AngioSupport: The design of an interactive tool to allow numerical modelling in clinical decision making

T. van den Boom

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Supervisors:
- dr.ir. I.M.M. Lammerts
- dr. ir. Marco Stijnen

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“AngioSupport: The design of an interactive tool to allow numerical modelling in clinical decision making”

Design project executed at:
LifeTec Group B.V.
Catharina Hospital Eindhoven

By:
ir. Tim van den Boom
Co-designer:
ir. B.G. van Willigen

The PDEng Thesis Evaluation Committee consisted of:

Supervisor: dr.ir. I.M.M. Lammerts (SMPE/e)
Scientific Program Director: prof.dr.ir. E.J.E. Cottaar (SMPE/e)
Company Representative: dr. ir. Marco Stijnen (LTG)
Hospital Representatives: 
dr. ir. W.A.L. Tonino (CZE)
dr.ir. M. van ’t Veer QME (CZE)

External Members: dr.ir. Marcel Rutten (TU/e)
External Scientific Member: prof.dr.ir.mr. B.A.J.M. de Mol (AMC)
scientific advisors: prof.dr.ir. F.N. van de Vosse (TU/e)
dr.ir. W. Huberts (TU/e)

Other members: dr.ir. M.D.I. Lansbergen (ZGT)

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The work described in this report is executed in accordance with the TU/e Code of Scientific Conduct

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Public Summary

Coronary Artery Disease (CAD) is the most common type of heart disease. It is caused by the buildup of plaque in the arterial walls, which narrows the vessel and reduces blood flow to the heart muscle. The remodeling of the heart can account for these changes, however, eventually increased plaque formation can result in insufficient oxygen in the heart muscle. Over time, CAD can cause heart failure, arrhythmias, ischemia, or a heart attack. CAD often develops slowly over time and the first emerging symptom is chest pain, often only during physical activity.

Treatment of CAD is either by medical therapy or revascularization. The two main revascularization techniques are coronary artery bypass graft (CABG) and percutaneous coronary intervention (PCI). To visualize the coronary vasculature, a coronary angiogram (CA) is made and the Fractional Flow Reserve (FFR) is measured invasively, which has shown to be an excellent indication of the presence of ischemia resulting from blocked blood flow. Currently, for patients with multivessel CAD, clinical outcomes following invasive revascularization depend on many characteristics, such as patient age, cardiac function, coronary disease distribution, previous interventions, diabetes, and/or the number of diseased vessels. Complicated cases are therefore discussed during a heart team meeting, where at least one cardiac surgeon and one intervention-cardiologist discuss each patient. However, choices (in the position, length or diameter) for a CABG or PCI can still be very difficult based on only experience, FFR measurement, and CA.

The aim of this project was to create a patient specific model based interactive tool, named AngioSupport, that could help the heart team in this process by simulating the outcome of PCI and CABG. AngioSupport is designed to fit in the current health care procedure of the Catharina Hospital Eindhoven and allows the heart team to use the models that have been developed at the Technical University of Eindhoven. In this design project, a ‘proof of concept’ has been given with a first prototype of AngioSupport, being developed at LifeTec Group.

In AngioSupport, a 3D representation of the full coronary vasculature of the patient is created by segmentation and pre-processing, using the angiogram images from the patient. Segmentation of the coronary arteries is performed with the help of CAAS software from Pie Medical Imaging. This 3D representation gives a more realistic insight of the patient specific vasculature and an easier interpretation of the blockages. It also allows the use of a one dimensional computational fluid dynamics code (1D CFD code), which can calculate the patient specific pressure throughout the coronary vasculature and is originally developed at the Eindhoven University of Technology (TU/e). With this 1D CFD code, the virtual FFR (vFFR) of the patient can be calculated, which is used to assess whether the heart muscle receives enough blood. AngioSupport also consists of an interface to be used during heart team meetings. The heart team only needs to load in the (pre-processed) patient data and can then start the 1D CFD code themselves. The interface also allows the heart team to virtually perform interventions and simulating the results, which greatly supports in deciding a treatment plan for each patient.

AngioSupport was tested on retrospective data from 10 patients during a user survey with 9 cardiologists. The cardiologists all stated that AngioSupport gives them more insight in each patient and that the AngioSupport interface is easy to use. However, improvements are still needed in AngioSupport, especially for the segmentation of the coronary vasculature. Also the accuracy of the 1D CFD code needs to be increased and validated if AngioSupport is to be used in clinical decision making.

During this project, a patient-specific model-based interactive tool has been developed that can support the heart team in clinical decision making. AngioSupport allows the heart team to use numerical models from TU/e to calculate the pre- and post-operative vFFR to support them in deciding a treatment plan for each patient.
Declaration concerning the TU/e Code of Scientific Conduct for the PDEng thesis

I have read the TU/e Code of Scientific Conduct.

I hereby declare that my PDEng thesis has been carried out in accordance with the rules of the TU/e Code of Scientific Conduct.

Date

8-8-2019

Name

Jouwe van den Boom

Signature

\[\text{Signature}\]

1 See: https://www.tue.nl/en/tue-university/about-the-university/organization/integrity/scientific-integrity/
The Netherlands Code of Conduct for Scientific Integrity, endorsed by 6 umbrella organizations, including the VSNU, can be found here also. More information about scientific integrity is published on the websites of TU/e and VSNU.
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1 Introduction

1.1 Coronary Artery Disease

Coronary Artery Disease (CAD) is the most common type of heart disease. It is caused by the buildup of plaque in the arterial walls, which narrows the vessel and reduces blood flow to the heart muscle. The remodeling of the heart can account for these changes, however, eventually increased plaque formation can result in insufficient oxygen in the heart muscle. Over time, CAD can cause heart failure, arrhythmias, ischemia, or a heart attack. Most heart attacks happen when a blood clot suddenly fully cuts off the blood supply to the heart, which causes permanent damage if not treated quickly. CAD often develops slowly over time and the first emerging symptom is chest pain (angina pectoris), often only during physical activity (stable angina pectoris). CAD is estimated to cost the EU economy 49 billion a year, about 2.6% of total healthcare expenditure [11].

The golden standard for assessing CAD severity in the Netherlands is coronary angiography (CA). This minimally invasive procedure involves the injection of contrast agent to visualize the coronary arteries using x-ray imaging. The excellent spatial resolution of CA provides diagnostic information about both proximal and distal part of the coronary tree [6]. However, CA often overestimates the severity of coronary stenosis while CA underestimates lesion length [5]. This poses problems in interpreting lesion severity and the impact of diffuse disease. CA also requires optimal angiographic views for lesions in tortuous segments, in bifurcations and in very short lesions [6]. To assist in the assessment of the coronary angiography images, quantitative coronary angiography (QCA) has been developed. QCA is an objective tool for quantification of the coronary lumen, using automatic edge detection algorithms to determine the vessel contours by assessing brightness along scan lines perpendicular to the vessel center (centerline). This is made by assessing one angiogram image (2D-QCA) or by combining two angiogram images into a 3D vessel (3D-QCA) [10].

Although CA gives insight in the location and radius of a stenosis, this does not assess whether the stenosis is hemodynamically significant and intervention is needed. Therefore, more complicated cases are reassessed in larger hospitals, such as Catharina Hospital Eindhoven, where the cardiac team can also perform a fractional flow reserve (FFR) measurement. This minimally invasive measurement is used to define the hyperemic flow with a stenosis \( Q_{hyp,sten} \) relative to the hyperemic flow without disease \( Q_{hyp,max} \) based on the ratio of the mean pressure distal to the stenosis (Pd) and the mean aortic pressure (Pa) \( FFR = \frac{Q_{hyp,sten}}{Q_{hyp,max}} \approx \frac{P_d}{P_a} \). FFR has shown to be an excellent objective measurement to assess the severity of a stenosis, since an FFR below 0.80 results in ischemia [9,22].

1.2 Treatment planning

Treatment of CAD is either by medical therapy or revascularization. The two main revascularization techniques are coronary artery bypass graft (CABG) and percutaneous coronary intervention (PCI). Comparison of CABG and PCI have provided conflicting results, with no difference in mortality evident between the methods after 1 year, however the adjusted all-cause mortality after 4 years was lower with CABG than with PCI [20]. These inferior results for PCI have recently been improving by the addition of second-generation drug eluting stents and the FFR guidance of PCI [21]. Currently, for patients with multivessel CAD, current data indicate that clinical outcomes following invasive revascularization depend on patient characteristics, cardiac function,
coronary disease distribution, previous interventions, diabetes, and/or the number of diseased vessels [22]. Complicated cases are therefore discussed during a heart team meeting, where one cardiac surgeon and one intervention-cardiologist discuss each patient. However, choices in the position, length or diameter for a CABG or PCI can still be very difficult based on only experience, FFR measurement, and CA.

Therefore, there is still a need to predict the outcome of an intervention. Many investigators have been developing computational fluid dynamics (CFD) models that describe the blood pressure and blood flow wave phenomena in arteries and veins to study the effects of vascular diseases on the pressure and flow waveforms [14,15]. These CFD models allow the calculation of a virtual fractional flow reserve (vFFR), which can be used in clinical decision making. Many companies are already developing a clinical tool which can calculate the pre-operative FFR, such as HeartFlow[16], Pie Medical Imaging[17] and Medis[18]. However, these clinical tools are not yet able to calculate the post-operative FFR after PCI or CABG, which is needed to help the heart team in deciding between PCI and CABG for each patient.

1.3 Aim and thesis outline

The aim of this project is to create an interactive tool that could help the heart team in this process by simulating the outcome of PCI and CABG, named AngioSupport. The tool will contain the research being developed at the Technical University of Eindhoven to create an interactive tool to assist in clinical decision making. By using the already made angiogram images, a 3D representation of the full coronary vasculature can be created. This gives a more realistic insight of the patient specific vasculature and an easier interpretation of the lesions. It also allows for computational fluid dynamics, which can calculate the patient specific pressure throughout the coronaries, allowing for calculation of virtual FFR (vFFR) [8]. Finally, the model can also allow to virtually perform the intervention and predict the post-FFR, which can greatly help the heart team in treatment planning. An example of this workflow is shown in Figure 2.

![Figure 2: Example of the workflow in AngioSupport to support the heart team in deciding between PCI and CABG](image)

This report therefore describes the development of AngioSupport. In Chapter 2, the project definition is described. This chapter will describe the approach of the project, such as the project organization, communication plan, design cycle and stakeholder analysis. In Chapter 3, the scope of the project is narrowed and the functional requirements are described. These functional requirements are then translated into technical requirements. In Chapter 4, the design alternatives and choices are described based on the requirements for the project. In Chapter 5, the final design of AngioSupport and each component is described. In Chapter 6, the results of the user survey are shown. In Chapter 7, the verification and validation of the project is described. In Chapter 8 the full project is discussed and a conclusion made. In Chapter 9, future steps for AngioSupport are explained and a possible planning is shown. In Chapter 10, a personal reflection on the total project is given.
2 Project definition

2.1 CompBioMed Consortium

This project is part of the CompBioMed (CBM) consortium. CompBioMed is a European Commission H2020 funded Center of Excellence focused on the use and development of computational methods for biomedical applications. The aim of this group is to bring the numerical models and methods that are being developed in universities to be used in a clinical and applicable setting. Within this Centre of Excellence is LifeTec Group (LTG) one of the core partners. LifeTec Group has defined this project together with the biomedical engineering department of Eindhoven University of Technology (Tue) and the Catharina Hospital Eindhoven (CHE). This project will combine the development and research that is currently in progress at the university. The focus is not to create new fundamental research, but to use the existing research and combine this into a working prototype to assist in clinical decision making. Finally, a proof of concept is made in this project to investigate whether this interactive tool is feasible and reliable.

2.2 Design Project: AngioSupport

The final product from which a prototype is created during this project, is named AngioSupport. It is a model-based interactive tool, which consists of a segmentation preprocessing part, a CFD numerical code and a clinical user interface. These elements will be further explained later in this report. AngioSupport has been created as part of the PDEng education of Qualified Medical Engineer (QME). QME is part of the School of Medical Physics and Engineering Eindhoven (SMPEe). The full project was executed together with Bettine van Willigen.

2.3 Stakeholders

Within this project, the stakeholders are identified. In order to develop cooperation between stakeholders and the developers of AngioSupport, the stakeholders are identified and their involvement assessed:

- **Bettine van Willigen**: Co-designer of the project.
- **LifeTec Group (LTG)**: AngioSupport is developed at LTG, where Marco Stijnen provides guidance. The AngioSupport software will be property of LTG and therefore Marco has a high interest and influence in the project.
- **CompBioMed (CBM)**: CBM is funding the project. LifeTec Group has obligations towards several work packages in this project and the development of AngioSupport is a part of the obligations.
- **Catharina Hospital Eindhoven (CHE)**: Pim Tonino is the intervention cardiologist and part of the heart team at Catharina Hospital. He is the desired end user of AngioSupport. Marcel van ’t Veer works as a qualified medical engineer at the cardiology research department at the Catharina Hospital Eindhoven. He will help us with the design of AngioSupport and the clinical modelling. He can also help us in acquiring hospital data and meetings with cardiologists.
- **Technical University of Eindhoven (Tue)**: Frans van de Vosse is the professor of the biomedical engineering department. The research in his group will be used in this project and he guides us in creating the 1D CFD code. Wouter Huberts is a assistant professor of medical engineering in the biomedical engineering department. He will help in creating the 1D CFD code and exploring new ideas in the interactive tool.
- **Pie Medical Imaging (PMI)**: Tristan Slots works at PMI and provided the segmentation tool to be used in the preprocessing. Pie Medical Imaging is not actively involved in creating AngioSupport, but is interested in the development and possible exploitation of AngioSupport combined with Pie Medical Imaging software.
School of Medical Physics and Engineering Eindhoven (SMPEe): Ward Cottaar is the director of SMPEe. Ivonne Lammerts is the education coordinator at SMPEe. She guides the development of the project and supervises the design method as proposed by the education.

Based on each stakeholders interest and power, a stakeholder analysis and communication plan are made and are shown in Figure 3 and Table 1. The full stakeholder analysis can be found in Appendix A.

<table>
<thead>
<tr>
<th>Name</th>
<th>Stakeholder analysis:</th>
<th>Communication:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bettine van Willigen</td>
<td>Co-designer</td>
<td>Daily meetings</td>
</tr>
<tr>
<td>Marco Stijnen</td>
<td>Supporter</td>
<td>Weekly meetings</td>
</tr>
<tr>
<td>Mariano Vazquez</td>
<td>Neutral</td>
<td>Monthly updates</td>
</tr>
<tr>
<td>Frans van de Vosse</td>
<td>Supporter</td>
<td>Progress meeting</td>
</tr>
<tr>
<td>Ward Cottaar</td>
<td>Supporter</td>
<td>Progress meeting</td>
</tr>
<tr>
<td>Pim Tonino</td>
<td>Supporter</td>
<td>Progress meeting</td>
</tr>
<tr>
<td>Marcel van ’t Veer</td>
<td>Supporter</td>
<td>Progress meeting</td>
</tr>
<tr>
<td>Wouter Huberts</td>
<td>Supporter</td>
<td>Progress meeting</td>
</tr>
<tr>
<td>Tristan Slots</td>
<td>Critic</td>
<td>Contacted when needed</td>
</tr>
<tr>
<td>Ivonne Lammerts</td>
<td>Supporter</td>
<td>Progress meeting</td>
</tr>
</tbody>
</table>

Table 1: Communication plan

2.4 Organization

The organization of the project is shown in Figure 4. The organization consists of a project board, project management and project delivery part. The project board consists of three persons: Senior User (the desired end-user of the project), Executive (the project owner and supervisor) Senior Supplier (the main supplier of input in the project). The project management consists of two project managers, since this project consists of more sub-projects:

- **1D CFD code**: patient specific model-based 1D CFD code for the simulations of interventions;
- **segmentation**: segmentation of the coronary angiograms and pre-processing for the simulations;
- **interface**: AngioSupport is used by the heart team as an interactive decision supporting tool.
Project assurance and change authority are performed by the project board and project managers together, which is common for smaller projects. In project delivery, two team leaders are assigned. Tim van den Boom (writer of this report) is mainly responsible for the 1D CFD code, Bettine van Willigen (co-designer of AngioSupport) is mainly responsible for the interface and the segmentation is a shared responsibility.

![Project Board](image)

**Figure 4: The organization of the project.**

### 2.5 Design Cycle

For the design of AngioSupport, the design cycle has been followed as proposed by SMPEe. An iterative process was chosen, which is usually the case when building software. This process is shown in Figure 5, with the iterative cycle shown in orange. Every new iteration involved the Plan-Do-Check-Act cycle. Mostly, new ideas were discussed during progress meetings and then executed. Therefore, this iterative cycle was usually from one progress meeting until the next progress meeting.

![Design cycle](image)

**Figure 5: Design cycle followed during this project.**

### 2.6 Project Deliverables and Non-deliverables

The aim of this project was the design of a patient-specific model-based interactive tool to support the heart team in clinical decision making. This project combines the research at the TUe into a usable tool for the heart
team. To complete this project, a prototype of AngioSupport has been realized, with the following deliverables:

- **Segmentation**: segmentation and pre-processing of the coronary vasculature of the patient;
- **1D CFD code**: model based fluid dynamics code for the computation of vFFR and for the simulation of the cardiac interventions PCI and CBAG (pre- and post-operative);
- **Interface**: interface for the heart team to perform virtual interventions for decision making;
- Investigate usability in the hospital.

However, to be able to successfully complete this project, the scope of the project was reduced during the project. The following choices were made during the project to reduce the scope:

- For the segmentation of the coronary angiograms, help was found at Pie Medical Imaging.
- Only the segmentation of the left coronary vasculature.
- Only the simulation of the placement of one stent during PCI
- Only the simulation of CABG using the Left Internal Mammary Artery (LIMA).
- No clinical validation of AngioSupport

### 2.7 Planning and Risk Analysis

The total project had a timespan of effectively one year, which was spread over 1.5 year. At the beginning of the project, the planning for the full project was made. This planning was updated every progress meeting. The definitive planning can be seen in Figure 6. The original planning and every updated version can be seen in Appendix B.

At the beginning of the project, the main risks of the project were discussed together with the stakeholders. These risks were assessed after each project meeting and the plans were explained. These projects risks and actions further explained in Appendix C. Most of the risks are finally mitigated at the end of the project, as shown in Table 2.

<table>
<thead>
<tr>
<th>Risk</th>
<th>Dependent on someone else?</th>
<th>Chance:</th>
<th>Impact</th>
<th>Color code</th>
<th>Risk mitigated?</th>
</tr>
</thead>
<tbody>
<tr>
<td>No segmentation of angiograms</td>
<td>Pie Medical Imaging</td>
<td>Average</td>
<td>Large</td>
<td>Green</td>
<td>Yes, at PM3</td>
</tr>
<tr>
<td>Not able to link segmentation with AngioSupport</td>
<td>No</td>
<td>Small</td>
<td>Large</td>
<td>Yellow</td>
<td>Yes, at PM3</td>
</tr>
<tr>
<td>Not able to build 1D CFD code</td>
<td>No</td>
<td>Small</td>
<td>Large</td>
<td>Yellow</td>
<td>Yes, at PM1</td>
</tr>
<tr>
<td>Not able to calculate FFR</td>
<td>No</td>
<td>Small</td>
<td>Large</td>
<td>Yellow</td>
<td>Yes, at PM2</td>
</tr>
<tr>
<td>vFFR not equal to mFFR</td>
<td>Catharina Hospital Eindhoven</td>
<td>Small</td>
<td>Large</td>
<td>Yellow</td>
<td>No</td>
</tr>
<tr>
<td>Code takes too much time</td>
<td>No</td>
<td>Large</td>
<td>Small</td>
<td>Orange</td>
<td>Yes, at PM4</td>
</tr>
<tr>
<td>Not able to create an interface</td>
<td>No</td>
<td>Small</td>
<td>Large</td>
<td>Orange</td>
<td>Yes, at PM2</td>
</tr>
<tr>
<td>Not able to perform virtual PCI</td>
<td>No</td>
<td>Small</td>
<td>Large</td>
<td>Orange</td>
<td>Yes, at PM3</td>
</tr>
<tr>
<td>Not able to perform virtual CABG</td>
<td>No</td>
<td>Average</td>
<td>Large</td>
<td>Orange</td>
<td>Yes, at PM4</td>
</tr>
</tbody>
</table>
Table 2: Risk matrix of the AngioSupport project. Final columns shows at which point during the project the risk was solved (PM = Progress Meeting).

<table>
<thead>
<tr>
<th>Risk</th>
<th>No</th>
<th>Average</th>
<th>Average</th>
<th>Not completely</th>
</tr>
</thead>
<tbody>
<tr>
<td>The virtual interventions are not realistic</td>
<td>No</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AngioSupport can not give advice between interventions</td>
<td>No</td>
<td>Small</td>
<td>Large</td>
<td>Yes, at PM4</td>
</tr>
<tr>
<td>No usability research possible</td>
<td>Catharina Hospital Eindhoven</td>
<td>Small</td>
<td>Large</td>
<td>Yes, during final weeks</td>
</tr>
<tr>
<td>No clinical patient data received</td>
<td>Catharina Hospital Eindhoven</td>
<td>Average</td>
<td>Average</td>
<td>Yes, at PM3</td>
</tr>
</tbody>
</table>

3 Detailed Project Aim

3.1 Design overview

As mentioned in 2.1, in this project a patient-specific model-based interactive tool (called AngioSupport) has been designed that consists of a segmentation preprocessing part, a 1D CFD code and a clinical user interface. Figure 7 shows a first overview of the workflow of AngioSupport. In this figure, the interface used by the heart team is shown in blue, while the underlying 1D CFD code is shown in grey. The heart team can use AngioSupport during the heart team meeting, which will first show the vFFR in the patient preoperatively. The heart team can then decide whether an intervention is needed and can virtually perform the PCI or CABG. By comparing the simulated (post-operative) results of the intervention with the pre-operative vFFR, the heart team can decide a treatment plan. The patient specific coronary vasculature is already created in the preprocessing and only needs to be loaded in. The 1D CFD code will be created as an executable: in this design process, it was created as an executable and can be started without any knowledge of the numerical model. The preprocessing, the 1D CFD code and the interface will be explained. First, the design choices are explained in Chapter 4 and the total design overview is shown in Chapter 5.

Figure 7: Overview of AngioSupport workflow. In blue, the interface parts visible for the heart team. In grey, the preprocessing segmentation and the 1D CFD code, not visible in the interface.
3.2 Functional Requirements

Before starting to design different concepts, it is important to identify the functional requirements. These functional requirements will later be translated into technical requirements. First, we talked with Pim Tonino (Senior User), since his requirements are leading in this project. Besides the conversations with the Senior User, some functional requirements resulted from conversations with Marco Stijnen (Executive) and Frans van de Vosse (Senior Supplier). For this project, the following 6 functional requirements were defined:

- Implementable in the current health care procedure.
- Segmentation of the patient specific coronary vasculature.
- Simulate the vFFR in the patient specific coronary vasculature.
- Visualize results of patient in interface.
- Compare results of interventions during heart team meeting.
- Start of simulation platform at LifeTec Group.

3.1 Technical Requirements

In the following section, each functional requirement (FR) is elaborated, while also narrowing the scope into the technical requirements, which were updated throughout the project.

**FR1: Implementable in the current health care procedure**

AngioSupport is designed to be used during heart team meetings. This means AngioSupport needs to fit in the current health care procedure to be used in hospitals. This requires AngioSupport to be used without the need to export data out of the hospital as well as to get correct CE marking. This resulted in the following technical requirements:

<table>
<thead>
<tr>
<th>Description:</th>
<th>Acceptance:</th>
</tr>
</thead>
<tbody>
<tr>
<td>TR1 No external connection outside hospital needed</td>
<td>Executable on single computer</td>
</tr>
<tr>
<td>TR2 No change in hospital to use AngioSupport</td>
<td>Same health care process</td>
</tr>
<tr>
<td>TR3 CE marking</td>
<td>Investigate required CE level</td>
</tr>
</tbody>
</table>

**FR2: Segmentation of the patient specific coronary vasculature**

To create 3D representation of the coronary vasculature, a segmentation of the coronary angiogram is needed. During the project start up meeting, it was decided to find help for the segmentation, since Tim and Bettine are not experienced in the segmentation of coronaries. Also, to reduce the scope of the segmentation, it was decided to only focus on the left coronary vasculature. To visualize the impact of interventions on each branch of the left coronary vasculature, we will combine the vessels into one vasculature. This resulted in the following technical requirements:

<table>
<thead>
<tr>
<th>Description:</th>
<th>Acceptance:</th>
</tr>
</thead>
<tbody>
<tr>
<td>TR4 Find segmentation tool</td>
<td>Software able to segment coronary angiogram</td>
</tr>
<tr>
<td>TR5 Use patient data</td>
<td>Receive retrospective data from hospital</td>
</tr>
<tr>
<td>TR6 Segment patient specific vasculature</td>
<td>Segment LAD, LCx and main side branches of patient</td>
</tr>
<tr>
<td>TR7 All coronaries connected together</td>
<td>One combined coronary vasculature</td>
</tr>
</tbody>
</table>

**FR3: Simulate the vFFR in the patient specific coronary vasculature**

For each patient, the vFFR will be calculated for the entire vasculature. This requires a computational fluid dynamics code. At the first meeting, it was already decided that only a 1D CFD code will be fast enough to be used during a heart team meeting. Therefore, a 1D CFD code is needed, which is executable for the heart team, without understanding the 1D CFD code. To create a realistic result of the simulations, patient data must be used to increase the accuracy of the simulations and the results of the interventions. This resulted in the following technical requirements:

<table>
<thead>
<tr>
<th>Description:</th>
<th>Acceptance:</th>
</tr>
</thead>
<tbody>
<tr>
<td>TR8 Code to simulate pressure and flow</td>
<td>Verified 1D CFD code</td>
</tr>
</tbody>
</table>
**FR4: Visualize results of patient in interface**

To visualize the 3D coronary vasculature, an interface for the heart team is needed. The heart team must be able to execute the CFD code from the interface and show the patient specific results. The interface should give the information to decide whether an intervention is needed, by visualizing the coronary vasculature, the stenotic vessels and the simulated vFFR. The results must be easy to understand and allow the heart team to decide if an intervention is needed. This resulted in the following technical requirements:

<table>
<thead>
<tr>
<th>Description</th>
<th>Acceptance</th>
</tr>
</thead>
<tbody>
<tr>
<td>TR15 Interface of AngioSupport</td>
<td>Software for interface</td>
</tr>
<tr>
<td>TR16 Heart team can easily load in patient</td>
<td>Positive user survey response</td>
</tr>
<tr>
<td>TR17 Interface can start 1D CFD code</td>
<td>1D CFD code executable from Interface</td>
</tr>
<tr>
<td>TR18 Show stenotic areas</td>
<td>Red parts for stenotic vessels</td>
</tr>
<tr>
<td>TR19 Show color coded vFFR</td>
<td>&gt;0.8 for healthy vessels &lt;0.8 for ischemic vessels</td>
</tr>
<tr>
<td>TR20 Investigate each segment of vasculature</td>
<td>Show plot with length and diameter of segment</td>
</tr>
<tr>
<td>TR21 Heart team understands results shown</td>
<td>Positive user survey response</td>
</tr>
<tr>
<td>TR22 Heart team can use results to decide of intervention is need</td>
<td>Positive user survey response</td>
</tr>
</tbody>
</table>

**FR5: Compare results of interventions during heart team meeting**

After each simulated intervention, the results are shown in AngioSupport. These results must be ready during a heart team and help them in deciding the best treatment plan. Therefore, it requires low simulation time. To reduce the scope of designing the interface, we decided to only simulate one single stent and to simulate the placement of a CABG using the LIMA. This resulted in the following technical requirements:

<table>
<thead>
<tr>
<th>Description</th>
<th>Acceptance</th>
</tr>
</thead>
<tbody>
<tr>
<td>TR23 Virtually perform PCI</td>
<td>Choose stent diameter and length</td>
</tr>
<tr>
<td>TR24 Virtually perform CABG</td>
<td>Choose position of placement LIMA</td>
</tr>
<tr>
<td>TR25 Calculate results in interface</td>
<td>Restart simulation when intervention created</td>
</tr>
<tr>
<td>TR26 Heart team can perform PCI easily</td>
<td>Positive user survey response</td>
</tr>
<tr>
<td>TR27 Heart team can perform CABG easily</td>
<td>Positive user survey response</td>
</tr>
<tr>
<td>TR28 Short simulation time</td>
<td>Simulation &lt;4 seconds</td>
</tr>
<tr>
<td>TR29 Show results of both interventions</td>
<td>Results PCI and CABG in one screen</td>
</tr>
<tr>
<td>TR30 Show results previous interventions</td>
<td>Buttons to reload previous simulations</td>
</tr>
<tr>
<td>TR31 AngioSupport improves decision making for heart team</td>
<td>Positive user survey response</td>
</tr>
</tbody>
</table>

**FR6: Start of simulation platform at LifeTec Group**

Besides developing an interactive tool, this project is the start of a simulation platform, combining the research from the biomedical engineering department and the business at LTG. Although this is not important for the success of AngioSupport, it would be good to keep these extra goals in mind when developing AngioSupport. This resulted in the following technical requirements:

<table>
<thead>
<tr>
<th>Description</th>
<th>Acceptance</th>
</tr>
</thead>
<tbody>
<tr>
<td>TR32 Software usable for future projects</td>
<td>Expandable and modular software</td>
</tr>
<tr>
<td>TR33 Explore possibilities for further development of simulation platform</td>
<td>Create a business case for AngioSupport</td>
</tr>
</tbody>
</table>
4 Design Choices

The design process during this project was a large iterative process with many design choices. In this chapter, these design choices are explained. For each design choice, the important technical requirements, are shown and the benefit compared to possible alternatives is explained. The design choice is then explained technically. For more in depth explanations, the reader will be referred to appendices. The design choices will result in the final product AngioSupport.

The design choices of AngioSupport are explained in four sections:

- **Section 4.1** explains how AngioSupport can be used in the hospital and explores the business case.
- **Section 4.2** explains the preprocessing of AngioSupport to create a patient specific coronary vasculature (shown in orange in Figure 7).
- **Section 4.3** explains the 1D CFD code used in AngioSupport (shown in grey in Figure 7).
- **Section 4.4** explains the interface used by the heart team (shown in blue in Figure 7).

4.1 Organization

This section explains how AngioSupport can be used in the hospital and explores the business case. The concepts described in this section will be used to meet the following technical requirements:

<table>
<thead>
<tr>
<th>Description</th>
<th>Acceptance</th>
</tr>
</thead>
<tbody>
<tr>
<td>TR2 No change in hospital to use AngioSupport</td>
<td>Same health care process</td>
</tr>
<tr>
<td>TR3 Implementable in hospital</td>
<td>Investigate required CE marking</td>
</tr>
<tr>
<td>TR33 Explore possibilities for further development of simulation platform</td>
<td>Create a business case for AngioSupport</td>
</tr>
</tbody>
</table>

**Same health care process**

*Resulting from technical requirement TR2 (Same health care process)*

Together with the stakeholders, it has been decided how AngioSupport can be used in the health care procedure. In principal, it should not need any extra process steps in the hospital. This choice makes AngioSupport an addition to the current health process and no structural changes are needed. This will improve the acceptance in the hospital and makes the implementation of AngioSupport in hospitals easier. As shown in Figure 8, patients with CAD in peripheral hospitals get a CA to visualize the coronary arteries. In case of a complicated CAD, these patients are sent to central hospitals to get a CA with an mFFR measurement. These patients are then discussed during the heart team meeting to decide for a treatment plan. AngioSupport would be used during these heart team meetings for these complicated cases. Although a CT scan has 3D spatial information and would be easier to create a 3D reconstruction, CT scans are not part of the current health care process in hospitals for patients with CAD. AngioSupport therefore relies on the angiogram images created for each patients. These angiogram images are stored in the picture archiving and communication system (PACS). AngioSupport will use the dicom images saved in the PACS. These dicom images are used to create the 3D coronary vasculature. These dicom images are then preprocessed with AngioSupport into a patient specific coronary vasculature. This segmentation will be done within the hospital and patient data do not need to go outside the hospital.
Legislation

*Resulting from technical requirement TR3 (Investigate required CE marking)*

For AngioSupport, the legislation needed for implementation in a hospital has been investigated. For each medical device, it is most important to elaborately specify the desired use. This desired use is then needed to classify the medical device using the demands for guideline medical devices [1]. For training purposes and to improve understanding of the interventions, no classification is needed. Hence, AngioSupport can be used during this project and to demonstrate this to cardiologists. However, whenever AngioSupport will be used as a device to decide a treatment plan for a patient, the risk of the medical device becomes high and AngioSupport is then classified as 2a. This means a notified body must judge AngioSupport.

Business Case

*Resulting from technical requirement TR33 (Create a business case for AngioSupport)*

To explore the business case for AngioSupport, several aspects were investigated before starting the project. This section explains the market, competition and unique selling points. In Chapter 10, a further future development plan is proposed.

Approximately two thirds of patients who require revascularization have multi-vessel disease and two thirds of this group have an anatomy that is treatable with percutaneous or open heart procedures[25]. In 2010, approximately 8.400 CABG[26] and 35.000 PCI were performed in the Netherlands[27]. Following prices as stated from Martini Hospital Groningen, these procedures cost €13.000 and €4.500 for CABG and PCI, respectively[28]. This results in total costs of CABGs of approximately €78 million and PCIs of approximately €158 million. Patients receiving a CABG are all discussed during a heart team meeting, while patients receiving PCI are not all discussed during a heart team meeting. No estimate could be made for how many of the total 35.000 PCI treatments were first discussed in a heart team meeting.
Virtual FFR model | Developed in | Imaging tool | CFD simulations | Extra requirements | diagnostic accuracy | Single or multi vessel | Approximate run time
--- | --- | --- | --- | --- | --- | --- | ---
HeartFlow [16] | California (US) | CT | 3D CFD | Myocardial mass | 86% | Multi | Remote core computation
VIRTU-1 [23] | Sheffield (UK) | CA | 3D CFD | - | 97% | Single | 12-24 h
FFRQCA [24] | Leiden (NL) | CA | Steady-state 3D | contrast velocity | 88% | Single | 5 min
CAAS [17] | Maastricht (NL) | CA | Geometry based | MAP | 95% | Single | 1 sec
Medis [18] | Leiden (NL) | CA | Geometry based | contrast velocity | 94% | Single | unknown
CathWorks [29] | Kfar-Saba (IS) | CA | Geometry based | MAP | 92% | Multi | 2-3 minutes
AngioSupport | Eindhoven (NL) | CA | 1D CFD | MAP | 70% | Multi | 4 sec

Table 3: Overview of software tools simulating vFFR. Data derived on the basis of best interpretation of the published data.

Table 3 gives an overview of software tools simulating the vFFR. These companies are all creating a tool to use for clinicians. Each already existing software tool have their own strategy in calculating the vFFR, but show good diagnostic accuracy. However, each software tool is only focused on simulating the pre-operative vFFR, which can result in not requiring an invasive mFFR to investigate whether revascularization is needed. However, for treatment planning, the post-operative vFFR would be needed, which none of the existing simulation tools currently predict. This gives the unique selling point of AngioSupport, which will be able to calculate the post-operative vFFR of the entire coronary vasculature, by allowing the heart team to test a PCI or CABG intervention during a heart team meeting. The Business plan is further explored in Chapter XXX.

4.2 Segmentation

An important part of AngioSupport is the 3D segmentation of the coronary arteries. As shown in Figure 8, the current procedure for patients with angina pectoris is to make an angiogram of the coronary vasculature. Therefore, in this project we used these 2D angiography images to create a 3D coronary vasculature. During this project, we collected retrospective data from patients which were in the health care process as described in Figure 8 and chose the segmentation tool CAAS from Pie Medical Imaging to segment the images. A timeline of this process is shown in Figure 9.

The concepts described in this section will be used to meet the following technical requirements:

<table>
<thead>
<tr>
<th>Description</th>
<th>Acceptance</th>
</tr>
</thead>
<tbody>
<tr>
<td>TR4 Find segmentation tool</td>
<td>Software able to segment coronary angiogram</td>
</tr>
<tr>
<td>TR5 Use patient data</td>
<td>Receive retrospective data from hospital</td>
</tr>
<tr>
<td>TR6 Segment patient specific vasculature</td>
<td>Segment LAD, LCx and main side branches of patient</td>
</tr>
<tr>
<td>TR7 All coronaries connected together</td>
<td>One combined coronary vasculature</td>
</tr>
</tbody>
</table>
Segmentation tool

*Resulting from technical requirement TR4 (Software able to segment coronary angiogram)*

To choose a segmentation tool, we investigated several options at the beginning of the project. These options are summarized in Table 4. During the first meeting with the stakeholders (Project Start Up meeting (PSU)), we decided together which option to choose. We quickly concluded that creating an entire new segmentation tool is not feasible during this project and would also require extra education and training for both project leaders, since both Tim and Bettine do not have much experience in image processing. At the PSU, we decided to contact Pie Medical Imaging for the segmentation. This is mainly because they already have a validated tool for segmentation of coronary arteries and also because there is already good contact with this company, since they partly originate from the department of biomedical engineering of Frans van de Vosse.

<table>
<thead>
<tr>
<th>Option</th>
<th>Description</th>
<th>Benefits</th>
<th>Downsides</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Create new</td>
<td>Free</td>
<td>Low knowledge of segmentation</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Full understanding of each part</td>
<td>Time needed to create</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Easier to connect with the rest of the software</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>CAAS</td>
<td>Full working software</td>
<td>License needed</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Validated in clinic</td>
<td>No knowledge how software works</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Good contact with company</td>
<td>Only one single vessel</td>
</tr>
<tr>
<td>3</td>
<td>pfire</td>
<td>Free software</td>
<td>No knowledge how software works</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Used in CompBioMed</td>
<td>Only validated</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Only for simple vasculatures</td>
</tr>
<tr>
<td>4</td>
<td>VMTK</td>
<td>Free software</td>
<td>No knowledge how software works</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Not ready for use</td>
</tr>
<tr>
<td>5</td>
<td>SimVascular</td>
<td>Free software</td>
<td>No knowledge how software works</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Not suitable for angiography</td>
</tr>
</tbody>
</table>

Table 4: Options for segmentation tool for coronary angiogram images.

Patient Data

*Resulting from technical requirement TR5 (Receive retrospective data from hospital)*

To receive the patient data from the hospital, first a nWMO agreement (niet-Medisch Wetenschappelijk Onderzoek) was made. This agreement can be found in Appendix L. This agreement was mandatory to receive data from the hospital as a company. This nWMO agreement was accepted in October 2018. We then received the first dataset from Marcel van ’t Veer from the Catharina Hospital Eindhoven. This dataset had both pre and post-operative data from patients which had a PCI or CABG. Unfortunately, not all of the dataset was compatible with the CAAS software and we were not able to correctly segment the coronary vasculature from this dataset. We then later received the dataset from Simon Dello, a cardiologist from Catharina Hospital who had prepared a dataset for Pie Medical Imaging which was suitable for the CAAS software. This dataset consisted of 75 patients, which were all discussed during a heart team meeting.

CAAS software

*Resulting from technical requirements TR6 (Segment LAD, LCx and main side branches of patient) and TR7 (One combined coronary vasculature)*

The CAAS software from PMI was used to create patient specific coronary vasculature of the left side. The software only needs two images and an angle larger than 30 degrees between these images. The CAAS software then needs the user to draw the outlines of the coronary vessels in both images and a 3D vessel is created by combining these two outlines. These outlines were drawn for each vessel and are combined into one single vasculature. To combine these coronary vessels, a python script was created which merges the vessels into one large coronary vasculature. The process of creating the coronary vessels in CAAS and merging them into a full coronary vasculature is explained in Appendix K. Fout! Verwijzingsbron niet gevonden. shows some examples of 3D vasculatures with their chosen corresponding 2D angiogram images. The total preprocessing of a patient takes approximately 90 minutes.
This section explains the concepts used in the 1D CFD code in AngioSupport. The concepts described in this section will be used to meet the following technical requirements:

<table>
<thead>
<tr>
<th>Description</th>
<th>Acceptance</th>
</tr>
</thead>
<tbody>
<tr>
<td>TR1  No external connection outside hospital needed</td>
<td>Executable on single computer</td>
</tr>
<tr>
<td>TR8  Calculate pressure and flow</td>
<td>Verified 1D CFD model</td>
</tr>
<tr>
<td>TR9  Simulate FFR</td>
<td>Verified coronary 1D CFD model</td>
</tr>
<tr>
<td>TR10 Make patient specific</td>
<td>Use patient parameters</td>
</tr>
<tr>
<td>TR11 Calculate accurate FFR</td>
<td>Accuracy &gt;70%</td>
</tr>
<tr>
<td>TR12 Detection of stenosis</td>
<td>Automatic stenosis detection</td>
</tr>
<tr>
<td>TR13 Easy to start simulation</td>
<td>Standalone executable</td>
</tr>
<tr>
<td>TR14 Able to perform interventions</td>
<td>Simulation of PCI and CABG</td>
</tr>
<tr>
<td>TR28 Short simulation time</td>
<td>Simulation &lt;4 seconds</td>
</tr>
</tbody>
</table>

**CFD code choice**

*Resulting from technical requirements TR1 (Executable on single computer), TR8 (verified 1D CFD model), TR13 (Standalone executable) and TR27 (Simulation <4 seconds)*

To simulate the flow and pressure in the coronaries, CFD simulations are needed. Since these simulations must be able to be used execute a full simulation under 4 seconds, the only option is to create a one dimensional CFD model, because higher dimensional models are computationally too expensive and therefore take too much time. One dimensional models are able to calculate the flow and pressure in the full vasculature while maintaining low computational cost. To implement a 1D CFD code in AngioSupport, first several options have been investigated, see in Table 5.
Table 5: Benefits and downsides of the 1D CFD code to implement in AngioSupport.

<table>
<thead>
<tr>
<th>Option</th>
<th>Origin</th>
<th>Language</th>
<th>Benefits</th>
<th>Downsides</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>TUE</td>
<td>Sepran</td>
<td>Matlab known by designers, Sepran fast</td>
<td>Linux server needed, Matlab license needed, Large extensive code, Sepran more difficult to program</td>
</tr>
<tr>
<td>2</td>
<td>TUE</td>
<td>Matlab</td>
<td>Matlab known by designers</td>
<td>Matlab license needed, Slow software</td>
</tr>
<tr>
<td>3</td>
<td>openBF</td>
<td>Julia</td>
<td>Free software, Used within CompBioMed</td>
<td>More time needed to understand, Different numerical scheme, Slower numerical scheme, No help available from TUE</td>
</tr>
<tr>
<td>4</td>
<td>Create new Python</td>
<td>Free Software, Full understanding each part</td>
<td>Time needed to create, Validation needed</td>
<td></td>
</tr>
</tbody>
</table>

At the beginning of the project is decided to create our own 1D CFD code using Python. Although this requires a longer start up time, since the code needs to be build and Verified, the software will be a standalone software package and no license is needed. This allows the 1D CFD code to be used in AngioSupport without being dependent of others. Python is also a free software package and can therefore easily be used when possibly selling AngioSupport as a software package.

**Version 1: 1D CFD code**

*Resulting from technical requirements TR8 (Verified 1D CFD model)*

In large arteries, the relation between pressure, flow, wall shear stress and cross sectional can be modelled using the 1D conservation of mass, the 1D momentum balance equation and a constitutive law. The 1D CFD code in this project is based on the model as proposed by Kroon et al. [7]. This model has the great advantage of only having pressure as a state variable, therefore greatly reducing the computational cost and decreasing simulation time. The 1D CFD method as proposed by Kroon et al [7] is explained in Appendix J and V. The python version that has been created in this project first only consisted of line elements and windkessel elements, which is explained in more detail in Appendix E and F, respectively. This first version was verified with the results from a benchmark study from Boileau et al. [4], which shows that the implementation is correct as can be found in Appendix M. The systemic geometry used in the benchmark study by Boileau et al. [4] is a reduced version of the anatomically detailed arterial network model developed by Blanco et al. [3]. This geometry is often used also in other studies [4, 3, 2] and verified with 3D simulations [4]. However, in this project not the entire systemic geometry is needed. The systemic geometry can be truncated at regions to reduce computational cost. Furthermore, this geometry does not include a Left Internal Mammary Artery (LIMA), which is often used in bypass surgeries. The truncation of the systemic geometry and the addition of the LIMA are explained in Appendix O.

**Version 2: 1D coronary vasculature**

*Resulting from technical requirements TR9 (Verified coronary 1D CFD model)*

The first version of the CFD code has been expanded using the research by van der Horst et al. [12]. An overview of these elements can be seen in Figure 11. The elements are briefly described in this section, but the reader is referred to the corresponding appendices for a more detailed explanation:

1. One fiber element (Appendix D): A mathematical model of the interaction between coronary flow and cardiac mechanics is presented, with a limited number of model parameters. This element also calculates the intramyocardial pressure, needed for the coronary windkessel elements.
2. Coronary line elements (Appendix G): The coronaries are modelled as coronary line elements, which is similar to the line elements as described in Appendix E. However, since the patient specific geometry created during the segmentation only has the centerline and radius, the wall thickness and Young’s modulus are unknown. We therefore use a different constitutive law in the coronary line elements as proposed by van der Horst et al. [12], which only needs the coronary radius.
3. **Coronary windkessel elements (Appendix H):** At each terminal coronary element, the vasculature is truncated with a coronary windkessel element, which models the effect of the intramyocardial pressure on the coronaries, therefore resulting in the expected flow profile in the coronaries, with low flow during systolic phase and high flow during diastolic phase.

4. **Stenosis elements (Appendix I):** At a stenotic vessel, the redirection of blood flow results in the formation of vortices and will cause energy dissipation. This loss of energy causes a pressure drop which is not accounted for in the line elements, which assumes a unidirectional flow. This means a new pressure flow relation is necessary. Based on two-dimensional simulations on the stenosis, a relation for the pressure drop over stenosis to the flow and the stenosis geometry was derived. The elements as implemented in the 1D CFD code are verified by comparing the results with the results from van der Horst et al. [12], which can be found in Appendix N.

![Diagram of 1D CFD code elements](image)

**Figure 11:** Second version of the 1D CFD code, with every element shown.

---

**version 3: Stenosis recognition**

*Resulting from technical requirements TR11 (Automatic stenosis detection) and TR12 (Standalone executable).*

During the verification of the second version of the 1D CFD code, a stenosis element was manually placed in the coronary vasculature. However, the 1D code needs to be a standalone software and should not extra manual steps in the code. Therefore, an automatic stenosis recognition is written in the 1D CFD code. A schematic representation is shown in Figure 12. First, the coronary vasculature is divided in segments and each segment is then analyzed separately. A linear line fit is made of the radius through this segment, which is then used to find which radius are significantly below this linear fit. These points are shown in red in Figure 12. The consecutive radii marked as stenosis will be removed as 1D line elements and replaced by a single stenosis element. For a larger explanation of the stenosis recognition, the reader is referred to Appendix I.
version 4: Use of steady inflow

Resulting from technical requirements TR28 (Simulation <4 seconds)

To be able to use AngioSupport during heart team meeting, the 1D CFD code needs to able to calculate the FFR through the coronaries within seconds (see TR14). With the reduction of the size of the systemic geometry, the simulation time was reduced from 2204 seconds to 1402 seconds. However, this is still much too long to be used in heart team meetings. We therefore changed the code from a pulsatile inflow to a steady inflow. This greatly reduced the computational cost, resulting in a simulation time of 2 seconds. To justify the use of steady inflow, the change in FFR in the coronaries was investigated. Especially the change in pressure drop over a stenosis element, which has a quadratic flow in the formula. Figure 4.6 shows the results of this comparison for a coronary vasculature with a stenosis at the red circle. The severity of this stenosis was gradually increased and the simulated FFR was compared at each cross. Figure 13 shows that the simulated FFR for an increasing stenosis severity does not change, therefore the steady inflow can be used instead of a pulsatile inflow. These results are further explained in Appendix P.

Figure 12: schematic representation of the automatic stenosis recognition in AngioSupport.

Figure 13: Results shown for the comparison between pulsatile and steady inflow. A stenosis element is placed at the red circle, with an increasing severity. The graph shows that for pulsatile and steady inflow, the FFR calculation is the same.
version 5: Sensitivity Analysis - Pressure
Resulting from technical requirements TR10 (Use patient parameters) and TR11 (Accuracy >70%)
This fourth version of the 1D CFD code is tested on the patient specific coronary vasculatures. Although the fourth version of the model is able to calculate the FFR in the patient specific coronaries and within 4 seconds, the parameters in the simulations used are generic and based on literature. In Figure 14, the simulated vFFR is compared to the measured mFFR. It shows a poor correlation with the invasively measured mFFR and has an accuracy of 40%, calculated with:

\[
\text{Accuracy} = \frac{TP + TN}{TP + TN + FP + FN}
\]

To improve this accuracy of the model, we investigated which parameters are important in the model, by performing a sensitivity analysis of the 1D CFD code. This sensitivity analysis shows which parameters are most influential on the output and therefore needs to be made patient specific, and which parameters have less influence on the output and can therefore be based on literature. The method used and the results of this sensitivity analysis can be found in Appendix Q.

The sensitivity analysis showed that the mean arterial pressure is the most influential parameter on the calculation of the vFFR in the 1D CFD model. Therefore, this parameter should be based on patient data. The systolic and diastolic pressure is measured during the FFR measurement and can be used to calculate the patient aortic pressure. When using the patient aortic pressure at the inlet of the 1D CFD model, the accuracy improves to 50%. The results of these simulations are shown in Figure 15.

version 6: Sensitivity Analysis – coronary outflow
Resulting from technical requirements T10 (Use patient parameters) and TR11 (Accuracy >70%)
With the mean arterial pressure based on patient data, again a sensitivity analysis was performed. With the mean arterial pressure excluded, the coronary terminal flow showed most important. This coronary terminal flow is chosen to be able to calculate the terminal resistance of the coronary vasculature. At each outlet at the coronaries, a coronary terminal resistance needs to estimated, which accounts for the peripheral vasculature. This coronary terminal resistance is currently calculated with:

\[
R_{cor,i} = \frac{P_{ao} - P_{ven}}{Q_{rest,i} \cdot C_{adenosine}}
\]

with \(R_{cor,i}\) the coronary terminal resistance, \(P_{ao}\) the mean aortic pressure, \(P_{ven}\) the mean venous pressure, \(Q_{rest,i}\) the terminal flow in rest and \(C_{adenosine}\) the adenosine factor. The terminal flow in rest \(Q_{rest,i}\) calculated by taking the total expected flow to the coronary vasculature, and dividing this using the radius of each outlet:

\[
Q_{rest,i} = Q_{rest,tot} \frac{r_i^3}{\sum r_i^3}
\]

with \(Q_{rest,tot}\) the expected total flow in rest to the coronaries and \(r_i\) the radius of the terminal coronary vessel. The expected total flow at rest \(Q_{rest,tot}\), the adenosine factor \(C_{adenosine}\) and the division of flow over each terminal coronary vessel (Equation 3) is currently based on the model of Van der Horst et al. [12].
To improve the results of the 1D code, several methods were tested to increase the accuracy. These methods are briefly explained in Table 6 and the resulting accuracy is shown.

<table>
<thead>
<tr>
<th>Option</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>First divide flow over LAD and LCx, then divide the flow over the outlets using terminal radius.</td>
</tr>
<tr>
<td>2</td>
<td>Use wall shear stress to add extra side branches.</td>
</tr>
<tr>
<td>3</td>
<td>Segment the volume of the heart muscle to estimate coronary rest flow.</td>
</tr>
<tr>
<td>4</td>
<td>Use patient description to estimate heart muscle volume.</td>
</tr>
<tr>
<td>5</td>
<td>Divide flow in the network, by using the radii at each bifurcation.</td>
</tr>
<tr>
<td>6</td>
<td>Use option 1, but then increase or decrease the coronary rest flow to simulate same vFFR as mFFR.</td>
</tr>
<tr>
<td>7</td>
<td>Use option 5, but then increase or decrease the coronary rest flow to simulate same vFFR as mFFR.</td>
</tr>
</tbody>
</table>

Table 6: Different options for modelling the coronary outflow and the resulting accuracy.

Interventions

**Resulting from technical requirements TR14 (Simulation of PCI and CABG)**

For each simulation with AngioSupport, the 1D code is adapted to simulate the desired intervention. For now, only the placement of a single stent (PCI) and a LIMA coronary artery bypass graft (CABG) is possible with AngioSupport. PCI is simply modelled by changing the radius of a coronary artery at the position of the stent. The position and radius of this stent is manually chosen in the interface. The CABG is modelled by connecting the end of the LIMA to the coronary geometry and removing the windkessel which was connected to the LIMA. A schematic overview can be seen in Figure 16.

![Figure 16: Schematic overview of the adaptations in the 1D CFD code when simulation PCI or CABG.](image)

4.4 Interface

This section explains the design concepts used to create the interface of AngioSupport. First, the basic version is explained and then the changes due to feedback received during demonstrations are shown. An overview of all demonstration given with AngioSupport is shown in Appendix S.

**Interface code**

**Resulting from technical requirements TR15 (Software for interface) and TR17 (Interface can start 1D code)**

To allow the heart to simulate the patient and their interventions, an interface is needed to start simulations and perform virtual interventions. Therefore, we created a user interface in Electron. Electron is an open-source framework and allows for the development of desktop GUI applications using web technologies. Electron serves as a universal interface with the operating system of any device. This makes the stand-alone program ready to use on any device. Within the Electron environment, we only need to make the user interface and connect this to the 1D CFD code. This user interface consists of three parts: HTML, CSS and
JavaScript. HTML creates the framework of each page, CSS creates the style and design of these pages and JavaScript creates the functionality of each part in a page. An overview of these components can be seen in Figure 17.

**Figure 17: The elements of the interface combined together in Electron.**

**Interface design process**

To create the interface of AngioSupport, we decided that this should be a user driven process. We therefore first created a basic version, which can do all basic functions and meets the first basic technical requirements. This first set of requirements are shown in Table 5. When this first version was ready, we demonstrated this version to the stakeholders and cardiologists.

<table>
<thead>
<tr>
<th>Description</th>
<th>Acceptance</th>
<th>Working in Interface:</th>
</tr>
</thead>
<tbody>
<tr>
<td>TR17 Interface can start 1D code</td>
<td>1D code executable from Interface</td>
<td>At PM2</td>
</tr>
<tr>
<td>TR18 Show stenotic areas</td>
<td>Red parts for stenotic vessels</td>
<td>At PM4</td>
</tr>
<tr>
<td>TR19 Show color coded FFR</td>
<td>&gt;0.8 for healthy vessels &lt;0.8 for ischemic vessels</td>
<td>At PM2</td>
</tr>
<tr>
<td>TR20 Investigate each segment of vasculature</td>
<td>Show plot with length and diameter of segment</td>
<td>At PM4</td>
</tr>
<tr>
<td>TR23 Virtually perform PCI</td>
<td>Choose stent diameter and length</td>
<td>At PM2</td>
</tr>
<tr>
<td>TR24 Virtually perform CABG</td>
<td>Choose position of placement LIMA</td>
<td>At PM4</td>
</tr>
<tr>
<td>TR25 Calculate results in interface</td>
<td>Restart simulation when intervention created</td>
<td>At PM4</td>
</tr>
<tr>
<td>TR29 Show results of both interventions</td>
<td>Results PCI and CABG in one screen</td>
<td>At PM4</td>
</tr>
<tr>
<td>TR30 Show results previous interventions</td>
<td>Buttons to reload previous simulations</td>
<td>At PM3</td>
</tr>
</tbody>
</table>

*Table 7: First basic requirements for the interface of AngioSupport*

After this basic version was finished, we demonstrated AngioSupport to stakeholders and cardiologists. Their feedback was used to improve the interface and increase the usability. This chapter gives a summation of the feedback we received which resulted in the biggest changes in the interface. For more information about these first demonstrations, the reader is referred to Appendix X, where each version of AngioSupport is shown in more detail. The final design of the interface and the total functionality is described in Chapter 5.
Dark lay out and color scheme
During a visit to Pie Medical Imaging to discuss collaboration in this project and to receive their help in segmentation of the coronary angiogram images, Tristan Slots gave some advice on the interface. First he indicated that we should not use the color red for healthy vessels, since red is associated with incorrect. Also, he indicated that the current angiogram visualization is also dark, because the angiogram images are also dark. It would give a more familiar view for the heart team to use a dark theme.
The feedback from Tristan resulted in a full update of the lay-out of AngioSupport. Now a darker theme is used as was also seen CAAS and CathWorks. A standard lay-out for each page is used, with all functionality at the left side bar, as is also in CAAS, CathWorks and the dicom viewer used in Catharina Hospital Eindhoven. A new color scheme is used, with red indicating low vFFR and blue high vFFR. These changes can be seen in Figure 18.

![Figure 18: Screenshots of first version before (left) and after (right) the lay out is renewed. The new lay-out has a darker theme and all functionality is placed at the left side of the screen.](image)

Different stent placement
In the first version, the user needs to select a predefined stent and click on the coronaries where to place this stent. This version was shown to Pim Tonino during progress meeting 3 and a new method for stent placement was proposed. AngioSupport should give information about the length of a stenosis, the proximal and distal diameter. The heart team can then decide themselves which stent should be placed. This improved method was implemented in AngioSupport as shown in Figure 19.

![Figure 19: New method for stent placement in AngioSupport.](image)

Systemic geometry not shown
A part of systemic geometry is shown in the interface. This is currently only based on literature and not patient specific. Showing this systemic geometry was only confusing during the progress meeting 3. The systemic geometry is no longer shown in AngioSupport.

3D Plot stenosis
This version of AngioSupport was demonstrated to Mohamed El Farassi and Jo Zelis, cardiologists in training at the Catharina Hospital in Eindhoven. They showed interest in the method to automatically recognize the stenosis parts and therefore the stenosis plot was added to AngioSupport. An example of this plot is shown
in Figure 20. This plot now shows the recognized stenosis by the 1D CFD model and gives a color coding for the severity of the stenosis.

**Diameter-Distance plot**

This version of AngioSupport also shows the radius of coronary vessel when selected. This plot was discussed during Progress meeting 4, which concluded that the plot should have a standardized axes and should show the fitted "healthy" line. Pim Tonino also told it might be better to show the radius starting from ostium until the selected segment. This Diameter-Distance was added to AngioSupport and can be seen in Figure 21.

![Flow plot](image)

**Flow plot**

Together with Bas de Mol, AngioSupport was demonstrated to Jose Henriques in AMC, the head intervention cardiologist. They were very interested and this especially turned into a long discussion about FFR related to flow. The people in AMC were a bit more skeptical about the use of FFR, with pressure as a measure of myocardial ischemia. They would be interested in the change of flow in the coronaries.

We discussed the addition of a flow plot with Pim Tonino, who indicated that the flow might be interesting, it gives no information about the state of the coronary vasculature. It might be a good addition to increase interest in AngioSupport, especially for hospitals still more skeptical in FFR, it is not an addition in clinical decision making.

AngioSupport now also has a button to plot the flow in the coronary vasculature.

![Erasmus MC](image)

**Erasmus MC**

Together with Frank Gijssen, a demonstration of AngioSupport was given to a cardiologist in Erasmus MC. They also showed interest in AngioSupport, but were skeptical about the results. Especially when we told we are using 1D CFD simulations. The cardiologists told flow in coronaries is in 3D and it was difficult to explain that this can be modelled in 1D. It showed that CFD simulation work is not accepted as clinical tool and we need to be careful in the way we explain the 1D CFD model of AngioSupport.
**FFR-Distance plot**
Marcel van ‘t Veer showed the idea to be able to plot the vFFR of a selected segment. This plot will then be similar to a ‘pull back’ of the coronary vessel, which is used to find the biggest pressure jump. This plot was added to AngioSupport interface.

![Figure 23: FFR-Distance plot of a selected coronary in the AngioSupport interface.](image-url)
5 Final design overview

The final design of AngioSupport is shown in Figure 24. It exists of a preprocessing part (orange part), a 1D CFD code (grey part) and an interface (blue part). The preprocessing part and the 1D CFD code are summarized. The functionality of each page of the interface is explained in more depth and the usability is described.

### Preprocessing

Before using AngioSupport at a heart team meeting, each coronary angiogram of a patient is preprocessed, as shown in Figure 24 in orange. This preprocessing can be summarized with:

| Requirements: | Dicom files: of coronary angiogram retrieved from PACS. |
| Work needed: | 90 minutes total per patient |
| Result: | Centerlines and radius of coronary vessels |
| | Connected left coronary vasculature |
| Explanation: | Section: 4.2 |
| | Appendix: K,L,T |

### 1D CFD Code

For the patient specific coronary geometry, the vFFR is calculated pre- and postoperative using the 1D CFD code. The 1D CFD code is shown in Figure 24 in grey. This 1D CFD can be summarized with:

| Requirements: | mFFR: Location and value of measured mFFR during CA. MAP: The mean aortic pressure. Python code: The 1D CFD code created in Python. |
| Work needed: | None |
| Result: | Standalone executable |
| | Calculation of vFFR pre- and postoperative |
| | Stenosis recognition |
| | Simulation time under 4 seconds |
| | Pre-operative accuracy 70% |
| Explanation: | Section: 4.3 |

### Interface

The interface is used during the heart team to support in clinical decision making. The interface is shown in Figure 24 in blue. This interface can be summarized with:

| Requirements: | Interface code: Combination of html, CSS and JavaScript. Electron: Connecting interface to local files and python. |
| Work needed: | None |
| Result: | Standalone executable |
| | Visualization of vFFR, recognized stenosis and flow |
| | Virtual PCI and CABG |
| | Comparison results interventions |
| Explanation: | Section: 4.4, 6.1 |
| | Appendix: S,U,X |
Figure 24: Schematic overview of final version of AngioSupport.
Page 1: Start AngioSupport
The first page of AngioSupport is only a welcoming page and has no further functionality for the user. In the interface, a new session number is started. Within this session, all results from simulations are saved locally. The user can continue to the next page by clicking 'continue'.

Page 2: Load Patient
The second page is used to load a patient and to add the patient parameters needed for the 1D simulations. This page has the following functionality:

- Load patient coronary vasculature: At the top, a patient can be loaded in by selecting the patient file number in the browser. The 3D plot of the coronary vasculature is shown in the interface.
- Add patient parameters: this page allows the user to add patient parameters, to be used for the 1D CFD code. Currently, only the pressure in the aorta and the measured FFR is used and are automatically added when loading a patient file.

The user can continue to the next page by clicking 'continue' and the 1D CFD simulation will start.

Page 3: Show Results Patient
When the simulation is finished, the results are shown. At this page, the heart team decides whether an intervention is needed for this patient. This can be investigated by using the following options in AngioSupport (corresponding number is shown in Figure 25):

1. vFFR: This button will plot the vFFR in all the coronaries and is automatically plotted when the simulation is finished. A color scheme is used to visualize healthy and unhealthy coronaries, for which red is used when vFFR is below 0.8.
2. Stenosis: This button will plot the recognized stenotic areas. The stenosis are recognized by the 1D CFD code and each stenosis is shown in red, while non stenotic vessels remain green.
3. Flow: This button will plot the flow through the coronaries. The vessels are colored red and become more transparent when the flow reduces.
4. Diameter-Distance plot: The diameter distance plot shows the diameter when clicked on a coronary vessel in the plot. It shows the diameter and distance from proximal at the ostium until the selected segment. This plot also shows the fitted "healthy" coronary vessel radius and shows how the stenotic areas are recognized.
5. vFFR-Distance plot: This plot is similar to the Diameter-Distance plot, but shows the vFFR in the selected coronary segment and thus gives the pull-back of the coronary.

When the heart team decides if this patient needs an intervention, the user can click 'continue'. The user continues to the page 'Compare Results Interventions', from which the user can perform a virtual PCI or CABG.

Figure 25 Screenshot of the 'show results patient' page. The numbers correspond to the numbers explaining the functionality.
Page 4: Perform Virtual PCI
When clicked on the button 'PCI' in the page of 'Compare Results Interventions page', the user can perform a virtual PCI. The PCI is performed by choosing the start and end of a stent and adapting the coronary vasculature. To perform a virtual PCI, the following steps are followed:

1. The user investigates the coronary vasculature with the plot. The stenosis plot can also show possible stenotic areas.
2. When clicked on 'Begin Stent' the user is able to select the starting position of the stent. The user can then select 'End Stent' to select the ending position of the stent.
3. The software returns the proximal and distal diameter of the selected points and the distance between these points. The user can then choose a desired stent diameter to be placed between the selected points.
4. The user can then click on 'Place Stent', which will adapt the coronary vasculature with the placed stent.
5. The user can change the position or radius of the stent by again clicking on the buttons.

When the intervention is finished, the user can click 'continue' and the user returns to the page 'Compare Results Interventions page'.

Page 5: Perform Virtual CABG
When clicked on the button 'CABG' in the page of 'Compare Results Interventions page', the user can perform a virtual CABG. The CABG intervention is performed by placing the LIMA on the coronary vasculature, as shown in Figure 24. Since this CABG only needs the position where the LIMA must be connected, the user only needs to click on the coronary vasculature. This position is then used to connect with the end of the LIMA. When planning the intervention is finished, the user can click 'continue' and the user returns to the page 'Compare Results Interventions page'.

Page 6: Compare Results Interventions
In this page, the results of interventions are compared to the pre-operative results. The vFFR can be compared and the heart team can decide which interventions gives the best result. The results of previous interventions are saved and can be loaded in at the bottom of the screen.
6 User survey

This chapter gives a total overview of the interface and explains all functionality of the final version of AngioSupport. This final version was demonstrated at the Catharina Hospital Eindhoven to cardiologists and a user survey was used to investigate the usability of AngioSupport. These cardiologists are shown in Table 8. For more information about the user survey and all answers, the reader is referred to Appendix U. For each statement, the cardiologists could respond with 1 (completely disagree) to 5 (completely agree). The questionnaire was divided into two parts:

1. Interface workflow: In this section the functionality of each page was questioned and the usability and ease of use was investigated.
2. General questions: To question the cardiologists what they think of AngioSupport and computer simulations.

The user survey also resulted in a many possible improvements and ideas for AngioSupport, which are all collected in Appendix U.

<table>
<thead>
<tr>
<th>Name</th>
<th>Function</th>
</tr>
</thead>
<tbody>
<tr>
<td>Annemieke de Vos</td>
<td>Cardiologist</td>
</tr>
<tr>
<td>Bastiaan Zwart</td>
<td>Cardiologist in training</td>
</tr>
<tr>
<td>Danielle Keulards</td>
<td>Cardiologist in training</td>
</tr>
<tr>
<td>Frederik Zimmermann</td>
<td>Cardiologist in training</td>
</tr>
<tr>
<td>Gijs van Steenbergen</td>
<td>Cardiothoracic surgeon in training</td>
</tr>
<tr>
<td>Jo Zelis</td>
<td>Cardiologist in training</td>
</tr>
<tr>
<td>Mohamed El Farissi</td>
<td>Cardiologist in training</td>
</tr>
<tr>
<td>Pieter-Jan Paulmers</td>
<td>Cardiologist</td>
</tr>
<tr>
<td>Simon Dello</td>
<td>Cardiologist</td>
</tr>
</tbody>
</table>

Table 8: List of cardiologists spoken during user survey.

6.1 Interface workflow

During the user survey, the functionality of each page of the interface was investigated. The averaged results for these questions are shown in Table 9. The questions and the results for each different functionality can be found in Appendix U.

<table>
<thead>
<tr>
<th>User survey</th>
<th>Average score:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Page 1: Start AngioSupport</td>
<td></td>
</tr>
<tr>
<td>Page 2: Load Patient</td>
<td></td>
</tr>
<tr>
<td>Page 3: Show Results Patient</td>
<td></td>
</tr>
<tr>
<td>Page 4: Perform Virtual PCI</td>
<td></td>
</tr>
<tr>
<td>Page 5: Perform Virtual CABG</td>
<td></td>
</tr>
<tr>
<td>Page 6: Compare Results Interventions</td>
<td></td>
</tr>
</tbody>
</table>

Table 9: Results user survey for each different page in AngioSupport interface.

6.2 General question

<table>
<thead>
<tr>
<th>User survey</th>
<th>Average score:</th>
</tr>
</thead>
<tbody>
<tr>
<td>AngioSupport is user friendly</td>
<td></td>
</tr>
<tr>
<td>AngioSupport provides me with more insight</td>
<td></td>
</tr>
</tbody>
</table>

In general, the usability of AngioSupport was rated good, even though the cardiologists still needed to be guided through the interface sometimes. However, most cardiologists stated here also this should be easier a second time. The cardiologists agreed with the workflow in AngioSupport and AngioSupport provided them with more insight of the patient.
To explore possible business cases for AngioSupport, we asked the cardiologists whether they want to use AngioSupport to explain the treatment plan to a patient. This resulted in a wide range of answers, some cardiologists absolutely agreed and stated that they already need a drawing to explain to a patient the treatment plan. Other cardiologists saw problems with using this software, since this requires a certain level of understanding of the patient. AngioSupport could perhaps result in many questions about, for instance, how FFR works, how the stenosis is recognized and how this can be simulated. This might take too much time, which is usually not available.

The cardiologists however did see the benefit to use AngioSupport for cardiologists in training or as a training for medical students. AngioSupport could give examples how pressure, flow and resistance relate to each other and how PCI and CABG affect these concepts. They explained that this is often not fully understood in other hospitals and FFR is not used correctly.

To explore the use of numerical modeling in a hospital, the use of computer simulations in general for clinical decision making was questioned to the cardiologists. The cardiologists agreed that computer simulations can support their daily decision making. Especially for guiding them through a patient status, such as color highlighting what a doctor needs to look at.

Whether a computer simulation can improve the clinical decision making depended on the personal trust in computer simulations. Some cardiologists indicated to have more trust in a computer simulation. Other stated to never really trust a computer simulation. Important part in this is whether the software is clinically validated. When a software tool is clinically validated, the computer simulation could improve their own decision making.

Every cardiologist completely disagreed that computer simulations can replace the clinical decision making of doctors. They stated that the wide range of elements that need to be considered, such as patient age, long term effects, procedure risks and patient medical history, can never be fully grasped by a computer simulation.

7 Verification and Validation

7.1 Verification

The technical requirements as described in Chapter 3 are all achieved. In Table 10, all technical requirements are summarized and the acceptance shown. For each technical requirement, the needed improvements for further development are described.

7.2 Validation

As has been described in Section 2.6, clinical validation of AngioSupport is not included in this design project. Only a first user survey could be conducted (chapter 6). Hence, the functional requirements can not be validated. However, for each functional requirement, the strong points, needed improvements and opportunities for further development are summarized in Table 10.
### FR1: Implementable in the current health care procedure

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>TR1 No external connection outside hospital needed</td>
<td>Executable on single computer</td>
<td>√ [sec 4.1]</td>
<td>Electron 1D CFD code</td>
<td>8.2.1</td>
</tr>
<tr>
<td>TR2 No change in hospital to use AngioSupport</td>
<td>Same health care process</td>
<td>√ [sec 4.1]</td>
<td>Use of CA Interface for heart team</td>
<td>8.2.1</td>
</tr>
<tr>
<td>TR3 CE marking</td>
<td>Investigate required CE level</td>
<td>√ [sec 4.1]</td>
<td>No CE for training/demonstration</td>
<td>8.2.11 8.2.10</td>
</tr>
</tbody>
</table>

**Strong Points:**
- No change in current health care process
- No connection outside hospital needed
- No CE level for demonstration or training

**Needed Improvements:**
- Reduction in preprocessing time
- CE level 2a for clinical use

### FR2: Segmentation of the patient specific coronary vasculature

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>TR4 Find segmentation tool</td>
<td>Software able to segment coronary angiogram</td>
<td>√ [sec 4.2]</td>
<td>CAAS software</td>
<td>8.2.2</td>
</tr>
<tr>
<td>TR5 Use patient data</td>
<td>Receive retrospective data from hospital</td>
<td>√ [sec 4.2]</td>
<td>nWMO request</td>
<td>8.2.7</td>
</tr>
<tr>
<td>TR6 Segment patient specific vasculature</td>
<td>Segment LAD, LCx and main side branches of patient</td>
<td>√ [sec 4.2]</td>
<td>CAAS software</td>
<td>8.2.2</td>
</tr>
<tr>
<td>TR7 All coronaries connected together</td>
<td>One combined coronary vasculature</td>
<td>√ [sec 4.2]</td>
<td>Python script</td>
<td>8.2.3</td>
</tr>
</tbody>
</table>

**Strong Points:**
- Connected coronaries into one vasculature

**Needed Improvements:**
- Automated process of segmentation
- Validation of connected vasculature
- Segmentation right coronary vasculature

### FR3: Compute the vFFR in the patient specific coronary vasculature

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>TR8 Code to simulate pressure and flow</td>
<td>Validated 1D CFD code</td>
<td>√ [sec 4.3]</td>
<td>1D CFD python code</td>
<td>8.2.4</td>
</tr>
<tr>
<td>TR9 Code to simulate coronaries</td>
<td>Validated coronary 1D CFD code</td>
<td>√ [sec 4.3]</td>
<td>Adapted code of van der Horst et al.</td>
<td>8.2.7</td>
</tr>
<tr>
<td>TR10 Make patient specific</td>
<td>Use patient parameters</td>
<td>√ [sec 4.3]</td>
<td>Use of MAP, CA, mFFR</td>
<td>8.2.6</td>
</tr>
<tr>
<td>TR11 Calculate accurate vFFR</td>
<td>Accuracy &gt;70%</td>
<td>√ [sec 4.3]</td>
<td>Use of patient mFFR, MAP</td>
<td>9.2</td>
</tr>
<tr>
<td>TR12 Detection of stenosis</td>
<td>Automatic stenosis detection</td>
<td>√ [sec 4.3]</td>
<td>Automatic stenosis detection</td>
<td>8.2.5</td>
</tr>
<tr>
<td>TR13 Easy to start simulation</td>
<td>Standalone executable</td>
<td>√ [sec 4.3]</td>
<td>Electron Python No manual steps required</td>
<td>8.2.1</td>
</tr>
<tr>
<td>TR14</td>
<td>Able to perform interventions</td>
<td>Simulation of PCI and CABG</td>
<td>√ [sec 4.3]</td>
<td>Adaptations in 1D geometry</td>
</tr>
<tr>
<td>------</td>
<td>-------------------------------</td>
<td>-----------------------------</td>
<td>-------------</td>
<td>-----------------------------</td>
</tr>
<tr>
<td><strong>Strong Points:</strong></td>
<td><strong>Needed Improvements:</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Simulates vFFR in coronary vasculature</td>
<td>Improved accuracy</td>
<td></td>
<td></td>
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<tr>
<td>Simulation time under 4 seconds</td>
<td>Validation post-vFFR</td>
<td></td>
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</tr>
<tr>
<td>Automatic stenosis detection</td>
<td>Modelling CABG</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Standalone executable</td>
<td></td>
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<tr>
<td>PCI and CABG interventions possible</td>
<td></td>
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</tbody>
</table>

**FR4: Visualize results of patient in interface**

<table>
<thead>
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<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td>TR16</td>
<td>Heart team can easily load in patient</td>
<td>Positive user survey response</td>
<td>√ [sec 6.1]</td>
<td>Electron Design process interface</td>
<td>8.2.10</td>
</tr>
<tr>
<td>TR17</td>
<td>Interface can start 1D CFD code</td>
<td>1D CFD code executable from Interface</td>
<td>√ [sec 4.4]</td>
<td>Electron</td>
<td>8.2.10</td>
</tr>
<tr>
<td>TR18</td>
<td>Show stenotic areas</td>
<td>Red parts for stenotic vessels</td>
<td>√ [sec 4.4]</td>
<td>Intuitive color code Design process interface</td>
<td>8.2.10</td>
</tr>
<tr>
<td>TR19</td>
<td>Show color coded vFFR</td>
<td>&gt;0.8 for healthy vessels &lt;0.8 for ischemic vessels</td>
<td>√ [sec 4.4]</td>
<td>Intuitive color code Design process interface</td>
<td>8.2.10</td>
</tr>
<tr>
<td>TR20</td>
<td>Investigate each segment of vasculature</td>
<td>Show plot with length and diameter of segment</td>
<td>√ [sec 4.4]</td>
<td>Design process interface Feedback from cardiologists</td>
<td>8.2.10</td>
</tr>
<tr>
<td>TR21</td>
<td>Heart team understands results shown</td>
<td>Positive user survey response</td>
<td>√ [sec 6.1]</td>
<td>Design process interface Feedback from cardiologists</td>
<td>8.2.10</td>
</tr>
<tr>
<td>TR22</td>
<td>Heart team can use results to decide of intervention is need</td>
<td>Positive user survey response</td>
<td>√ [sec 6.1]</td>
<td>Design process interface Feedback from cardiologists</td>
<td>8.2.10</td>
</tr>
</tbody>
</table>

**Strong Points:**
- Visualization patient coronary vasculature
- Investigate individual segments
- Visualization vFFR, stenosis and flow
- Excellent usability
- Supports in decision making

**Needed Improvements:**
- Faster connection Electron and Python
- User survey feedback, see Appendix U

**FR5: Compare results of interventions during heart team meeting**

<table>
<thead>
<tr>
<th>TR23</th>
<th>Virtually perform PCI</th>
<th>Choose stent diameter and length</th>
<th>√ [sec 4.4]</th>
<th>Design process interface Feedback from cardiologists</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Choose stent position</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

37
| TR24 | Virtually perform CABG | Choose position of placement LIMA | ✓ [sec 4.4] | Design process interface Feedback from cardiologists | 8.2.10 |
| TR25 | Calculate results in interface | Restart simulation when intervention created | ✓ [sec 4.4] | Electron | 8.2.10 |
| TR26 | Heart team can perform PCI easily | Positive user survey response | ✓ [sec 6.1] | Design process interface Feedback from cardiologists | 8.2.10 |
| TR27 | Heart team can perform CABG easily | Positive user survey response | ✓ [sec 6.1] | Design process interface Feedback from cardiologists | 8.2.10 |
| TR28 | Short simulation time | Simulation <4 seconds | ✓ [sec 4.3] | Use of steady inflow Reduction systemic geometry | 8.2.10 |
| TR29 | Show results of both interventions | Results PCI and CABG in one screen | ✓ [sec 4.4] | Electron | 8.2.10 |
| TR30 | Show results previous interventions | Buttons to reload previous simulations | ✓ [sec 4.4] | Electron | 8.2.10 |
| TR31 | AngioSupport improves decision making for heart team | Positive user survey response | ✓ [sec 6.1] | Design process interface Feedback from cardiologists | 8.2.10 |

**Strong Points:**
- Virtual PCI
- Virtual CABG
- Comparing results interventions
- Excellent usability
- Supports in decision making

**Needed Improvements:**
- Multiple stents
- Venous grafts
- User survey feedback, see Appendix U

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**FR6: Start of simulation platform at LifeTec Group**

| TR33 | Explore possibilities for further development of simulation platform | Create a business case for AngioSupport | ✓ [sec 4.1] | Feedback from cardiologists | 9.1-9.5 |

**Strong Points:**
- Verified 1D CFD code
- Modular software
- Possible business opportunities

**Needed Improvements:**
- Connecting 1D CFD with 3D CFD simulations

*Table 10: Overview of all technical requirements, achieved acceptance and future steps required*
8 Conclusion and Discussion

8.1 Conclusion

During this project, a model-based interactive tool to support the heart team in clinical decision making has been successfully developed. AngioSupport combines developed at the Technical University of Eindhoven, which allows the heart team to use the numerical models to calculate the pre-operative vFFR and post-operative vFFR to support in deciding a treatment plan for each patient. The aim of this project is reached and the project is successfully finished.

During this project, a patient-specific model-based interactive tool has been successfully developed, that supports the heart team in clinical decision making. AngioSupport combines numerical models that have been developed at the Technical University of Eindhoven with patient-specific data (angiograms, mFFR and MAP) such a to perform simulations with these numerical models to calculate the pre-operative vFFR and post-operative vFFR. Hence, with the help of an interface, AngioSupport is able to support the cardiac team in deciding a treatment plan for each patient. The aim of this project has been reached and the project is successfully finished. In the following section, the obtained results will be discussed and recommendations will be given for further development of AngioSupport.

8.2 Discussion and recommendations

8.2.1 Implementable in the current health care procedure

By using the already made coronary angiograms and creating an interface which is usable during a heart team meeting, AngioSupport fits in the current health care procedure. Since preprocessing can be done within the hospital, patient data do not require to leave the hospital. However, this preprocessing is still not fully automated and requires much manual work, resulting in a preprocessing time of 90 minutes per patient. Furthermore, this manual work has still to be done by an expert. Hence, before AngioSupport can be used in a hospital, this needs to be improved.

8.2.2 Segmentation

The segmentation of the measured coronary vessels is performed with the CAAS software. Although this software is able to segment the coronary vessels from a coronary angiogram, it is unclear how the software is able to do this. The CAAS software also does not show the accuracy of this segmentation and when questioned to PMI, no explanation was given. They only stated that the length and radius estimation is accurate, but the final vessel could be differently rotated in space. Besides the accuracy of the segmentation, the CAAS software was also not able to easily segment multiple vessels: therefore, in this design project a python script has been created to combine the segmented coronaries semi-manually. This resulted in a final coronary vasculature with multiple vessels, however no real validation could be performed and there is great uncertainty whether the result really shows the coronary vasculature of the patient accurately enough. These problems were recognized during the project and we tried to search for different segmentation tools, talked with other experts and even tried to segment the coronary angiograms ourselves. However, due to the limited time of this design project, it was decided to remain with the CAAS software.

To improve this segmentation process with CAAS, a further collaboration with PMI is needed. However, during this project, it was difficult to receive more insight in the CAAS software. Therefore, for the further development of AngioSupport other research groups or companies need to be contacted to find a more suitable segmentation process. Another improvement that has to be performed in AngioSupport is to also segment the right coronary arteries, which is needed to evaluate patients with multiple stenosis and patients with three-vessel disease. The segmentation of the right coronary vasculature was kept out of scope in this design project, but should be added in AngioSupport.
Patient data
The patient data received from Simon Dello were from 75 patients, with both the measured FFR and the coronary angiogram images. Although these patients all had been discussed during a heart team meeting, therefore being the target group for which AngioSupport has been designed for, this dataset was unfortunately very complicated. Mainly, because the CAAS software showed unable to segment a full left coronary vasculature. PMI also stated that they were only able to segment 25 patients of this dataset, while PMI only segments one single vessel. In the scope of this design project, finally the segmentation of a left coronary vasculature of only 10 patients was possible. Hence, it is a better step to first validate AngioSupport on single stenosis patients with no complicated CAD and investigate the accuracy before using AngioSupport for more complicated cases.

8.2.4 Steady or pulsatile inflow for simulations
In the design process, the choice was made to use steady inflow for simulations instead of pulsatile inflow. This resulted in a great reduction in computational costs and therefore simulation time. This choice has been justified, since the corresponding change in vFFR calculation in the entire coronary vasculature was minimal. Although this justifies this choice for the current prototype of AngioSupport, this might also indicate that the 1D CFD code is currently too simplified for the final product AngioSupport. The time varying effects, such as the intramyocardial pressure, the extravascular pressure of the proximal coronary arteries or the flow through a stenosis might have more impact than is currently modelled. This has to be investigated for further development of AngioSupport.

8.2.5 Modelling of the stenosis
The automatic stenosis recognition in the 1D CFD code that has been developed in this design project allows for the interface to visually highlight stenotic parts in the coronary vasculature. During demonstrations with cardiologists, this automatic recognition excellently highlighted each stenosis for each patient and therefore showed to be functioning. In the current 1D CFD code, after recognition of stenotic parts, the corresponding 1D line elements are being replaced with stenosis elements based on a sinusoidal shape. For each stenosis element, the minimum stenosis radius, the ‘healthy’ normal radius and an average radius is needed. Although these can be estimated for each stenosis, it has shown to be difficult for the tapered vessels which in reality never have a sinusoidal shaped stenosis. Also, in this design project recognized stenoses close to a bifurcation were excluded, because those usually only were a narrowing. For the further development of AngioSupport, research is required to better model this replacement of line elements with stenosis elements. Another solution however, is probably given by the research of Schrauwen et al. [13], which recreates a velocity field for each 1D line element, therefore not requiring any stenosis elements.

8.2.6 Sensitivity analysis
The sensitivity analysis performed in this design project has shown that the mean aortic pressure is the most influential parameter on the calculation of the vFFR. The mean aortic pressure is measured and saved with the coronary angiogram in the hospital. This mean aortic pressure is therefore a patient-specific input parameter for the model. However, the mean aortic pressure is not a single value that is stable over time: it changes during the day and is most likely increased during the coronary angiogram procedure. It should be further investigated how this might affect the results of AngioSupport. Besides the mean aortic pressure, the (expected) total coronary flow has been shown to be relatively influential. This parameter is used to estimate the windkessel resistance at each terminal coronary vessel. Although different methods were tested, this did not resulted in a satisfying approach to estimate the parameters for the coronary windkessel. The addition of collateral coronaries could be needed to change the flow distribution in the coronary arteries. However, no good method was found to add these collateral coronaries. This should be investigated for the further development of AngioSupport.

8.2.7 Use of mFFR
In the current version of AngioSupport, the measured FFR (mFFR) is needed to estimate the boundary conditions of the coronary terminal windkessel elements. mFFR is mostly already measured for these complicated cases that are being discussed during a heart team meeting. However, these invasive FFR
measurements are only performed in centralized hospitals; patients who are diagnosed with CAD using CA at peripheral hospitals therefore need a second CA at a centralized hospital to measure the FFR. If AngioSupport can accurately simulate the vFFR without requiring the mFFR, this second CA at a centralized hospital is not needed. This would be a great selling point for AngioSupport, since this would result in a reduction of costs in hospitals.

8.2.8 Modelling of PCI
The placement of a stent is currently only modelled by changing the radius of the coronary vessel at a location in the coronary vasculature as chosen in the interface. To increase the accuracy of AngioSupport, the modelling of a stent could be expanded, for instance by changing the stiffness or allowing for extra dilation at the distal part of a stent in the interface. The placement of multiple stents should also be easily possible with AngioSupport. Finally, the calculation of in-stent restenosis could also be a good addition for AngioSupport, which is a risk when planning for PCI.

8.2.9 Modelling of the CABG
The CABG intervention is modelled in AngioSupport by connecting the LIMA to a coronary artery. Since no data was available of the systemic geometry and the LIMA of each patient, a literature based generic geometry is created. This resulted in almost no pressure drop in the LIMA and thus an FFR of 1.0 at the location of the anastomosis. This has shown to be not realistic, since the cardiologists all stated this is too high and even provided an article about this issue [19]. To improve the CABG simulations, the pressure drop in the LIMA and at the anastomosis needs to be modelled. Furthermore, for further development of AngioSupport, a venous graft and a jump graft can also be added to the CABG simulations in AngioSupport.

8.2.10 User survey
The cardiologists were all very interested in the model and the demonstrations resulted in many ideas to be added in the interface. Especially for the placement of stents, many improvements were suggested. However, whether cardiologists would like to use this during a heart team was mostly based clinical validation. They all stated that they would like to use AngioSupport, but only after clinical validation and AngioSupport is accepted in the guidelines. Only then the use of AngioSupport is allowed in clinical decision making.

8.2.11 Other opportunities with AngioSupport
Although the current version of AngioSupport can not be used for clinical decision making, the tool might already be useful for training of cardiologists and explaining the treatment plan to patients. This was also confirmed by the cardiologists. In the development of AngioSupport, this could be a good first step for the business case for AngioSupport.

9 ‘Proof of concept’, what’s next?

With the completion of a prototype of AngioSupport, a ‘proof of concept’ has been shown. However, the development of AngioSupport is not yet finished: the final version of our prototype still has many shortcomings. Therefore it needs further research and development, as has been discussed in the previous chapter, before this can be used during a heart team meeting by the clinicians themselves. For further development of AngioSupport, in Figure 26 several steps are defined and intermediate milestones are described. In this Chapter, I will give my personal view on the next steps needed for AngioSupport (with steps highest priority first).
9.1: Automatic and fast segmentation (and pre-processing) process
AngioSupport relies on the segmentation of the coronary vasculature. This segmentation currently includes many manual (and time-consuming) steps and no reliable full coronary vasculature can be created. If the segmentation of the entire coronary vasculature can finally become a fully automatic software tool (optimally included in the backend of the interface), this can then be used to automatically produce the 3D visualization of the coronary vasculature. The segmentation is also being developed elsewhere and could be contacted for further development [29][30]. These segmentation tools need at least 4 coronary angiograms per patient, with each a specific angle for each main coronary vessel. A full segmentation of the coronary vasculature could already allow for QCA on the entire vasculature, highlighting the each significant stenosis for a heart team. Also, the SYNTAX score could be calculated automatically, which is a clinical number used to choose between PCI and CABG. Hence, work in progress to achieve this; summarizing:

<table>
<thead>
<tr>
<th>Further Development:</th>
<th>Automatic segmentation of full coronary vasculature.</th>
</tr>
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<tbody>
<tr>
<td>Work in progress to achieve this:</td>
<td>Student in AMC working on segmentation of angiogram Contact with group in Oxford, developing automatic full segmentation Further contact with Pie Medical Imaging</td>
</tr>
<tr>
<td>Examples:</td>
<td>[29],[30]</td>
</tr>
<tr>
<td>Result:</td>
<td>3D plot of full coronary vasculature</td>
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<tr>
<td>Intermediate milestones:</td>
<td>QCA assessment SYNTAX score calculation</td>
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</table>

9.2 Pre-operative vFFR calculation
During the development of the first prototype of AngioSupport, the programming of the model-based 1D CFD code to compute the vFFR was hampered by the reliability of the segmented coronary, furthermore it was only the left coronary artery. As soon as a reliable segmentation of the full coronary vasculature is possible, the pre-operative vFFR can be computed and used in the simulations instead of the mFFR. Ideally, the automatic segmentation of the coronary vasculature includes all coronary arteries, all collateral arteries and the myocardial mass of the heart. This can then be used for creating the 1D CFD code and computing the vFFR. Since this is probably too much to expect soon (in the further development of AngioSupport), the shortcomings of the automatic segmentation should be included in the 1D CFD code. If known exactly to what extent the coronaries are segmented, the 1D CFD code can be adjusted to compensate for these the shortcomings. The 1D CFD code can then calculate pressure drops in the segmented coronaries, while the boundary conditions for the 1D part should be modeled with information from the segmentation. For instance by adding collateral arteries, estimating terminal resistance using contrast velocity and estimating total flow to coronaries based on the angiogram. Ideally the use of the mFFR is then not needed, as already shown in other simulation tools.
| Needed: | Full segmentation coronary vasculature  
| Exact shortcomings of segmentation known |
| Further Development: | 1D CFD code  
| Accuracy pre-operative simulations |
| Work in progress to achieve this: | Collateral arteries added in coronary vasculature  
| Boundary condition estimation based on contrast fluent velocity |
| Examples: | [17],[18],[23],[24] |
| Result: | Calculation of pre-operative vFFR |
| Intermediate milestones: | Pre-operative vFFR calculation |

9.3 Further development of the interface
During the previous steps, the interface should be further developed continuously. Each extra functionality of the model (such as an automatic segmentation/pre-processing tool) should be implemented in the interface, by using the feedback from cardiologists. This makes the interface more and more usable for cardiologists.

| Needed: | Feedback cardiologists |
| Further Development: | Interface functionality |
| Work in progress to achieve this: | Programming feedback received from cardiologists |
| Examples: | [16],[17],[18],[29] |
| Result: | Interface easy to use for heart team |
| Intermediate milestones: | Interface immediately implementable in health care process |

9.4 Post-operative vFFR calculation
When the pre-operative simulations are accurate, the next step is the computation of the post-operative vFFR. This requires the correct modelling of the interventions, while the same boundary conditions of the pre-operative simulations can be used. To model the interventions, post-operative patient data are needed. Especially for CABG interventions, not much data is available.

| Needed: | Post-operative data PCI  
| Post operative data CABG |
| Further Development: | Modeling interventions  
| Accuracy post-operative simulations |
| Examples: | |
| Result: | Calculation of pre-operative vFFR |
| Intermediate milestones: | Post-operative vFFR calculation |

9.5 Clinical Validation
After a high accuracy of post-operative vFFR is achieved, finally clinical validation is needed. Only with clinical validation will the tool be used in daily use during heart team meetings.

| Needed: | High accuracy post-operative vFFR |
| Further Development: | Validation AngioSupport |
| Examples: | |
| Result: | Validated AngioSupport |
10 Reflection

I think the project is a success and we can be happy with the result in the end. If I could have known at the beginning how far we would come, I would have been happy. I look back on a project I have done happily and with a satisfying result. Especially at the beginning we made fast progress, which was mostly the development of the 1D CFD code and the interface, while still doing many courses. I hope that I can stay involved in the development of AngioSupport and one day implement this in a hospital. I really believe that AngioSupport, or something similar, can one day be used during a heart team meeting to improve clinical decision making.

The development of AngioSupport has thought me that although the modelling of the blood flow in arteries in developing, these models are not exploited in clinical practice. The problem of these models is mostly in estimating correct patient specific boundary conditions. Acceptance of these models is required by achieving a high accuracy and these models will only be implemented by clinical validation. I learned during this project that the models from the technical university can greatly improve insight for clinical use, but clinicians need to be involved in the development of these tools. Otherwise these two worlds will never combine.

The entire project was together with Bettine. Although a strong focus at the start was to split the project in two project, this showed very unpractical in developing AngioSupport. I think me and Bettine showed that codesigning a PDEng project is possible, if these two people can work together. During the entire project, the collaboration was naturally. We were able to work together on the same project, finishing each others work. I think this greatly improved the development of AngioSupport. I am grateful for this friendly and productive collaboration with Bettine.

A disappointment in the project is the result in the segmentation process. Although the technical requirement are met, the final result is not trust-worthy and the following modeling steps are based on this segmentation. Although several times help was requested from PMI to segment full coronary vasculature, this did not result in a better collaboration or commitment. This was not expected, because there is good collaboration between PMI and TUe. Hopefully this can still be improved or other strategies can be explored to improve the segmentation process.

Working in the Catharina hospital was an interesting period and really showed me the limitations of numerical modelling for daily clinical use. I think this gap is a result from each research group being focused on new theories and creating papers, while daily use in clinical practice is not interesting for a research group. Basic simple simulation work could already improve clinical practice. Me and Bettine had a working position in the Catharina hospital for the last 5 months of the project. We could have had a position earlier in the hospital, but I think this would not have been useful. In the beginning, we started with nothing and needed to build the entire code and interface from nothing. We would have been at Catharina hospital with nothing to show, which I think would have been a waste of time.

Working at LifeTec Group was a great and fun time. The people are really friendly and the open environment between employee and employers is really good. The amount of new research which passes through LifeTec Group is amazing and I really learned something new constantly. Especially the development of the platforms was very interesting to see. Besides the research, I think the freedom LifeTec Group provides in personal development is unique.
11 Abbreviations

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
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<tbody>
<tr>
<td>1D</td>
<td>One Dimensional</td>
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<tr>
<td>2D</td>
<td>Two Dimensional</td>
</tr>
<tr>
<td>3D</td>
<td>Three Dimensional</td>
</tr>
<tr>
<td>1D CFD</td>
<td>One Dimensional Computational Fluid Dynamics</td>
</tr>
<tr>
<td>2D CFD</td>
<td>Two Dimensional Computational Fluid Dynamics</td>
</tr>
<tr>
<td>3D CFD</td>
<td>Three Dimensional Computational Fluid Dynamics</td>
</tr>
<tr>
<td>2D-QCA</td>
<td>Two Dimensional Quantitative Coronary Angiography</td>
</tr>
<tr>
<td>3D-QCA</td>
<td>Three Dimensional Quantitative Coronary Angiography</td>
</tr>
<tr>
<td>AMC</td>
<td>Amsterdam Medical Center</td>
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<tr>
<td>CA</td>
<td>Coronary Angiogram</td>
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<td>CAAS</td>
<td>Cardiovascular Angio Graphic Analysis System</td>
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<td>CAD</td>
<td>Coronary Artery Disease</td>
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<td>CABG</td>
<td>Coronary Artery Bypass Graft</td>
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<td>CBM</td>
<td>CompBioMed</td>
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<td>CE</td>
<td>Conformité Européenne</td>
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<td>CFD</td>
<td>Computation Fluid Dynamics</td>
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<td>CHE</td>
<td>Catharina Hospital Eindhoven</td>
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<tr>
<td>CSS</td>
<td>Cascading Style Sheets</td>
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<tr>
<td>CT</td>
<td>Computed Tomography</td>
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<td>FFR</td>
<td>Fractional Flow Reserve</td>
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<td>FN</td>
<td>False Negative</td>
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<tr>
<td>FP</td>
<td>False Positive</td>
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<td>Functional Requirement</td>
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<td>HTML</td>
<td>HyperText Markup Language</td>
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<tr>
<td>LAD</td>
<td>Left Anterior Descending artery</td>
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<td>LCx</td>
<td>Left Circumflex artery</td>
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<tr>
<td>LIMA</td>
<td>Left Internal Mammary Artery</td>
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<tr>
<td>MAP</td>
<td>Mean Arterial Pressure</td>
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<td>Medical Center</td>
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<tr>
<td>mFFR</td>
<td>Measured Fraction Flow Reserve</td>
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<td>nWMO</td>
<td>niet-Medisch Wetenschapelijk</td>
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<tr>
<td>Onderzoek</td>
<td></td>
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<tr>
<td>Pa</td>
<td>Aortic pressure</td>
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<td>PACS</td>
<td>Picture Archiving and Communication System</td>
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<td>PDCA</td>
<td>Plan Do Check Act cycle</td>
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<td>PCI</td>
<td>Percutaneous Coronary Intervention</td>
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<td>PM</td>
<td>Progress Meeting</td>
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<td>Pie Medical Imaging</td>
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<td>Project Start Up meeting</td>
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<td>School of Medical Physics and Engineering Eindhoven</td>
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<td>True Positive</td>
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<td>Technical Requirement</td>
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<tr>
<td>vFFR</td>
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</tr>
<tr>
<td>VMTK</td>
<td>The Vascular Modeling ToolKit</td>
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</tbody>
</table>

12 References


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## 13 Appendix

The appendices are created in Latex and can be found in the attachment.

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<thead>
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<th>Appendix</th>
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