}} \vec{v} \cdot \vec{n} \, d\Gamma \, ds - V_{LV,0} \right\} \underbrace{I}_{\sim} \\ &- \left(R_{LV-art} + L_{LV-art} \, \frac{d}{dt} \right) \int_{\Gamma_{in}} \vec{v} \cdot \vec{n} \, d\Gamma \, \underbrace{I}_{\sim} + \underbrace{\tau}_{\sim} \\ &- (\vec{n} \cdot \tau \cdot \vec{n}) \, I \end{split}$$
(7)

 $[\vec{M}_c(\vec{v}, p) + \vec{H}_c]_{\Gamma_{in}} = \vec{v} | \Gamma_{in}$

Here, $t_{ao,LV}$ is the time the aortic valve opens. When the valve is closed, we switched the inlet boundary to a Dirichlet boundary and assigned a zero velocity condition.

2.2.3. Boundary conditions for other outlets

For the other boundaries Γ'_h , we used the same method to couple three-element Windkessel models and modeled the continuity of momentum and mass using the following

Table 2

Parameter values of the three-element Windkessel models at rest and during exercise for the simulations of coronary flow and pressure with normal coronary anatomy. Note that the parameter values of the upper branch vessels are the same for the light exercise condition.

	B: Right subclavian	C: Right carotid	D: Right vertebral
Parameter values of the Windkessel is $R_p (10^3 \text{ dynes s/cm}^5)$ $C(10^{-6} \text{cm}^5/\text{dynes})$ $R_d (10^3 \text{ dynes s/m}^5)$	nodels 1.49 235 15.1	1.41 248 14.3	10.7 32.9 108
	E: Left carotid	F: Left vertebral	G: Left subclavian
$R_p (10^3 \text{ dynes s/m}^5)$ $C(10^{-6} \text{cm}^5/\text{dynes})$ $R_d (10^3 \text{ dynes s/m}^5)$	1.75 201 17.6	7.96 44.0 80.5	1.80 195 18.2
	H: Descending thoracic aorta (rest)	H: Descending thoracic aorta (exercise)	
$R_p (10^3 \text{ dynes s/m}^5)$ $C(10^{-6} \text{ cm}^5/\text{dynes})$ $R_d (10^3 \text{ dynes s/m}^5)$	0.227 1540 2.29	0.180 1600 0.722	

operators [42]:

$$\begin{split} [\underbrace{M}_{\sim m}(\vec{v},p) + \underbrace{H}_{\sim m}]_{\Gamma'_{h}} &= -\left\{ R_{p} \int_{\Gamma'_{h}} \vec{v} \cdot \vec{n} ds + (R_{p} + R_{d}) \int_{0}^{t} \frac{e^{-(t-t_{1}/\tau)}}{C} \int_{\Gamma'_{h}} \vec{v} \cdot \vec{n} ds dt_{1} \right\} \\ &+ \{ (P(0) - R \int_{\Gamma'_{h}} \vec{v}(0) \cdot \vec{n} ds - P_{d}(0)) e^{-t/\tau} - p_{d}(t) \} \underbrace{I}_{\sim} \\ &+ \underbrace{\tau}_{\sim} - \vec{n} \cdot \underbrace{\tau}_{\sim} \cdot \vec{n} \underbrace{I}_{\sim} \end{split}$$

 $[\vec{M}_c(\vec{v}, p) + \vec{H}_c]_{\Gamma'_h} = \vec{v}$

2.3. Closed loop model

The boundary conditions combined with the three-dimensional finite element model of the aorta constitute a closed loop model of the cardiovascular system. The closed loop model consists of two lumped parameter heart models representing the left and right sides of the heart, a three-dimensional finite element model of the aorta with coronary arteries, threeelement Windkessel models and lumped parameter coronary vascular models that represent the rest of the systemic circulation, and a three-element Windkessel model to approximate the pulmonary circulation. This closed loop model is used to compute the right ventricular pressure, which is used to approximate the intramyocardial pressure acting on the right coronary arteries.

2.4. Parameter values

2.4.1. Choice of the parameter values for coronary boundary conditions

The boundary condition parameters determining the mean flow to each primary branch of the coronary arteries were obtained using morphology data and data from the literature [12,49]. We assumed that the mean coronary flow is 4.0 % of the cardiac output [1]. For each coronary outlet surface, coronary venous resistance was calculated on the basis of the mean flow and assigned venous pressure according to literature data [1]. We then obtained the coronary arterial resistance and coronary arterial microcirculation resistance on the basis of mean flow, mean arterial pressure, and the coronary impedance spectrum

Table 3

Parameter values of the lumped parameter models of the coronary vascular beds for the simulations of coronary flow and pressure with normal coronary anatomy.

	Ra	R _{a-micro}	$R_{\nu} + R_{\nu-micro}$	Ca	Cim	
Parameter values of the coronary models at rest						
(Resistance in 10^3 dynes s/m ⁵ and capacitance in 10^{-6} cm ⁵ /dynes)						
a: LAD1	183	299	94	0.34	2.89	
b: LAD2	131	214	67	0.48	4.04	
c: LAD3	91	148	65	0.49	4.16	
d: LAD4	55	90	40	0.80	6.82	
e: LCX1	49	80	25	1.28	10.8	
f: LCX2	160	261	82	0.39	3.31	
g: LCX3	216	353	111	0.29	2.45	
h: LCX4	170	277	87	0.37	3.12	
i: RCA1	168	274	86	0.37	3.15	
j: RCA2	236	385	121	0.26	2.24	
k: RCA3	266	435	136	0.23	1.99	
	Ra	R _{a-micro}	$R_{\nu} + R_{\nu-micro}$	Ca	C _{im}	
Parameter values of the coronary models at exercise						

(Resistance in 10^3 dynes s/m ⁵ and capacitance in 10^{-6} cm ⁵ /dynes)					
a: LAD1	76	24	18	0.75	6.88
b: LAD2	52	16	13	1.02	9.34
c: LAD3	51	16	12	1.07	9.74
d: LAD4	31	10	7	0.74	15.9
e: LCX1	20	6.2	5	2.79	25.4
f: LCX2	65	20	15	0.85	7.78
g: LCX3	87	27	21	0.63	5.74
h: LCX4	68	21	16	0.80	7.29
i: RCA1	71	22	16	0.83	7.60
j: RCA2	98	31	23	0.59	5.38
k: RCA3	110	35	25	0.52	4.72

using literature data [6,40,45]. The capacitance values were adjusted to give physiologically realistic coronary flow and pressure waveforms.

During simulated exercise, the mean flow to the coronary vascular bed was increased to maintain the mean flow at 4.0% of the cardiac output. The coronary parameter values for each coronary outlet surface were modified by increasing the capacitances and the ratio of the coronary arterial resistance to the total coronary resistance [6,40,45].



Fig. 2. Flow and pressure waveforms of the upper branch vessels and the descending thoracic aorta at rest and during exercise.



Fig. 3. Pressure-volume loops of the left and right ventricles and flow and pressure waveforms of the aortic inlet. The aortic pressure waveforms are plotted with the left and right ventricular pressure.

2.4.2. Choice of the parameter values for the inflow boundary condition

The parameter values of the lumped parameter heart model were determined as follows [29,30]:

 $t_{max,LV} = t_{max,RV}$ = $\begin{cases} \frac{T}{3} & \text{at rest, where } T \text{ is the measured cardiac cycle} \\ 0.5T & \text{during exercise} \end{cases}$

 $E_{max,LV} = \frac{\gamma \cdot R_S}{T}$, where R_S

is the total resistance of the systemic circulation and $1 \leq \gamma \leq 2$

 $E_{max,RV} = \frac{\gamma \cdot R_P}{T}$, where R_P is the total resistance of the pulmonary circulation and $1 \le \gamma \le 2$

$$V_{LV,0} = V_{LV,esv} - \frac{0.9P_{sys}}{E_{max,LV}}$$
, where $V_{LV,esv}$

is an end - systolic volume of the left ventricle and

 P_{sys} is an aortic systolic pressure

2.4.3. Choice of the parameter values for other outlet boundary conditions

For the upper branch vessels and the descending thoracic aorta, three-element Windkessel models were adjusted to match mean flow distribution and the measured brachial artery pulse pressure by modifying the total resistance, capacitance, and the ratio between the proximal resistance and distal resistance based on literature data [16,28,33,46].

2.5. Constraining shape of velocity profiles to stabilize blood flow simulations

Using these sets of boundary conditions, we simulated physiologic coronary flow of subject-specific computer models. When we first simulated blood flow in complex subject-specific models with high mesh resolutions, however, we encountered instabilities in the outlet boundaries caused by complex flow structures, such as retrograde flow or complex flow propagating to the outlets from the interior domain due to vessel curvature or branches.

To resolve these instabilities, we developed an augmented Lagrangian method to enforce the shape of the velocity profiles of the inlet boundary and the outlet boundaries with complex flow features or retrograde flow [13]. The constraint functions enforce a shape of the velocity profile on a part of Neumann partition Γ_{h_k} and minimize in-plane velocity components:

$$c_{k1}(\vec{v}, \vec{x}, t) = \alpha_k \int_{\Gamma_{h_k}} (\vec{v}(\vec{x}, t) \cdot \vec{n} - \Phi_k (\vec{v}(\vec{x}, t), \vec{x}, t))^2 \, ds = 0, \quad \vec{x} \in \Gamma_{h_k}$$

$$c_{ki}(\vec{v}, \vec{x}, t) = \alpha_k \int_{\Gamma_{h_k}} (\vec{v}(\vec{x}, t) \cdot \vec{t}_i)^2 \, ds = 0 \quad \text{for } i = 2, 3 \tag{8}$$

Here, $\Phi_k(\vec{v}(\vec{x},t),\vec{x},t)$ defines the shape of the normal velocity profile, \vec{n} is the unit normal vector of face Γ_{h_k} , $\vec{t_2}$ and $\vec{t_3}$ are unit in-plane vectors which are orthogonal to each other and to the unit normal vector \vec{n} at face Γ_{h_k} . α_k is used to nondimensionalize the constraint functions.

The boxed terms below are added to the weak form of the governing equations of blood flow and wall dynamics. The weak form becomes:

Find $\vec{v} \in S$, $p \in \mathcal{P}$ and $\vec{\lambda}_1, \vec{\lambda}_2, \dots, \vec{\lambda}_{n_c} \in (L^2(0,T))^{n_{sd}}$, $\vec{\kappa}_k \in \mathcal{R}^{n_{sd}}$, Penalty numbers where $k = 1, \dots, n_c$, and $\vec{\sigma}_k \in \mathcal{R}^{n_{sd}}$, Regularization parameters such that $|\vec{\sigma}_k| \ll 1$, $k=1,\dots,n_c$ such that for any $\vec{w} \in \mathcal{W}$, $q \in \mathcal{P}$ and $\delta \vec{\lambda}_1, \delta \vec{\lambda}_2, \dots, \delta \vec{\lambda}_{n_c} \in (L^2(0,T))^{n_{sd}}$, the following is satisfied:

$$\begin{split} B_{G}(\vec{w},q,\delta\vec{\lambda}_{1},\ldots,\delta\vec{\lambda}_{n_{c}};\vec{v},p,\vec{\lambda}_{1},\ldots,\vec{\lambda}_{n_{c}}) \\ &= \int_{\Omega} \{\vec{w}\cdot(\rho\vec{v}_{,t}+\rho\vec{v}\cdot\nabla\vec{v}-\vec{f})+\nabla\vec{w}:(-p\,\underline{l}+\tau)\}\,d\vec{x}-\int_{\Omega}\nabla q\cdot\vec{v}\,d\vec{x} \\ &-\int_{\Gamma_{h}}\vec{w}\cdot(-p\,\underline{l}+\tau)\cdot\vec{n}\,ds+\int_{\Gamma}q\vec{v}\cdot\vec{n}\,ds+\xi\int_{\Gamma_{h}^{s}}\{\vec{w}\cdot\rho^{s}\vec{v}_{,t} \\ &+\nabla\vec{w}:\,\underline{\sigma}_{}^{s}(\vec{u})-\vec{w}\cdot\vec{f}^{s}\}\,ds-\xi\int_{\partial\Gamma_{h}^{s}}\vec{w}\cdot\vec{h}^{s}\,dl \\ &+\sum_{i=1}^{n_{sd}}\sum_{k=1}^{n_{c}}\{\lambda_{ki}\cdot(\sigma_{ki}\delta\lambda_{ki}-\delta c_{ki}(\vec{w};\vec{v},\vec{x},t))\} \end{split}$$



Fig. 4. Flow and pressure waveforms of coronary arteries for resting and exercise cases.

$$+\sum_{i=1}^{n_{sd}}\sum_{k=1}^{n_c}\delta\lambda_{ki}\cdot(\sigma_{ki}\lambda_{ki}-c_{ki}(\vec{v},\vec{x},t))$$
$$+\sum_{i=1}^{n_{sd}}\sum_{k=1}^{n_c}\kappa_{ki}\cdot c_{ki}(\vec{v},\vec{x},t)\delta c_{ki}(\vec{w};\vec{v},\vec{x},t) = 0$$
where $\delta c_{ki}(\vec{w};\vec{v},\vec{x},t) = \lim_{\epsilon \to 0} \frac{dc_{ki}(\vec{v}+\epsilon\vec{w},\vec{x},t)}{d\epsilon}$ (9)

Here, $L^2(0,T)$ represents the Hilbert space of functions that are square-integrable in time [0,T]. n_{sd} is the number of spatial dimensions and is assumed to be three and n_c is the number of constrained surfaces. Here, in addition to the terms required to impose the augmented Lagrangian method, we added the regularization term $\sum_{i=1}^{n_{sd}} \sum_{k=1}^{n_c} 2\sigma_{ki}\lambda_{ki}\delta\lambda_{ki}$ to obtain a system of equations with a non-zero diagonal block for the Lagrange multiplier degrees of freedom. This method was shown not to

alter the solution significantly except in the immediate vicinity of the constrained outlet boundaries and stabilize problems that previously diverged without constraints [13].

3. Results

The computer model used in these simulations was constructed using cardiac-gated computer tomography data corresponding to a 36-year-old healthy male subject. The model started from the root of the aorta, ended above the diaphragm, and included the major coronary arteries (left anterior descending, left circumflex, and right coronary arteries) and the main upper branch vessels (right subclavian, left subclavian, right vertebral, left vertebral, right carotid, and left carotid arteries). For the inlet, we coupled the lumped parameter heart model [14],



Fig. 5. Volume rendering of velocity magnitudes for peak systole, peak left coronary flow rate, and mid-diastole at rest and during exercise.

which is a part of the closed loop model. For the coronary outlets, we assigned lumped parameter coronary vascular models [18]. Similarly, for the upper branch vessels and the descending thoracic aorta, we assigned three-element Windkessel models. Additionally, we found tethering areas using this patient's cardiac-gated computer tomography data and fixed those areas in space and time in the computer model. For the coronary vessels, we identified thin strips approximating the intersection between the coronary arteries and epicardial surface of the heart and fixed the surface of the coronary arteries along the strips. To assign Young's modulus of the blood vessel walls, we measured the wall deformations over the cardiac cycle at different locations of the thoracic aorta and adjusted the modulus until the computed wall deformations approximated the measured deformation of the thoracic aorta. The assigned Young's modulus was 6.26×10^6 dynes/cm². The same value of Young's modulus was used for the exercise simulation. Finally, we enforced the constraints on the velocity profile shape to the inlet, upper branch vessels of the aorta and the descending thoracic aorta [13].

In this study, we approximated blood as an incompressible Newtonian fluid with a density of 1.06 g/cm^3 and a dynamic

viscosity of 0.04 dynes/cm² s. We modeled the blood vessel walls with a linearly elastic material within a physiologic pressure range with Poisson's ratio of 0.5, a wall density of 1.0 g/cm³, and a uniform wall thickness of 0.1 cm. The inlet and the outlet rings were fixed in space and time [8].

We generated an anisotropic finite element mesh with extra local refinement on the exterior surfaces and coronary vascular beds, and five layers of semi-structured (boundary layer) mesh [26] to compute wall shear stress fields more accurately. We ran the solutions until the relative pressure fields at the inlet and outlets did not change more than 1.0% compared to those in the solutions from the previous cardiac cycle. We studied flow and pressure of a normal thoracic aorta with coronary arteries for rest and light exercise conditions. Solutions were obtained using a 1,325,518 element and a 256,856 node mesh with a time step size of 0.25 ms to simulate a resting condition and 0.125 ms to simulate a light exercise condition (Fig. 1).

To simulate light exercise, we decreased the resistance value of the descending thoracic aorta and increased flow to the lower extremities. We doubled the heart rate during exercise so that the systolic pressure of the thoracic aorta increased by 20% compared



Fig. 6. Volume rendering of velocity magnitudes of coronary arteries for peak right coronary flow rate and peak left coronary flow rate at rest and during exercise.

to that of the resting state [5]. We did not change the boundary conditions of the upper branch vessels. The parameter values of the closed loop system and the three-element Windkessel models are shown in Tables 1 and 2. Note that we used the same contractility functions for the left and right ventricles for the light exercise simulation.

The parameter values of the lumped parameter coronary vascular model were adjusted for each coronary outlet to obtain assigned mean flow and pulse pressure while maintaining a physiologically realistic coronary impedance spectrum. Total coronary flow was maintained to be 4% of total cardiac output for both rest and exercise conditions. The parameter values of the lumped parameter coronary vascular models for each coronary outlet are shown in Table 3 for rest and exercise conditions.

Fig. 2 shows computed flow and pressure waveforms of the outlets for rest and exercise conditions of the normal thoracic aorta. We observe a significant flow increase to the descending thoracic aorta during exercise. The upper branch vessels experienced retrograde flow in diastole. We can see how the flow and pressure waveforms change due to the changes in the boundary conditions of the descending thoracic aorta and the heart even though the same boundary conditions were assigned to the upper branch vessels. Fig. 2 also shows the pressure waveforms of the upper branch vessels and the descending thoracic aorta. The pressure waveform of the upper branch vessels and the descending thoracic aorta decay faster during exercise than in the resting condition, facilitating the influx of blood from the heart in systole.

Fig. 3 shows aortic flow and pressure waveforms with the left and right ventricular pressure waveforms at rest and during exercise. It also shows the pressure–volume loops of the left and right ventricles for rest and exercise conditions. The cardiac output increased from 5.0 L/m to 10.3 L/min, the systolic aortic pressure increased from 124 to 149 mmHg, and the stroke volume increased from 83 to 86 cc. The diastolic aorta pressure remained unchanged at 78 mmHg. The left ventricular pressure increased as the aortic pressure increased but the right ventricular pressure changed little.

In Fig. 3, the left ventricular pressure is higher than or as high as the aortic pressure in systole. On the contrary, the right ventricular pressure is much smaller than the aortic pressure even in systole. Thus, the compressive force acting on the right coronary networks does not change the flow to the right coronary arteries significantly.

Fig. 4 depicts coronary flow and pressure waveforms of the left anterior descending, left circumflex, and right coronary arteries for rest and exercise conditions. As expected from the pressure waveforms in Fig. 3, the left anterior descending and circumflex coronary arteries have high flow in diastole and low flow in systole because the intramyocardial pressure approximated by the left ventricular pressure is elevated in systole. On the contrary, the right coronary artery has high flow in systole and low flow in diastole because the intramyocardial pressure represented by the right ventricular pressure operates in a low pressure range.

For the resting condition, the mean coronary flow to the left anterior descending coronary artery was 1.32 cc/s, the mean flow to the left circumflex coronary artery was 1.45 cc/s, and the mean flow to the right coronary artery was 0.55 cc/s, to yield a total coronary flow of 3.32 cc/s. During exercise, the coronary flow doubled achieving a mean flow of 2.65 cc/s to the left anterior descending coronary artery, 3.00 cc/s to the left circumflex coronary artery, and a total coronary flow of 6.64 cc/s.



Fig. 7. Mean wall shear stress and oscillatory shear index of the thoracic aorta and coronary arteries at rest and during exercise.

In Fig. 5, volume rendered velocity magnitudes are shown for peak systole, peak left coronary flow rate, and mid-diastole. The velocity magnitudes illustrate complex flow features in the thoracic aorta, in particular for peak left coronary flow rate during exercise because the high inertia of blood travels through the aortic arch. For the light exercise condition, the flow to the descending thoracic aorta increased significantly, increasing the retrograde flow in the upper branch vessels.

Fig. 6 shows volume rendered velocity magnitudes of the coronary arteries for peak right coronary flow and peak left coronary flow. We observe asynchrony between the peaks of the left coronary artery flow and right coronary artery flow. The left coronary arteries have high flow in diastole and low flow in systole whereas right coronary arteries have high flow in systole and low flow in diastole.

Mean wall shear stress and oscillatory shear index of the thoracic aorta with coronary arteries are also plotted for the resting condition and the light exercise condition in Fig. 7. For the light exercise condition, mean wall shear stress to the aorta and coronary arteries increased as higher flow traveled to the aorta and the coronary arteries. The oscillatory shear index of the upper branch vessels increased during exercise due to the increase of the retrograde flow to the vessels in diastole. Note that the oscillatory shear index of the coronary arteries is zero because they have unidirectional flow for these simulations.

4. Discussion

We have successfully developed and implemented a method that enables the prediction of realistic coronary flow and pressure waveforms. This method couples a lumped parameter coronary vascular model to each coronary outlet of a three-dimensional finite element model of the aorta with epicardial coronary arteries. It also utilizes an inflow boundary condition coupling a lumped parameter heart model and a closed loop model to represent the intramyocardial pressure by considering the interactions between the heart and arterial system. Fluidstructure interaction simulations were performed to better represent flow and pressure waveforms. Additionally, we obtained robust and stable solutions by constraining the shape of the velocity profiles of the boundaries that experienced retrograde flow.

Using these methods, we can study the changes in cardiac properties, arterial system, and coronary arteries interactively. In this paper, we studied how the coronary flow and pressure change for resting and light exercise conditions for normal coronary anatomy. For light exercise, the coronary flow doubled compared to that at rest as the metabolic demands of the heart increased. The coronary pressure range also increased during light exercise compared to that at rest. Computed coronary flow and pressure waveforms were realistic for both the resting and exercise conditions and the asynchrony of the left and right coronary arteries was represented as we approximated the intramyocardial pressure of the left and right ventricles realistically.

Our method has four primary limitations. First, we did not consider the motion of the heart during the cardiac cycle and fixed the surfaces of the coronary arteries attached to the epicardial surface of the heart in space and time. In reality, the heart moves significantly to contract and relax during the cardiac cycle. This movement is large and cannot be modeled using a fixed grid configuration for the fluid–solid domain [8]. A different approach, such as an arbitrary Lagrangian–Eulerian formulation, would be needed to represent the movement of the heart over the cardiac cycle. However, previous studies showed that the effects due to the movement of the heart were secondary and did not affect the pressure and flow fields as much as boundary conditions and geometry [23,25,27,47,48].

Second, we assumed a uniform intramyocardial pressure for all the left and right coronary outlets. In reality, the coronary vascular networks experience nonuniform intramyocardial pressure depending on the location of the coronary networks. To consider nonuniform intramyocardial pressure, a three-dimensional nonuniform model of the heart as well as the mapping of the coronary arteries to the location of the myocardium that the arteries perfuse should be considered.

Third, we assumed a uniform Young's modulus for the entire computer model even though the vessel wall properties vary spatially. To consider nonuniform vessel wall properties, we are developing noninvasive methods of estimating wall thickness and elastic (viscoelastic) wall properties. In this study, however, we adjusted the vessel wall properties so that the wall deformation of the descending thoracic aorta fit the experimental data reasonably well.

Fourth, we simulated the resting and exercise conditions by manually changing the parameter values of the lumped parameter models. However, we are currently developing feedback control loop models that consider autoregulatory mechanisms of the cardiovascular system. These models will enable us to replicate temporary physiologic changes due to the cardiovascular interventions or changes in physiologic conditions automatically.

5. Conclusions

We have developed methods that predict coronary flow and pressure by considering a hybrid numerical/analytic closed loop system comprising a numerical finite element model, two lumped parameter heart models representing the left and right sides of the heart, lumped parameter coronary vascular models of the downstream vasculature of the coronary beds, and three-element Windkessel models approximating the rest of the systemic circulation and the pulmonary circulation. Using this closed loop system, we can study effects on the coronary flow and pressure due to the changes in the heart, systemic circulation, pulmonary circulation, and coronary vascular beds. Furthermore, we can use these methods to predict the outcome of various cardiovascular interventions and thus determine the optimal intervention for cardiovascular disease in individual patients.

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