Validation of patient specific multi-scale hemodynamic computational model for planning vascular access surgery in hemodialysis patients

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Introduction

More than 940 patients affected by end-stage renal disease per million population in Europe are on chronic therapy by hemodialysis (HD) (EDTA (2011)) and this number increases annually at a constant rate of about 8%. The Achilles heel of HD is the vascular access (VA) used to connect patient circulation to the artificial kidney. Medical societies and guidelines [1][2] strongly recommend the use of native arteriovenous fistula (AVF), surgically created in the arm with the anastomosis of an artery and a vein. However, short- and long-term VA dysfunctions, including non-maturation (inadequate increase in blood flow volume after surgery), stenosis due to intimal hyperplasia, and ultimately thrombotic occlusion, are the major cause of morbidity and hospitalisation in HD patients, with more than 90,000 procedures/year performed in Europe for revision or reoperation. The extent of this major clinical problem points out the need of prediction and prevention of VA dysfunction. However, to date, they still represent open clinical challenges. A number of computational approaches have been proposed for the simulation of hemodynamics and vascular wall dynamics in complex vascular networks, which could potentially be used to simulate blood flow volume change after VA creation. Among them, 0D and 1D pulse wave propagation methods allow to efficiently model flow and pressure distributions and wall displacements throughout vascular networks at low computational costs. Although several techniques are documented in the literature, widely available, open-source computational tools are still lacking. During the VPH-I ARCH project, specific computational modelling tools were developed to simulate both pre- and post-operative volumetric blood flow rate, and embedded in an open-source framework (archTk, http://archtk.github.com). At the same time, a prospective observational pilot study (ARCH clinical study) was performed in patients with end stage renal disease (ESRD) awaiting VA creation for HD treatment, in order to collect longitudinal data on vascular access function. In this work we used the archTk framework to simulate blood flow volume 40 days after surgery based on pre-surgery measurements in a group of patients with newly created AVFs taken from the ARCH clinical study, and we compared simulated to measured data.

Methods

The archTk framework, developed during the VPH-I ARCH project, includes a modular solver for 0D/1D problems (pyNS) which implements 1D wave propagation computational models [3]. The relation between pressure p and volumetric flow rate q are derived from conservation of mass and momentum by assuming fully-developed incompressible Newtonian volumetric flow rate in a straight vessel [4]. The convection term, the axial diffusion term and the effect of body forces in the momentum equation are neglected because their contributions are expected to be small [3][5]. An expression for the wall shear stress (WSS) as function of p and q is derived from a time and frequency dependent approximated velocity profile [6], which is based on boundary layer theory. pyNS, on the basis of the momentum equation, represents the vascular network as a graph in which each edge is associated to a mathematical model of pressure (p), volumetric flow rate (q) and wall-shear stress in that segment. In addition, a computational 0D model of the anastomosis, i.e. the surgical connection between the feeding artery and the outflow vein, was developed and included in the vascular network. The anastomosis element cannot be modeled using fully developed flow because the radial velocity component is no longer infinitesimally small compared to the axial velocity and flow separation are expected to occur. In order to properly account for non-linear pressure losses anastomosis, 3D computational fluid dynamics (CFD) models were employed in order to estimate pressure drops occurring over the anastomosis

for a clinically relevant range of input flow rates and for a variety of anastomosis configurations. The resulting pressure-flow relations were then lumped as a non-linear resistance in the anastomosis element. Furthermore, a vascular adaptation algorithm [7] based on the assumption that blood vessel diameter changes upon change in blood flow volume to maintain a pre-set value of the peak WSS was implemented in the solver.
During the ARCH project, a multicenter longitudinal clinical prospective observational study was performed to systematically collect anatomical, clinical, and physiological data, aimed to calibrate and validate patient-specific modelling tools. A total of 94 consecutive patients with ESRD awaiting VA creation were enrolled in the ARCH clinical study. All patients underwent pre-operative clinical and US examinations and, after VA surgery, they were systematically followed up through clinical and US examinations for a period of two years. In 38 patients AVF was created in the upper arm, and was either brachio-cephalic (n=28) or brachio-basilic (n=10), while in 56 patients AVF was created in the lower arm, and was either radio-cephalic (n=55) or ulnar-cephalic (n=1). Anastomoses were either end-to-side (20 brachio-cephalic, 10 brachio-basilic, 23 radio-cephalic and 1 ulnar-cephalic), end-to-end (28 radio-cephalic), or side-to-side (8 brachio-cephalic and 4 radio-cephalic). Both patients with ulnar-cephalic AVF and patients with side-to-side anastomosis were excluded from the simulation dataset. Patients with missing or inconsistent data were further excluded.
For all patients in the simulation dataset, brachial blood flow volume 40 days after AVF surgery was simulated using archTk according to AVF configuration, and compared to measured flow volume. For diabetic patients with upper arm AVF, a second simulation was performed without applying the adaptation algorithm. The agreement between simulated and measured data in the whole simulation dataset was investigated using Bland-Altman plots. In addition, Pearson's correlation between simulated and measured data was evaluated.

Results

Sixty-five patients with newly created AVF were included in the simulation dataset, and divided in 4 groups, based on AVF configuration: lower arm radio-cephalic end-to-end (n=25) and end-to-side AVF (n=18), upper arm brachio-cephalic (n=18) and brachio-basilic end-to-side AVF (n=5). Since in diabetic patients brachial artery diameters were found not to increase after surgery (mean brachial artery diameter: 4.87 ± 0.64 mm (pre-operative) and 4.72 ± 0.68 mm (40 days post-operative)), no vascular adaptation was considered for the simulation in all diabetic patients with upper arm AVF. Figure 1 shows the comparison between predicted and measured blood flow volumes 40 days after surgery, for each of the four AVF configurations.

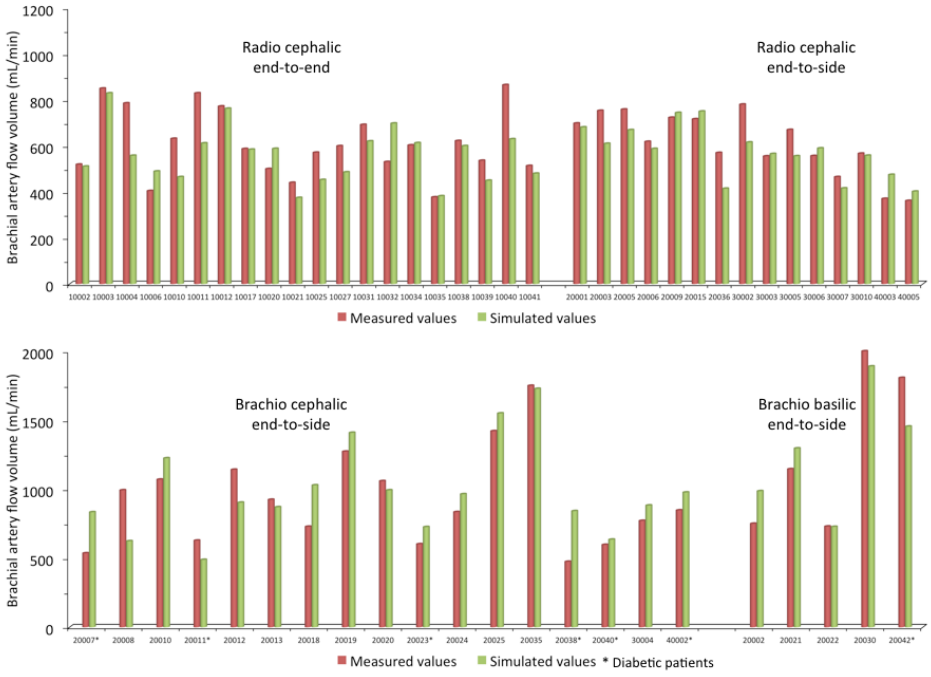

Figure 1: Measured vs Simulated brachial artery blood flow volume at 40 days after AVF surgery.

Bland-Altman plots show good agreement between simulated and measured flow volumes in the whole simulation dataset (Figure 2). Furthermore, predicted and measured data were significantly correlated, regardless of AVF configuration (Pearson's $r = 0.925$, $p < 0.01$)(Figure 2).

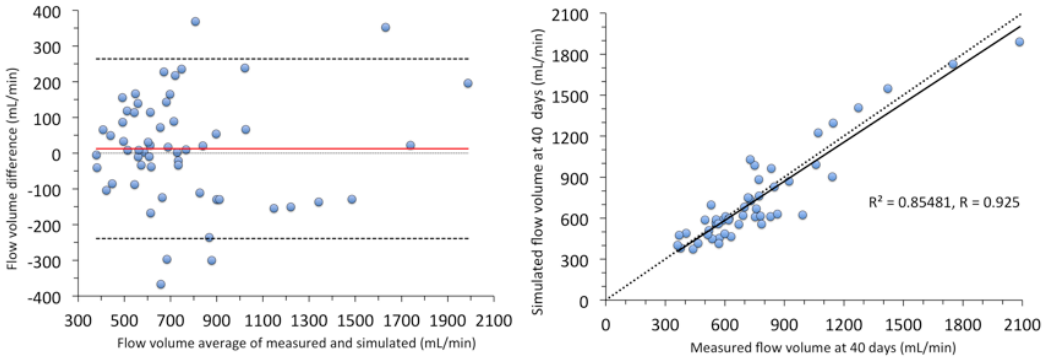

Figure 2: Bland-Altman (left) and correlation (right) between measured data and simulated results on brachial artery.

Conclusions

In this study we showed that the archTk computational modelling tool reliably simulates changes in blood flow volume during AVF maturation. Therefore, this computational tool could potentially be used for surgical planning of AVF, to predict VA outcome. Predicting patient-specific blood flow volume increase, resulting from VA creation and vascular adaptation using different AVF configurations, could help the surgeon choosing the most appropriate AVF location (e.g. in case of too low predicted blood flow resulting from a lower arm AVF, a more proximal location should be preferred), ultimately leading to a lower proportion of post-operative VA dysfunctions.
Following validation of the computational model and in view of its potential use in clinics, a large-scale, randomised and controlled clinical study aimed to evaluate the potential beneficial effect of the use of archTk in reducing VA-related clinical problems has been designed. To this purpose, AVF.SIM, a web-application based on archTk is currently under development. AVF.SIM is being designed to be used directly by clinicians and surgeons in a clinical environment, and will provide simulation results (including vascular adaptation and blood flow volume increase up to 40 days from surgery) based on patient-specific data.

Acknowledgement(s)

The research leading to these results has received funding from the European Communitys Seventh Framework Programme (FP7-ICT-2007-2: Project ARCH n. 224390).
Partners of the ARCH Consortium are: Mario Negri Institute, Bergamo (IT); Academisch Ziekenhuis Maastricht (NL); Philips Medical Systems, Eindhoven (NL); Philips Research, Eindhoven (NL); Esaote Europe BV, Maastricht (NL); Ghent University (BE); Sheffield University (UK); Lubljana Medical University (SL).

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