Medical Engineering & Physics 35 (2013) 810–826

Contents lists available at SciVerse ScienceDirect

Medical Engineering & Physics

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

A sensitivity analysis of a personalized pulse wave propagation model for arteriovenous fistula surgery. Part A: Identification of most influential model parameters

W. Huberts[a,c,*], C. de Jonge[d], W.P.M. van der Linden[d], M.A. Inda[d], J.H.M. Tordoir[b], F.N. van de Vosse[a,c], E.M.H. Bosboom[a,c]

[a] Department of Biomedical Engineering, Eindhoven University of Technology, The Netherlands
[b] Department of Surgery, Maastricht University Medical Center, The Netherlands
[c] Department of Biomedical Engineering, Maastricht University Medical Center, The Netherlands
[d] Healthcare Information Management Group, Philips Research Laboratories Eindhoven, The Netherlands

ARTICLE INFO

Article history:
Received 20 July 2011
Received in revised form 11 April 2012
Accepted 18 August 2012

Keywords:
Pulse wave propagation model
Personalized modeling
Predictive surgery
Global sensitivity analysis
AVF surgery
Measurement protocol

ABSTRACT

Previously, a pulse wave propagation model was developed that has potential in supporting decision-making in arteriovenous fistula (AVF) surgery for hemodialysis. To adapt the wave propagation model to personalized conditions, patient-specific input parameters should be available. In clinics, the number of measurable input parameters is limited which results in sparse datasets. In addition, patient data are compromised with uncertainty. These uncertain and incomplete input datasets will result in model output uncertainties. By means of a sensitivity analysis the propagation of input uncertainties into output uncertainty can be studied which can give directions for input measurement improvement. In this study, a computational framework has been developed to perform such a sensitivity analysis with a variance-based method and Monte Carlo simulations. The framework was used to determine the influential parameters of our pulse wave propagation model applied to AVF surgery, with respect to parameter prioritization and parameter fixing. With this we were able to determine the model parameters that have the largest influence on the predicted mean brachial flow and systolic radial artery pressure after AVF surgery. Of all 73 parameters 51 could be fixed within their measurement uncertainty interval without significantly influencing the output, while 16 parameters importantly influence the output uncertainty. Measurement accuracy improvement should thus focus on these 16 influential parameters. The most rewarding are measurement improvements of the following parameters: the mean aortic flow, the aortic windkessel resistance, the parameters associated with the smallest arterial or venous diameters of the AVF in- and outflow tract and the radial artery windkessel compliance.

1. Introduction

A well-functioning vascular access is crucial for successful hemodialysis therapy. Such a vascular access is used to connect the patient's circulation to the artificial kidney and should provide the blood flow rate of 300 ml/min required for efficient treatment [1,2]. The best option for a vascular access is an arteriovenous fistula (AVF) in the arm, which is a surgically created permanent connection between an artery and vein [1,2] resulting in a five- to thirtyfold flow increase and vessel dilation and remodeling. An AVF can be created at several positions in the arm and the optimal location is preoperatively selected by a vascular surgeon. Functioning lower arm AVFs have statistically better long-term patency rates and lower complication rates than upper arm AVFs [1,2] and are therefore preferred. However, for a significant number of patients (up to 50%), the resulting blood flow after creation of a lower arm AVF can be too low to enable hemodialysis [3–5]. Conversely, the blood flow in upper arm AVFs may be too high, leading to cardiac problems and/or distal hand ischemia in 20% of all upper arm AVFs [2–4,6]. In addition to the high blood flow, also a low systolic finger pressure after AVF creation is indicative for the development of distal ischemia [1,2,4].

In previous work, a distributed lumped parameter pulse wave propagation model was presented that simulates the hemodynamical conditions directly after AVF creation [7]. In order to make personalized predictions that might assist the surgeon during vascular access planning, the model parameters were adapted to patient-specific conditions and the model was able to select the

---

* Corresponding author at: Department of Biomedical Engineering, Maastricht University Medical Center, PO Box 616, NL-6200 MD Maastricht, The Netherlands. Tel.: +31 43 388 16 56.
E-mail address: w.huberts@tue.nl (W. Huberts).

1350-4533/$ – see front matter © 2012 IPEM. Published by Elsevier Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.medengphy.2012.08.013

same AVF configuration (upper or lower arm) as an experienced surgeon (more than 1000 interventions) in nine out of ten patients. Furthermore, the predictions of the mean brachial flows were similar to ultrasound flow measurements in six out of ten patients [7]. Although these preliminary results were promising, to further optimize the use of this personalized pulse wave propagation model we need to be able to deal with the uncertainty in and incompleteness of input datasets obtained by clinical measurements. This uncertainty in input parameters will propagate to the pressure and flow predictions and therefore it is necessary to analyse the uncertainty in the predictions before inferences with the model can be made reliably. The knowledge of which model parameters influence output uncertainty the most can be used to determine which clinical measurements are most important for obtaining reliable predictions. Developing more accurate measurement methods for these model parameters will be most rewarding as this will result in the best improvement of the predictions (parameter prioritization). Model parameters that hardly influence the output uncertainty can be fixed within their measurement uncertainty interval (parameter fixing), and improving measurements of these parameters is not beneficial for a more reliable output (i.e. reduction in output uncertainty).

To select which model parameters can be fixed and which model parameters need to be prioritized for measurement improvements, a sensitivity analysis needs to be performed [8,9]. A sensitivity analysis can either be local or global [8–11]. In a local sensitivity analysis, changes in the output are investigated by varying one input parameter around its initial value, while all other input parameters are kept fixed. The conclusions, therefore, only hold when the input conditions are kept around the initial state and neglect the influence of interactions between input parameters. In a global sensitivity analysis, sensitivity measures are determined while all model parameters are changed simultaneously and thus the complete input domain is sampled and interactions between model parameters are taken into account. Because the wave propagation model is nonlinear and interactions between parameters are expected, a global sensitivity analysis is the most suitable for our application.

Xiu et al. [12] performed uncertainty and sensitivity analysis in a wave propagation model of a human arterial tree based on generalized polynomial chaos expansion. The uncertain model parameters were modeled as random variables directly within the governing equations, transforming them into stochastic equations. This method gives a global description of the effect of model parameter uncertainties on the output. However, the deterministic properties of the model are lost and therefore apportioning the output uncertainty to the input uncertainties is not easy. An alternative is a Monte Carlo approach, in which the input parameters are randomly varied within their uncertainty domain [8,9]. Leguy et al. [13] used Monte Carlo simulations to perform a global sensitivity analysis of a wave propagation model and showed that the majority of model parameters affected the output significantly. However, Leguy et al. used the Pearson correlation coefficient and the ranked Spearmann correlation coefficient as sensitivity measures [13]. These correlation coefficients can only be applied for monotonic models and do not reveal interactions between model parameters [8,9,14,11]. Variance-based methods are independent of the model's behavior with respect to linearity, monotonicity or additivity, and these methods also take into account possible interactions between parameters. Wenk et al. [15] used a variance-based method in their application of finite element stress analysis of atherosclerotic plaques. However, they only had a limited number of three input parameters. To our knowledge, variance-based methods have not yet been applied to wave propagation models which typically have 50 parameters. The aim of this study is to identify the influential and (non)-influential model parameters of our pulse wave propagation model for AVF surgery. A variance-based method and Monte Carlo simulations are used, which is considered to be the current best available practice to perform a global sensitivity analysis [8,9,16]. This analysis will generate more insight into the model and into which model parameters should be determined more accurately to reduce output uncertainty. It is important to realize that the parameters to prioritize and which parameters to fix depend on the specific output parameter of interest. Here the output parameters are the mean brachial flow and systolic radial artery pressure distal to the anastomosis after AVF creation. These outputs are chosen as mean brachial flow is related to AVF short-term failure, while distal systolic pressure in the radial artery is used as measure for finger pressure, which is related to distal ischemia [1,2,4]. Radial pressure is chosen as it is difficult to assess vessel diameters and lengths in the hand vasculature.

In this paper, we briefly describe the distributed lumped parameter pulse wave propagation model, and, thereafter, present the variance-based global sensitivity analysis. In the description of the global sensitivity analysis, an overview of the model parameters and their uncertainty intervals are given. In addition, the computational framework to calculate the sensitivity indices is presented. Results with regard to mean brachial flow and finger pressure are presented and conclusions on how to improve the measurement protocol to obtain the most reliable model outcomes are drawn.

2. Methods

2.1. The wave propagation model

In this section, we give a short description of the distributed lumped parameter wave propagation model that we use. For details the reader is referred to Huberts et al. [7].

In this study two different vascular topologies (computational domains) were used (Fig. 1) for the pulse wave propagation model, representing respectively an lower and upper arm AVF. The first topology consists of the main arteries of the right arm, i.e. the innominate artery, subclavian artery, axillary artery, brachial artery, interosseus artery, radial artery and ulnar artery. A truncated part of the aorta, of the vertebral artery and of the right and left common carotid arteries are also included. The arterial tree is extended with a venous outflow tract to mimic a lower arm AVF. The outflow tract consists of the cephalic vein in the upper and lower arm, the median cubital vein, the basilic vein in the upper arm and the axillary and subclavian vein. The second topology represents an upper arm AVF. The arterial tree is as described above but the outflow tract now consists of the basilic, axillary and subclavian vein.

Each vessel in the computational domain is divided into segments (Fig. 2) with a maximum length of 5 cm. In each segment the local relation between pressure and flow is described by using a lumped parameter approach based on local mass and momentum equations [7,17]. For the scope of modeling the effect of vascular access creation on blood pressure and flow distribution, segments that represent arteries, veins and the anastomosis are needed (Fig. 2). For arterial and venous segments, the lumped parameter model consists of a Womersley number dependent resistor and inductor in series representing respectively the viscous blood flow resistance and the blood inertance, whereas the storage capacity of the vessel segment was captured by two capacitors. The anastomosis segment consists of nonlinear resistors that depend on anastomosis angle and blood flow. Parts of the cardiovascular system are truncated and terminated with three-element windkessel models [18]. Assembling the equations for all segments results in a system of differential equations that is solved by numerical integration applying the trapezium rule for implicit time integration [7]. On the first aortic node, the aortic flow (measured with MR) is