Medical Engineering & Physics 35 (2013) 1573–1583

Contents lists available at ScienceDirect

Medical Engineering & Physics

journal homepage: www.elsevier.com/locate/medengphy

Validation of a 1D patient-specific model of the arterial hemodynamics in bypassed lower-limbs: Simulations against in vivo measurements

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ARTICLE INFO

Article history:
Received 11 September 2012
Received in revised form 11 April 2013
Accepted 26 April 2013

Keywords:
In vivo data acquisition
One-dimensional model
Hemodynamics
Lower-limb bypass
Parameter fitting

ABSTRACT

The validation of a coupled 1D–0D model of the lower-limb arterial hemodynamics is presented. This study focuses on pathological subjects (6 patients, 72.7 ± 11.1 years) suffering from atherosclerosis who underwent a femoro-popliteal bypass surgery. The 1D model comprises four vessels from the upper-leg, peripheral networks are modeled with three-element windkessels and in vivo velocity is prescribed at the inlet.

The model is patient-specific: its parameters reflect the physiological condition of the subjects. In vivo data are acquired invasively during bypass surgery using B-mode ultrasonography and catheter.

Simulations from the model compare well with measured velocity (u) and pressure (p) waveforms: average relative root-mean-square error between numerical and experimental waveforms are limited to $\epsilon_p = 9.6\%$, $\epsilon_u = 16.0\%$. The model is able to reproduce the intensity and shape of waveforms observed in different clinical cases. This work also details the introduction of blood leakages along the pathological arterial network, and the sensitivity of the model to its parameters.

This study constitutes a first validation of a patient-specific numerical model of a pathological arterial network. It presents an efficient tool for engineers and clinicians to help them improve their understanding of the hemodynamics in diseased arteries.

1. Introduction

In recent years, mathematical models of the cardiovascular system have been extensively used to simulate arterial hemodynamics in both healthy and pathological conditions. Depending on the application, the models vary from complex 3D to simple lumped parameter models, representing different levels of accuracy, complexity and computing time. An interesting approach consists of coupling models of different scales in order to benefit from their multiple advantages. In this study, we will focus on a coupled 1D–0D model: simple and fast-computing, it describes efficiently the propagation of arterial pressure and flow waves in the entire human body or in parts of it. While this type of model has been widely used, its validation has been mostly restrained to healthy data, acquired in an in vitro or in vivo setting. 1D numerical models were assessed against in-vitro measurements [1–3]. These studies showed the ability of the 1D time-domain formulation to capture the main features of pulse wave propagation. In Reymond et al. [4,5], healthy in vivo data were used to validate a 1D numerical model. In their work, results from a 1D–0D model of a complete arterial tree (including the heart, cerebral arteries and coronaries), with values of parameters taken from the literature or extracted from measurements, were compared against in vivo measurements performed on healthy subjects. In other studies [6,7], simulations of parts of the arterial network were also validated against in vivo data, with parameters computed from in vivo measurements. Besides these healthy validation, few studies have focused on model validation of subjects in pathological conditions [8,9]. Steele et al. [10] validated a 1D model of a stenosis with thoraco–thoraco bypass in pigs by comparing flow measurements.

In this work, we intend to validate a patient-specific coupled 1D–0D model of the hemodynamics in atherosclerosed bypassed lower-limb arteries using in vivo measurements in these arteries. This validation will be performed on 6 patients. As the hemodynamics in pathological arteries greatly fluctuates between subjects, our model is designed to produce patient-specific results. This characteristic is achieved by fixing the values of the model parameters so that they are representative of the physiological condition of the patient. Because measurements we have at our disposal focus on

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http://dx.doi.org/10.1016/j.medengphy.2013.04.012

the lower-limb, we will consider a truncated arterial model; the 1D model will be limited to the arteries of the upper leg. Another hypothesis is to consider only post-operative conditions, i.e. once the bypass is inserted in the patient's leg and that blood flows to the distal arteries. The modeling of a pre-operative condition (with a long section of the arterial path occluded) is indeed different as it is based on other modes of blood displacement (perfusion) through small collateral arteries and arterioles, and will not be considered in the framework of this work.

From a clinical point of view, the ultimate goal of our model is to help surgeons choose the best patient-specific bypass parameters on basis of pre-operative measurements. Post-operative hemodynamic factors of graft failure could then be computed from a pre-operative state for a defined set of bypass parameters. Nevertheless, before reaching this goal, a necessary step is to examine whether the pulse wave propagation model is able to reproduce post-operative hemodynamics is atherosclerotic patients.

In a patient-specific approach, model parameters represent the physiological condition of the subject. The determination of their value results from a process involving multiple steps, i.e. the experimental data acquisition, their computation based on particular algorithms and model hypotheses. For optimal results, uncertainties and bias should be reduced to a minimum in each step. It is therefore interesting to know the parameters which have the largest influence on the model results in order to further improve their determination. This can be achieved with a local sensitivity analysis.

This work is organised as follows. The in vivo data acquisition, the 1D–0D model and its parameters, the tools introduced to compare in vivo and simulated waveforms, and the design of the local sensitivity analysis are presented in Section 2. In Section 3, we consider the validation of our model against in vivo measurements on the entire population (6 subjects). By focusing on one clinical case, an improvement to the model (introduction of blood leakage) is presented. Finally, we also study the influence of the model parameters on the simulated waveforms. Section 4 discusses results and observations.

2. Materials and methods

When assessing a model based on experimental data, one must consider the entire process of transformation of the data: from their acquisition to the generation of the simulations. Indeed, new hypotheses, data acquisition errors, approximations or manual interactions are present at each step of the process. The evaluation of the performance of the numerical model requires to consider all of these inputs. The process of transformation of the in vivo lower-limb raw data to the numerical simulations is presented in Fig. 1. In this schema, the different inputs and outputs of the process are identified. Boxes on the left represent the origin of the data (in vivo measurements or literature), the central panel represents the process of transformation of the raw data towards inputs of the model. The 1D–0D model appears in the box on the right. Variables are represented on arrows. We use the notation [.] to represent a variable in the four vessels (the common femoral artery (CF), the deep femoral artery (DF), the bypass conduit (BP) and the popliteal artery (PO)), and the notation $\langle . \rangle$ to represent a variable in the DF and PO only. All variables are defined in the legend of Fig. 1.

This section details the different steps of this process: the in vivo data acquisition performed on 6 patients operated with lower-limb bypass surgery, the 1D–0D model, the patient-specific parameters of the model and their computation and, finally, the tools introduced to compare in vivo and simulated waveforms as well as the parameters of the local sensitivity analysis.

Table 1
Clinical characteristics of the 6 pathological subjects participating in the study (mean data ± standard deviation).

Gender	5 Men, 1 woman
Age (year)	72.7 ± 11.1
Heart rate (beats/min)	64.0 ± 8.4
Common femoral SBP (mm Hg)	104.8 ± 18.9
Common femoral DBP (mm Hg)	53.0 ± 6.8
Body mass index (kg/m^2)	22.4 ± 1.1
Distal anastomosis	2 BK, 4 AK
Type of bypass graft	3 GT, 1 DA, 2 ISV
Length of AK bypass graft (cm)	35.0 ± 4.8
Length of BK bypass graft (cm)	53.8 ± 2.8
Acquisition protocol	4 (# 1), 2 (# 2)
ABI before surgery*	0.37 ± 0.06
ABI after surgery†	0.77 ± 0.18
$\overline{Q}$ in bypass (ml/min)	145 ± 101
PSV in bypass (cm/s)	74 ± 26
EDV in bypass (cm/s)	7 ± 9

SBP: systolic blood pressure; DBP: diastolic blood pressure; AK/BK: above/below-knee; GT: gore-tex, DA: dacron, ISV: in-situ saphenous vein. Acquisition protocol (# 1) uses catheter and Doppler ultrasound measurements, while protocol (# 2) uses a guide wire. In ABI (ankle-brachial index) computation, data available for 3* and 5† subjects. PSV: peak systolic velocity; EDV: end diastolic velocity.

2.1. In vivo data acquisition

2.1.1. Subjects

Six in-hospital patients in an advanced stage of atherosclerosis took part in this study (see clinical parameters in Table 1). Informed consent was obtained from all subjects and the study was approved by the biomedical ethics committee of Université catholique de Louvain, Faculté de Médecine (Authorization reference number F:2006/02). All subjects suffered from occlusion of the superficial femoral artery and were treated with femoro-popliteal bypass (see Fig. 2). Materials used for the bypass were either a synthetic material of 6 mm diameter (Dacron, Gore-Tex), or the native saphenous vein used in-situ. The severity of the peripheral arterial disease is characterized with ankle-brachial index (ABI) before surgery [11]. Value of the ABI after surgery is also given, as an indicator of the success of the surgery. The ABI is computed as the ratio of the systolic blood pressure at the ankle to the systolic blood pressure at the arm. Before surgery, patients presented a severe disease, close to critical ischemia (ABI: 0.37 ± 0.06). After surgery, due to the bypass graft, their ABI index increased to a normal range with moderate disease (ABI: 0.77 ± 0.18). In clinical practice, surgeons also assess the success of the bypass with measurements of the hemodynamics in the graft, performed a few days after surgery. Three indicators of early graft failure are: a low mean flow in the bypass ($\overline{Q} < 50$ ml/min), a low peak systolic velocity (*PSV* < 45 cm/s) and a low end-diastolic velocity (*EDV* < 8 cm/s) [12,13]. Notice that the *PSV* considered here corresponds the maximal centerline velocity in the vessel. For the subjects studied (detailed results by patient can be found in Table 4), average values of flow and *PSV* are representative of the success of the bypass graft ($\overline{Q} = 145 \pm 101$ ml/min, *PSV* = 74 ± 26 cm/s), while the *EDV* criteria indicates failure of the bypass in half our patients (average *EDV* = 7 ± 9 cm/s). Status of the bypass conduit in each patient is also displayed in Table 4.

2.1.2. Data acquisition

Data acquisition was performed during the bypass surgery, while patients were under anesthesia. Patients were in a stable hemodynamic state and no vasodilatory drug was administrated at least 30 min before measurements. For all 6 subjects, measurements were performed after the suture of the graft, at four different locations in the leg: in the proximal CF, DF, BP and PO (see red points in Fig. 3). Two different acquisition protocols have been used, the data of each patient was analyzed by one of them. In the