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Global sensitivity analysis of a wave propagation model for arm arteries

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ABSTRACT

Wave propagation models of blood flow and blood pressure in arteries play an important role in cardiovascular research. For application of these models in patient-specific simulations a number of model parameters, that are inherently subject to uncertainties, are required. The goal of this study is to identify with a global sensitivity analysis the model parameters that influence the output the most. The improvement of the measurement accuracy of these parameters has largest consequences for the output statistics. A patient specific model is set up for the major arteries of the arm. In a Monte-Carlo study, 10 model parameters and the input blood volume flow (BVF) waveform are varied randomly within their uncertainty ranges over 3000 runs. The sensitivity in the output for each system parameter was evaluated with the linear Pearson and ranked Spearman correlation coefficients. The results show that model parameter and input BVF uncertainties induce large variations in output variables and that most output variables are significantly influenced by more than one system parameter. Overall, the Young's modulus appears to have the largest influence and arterial length the smallest. Only small differences were obtained between Spearman's and Pearson's tests, suggesting that a high monotonic association given by Spearman's test is associated with a high linear corelation between the inputs and output parameters given by Pearson's test.

1. Introduction

In the last few decades, lumped parameter [1–6] and one dimensional wave propagation models [7–11] of blood flow and blood pressure in arteries are increasingly used in cardiovascular research. Experimental and clinical validation of wave propagation models demonstrated the ability to qualitatively describe blood pressure and blood volume flow waveforms [7,12,13]. Furthermore, wave propagation models were employed to estimate arterial properties [14] or predict the effects of (surgical) interventions [15].

One dimensional wave propagation models of an arterial tree require an input blood volume flow (BVF) waveform and many system parameters to define geometry, boundary conditions and mechanical behavior of the vessel wall. For patient-specific simulations, input BVF and system parameters should be obtained from in vivo measurements employing high resolution techniques such as ultrasound, magnetic resonance imaging or tonometry. However, these measurements are exposed to uncertainties which can significantly influence the output obtained, e.g. vessel distension, blood velocity, and blood pressure waveforms at arbitrary locations. Moreover, the number of measurements for each patient is constrained by the duration of the measurement session. To optimize the measurement protocol, it would be of great interest to identify the input parameters that influence the output the most. Improved measurement of those parameters is the more beneficial [16,17].

The effect of system parameter uncertainty can be studied with sensitivity analysis (SA) methods. Local SA is the standard method; it evaluates the elementary effect of each parameter at a specific initial state of the model [18,19]. However, the results obtained are only valid at the initial state chosen, and can not be extrapolated to other points in the input space. Global SA quantifies the effect of each parameter within the entire input space and can be performed by a Monte-Carlo study based on multiple runs of the model. The simulated data-set corresponds to a random sampling of the system parameters within their uncertainty ranges. The global sensitivity of the system parameters follows then from appropriate statistical tests. As shown by local SA studies [14,18], blood pressure wave propagation models exhibit a complex relationship between the system parameters and the output. However, a global sensitivity analysis that considers in vivo measurement uncertainties in a wave propagation madel, has not been performed previously.

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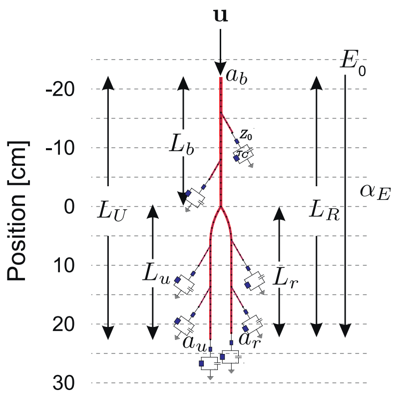

Fig. 1. Arterial tree model geometry and representation of the model parameters constrained to uncertainties: the centerline input flow velocity **u**; the arterial radius at the brachial (a_b), radial (a_r) and ulnar (a_u) artery; the length of the brachial (L_b), radial (L_r) and ulnar (L_u) artery (L_R and L_U are defined as $L_b + L_r$ and $L_b + L_u$, respectively); the Young's modulus at the brachial artery (E_0); the stiffening factor (α_E); the characteristic impedance Z_0 and the time constant τ_C.

The goal of this study is to identify with a global sensitivity analysis the input properties and model parameters that influence the output the most. We focus on a model of the arteries of the arm because these arteries are frequently subject of medical investigations [20–22]. Furthermore, the local systolic and diastolic blood pressure can be measured directly in the brachial artery and ultrasound measurements can be performed in the main arteries. In the first part of this paper, the subject-specific model of the arm, system parameters and their uncertainty ranges are described. Then, a global sensitivity analysis, based on a Monte-Carlo study, is performed. The results of the model evaluations are quantitatively illustrated employing Cobweb's graphical method. Further, the linear Pearson and ranked Spearman correlation coefficients are calculated to evaluate quantitatively the sensitivity of the model output to system parameters. Subsequently, the derived correlation coefficients are classified and discussed.

2. Methods

2.1. Wave propagation model

The wave propagation model developed by Bessems et al. [12,23] was employed, see Fig. 1. The mass and momentum conservation equations were solved using the spectral element method considering blood as a Newtonian fluid and the arterial wall as a thick walled linear-elastic material and the arteries were terminated by a 3-element Windkessel model [24].

The model in this study consisted of the three main arteries of the arm, the brachial artery (BA), the radial (RA) and the ulnar artery (UA). Six extra side branches were added to model the arterial network which supplies blood volume to the surrounding tissue (arm's muscles).

2.2. Measurement protocol

A set of local ultrasound measurements was obtained to provide arterial distension and blood flow velocity waveforms. These measurements were performed distal and proximal in the brachial, ulnar and radial arteries. The distance between the measurement location and the bifurcation was measured on the body surface using a tape measure. Each measurement covered 4 consecutive heartbeats and was repeated at least three times. Brachial systolic (P_s) and diastolic (P_d) blood pressures were measured at the start and end of the measurement session. For more details, the reader is referred to [14].

Table 1
Average and uncertainty range of input blood velocity waveform properties and model parameters depicted by the time average, the maximum and minimum blood velocity $\bar{U}$, U_M and U_n respectively; the proximal Young's modulus E_0; the stiffening factor α_E; the time average radius $\bar{a}$; the arterial length L; the time constant τ_C and the characteristic impedance factor K_{Z_0}. The indices b, r, and u refer to the *BA*, *RA* and *UA*.

Parameters	Average	Range	Range (%)
$\bar{U}$ (cm/s)	3.8	3.0–4.5	40
U_M (cm/s)	29	28–31	9.4
U_n (cm/s)	−9	(−12)–(−6)	69
E_0 (MPa)	5.0	4.0–6.0	40
α_E (MPa)	−0.5	(−1)–0	×
$\bar{a}_b$ (mm)	2.39	2.31–2.46	6
$\bar{a}_r$ (mm)	1.48	1.41–1.56	10
$\bar{a}_u$ (mm)	1.31	1.24–1.39	12
L_b (cm)	22	21–23	9
L_r (cm)	22	21–23	9
L_u (cm)	23	22–24	9
τ_C (s)	1.1	0.8–1.4	54
K_{Z_0}	1.0	0.8–1.2	40

2.3. Model system parameters and input blood volume flow

2.3.1. Model geometry

The three main arteries of the arm were represented by the BA bifurcating into the RA and UA artery, see Fig. 1. The measured lengths L_b of the BA, L_r of the RA and L_u of the UA were used to build the arterial tree and six extra side branches, having a length of 4 cm, were added to model the arterial network of smaller sized arteries like the superior and inferior ulnar, the radial recurrent and the dorsal interosseous arteries. Each arterial segment was divided into elements with a length of 1 cm (sufficiently small to ensure numerical convergence), whereas a bifurcation element ensured continuity of pressure and flow, see Fig. 1.

The vessel radius was assumed to decrease exponentially along the arterial tree. The vessel radius $\bar{a}$ at a position z along the artery was then defined as

$$\bar{a}(z) = \bar{a}_{z_0} \exp(-\alpha_{\bar{a}} z) \tag{1}$$

with $\bar{a}_{z_0}$ the radius at $z = 0$ and $\alpha_{\bar{a}}$ the tapering factor [4,25,26]. According to Murray's law, the third power of the mother artery radius, a_m, is equal to the sum of the third power of the two daughter artery radii, a_{d_1} and a_{d_2} [27,28]:

$$\bar{a}_m^3 = \bar{a}_{d_1}^3 + \bar{a}_{d_2}^3 \tag{2}$$

Eqs. (1) and (2) were applied to the BA, RA and UA. The obtained system of 4 equations with 4 unknowns (the radii of the brachial, radial and ulnar arteries at the bifurcation and the tapering factor $\alpha_{\bar{a}}$) was then solved to determine the tapering factor $\alpha_{\bar{a}}$ using the measured radii at the BA, RA and UA. For the side branches, as it was not possible to assess the radius of these small vessels using ultrasound, an estimate of the radius has been obtained. We could determine using radius measurements that the blood flow should decrease by 30% along the BA. Considering two side branches in the BA, and a constant time average wall shear stress, the following relation could then be used:

$$\bar{a}_s^3 = 0.15\bar{a}_m^3 \tag{3}$$

with $\bar{a}_s$ and $\bar{a}_m$ the radius of the side branch and the mother artery, respectively.

2.3.2. Arterial wall properties

Since arterial stiffness (defined as $E\bar{h}$ with E the Young's modulus and $\bar{h}$ the wall thickness) increases toward the periphery, an exponential model is used to describe the Young's modulus, E,

$$E(z) = E_0 \exp(-\alpha_E z) \tag{4}$$