Development of a myocardial perfusion phantom

Gijs de Vries, s1854526

Revision 0.26

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Preface

The system requirements specify all the requirements for the myocardial perfusion phantom. These requirements are based on research and interviews with stakeholders.

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Enschede, 7th of January 2019

Version

Requirement	Old description	Date
R0.1	Initial version. Discussed in progress meeting of 2019/01/15.	2019/01/15
R0.2	Added following items: •TR-PR02, TR-PR03, TR-PR04, TR-PR05, TR-PR06, TR-PR07, TR-PR08, TR-PR09, TR-PR10 •TR-ER02, TR-ER03 •TR-IC04, and TR-IC05 •Added appendices C & D.	2019/01/16
R0.21		2019/01/18
R0.22	Added following items: •TR-IC03 A) through E). •TFR-SIM04 A) through E) •TR-PR02 A) through E).	2019/01/20
R0.23	Added following items: •TFR-SIM05 A) through C).	2019/01/23
R0.24	Modified: •Section 2.2.1, to correspond to interview at ZGT. Added following items: •Figure 3.1, 3.2, and 3.3 Removed following items: •FR08 (combined with FR07) Inserted following items: •TFR-SIM04 B) & C). Other requirements are shifted down.	2019/01/28
R0.25	Modified: •Section 2.2.2, rephrased. Removed following items: •TFR-SIM04 E), combined with TFR-SIM04 D), AIF initially in left atrium but alternatively in left ventricle. Added following items: •TFR-GF09.	2019/01/29
R0.26	Textual (argumentative) requirements are separated from the quantitative requirements. Modified following items: •Caption of figure 2.2 to make it clear that it is not definitive. •Business model, rephrased and added business cases as discussed in work meeting of January 29, 2019. Added following items: •TFR-GFQ03, TFR-GFQ04, TFR-GFQ09, TFR-GFQ10.	2019/01/30

Changelog

Requirement	Old description	Change reason
TR-IC01	A variable amount of contrast can be injected.	Rephrased.
TFR-SIM01	An Arterial Input Function (AIF) must be extractable from either the aorta or the left ventricle chamber.	The AIF, in the D-SPECT software, is taken from the left ventricle. This requirement is moved to TFR-SIM04.
TFR-SIM04	Multiple chambers, or areas, should be present, such that ischaemic and non-inschaemic tissue can be visualised simultaneously. Typical software divide the heart into 17 chambers.	Rephrased due to misunderstanding of the 17 section model.
TR-PR10	The phantom's chambers must match the dimensions of an average human heart, between 60-90x30-50x60-90mm [LxWxD]	Sizes are specified for the ventricles.
TR-PR02	The phantom must be anatomically correct; four heart chambers, myocardium around the chambers, arrow shaped bottom.	Rephrased after interview at ZGT.
TFR-SIM05	Phantom's compartment model should match the currently practised protocol. Does the tracer diffuse, is it trapped in tissue et cetera.	Rephrased and linked to contrast section.
FR03	The high flow should be suitable for an AIF, either in a ventricle chamber or an aorta depending on the clinical software.	The D-SPECT software extracts the AIF in the left atrium.
FR04	Cardiac defects should be simulated such that the complex relation between stenotic and non-stenotic arteries is modelled.	Rephrased.
FR05	The phantom must be able to visualise both control and stenotic areas, similar to clinical scans.	Rephrased, it should be compatible with the 17 segment model.
FR06	The phantom must initially simulate the compartment model typically used in clinical scans, but be flexible enough such that other compartment models are achievable.	Rephrased to be more specific.
FR07	The contrast agent should be equivalent to that used in clinical scans.	Rephrased and combined with FR08 to be more global.
TFR-SIM04 A)	The three coronary arteries should be present (RCA, LAD, LCx) and connected to a myocardium.	Rephrased to make it more clear.
TFR-SIM04 F)	The myocardium has a longitudinal cross-sectional shape of a horseshoe.	Rephrased to be more specific.
TFR-SIM04 G)	The myocardium has a transverse cross-sectional shape of a circle.	Rephrased to be more specific.
TFR-SIM04 D)	An ROI can be taken in the left ventricle.	Combined with TFR-SIM04 E), AIF is taken in left atrium. If it has poor results, the AIF's ROI can be moved to the left ventricle.

Requirement	Old description	Change reason
TFR-SIM04 E)	An AIF can be taken from the left atrium.	Removed, combined with TFR-SIM04 D).
TR-PR02 A)	In correspondence with requirements TFR-SIM04 D) and E)	TFR-SIM04 requirements were modified, therefore TR-PR02 is modified in accordance.
TFR-GF03	Minimum achievable upper limit of myocardial perfusion is 300 mL/min/100g.	Added more specificity for stress perfusion.
TFR-GF04	Minimum achievable lower limit of myocardial perfusion is 60 mL/min/100g.	Added more specificity for rest perfusion.
FR05	The phantom must be able to visualise (and measure) the 17-segment cardiac model.	17 active segments will be too much for the initial version.
FR03*	The high flow should be suitable for an AIF extracted from the left atrium.	Rephrased to be more specific.
FR07	The contrast protocol must be equivalent to that used in clinical scans with D-SPECT.	For SPECT, the terminology is "tracer" in stead of "contrast".

Contents

1 Introduction

Myocardial Perfusion Imaging (MPI), or, simply put, the imaging of the blood flow in the heart muscle, plays an important role in diagnosing heart failure or detecting Coronary Artery Disease (CAD). Imaging systems like Computed Tomography (CT), Magnetic Resonance Imaging (MRI), Single-Photon Emission Computed Tomography (SPECT), or Positron Emission Tomography (PET) can visualise a (radioactive) contrast bolus in the supplying arteries and in underlying myocardial tissue, whose flow can give an indication of narrowed or blocked blood vessels.

Many variations in the visualisation process of myocardial perfusion, including variations in hard- and software, can (significantly) influence the outcome and in turn have consequences for patient treatment. These variations need to be validated against a well-known baseline.

A myocardial perfusion phantom will be developed that is able to simulate the blood flow in the heart muscle, i.e. the myocardium, and is able to mimic cardiac defects like (significant) stenosis.

Document overview

[todo] This section

Abbreviations

AIF Arterial Input Function

CAD Coronary Artery Disease

CT Computed Tomography

LA Left Atrium

LV Left Ventricle

MPI Myocardial Perfusion Imaging

MRI Magnetic Resonance Imaging

MV Maximal Vasodilation

PET Positron Emission Tomography

RA Right Atrium

ROI Region of Interest

RV Right Ventricle

SPECT Single-Photon Emission Computed Tomography

2 Functional system overview

This chapter goes into detail on the functional aspects of the myocardial perfusion phantom.

2.1 Drivers

Many factors influence the outcome of MPI. Some of these factors are:

Tracer	Patient	Technology	Software
- Concentration,	- Breathing artefacts,	- Modality,	- Package,
- Volume,	- Cardiac motion,	- Spatial resolution,	- Mathematical model,
- Molecule size,	- BMI.	- Temporal resolution.	- Filters,
- Injection speed.			- ROI.

The strength of a phantom is that small modifications, for example, in contrast concentration or volume, or the mathematical model, can be directly mapped to the outcome. It provides insight into dependent and independent factors in perfusion imaging.

Current phantoms either require modifications to software packages or do not model defects in a physiological way. Defects are typically modelled by reducing the flow through the myocardium by reducing the pump rate, effectively ignoring the complex relation between stenotic and non-stenotic arteries. Therefore, a myocardial perfusion phantom is needed that is compatible with clinical software and is able to mimic cardiac defects in a physiological way. This will increase the similarity with patient studies resulting in more reliable validation.

In addition to being a tool for validation of scanners and/or software packages, the phantom can be used for educational and training purposes to demonstrate the impact of hard- and software variables (sampling rate, Region of Interest (ROI), mathematical model), patient variables (BMI, blood flow and -pressure), tracer variables (concentration, type, injection speed), and many more.

2.2 Approach

The V-Model defines the project's development cycle.

2.2.1 Concept of operations

Is the D-SPECT's dynamic scanning, in comparison with other modalities (CT, MRI, PET, or SPECT), suitable for quantitative myocardial perfusion imaging?

Quantitative flow measurements is made possible due to dynamic scanning. Dynamic scanning is not a newly emerged technique, it has been used with CT in past research. Due to the solid-state detectors (Cadmium-Zinc Telluride), dynamic scanning is made possible for SPECT. The D-SPECT is relatively new in the Netherlands. However, it has been employed in Japan, Canada, France, and Great-Britain. The D-SPECT is a highly specialised cardiac system. Due to the relatively small patient population, clinics often choose more all-purpose systems. The D-SPECT is very patient friendly due to its design in contrast to alternatives, e.g. GE uses a gantry design.

CT is a well established modality with the highest spatial resolution. However, its largest drawback is that the radiation dose is directly proportional to the number of images, therefore increasing the likelihood of complication due to radiation exposure. MRI does not rely an ionising radiation, but its lower temporal resolution makes it less suitable for dynamic imaging. SPECT and PET use radioactive tracers to image blood flow, thus exposing the patient to some degree of radiation. However, it is not directly proportional to the amount of images taken and is therefore less dangerous than CT.

In addition, traditional SPECT is, on average, 22% less expensive than the current gold standard, PET. D-SPECT is supposed to be even less expensive and faster. Furthermore, significant dose reduction, due to more sensitive solid-state detectors, reduces the strain and risk for patients. In addition, these solid-state detectors improve the image resolution.

In summary, although the D-SPECT is relatively new in the Netherlands, it is more widely employed in Japan, Canada, France, and Great-Britain. The highly cardiac specialised system, its patient friendly design, the ability to scan faster and more accurate at significant dose reductions, make the D-SPECT suitable for quantitative myocardial perfusion imaging.

2.2.2 What must the myocardial perfusion phantom be able to simulate to validate quantitative MPI?

The phantom must be compatible with clinical practice, i.e. use clinical protocols and hard-/software. Patients are scanned in a D-SPECT scanner while lying down. The scans are evaluated using 4DM software.

The phantom must be suitable for an ROI in the left atrium for AIF extraction. However, in case of poor results, the ROI can be reshaped and moved to the left ventricle. The software determines the perfusion in 17 areas, i.e. the 17-segment heart model, of the myocardium, at a basal, mid and apical level, and at the apex. These segments are supplied via branches of the three coronary arteries, i.e. the RCA, LAD, and LCx. 4DM calculates individual flow rates for each segment. Therefore, the phantom should contain 17 segments where each segment's flow can be measured.

A single flow source is to be used that supplies the RCA, LAD, and LCx. From an anatomical viewpoint, the coronary arteries are supplied from the aorta. The phantom could mimic this anatomical structure, which, from a practical viewpoint, is impractical. Instead, it is possible to supply the coronary arteries from a dedicated flow source significantly decreasing the total volume of liquid being displaced. Care must be taken such that the ratio of contrast remains equivalent. Since the entire myocardium is supplied by three coronary arteries, stenosis in one of the arteries, or its branches, results in different flow behaviour which cannot be mimicked by reducing the overall flow to the myocardium alone.

Every tracer behaves differently. For D-SPECT, Technetium (^{99m}Tc) Tetrofosmin is used. This tracer is absorbed by the myocardium. The phantom will thus have to mimic this behaviour in the myocardium.

2.3 Business model

Dynamic scanning yield quantitative results, i.e. absolute perfusion rates, which require proper validation. Phantom studies are, to a high degree, suitable for such purpose. An added benefit of these studies, is that it provides insight into the effect of different parameters on the outcome, which in turn influences patient treatment. These insights can be used for calibration or protocol optimisation, e.g. tracer protocol. Examples would be determining optimal (patient dependable) activity or injection speed.

In short, the phantom can be used for educational and training purposes, as well as for calibration or optimisation.

The phantom will distinguish itself from other phantoms due to its more true-to-nature design, ability to physiologically mimic cardiac defects, and the possibility of modelling different compartment models.

The primary focus remains on the current application of MPI as performed at the ZGT in Hengelo, Overijssel.

2.4 Requirements

[todo] Verify the AIF requirements.

The functional requirements are summarised in table 2.1.

Table 2.1: Functional requirements

This table summarises the functional requirements for the prototype myocardial perfusion phantom.

Requirement number	Description
FR01	The phantom must be able to simulate blood flow, either using water of blood-mimicking fluid, at high flow rates (aortic flow).
FR02	The phantom must be able to simulate blood flow, either using water or blood-mimicking fluid, at low flow rates (myocardial flow).
FR03*	An AIF can be extracted from the left atrium, or alternatively from the left ventricle.
FR04	Cardiac defects must simulate the complex relation between stenotic and non-stenotic arteries.
FR05	The phantom must be able to visualise (and measure) at least two active segments of the 17-segment ventricle model.
FR06	The phantom must use a 2-compartment model (simulating contrast uptake in tissue).
FR07	Tracer protocol must be equivalent to that used in clinical scans with D-SPECT.
~~FR08~~	~~Contrast should be mixed equivalently to contrast mixing in patients.~~

** Depending on the flexibility of the clinical software.*

2.5 Business and system use cases

The myocardial perfusion phantom is used by researchers with varying goals. Primarily, the phantom set-up is a tool to validate perfusion imaging hard- and software and to educate on independent and dependent factors, see section 2.1. The researcher should be able to adjust the blood flow, both in the myocardium and in the aorta, and be able to set a cardiac defect.

Please note, setting the imaging and contrast parameters are not part of the phantom itself.

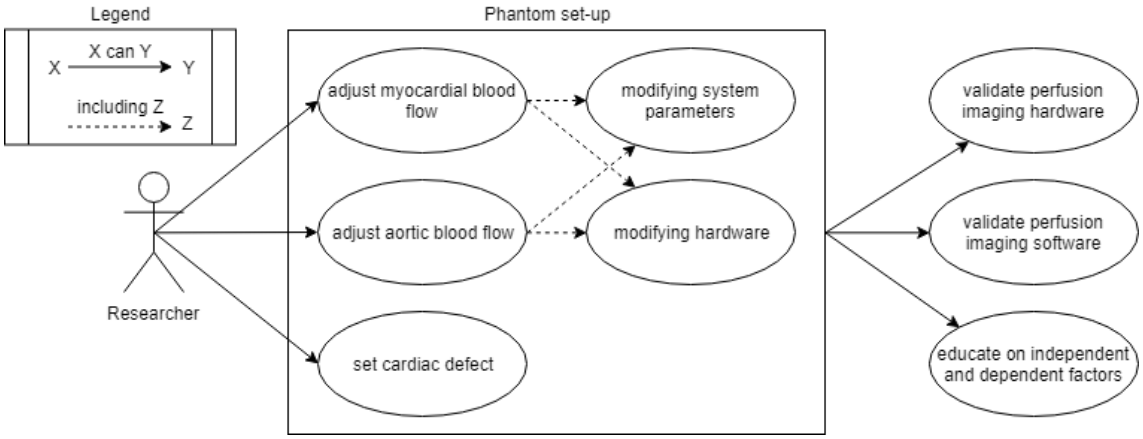

Figure 2.1: Use case diagram for the prototype myocardial perfusion phantom

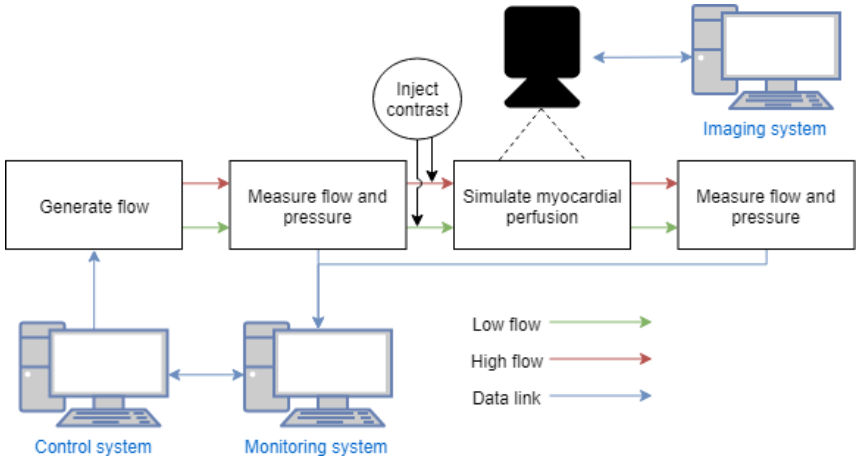

Figure 2.2: Functional architecture for the myocardial perfusion set-up, **not yet definitive.**

2.6 Architectural overview

A schematic overview of the flow set-up is shown in figure 2.2. The set-up consists of a flow generating system, e.g. mechanical pumps or pressure based, to generate the required aortic and myocardial flow, measuring systems, e.g. flow and pressure sensors, and the phantom itself, simulating the heart. The flow is controlled by means of a control system, over which the user has control. The flow parameters, i.e. flow and pressure, are measured by sensors which are monitored by a monitoring system. The monitoring system and control system cooperate such that user parameters are maintained. Figure 2.2 shows a distinction between high and low flow, which is not a requirement. Low flow can be created by means of pressure difference in high and low flow circuit; increasing pressure in low flow circuit results in less volume passing through.

3 Technical system overview

3.1 Function requirements

This section specifies the requirements set for the functions mentioned in figure 2.2.

3.1.1 Generate flow

In the project plan, a literature overview is given on perfusion phantoms, for a variety of organs, but also on physiological factors: perfusion rates, blood pressures, rates of stenosis et cetera. The TFR-GF requirements are based on the estimates by Uren et al. (1994), summarised in appendix A, Chiribiri et al. (2013a), Ho et al. (2014), summarised in appendix B, and Slart (2015).

Decisions and design choices are given in table 3.1, quantitative requirements are given in table 3.2.

Table 3.1: Textual requirements for function: Generate flow

Requirement number	Description
TFR-GFT01	A constant flow is to be generated, i.e. non-pulsatile.
TFR-GFT02	Flow generators need to be interchangeable.
TFR-GFT03	Flow feedback control for flow generators.

TFR-GFT01 is based on reducing the complexity of the set-up. The ROI based AIF averages the intensity over time, which removes the pulsatile nature. Furthermore, the heart rate cannot be determine in the measurements results. Therefore, pulsatile flow is not a priority. **TFR-GFT02** is based on maintaining flexibility such that the most optimal flow generator can be chosen based on the requirements for a specific experiment.

TFR-GFT03 is based on ensuring reliability; no validation can be performed when the flow is not controlled.

Table 3.2: Quantitative requirements for function: Generate flow

Requirement number	Description		Value	Unit
TFR-GFQ01*	Upper limit myocardial perfusion.	=	300	mL/min/100g
TFR-GFQ02*	Lower limit myocardial perfusion.	=	60	mL/min/100g
TFR-GFQ03*	Typical perfusion rate during stress.	>..<	190..300	mL/min/100g
TFR-GFQ04*	Typical perfusion rate during rest.	>..<	60..95	mL/min/100g
TFR-GFQ05**	Upper limit cardiac output.	=	8	L/min
TFR-GFQ06+	Lower limit arterial pressure.	=	56	mmHg
TFR-GFQ07+	Upper limit arterial pressure.	=	155	mmHg
TFR-GFQ08	Mean Arterial Pressure (MAP)[1].	=	89	mmHg
TFR-GFQ09	Typical MAP.	>..<	70..110	mmHg
TFR-GFQ10	Feedback control accuracy	=	5	%

** combined flow to myocardium, indicated by blue arrows in figure 3.1.*
*** flow **not** entering the myocardium, indicated by red arrow in figure 3.1.*
+ based on diastolic and systolic blood pressures, respectively. Measured at dashed line P in figure 3.1.

[1] Calculated as: $MAP \simeq DP + {}^1/_3(SP - DP)$

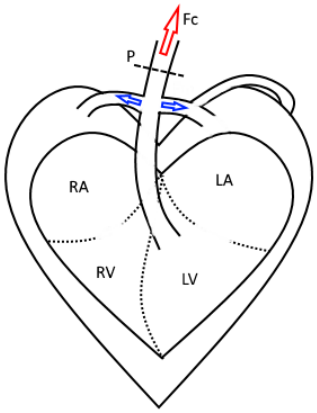

Figure 3.1: Simplified, schematic overview of the heart.

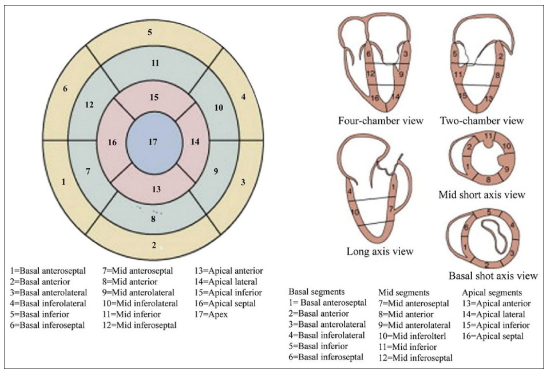

Figure 3.2: 17-segment heart model

3.1.2 Measuring flow and pressure

Table 3.3: Quantitative requirements for function: Measure flow and pressure

Requirement number	Description		Value	Unit
TFR-MFPQ01	Flow measuring accuracy.	<=	5	%
TFR-MFPQ02	Pressure measuring accuracy.	<=	5	%
TFR-MFPQ03	Absolute flow resolution.	>=	1	mL/min
TFR-MFPQ04	Sampling rate.	>=	10	Hz

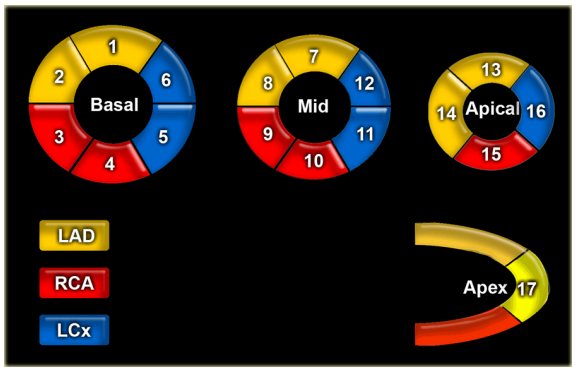

Figure 3.3: Schematic representation of the supply to each segment (simplified).

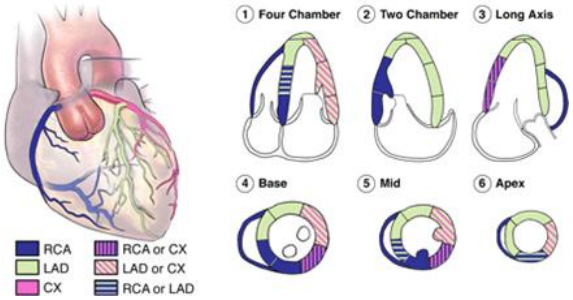

Figure 3.4: Schematic representation of the supply to each segment.

3.1.3 Simulate myocardial perfusion

Table 3.4: Function requirements for function: Simulate myocardial perfusion

This table specifies the requirements specific for the phantom that simulates the myocardial perfusion.

Requirement number	Description
~~TFR-SIM01~~	~~An AIF must be extractable from the left ventricle, as per software requirement.~~
TFR-SIM02	Stenotic arteries are mimicked in a physiological way by physically narrowing (or increasing flow resistance) of certain arteries.
TFR-SIM03	Different stenotic severity, should be possible by, for example, variable flow resistors or interchanging components.
TFR-SIM04	The phantom must be compatible with D-SPECT protocol.
A)	Flow to the myocardium is supplied by the RCA, LAD, and LCx.
B)	Flow for each segment is supplied individually by branches of the RCA, LAD, and LCx, see figure 3.3.
C)	Flow from each segment is measured separately such that they can be compared to the 17-segment model.
D)	An ROI for the AIF can be taken in the left atrium. Alternatively, the ROI for the AIF can be taken in the left ventricle.
~~E)~~	~~An AIF can be taken from the left atrium.~~
F)	The left ventricle's myocardium has a Vertical and Horizontal Longitudinal Axial (VLA/HLA) cross-sectional shape of a horseshoe.
G)	The left ventricle's myocardium has a Short Axial (SA) cross-sectional shape of a circle.
TFR-SIM05*	Phantom's compartment model should match the currently practised protocol.
A)	The contrast agent specified as Technetium (^{99m}Tc) tetrofosmin, see section 3.1.4.
B)	The contrast agent is absorbed by the myocardium to approximately 1.2% of administered activity in 5 minutes.
C)	Contrast accumulates in skeletal muscles, spleen, liver, and kidneys (potential interference).

*https://pubchem.ncbi.nlm.nih.gov/compound/131704316#section=Absorption-Distribution-and-Excretion

3.1.4 Inject contrast

The injection protocol is not part of the development of the phantom. However, there are certain requirements to be monitored:

Table 3.5: Contrast requirements

This table summarises the requirements on the contrast and contrast injection protocol.

Requirement number	Description
TR-IC01	Contrast volume is variable.
TR-IC02	Contrast injection is reproducible.
TR-IC03	Contrast protocol should match the currently practised protocol.
A)	Contrast agent is Technetium (^{99m}Tc) tetrofosmin.
B)	Contrast agent is injected, as bolus, via infusion pump.
C)	A pre-bolus is to be used of 37mBq, for proper placement of the heart in the scanner.
D)	A main bolus is to be used of 500mBq.
E)	A main bolus is to be used of 700mBq, for more hefty patients.
TR-IC04	Contrast concentration is variable.
TR-IC05	Contrast agent is variable.

3.2 Physical requirements

[inpr] Determine size of seating of D-SPECT

[done] Determine weight limit of seating of D-SPECT

[inpr] Must it be completely anatomical?

[inpr] Adjust requirements if the phantom does not have to be anatomical.

The following requirements state the physical aspects of the phantom and of the .

Table 3.6: Physical requirements

This table summarises the physical requirements.

Requirement number	Description
TR-PR01	The phantom, and its set-up, must fit on the D-SPECT's chair.
TR-PR02	The phantom must be anatomically shaped.
A)	In correspondence with requirements TFR-SIM04 D).
B)	Four chambered phantom that correspond to left/right ventricle and left/right atrium.
C)	Myocardium surrounds heart chambers.
D)	Three coronary arteries, RCA, LAD and LCx, supply the myocardium.
E)	The coronary arteries run outside of the myocardium.
TR-PR03	The phantom must be placed inside a thorax phantom, QRM TRX-116, with maximum diameter of 100mm.
TR-PR04	Total weight, on patient chair, cannot exceed 171kg.
TR-PR05	The flow set-up must remain horizontal, to prevent additional flow resistance.
TR-PR06*	The phantom must match the size of an average human heart, 12x8x6cm [LxWxD] (OpenStax College, 2013).
TR-PR07	The phantom must resemble the weight of an average human heart, 250-300g (female) or 300-350g (male) (OpenStax College, 2013).
TR-PR08+	The phantom's ventricles must match the volume of average human ventricles, between 40 and 180mL.
TR-PR09+	The phantom's atria must match the volume of average human atria, between 80 and 115mL.
TR-PR10**	The phantom's ventricles must match the dimensions of an average human heart, between 60-90x30-50x60-90mm [LxWxD]
TR-PR11	The phantom cannot contain air bubbles.

**Length (L): longitudinal axis (apex-basal), width (W): transverse axis (septal - lateral), Depth (D): transverse axis (anterior-inferior).*
***Length (L): longitudinal axis (apical-annular), width (W): transverse axis (septal-lateral (LV) or septal-medial (RV)), depth (D): transverse axis (apical-annular)*
+Chiribiri et al. (2013b) uses LA/RA of 105mL and LV/RV of 120mL.

3.3 Environmental requirements

[todo] Determine how much noise output it may have.

[done] Determine the height of the chair of the D-SPECT

In what environment is the system operating.

Table 3.7: Environmental requirements

This table summarises the environmental requirements, i.e. the restrictions set by the environment to the phantom.

Requirement number	Description
TR-ER01*	No high-density or "High-Z" material is to be used.
TR-ER02	The phantom's left and front side must remain free such that the D-SPECT camera image around it.
TR-ER03**	Any part of the flow set-up and/or phantom, that does not fit directly on the patient chair, must remain horizontal with the remaining parts between 63 and 93cm.

** High-density and "High-Z" material, i.e. material with high atomic number, tend to block gamma radiation emitted by SPECT tracers. Examples are Titanium (Ti), Chromium (Cr), Vanadium (V), Iron (Fe), or Lead (Pb); atom number >22, Lead is 82.*
*** The patient chair's seating is adjustable between 63 and 93cm.*

3.4 External interfaces

Table 3.8: External interface requirements

This table summarises the requirements for the external interface.

Requirement number	Description
TR-EI01	Live plotting, at 10Hz, of system system flow and pressure.
TR-EI02	Ability to adjust the output of the flow generators.
TR-EI03	Serial communication between control/monitoring systems and external interface.

3.5 System qualities

[todo] Specify pressure threshold.

Define the quality of the system: such as reliability, availability, serviceability, security, scalability, maintainability.

Table 3.9: System qualities

This table summarises the system qualities.

Requirement number	Description
TR-SQ01	The flow set-up must perform an emergency shut down when the arterial pressure exceeds specified threshold.
TR-SQ2	The flow set-up must perform an emergency shut down when the flow cannot be controlled, i.e. erratic.

3.6 Constraints and Assumptions

Design constraints that have been imposed and assumptions that have been made by the requirements engineering team when gathering and analyzijng the requirements.

Table 3.10

This table summarises constraints placed on the design and assumptions made to yield the system requirements.

Reference number	Description
TR-CA01	Cardiac artefacts, beating of the heart, is initially too complex. The phantom will be static.
TR-CA02	Breathing artefacts are not simulated in the phantom itself. A breathing thorax phantom can be used if available.
TR-CA03	Chest size, the amount of tissue between heart and scanner, is not simulated in the phantom itself. Thorax phantoms with modular rings are available to simulate tissue patients with varying BMIs.

A Appendix: Normal heart rate/blood pressure and myocardial perfusion rates by Uren et al. (1994)

The following tables summarise Uren et al. (1994).

Table A.1: Heart rate and blood pressure according to Uren et al. (1994).

This table shows the heart rate and blood pressure in (Uren et al., 1994) among 35 patients with single-vessel CAD and 21 control patients.

		Control	**Stenosis**
Heart rate [BPM]	Base line	65 ± 7	63 ± 10
	MV*	84 ± 10	88 ± 16
Blood pressure [mmHg]	Diastolic (B)	76 ± 8	74 ± 11
	Diastolic (MV)	75 ± 12	72 ± 12
	Systolic (B)	132 ± 19	148 ± 22
	Systolic (MV)	140 ± 20	153 ± 21

** Maximal Vasodilation (MV)*

Table A.2: Myocardial blood flow according to Uren et al. (1994).

This table shows the determined perfusion rates in (Uren et al., 1994), converted to ml/min/100g.

	Control	**Stenosis**			
		<40%	40-59 %	60-79%	>80%
Base line	113 ± 26	96 ± 19	125 ± 34	123 ± 57	92 ± 33
MV*	337 ± 125	344 ± 147	207 ± 83	151 ± 37	122 ± 36

** Maximal Vasodilation (MV)*

B Appendix: Normal heart rate/blood pressure and myocardial perfusion rates by Ho et al. (2014)

The following tables summarise Ho et al. (2014).

Table B.1: Heart rate and blood pressure according to Ho et al. (2014).

This table shows the heart rate and blood pressure in (Ho et al., 2014) among 35 patients with documented CAD and 35 control (low-risk) patients. The 35 documented CAD patients are from a previous study.

		Control	**Stenosis**
Heart rate [BPM]	Base line	66 ± 10	73 ± 14
	MV*	88.54 ± 11.45	82 ± 16
Blood pressure [mmHg]	Diastolic (B)	63 ± 13	–
	Diastolic (MV)	56 ± 10	–
	Systolic (B)	111 ± 17	–
	Systolic (MV)	105 ± 21	–

** Maximal Vasodilation (MV)*

Table B.2: Myocardial blood flow according to Ho et al. (2014).

This table shows the myocardial perfusion rates by Ho et al. (2014), given in mL/min/100g.

	Low risk	**Historic ischaemia**	**Previous infarction**
Global rest	74.08 ± 16.3	82.29 ± 16.87	81.98 ± 18.54
Global stress	141.92 ± 30.83	107.95 ± 25.25	106.93 ± 32.91

C Appendix: heart chamber volumes by Lin et al. (2008)

The following tables summarise Lin et al. (2008) who investigated the ventricles and atria of 103 non-obese adults using 1D, 2D, and 3D techniques.

Table C.1: Heart chamber volumes according to Lin et al. (2008).

		End-systolic volume [mL]	**End-diastolic volume** [mL]	**Average wall thickness** [mm]
LV	2D	65.2 ± 20.9	150 ± 35.6	7.3 ± 1.3
	3D	52.6 ± 19.2	143.6 ± 36.4	
RV	2D	–	–	2.4 ± 0.7
	3D	82.10 ± 29.2	174.9 ± 48.0	
LA	2D	86.5 ± 29.1	-	–
	3D	102.3 ± 24.4	–	
RA	2D	–	–	–
	3D	111.9 ± 29.1	–	

Left Ventricle (LV), Right Ventricle (RV), Left Atrium (LA), Right Atrium (RA)

Table C.2: Heart chamber sizes according to Lin et al. (2008).

	LV [mm]			**RV** [mm]	
	End-Systolic	End-Diastolic		End-Systolic	End-Diastolic
SL	–	47.4 ± 4.7	SM	29.6 ± 5.3	37.0 ± 5.7
AI	–	57.7 ± 5.5	AI	29.6 ± 5.3	72.6 ± 9.0
AA	–	87.6 ± 9.3	AA	62.0 ± 8.8	77.7 ± 10.4

Left Ventricle (LV), Right Ventricle (RV), Septal-Lateral (SL), Anterior-Inferior (AI), Apical-Annular (AA), Septal-Medial (SM)

D Appendix: heart chamber volumes by Maceira et al. (2006a,b)

The following table summarises Maceira et al. (2006a,b), who investigated the left and right ventricles, respectively, of 120 patients.

Table D.1: Heart chamber volumes according to Lin et al. (2008).

		End-systolic volume [mL]	**End-diastolic volume** [mL]
LV	All	47 ± 10	142 ± 21
	Female	42 ± 9.5	128 ± 21
	Male	53 ± 11	156 ± 21
RV	All	50 ± 14	144 ± 23
	Female	43 ± 13	126 ± 21
	Male	57 ± 15	163 ± 25

Left Ventricle (LV), Right Ventricle (RV), Left Atrium (LA), Right Atrium (RA)

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