AngioSupport: an interactive tool to support coronary intervention

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1. Introduction

Every year about 735.000 Americans suffer from Coronary Artery Disease (CAD); one of the leading causes of death in the United States; therefore, diagnosis and treatment should be convenient and accurate with costs as low as possible. Currently, medium to high risk stable patients have been assessed based on invasive coronary angiography (ICA). In other words, ICA was the 'gold standard' to determine the appropriate treatment (pharmaceutical treatment, percutaneous coronary intervention (PCI), or coronary artery bypass graft (CABG)) for CAD by revealing the location and anatomy of the stenosis. This diagnostic method is based on the research of Gould et al., which demonstrates the relationship between the stenosis (lumen diameter) and ischemia (determined based on myocardial blood flow) during the hyperemic state (Gould et al., 1974). Despite the subjective visual interpretation of the clinician to interpret the ICA, the percentage stenosis defined by ICA is a decent indication for revascularization for single vessel stenosis. However, for diffuse coronary disease or multiple stenosis (Tonino et al., 2009), ICA is unreliable for the diagnosis, because hemodynamics are unpredictable based on the anatomy of the stenosis. This may result in unnecessary revascularization of patients.

To improve the diagnostic method, Pijls et al. developed a new method to determine the impact of the stenosis by measuring invasively the myocardial fractional flow reserve (FFR) (Pijls et al., 1996). This fraction defines the hyperemic flow with a stenosis (Q_s^{hyp}) relative to the hyperemic flow without disease (Q_{max}^{hyp}) based on the ratio of the mean pressure distal to the stenosis (P_d) and the mean aortic pressure (P_a) ($FFR = \frac{Q_s^{hyp}}{Q_{max}^{hyp}} \approx \frac{P_d}{P_a}$). The invasive FFR is used in combination with ICA by inserting a pressure wire in the desired coronary artery to measure the P_d. The FFR, in combination with ICA, improves the diagnosis of multi-vessel and diffuse disease, because the P_d covers all changes in the vessel diameter distal to the stenosis. Furthermore, the use of the mean pressures to compute the FFR makes the method more robust to changes of pressure. In order to verify its diagnostic ability, three clinical studies were performed: 1) Fractional Flow Reserve versus Angiography for Multi-vessel Evaluation (FAME), 2) FAME 2, and 3) DEFER these studies show that invasive FFR in combination with ICA improves the decision between pharmaceutical treatment and PCI for CAD than ICA alone. As a result, FFR with ICA has become the new 'gold standard' to assess CAD. However, a part of the patients only requires pharmaceutical treatment while an invasive procedure was already performed. Therefore, multiple companies developed software to assess CAD minimal- or non-invasive.

For assessment of lesions based on coronary ICA, multiple software tools are available to quantify the length and percentage of stenosis by generating 3D construction of the vessel with stenose. Examples are the software tools of Pie Medical Imaging (CAAS) and Medis (QAngio XA 3D). Although these tools can quantify lesions accurately, a 3D construction of only one vessel can be generated, so assessing multi-vessel lesions is inconvenient. Cathworks and Heartflow generate the entire coronary tree in 3D and computes the FFR virtually based on ICA and compute tomography (CT), respectively. CT is non-conventional to assess CAD; therefore, tools based on ICA is preferred over CT. Nevertheless, both tools have shown a high correlation with invasive FFR and a reduction in invasive treatments. However, for treatment planning it may still be difficult to determine the position, length or diameter for a CABG or PCI based on ICA and FFR due to multiple occlusions, diffuse coronary disease or complicated vasculature.

A tool that can predict the treatment outcome may support the cardiac team that discusses the treatment of multiple patients with CAD, every morning.

An existing tool to predict the FFR after PCI is VIRTUheart. However, the computational time is 95s per case, which is not feasible in a dynamic environment, such as a cardiac team meeting where multiple patients with CAD are discussed and multiple interventions per patient will be analysed within minutes. Furthermore, predicting the outcome of CABG next to PCI would be beneficial to compare PCI with CABG. Therefore, AngioSupport is developed to provide clinicians useful information while using conventional ICA and predicting the outcome of CABG or PCI within seconds to support clinical decision making.

2. Method

AngioSupport is a toolchain consisting of a segmentation tool and a 1D wave propagation model. The segmentation of the coronary arteries is performed by CAAS (Coronary Angiographic Analysis Systems, Pie Medical Imaging) and requires two single plane angiograms with an angle $\geq 30^{o}$ obtained by conventional ICA. The segmented coronaries are combined to create a patient specific full coronary vasculature. An existing 1D wave propagation model of the human vascular system was simplified and extended with the patient coronary system, as developed at the Eindhoven University of Technology (van der Horst et al., 2013). To simulate the pressure and flow propagation, the model is provided with patient specific clinical measures, such as patient length, weight, heart rate and aortic blood pressure, to compute the pre-operative FFR (pre-FFR) throughout the patient's system. In additions, an interactive interface is developed, such that clinicians can select standard stent sizes and deploy them virtually in the area that seems affected by disease. Alternatively, the CABG option can be simulated by selecting the location of the anastomosis on the coronary tree. To be able to compare coronary interventions with AngioSupport, the post-operative FFR (post-FFR) is calculated throughout the coronaries. In practice, the clinician will only have to load the ICA and, subsequently, perform multiple interventions virtually.

3. Results

The post-FFR is computed within seconds and can be compared between the different interventions (Figure 1). This allows AngioSupport to be used during the cardiac team meetings, where patient treatment plans are determined in a short time span. By allowing clinicians access to the numerical models through the straight-forward AngioSupport user interface, clinicians will have an additional tool to support this difficult, but vital decision. The validation of AngioSupport is currently ongoing in cooperation with multiple hospitals in the Netherlands.

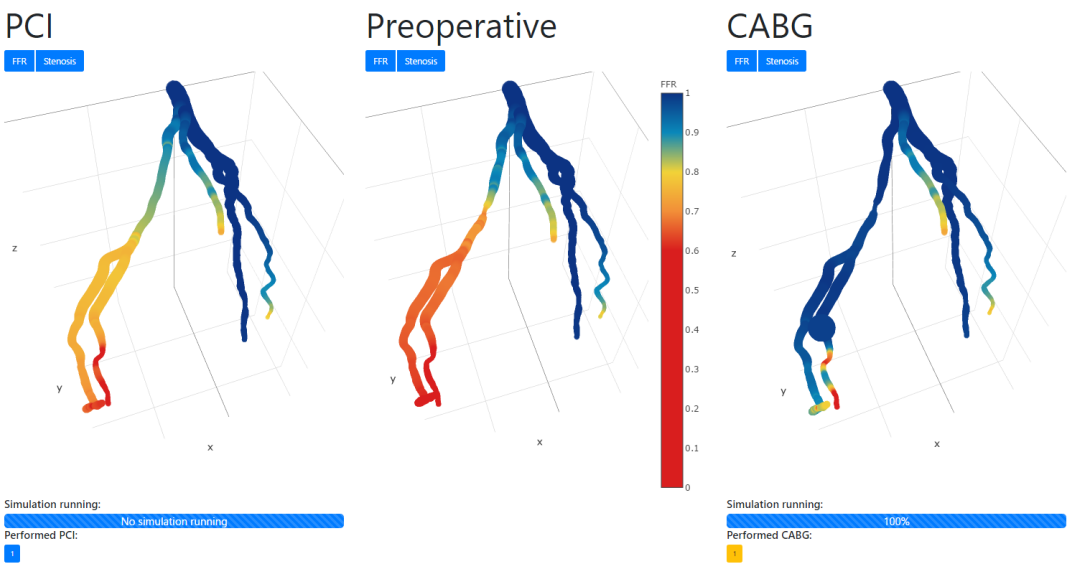

Figure 1 *The result of AngioSupport calculations within the middle the pre-operative FFR calculation and left and right the results from a PCI and CABG. The heart team can now directly compare the post-operative FFR and determine a patient-specific treatment.*

4. Discussion

An interactive interface for clinicians is developed as front-end for the physiological model developed by van der Horst et al. to compute blood pressure and flow throughout the coronary arteries (van der Horst et al., 2013) to analyse stenoses, compute pre-FFR, perform interventions, and predict post-FFR. AngioSupport aims to support clinicians with treatment planning, especially for multi-vessel and serial stenoses and diffuse diseased vessels. In addition, it could potentially reduce the number of repeat revascularization and stents for patients with multiple stenoses. This contributes to lower medical costs and an increase in convenience of the patient. In order to prove those benefits of AngioSupport, validation of AngioSupport with its assumptions should be performed. These assumptions with upcoming validations are discussed in the following paragraphs.

First, the segmentation of the coronary arteries is performed with CAAS. This software is developed to segment only one vessel, not an entire tree. Therefore, post processing was needed to connect the coronary arteries to each other. In addition, to generate a 3D image, the assumption is made that the vessels are ellipsoid. In order to validate that circular vessels and segmentation of CAAS is accurate enough to compute the FFR (pre- and post-operative) throughout the entire coronary tree, the virtual FFR values should be compared with measured FFR values.

Second, there has been chosen for a steady inflow as boundary condition to reduce computational time in respect to pulsatile inflow. Steady flow is assumed accurate enough to compute the FFR (pre- and post-operative). This is verified by comparing the FFR generated by pulsatile inflow simulated with the model of Bovendeerd et al. (Bovendeerd et al., 2006) and the FFR resulted of steady inflow. Both outcomes are considered equal, because the difference is smaller than 0.02, which is equal to the standard deviation of the repeatability of invasive FFR (Johnson et al., 2015).

Third, to simulation the blood pressure and flow real-time, the simulations are 1D assuming that flow is unidirectional. This is assumed to be accurate for calculation of mean pressures. This can be validated by performing the same simulations with the same boundary conditions with a 3D model and compare those results with the 1D results.

Fourth, AngioSupport consists of a multiple boundary conditions with parameters, which are population based defined. Therefore, a sensitivity analysis is performed to discover the influential parameters to subsequently couple those to patient data to define patient specific parameters. This could be validated against invasive pre- and post-FFR data.

Finally, the clinical relevance of AngioSupport should be proved by a clinical trial where a treatment plan will be defined for a group of patients based on the current procedure and for a patient group based on AngioSupport. For both groups follow-up data will be collected, such as repeated revascularization, number of stents, and end point of death and those data will be compared between the groups.

In summary, current results of AngioSupport looks promising; however, more validation must be performed to confirm its accuracy and clinical relevance.

5. References

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