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A global mathematical model for the simulation of stenoses and bypass placement in the human arterial system

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ABSTRACT

This paper is concerned with a global mathematical model for the human circulation; we describe its construction, its validation and its application to study the haemodynamical effect of stenoses and bypass placement in the arterial system. A geometric multiscale approach is adopted combining one-dimensional (1D) descriptions to represent 55 major arteries and zero-dimensional (0D) compartmental descriptions for the heart, lungs, the venous system and the microcirculation. Modern non-linear numerical methods are implemented for solving the 1D systems of hyperbolic partial differential equations and high-order Runge–Kutta methods are used to solve the systems of Ordinary Differential Equations resulting from the compartmental models. The complete global mathematical model is then validated for healthy and stenotic cases comparing numerical predictions from the model against *in-vivo* measurements. Results show overall satisfactory agreement. In addition, a sensitivity analysis is conducted in order to assess the influence of the most important parameters on some haemodynamical quantities of interest. We then apply the model to simulate the haemodynamics for healthy controls and subjects with arterial stenosis. We study the haemodynamical effect of bypass placement, considering different locations in the arterial system, different degrees of severity, for both single and multiple arterial stenoses. Haemodynamical quantities of interest in the study are local pressure and flow rate. We observe that large stenotic plaques near the heart cause abnormally strong pressure waves in the circulatory system and two adjacent occlusions worsen the phenomenon. We find that the mathematical model is capable of predicting the most convenient bypass location and graft dimensions, consistent with normal haemodynamics.

1. Introduction

Arterial stenoses, a frequent and often fatal disorder in most industrialized countries, consist of the formation of an atherosclerotic plaque in the inner walls of vessels. This causes large increases in pressure drop across the stenosis and can affect perfusion to downstream tissues. If left untreated, more serious pathologies may develop, leading to hypertension and possibly to heart failure. The severity of this condition has drawn the attention of medical researches and a large body of works are available in the current literature, see for instance [1–7]. There are many therapeutic approaches to treat it

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and *a-priori* surgical decision-making is not always easy. It is here where mathematical modeling could assist in providing information, in a predictive manner, about various possible scenarios prior to the actual surgical intervention.

One of the first attempts at describing blood flow across an arterial stenosis through a mathematical model dates back to the work of Avolio [8], where the author used a lumped-parameter model. This approach, despite its simplicity, gave useful results and signalled a step forward in computational haemodynamics. More advanced models have been developed, see for example [9–13]. Other works to simulate arterial stenoses have been reported in [14–17].

Bypass placement has also been investigated extensively, since it is one of the most efficient interventions used to treat arterial occlusions, see [18–20]. Mathematical modeling of this medical problem could give to surgeons useful information about the effect of the treatment before intervention, see [21,22]. For instance, Steele et al. [23] solved the 1D blood flow equations allowing for different arterial stenoses and slopes of aortic grafts. They also carried out an *in-vivo* validation of local flow rate computations. Analogous work was done in [24], where, although a simple 0D model was used for the blood flow, the authors also included a model for the heart.

In the present paper we construct a global mathematical model based on the multi-scale approach proposed in [16]. This mathematical model gives a detailed description of the arterial system (1D) and simplifies the remaining components by using a lumped approach. Other global mathematical models of the cardiovascular system have been proposed [12,13,25,26] and give a more detailed spatial description of pressure and flow waves in the venous system as well, but since in the present paper we are only interested in analyzing the haemodynamical effects on the arterial tree, we decided to use the simpler model proposed by Liang et al. [16]. We used an ADER scheme [27] to discretize the 1D blood flow equations. The ADER scheme is a non-linear numerical method which allows us to achieve high-order in space and time, to circumvent the Godunov's theorem and use an optimal Courant–Friedrichs–Lewy (CFL) number. We note that all ADER schemes emerge from [27]. The present ADER scheme is different (simpler) to the ADER scheme of Refs. [12,13]. An high-order Runge–Kutta method is used to solve the systems of Ordinary Differential Equations resulting from the compartmental models. We identify the most important parameters by conducting a sensitivity analysis, in order to see their influence on some significant haemodynamical quantities. In addition, we validate our numerical results for healthy and stenotic cases with *in-vivo* measurements. We then consider different locations and severities for single and multiple arterial stenoses to examine how these factors affect local pressure and flow rate. We conclude that large plaques developing near the heart cause abnormally strong waves in the circulatory system. In particular, two adjacent occlusions worsen the phenomena. To conclude, we perform a systematic analysis of the effect of bypass placement on the resulting haemodynamics. As distinct from [23], to preserve the general structure of the 1D blood flow equations, we do not consider different slopes of the bypass. This allows us to include the bypass sub-model in a global model and to inspect the effect of the surgery on different regions of the human circulation. We find that the mathematical model is capable of predicting the most convenient dimensions of the graft, consistent with normal haemodynamic quantities. The overall dynamics are comparable with the healthy control.

The rest of this article is structured as follows. In Section 2, the global mathematical model is presented. In Section 3 the numerical schemes that are employed to solve the equations are given. In Section 4 a study about the influence of the parameters on our outcome is carried out. In Sections 5 and 6 results for the healthy, sick and cured cases are displayed and discussed. In Section 7 some concluding remarks about our study are drawn.

2. A global mathematical model

Several mathematical model of the cardiovascular system have been proposed in the lite For the purpose of this paper, we construct a global mathematical model following the multi-scale approach of Liang [16]. The 55 main arteries of the human body are modeled with the 1D blood flow equations in which the vessels are assumed to have no taper. Junctions between vessels are treated following [28]. Microcirculation, veins, the inferion vena cava, the superior vena cava, the heart and the pulmonary circulation are simulated with 0D models, see [29]. 1D and 0D formulations are coupled, as suggested in [30]. Arterial stenoses are simplified as single interfaces, across which flow rate is computed by solving an ODE depending on the pressure drop [16]. The placement of the bypass is modeled by modifying the local connectivity around the obstruction. A complete description of the global model for the healthy control is given in Fig. 1.

In Section 2.1 the 1D blood flow equations are presented in conservative form; in Section 2.2 the governing equations for a lumped-parameter model are given and in Section 2.3 the arterial stenosis sub-model is described.

2.1. One-dimensional blood flow equations

The 1D blood flow equations for a compliant vessel are the following

$$\begin{cases} \partial_t A + \partial_x q = 0, \\ \partial_t q + \partial_x\left(\alpha \dfrac{q^2}{A}\right) + \dfrac{A}{\rho}\partial_x p = -R\dfrac{q}{A}, \end{cases} \tag{1}$$

where x is the space variable, t is time, α is the Coriolis coefficient assumed to be $\alpha = 1$, $A(x, t)$ is the cross-sectional area of the vessel, $q(x,t) = A(x,t)u(x,t)$ is the flow, $u(x, t)$ is the velocity, $p(x, t)$ is the pressure, $\rho = 1060$ kg/m^3 is the blood density, $R = 22\pi\nu$ is the friction force per unit length of the tube with the dynamic viscosity of the blood ν equal to