DOCTOR OF PHILOSOPHY

Workflow Analysis, Modelling and Simulation for Improving Conventional and MRI-guided Vascular Interventions

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A mis padres y a mi hermana Leticia

Contents

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Declaration

I hereby declare that this thesis titled 'Workflow Analysis, Modelling and Simulation for Improving Conventional and MRI-guided Vascular Interventions' has been compiled by myself, that it is a record of work completed by myself and that it has not previously been accepted for a higher degree at this University or any other institution of learning. Where other sources of information have been used, they have been acknowledged.

Signature: Fabiola Fernández-Gutiérrez Date: 15th May 2014

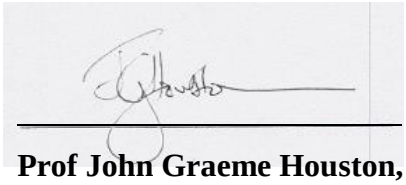
Statement by supervisors

I, Andreas Melzer, have read this thesis titled 'Workflow Analysis, Modelling and Simulation for Improving Conventional and MRI-guided Vascular Interventions' and certify that the conditions of Ordinance 39 of the University of Dundee have been fulfilled.

Signed:  Date: 14/05/214

Prof Andreas Melzer, First Supervisor

I, John Graeme Houston, have read this thesis titled 'Workflow Analysis, Modelling and Simulation for Improving Conventional and MRI-guided Vascular Interventions' and certify that the conditions of Ordinance 39 of the University of Dundee have been fulfilled.

Signed:  Date: 14/05/214

Prof John Graeme Houston, Second Supervisor

Abstract

This thesis proposes a multidirectional methodological framework for a comprehensive ergonomic analysis and modelling of workflow for multi-modal vascular image-guided procedures (IGPs). Two approaches are employed to analyse the workflow: Discrete Event Simulation (DES) and purpose-oriented physical models. In contrast to previous studies, the proposed methodology looks in detail the actions carried out within the intervention rooms and the clinical experience during the procedures with three main objectives: to provide a deeper understanding of vascular procedures, to predict the impact of protocol modifications and to offer a framework to develop new image-guided protocols for the alternative use of Magnetic Resonance (MR) imaging in comparison with X-Ray Digital Subtraction Angiography (DSA). The methodological framework includes an assessment of commercial simulation software packages to evaluate their fitness to the specific requirements of this research. The novel methodology is applied to several cases studies of common vascular IGPs. In addition, a case of MR – guided focused ultrasound intervention demonstrates how it is possible to extend the framework to study non-vascular IGPs. The multi-disciplinary methodological framework described opens a new way to understand IGPs that could be used in prospective applications such as medical education and medical devices regulations.

Resumen

Esta tesis presenta un marco metodológico multidireccional para el análisis y modelado ergonómicos detallado de flujos de trabajo de intervenciones vasculares guiadas por imágenes (IGPs en sus siglas en inglés) multimodales. Para el análisis del flujo de trabajo se han utilizado dos enfoques: Simulación por Eventos Discretos (DES en sus siglas en inglés) y modelado físico orientado a resultado. En contraste con estudios previos, la metodología propuesta analiza en detalle las acciones llevadas a cabo dentro de las salas de intervenciones y la experiencia del personal clínico durante los procedimientos, todo ello con tres objetivos principales: proporcionar un conocimiento más profundo de las intervenciones vasculares, predecir el impacto de modificaciones en los protocolos y ofrecer un marco de trabajo para desarrollar nuevos protocolos en intervenciones vasculares guiadas por imagen para el uso alternativo de Resonancia Magnética (MR en sus siglas en inglés) en comparación con la Angiografía por Sustracción Digital (DSA en sus siglas en inglés). Como parte de este marco metodológico, se presenta una evaluación comparativa de cumplimiento con los requerimientos específicos de esta investigación sobre paquetes de software de simulación comerciales. La nueva metodología se aplica a varios casos de estudio de IGPs vasculares típicos. Además, otro caso que se presenta es el de intervención de ultrasonidos focalizados guiados por Resonancia Magnética, que demuestra cómo es posible extender el ámbito de trabajo para estudiar IGPs no vasculares. El marco metodológico multi-disciplinario descrito abre una nueva vía para entender IGPs que puede ser utilizada en futuras aplicaciones tales como la educación médica o la regulación de instrumental médico.

Glossary

Symbols

A^2 – *Anderson-Darling test statistic*

d^*, h_1 , n_0 , N_i – *parameters for the Dudewicz and Dalal Ranking and Selection method for optimisation analysis*

E(X) – Expected value of the IID random variable X

f – Degree of freedom

F – Cummulative distribution function

S^2 – *Variance of an IID random variable*

SD – Standard deviation

SE – Standard error

t – Student t

W – Weights calculated for optimisation analysis

X – Independent and identically distributed (IID) random variables

$\bar{X}$ – *mean of an IID random variable*

$\tilde{X}$ – *Weighted sample mean for optimisation analysis*

Acronyms

ACR – America College of Radiology

AMIGO – Advanced Multimodality Image-Guided Operating

CAD – Computer aided design

CDF – Cumulative distribution function

CI – Confidence Interval

CRC – Clinical Research Centre

CRPA – Cued Retrospective Protocol Analysis

CT – Computed Tomography

CVIR – Cardiovascular interventional radiology

DES – Discrete Event Simulation

DHM – Digital Human Model

DSA – Digital Subtraction Angiography

D&D – Dudewicz and Dalal ranking and selection method for optimisation analysis

FUS – Focussed Ultrasound

FUSIMO - Patient specific modelling and simulation of focused ultrasound in moving organs

GEE – Generalised Estimating Equations

GPL – General Public License

GUI – Graphical user interface

HCC – Hepatocellular carcinoma

HD – High definition

HF – High frequency

IC – the Interventional Centre

ICRP – International Commission on Radiological Protection

IEEE – Institute of Electrical and Electronics Engineers

IIIOS – Integrated Interventional Imaging Operating System

IGP – Image-guided Procedure

IR – Interventional Radiology

KPI – Key Performance Indicator

MCAR – Missing Completely at Random

MCM – Monte Carlo model

MI – Multiple Imputation

MIDAS – Medical Intervention Data Analysis System

MITOS – Multimodality Imaging Therapy Operating System

MKC – Markov Chain

MR – Magnetic Resonance

MRgFUS – Magnetic Resonance guided Focussed Ultrasound

MRI – Magnetic Resonance Imaging

NHS – National Health System

NIOSH – National Institute for Occupational Safety and Health

OT – Operating Theatre

OR – Operational Research

PCI – Percutaneous Coronary Interventions

PET – Positron Emission Tomography

PN – Petri Nets

PTA – Percutaneous Transluminal Angioplasty

PTA-IA – Percutaneous Transluminal Angioplasty of the Iliac Artery

R&S – Ranking and Selection

RAD – Role Activity Diagrams

RF - Radiofrequency

RULA – Rapid Upper Limb Assessment

SMEs – Subject- matter experts

SSM – Soft Systems Methodology

STL – Stereo Lithography

TACE - Transarterial Chemoembolisation

TAVI – Transcatheter Aortic Valve Implantation

UML – Unified Modelling Language

US – Ultrasound

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Chapter 1.
Introduction

1.1. Context

Image-guided therapy is considered as alternative to open surgery in a multitude of procedures motivated by same or better results and fewer complications. However, the introduction of complex technologies in imaging operating systems is increasing costs and challenges in the training of clinical staff members. The current economic situation worldwide is steadily increasing the pressure on improving effectiveness and efficiency in healthcare systems.

Operational research (OR) methods for workflow analysis, modelling and simulation have been used for decades in the manufacturing industry in order to optimise processes (also called systems in this context), design new layouts or modify areas to improve productivity and explore more efficient ways in the use of human resources and equipment. This concept has been successfully applied to health systems, especially in high demanding areas, such as surgical rooms and emergency departments (Sobolev, Sanchez, and Vasilakis 2011). Recent studies indicate the increasing interest on applying simulation to improve radiology departments, including radiotherapy treatments (Santibáñez et al. 2009; Werker et al. 2009).

However, the majority of the studies in radiology environments focus on a department level and interventional procedures are judged in overall procedure times. The impact of actions and decisions within the procedures is then usually not assessed. In addition, many studies disregard the interactions among the clinicians and the effect that elements of the workspace may have in the clinical practice.

This thesis aims to deliver a comprehensive analysis of ergonomic workflow for image-guided interventions with a focus on vascular procedures. A methodological framework was designed to study the workflow from multiple perspectives, providing a better understanding of vascular procedures. Treating interventions as

systems, this thesis uses two approaches to analyse the workflow: simulation and physical models.

1.2. Research objectives, hypotheses and propositions

An image-guided procedure (IGP) can be described in three phases (Yaniv and Cleary 2006):

- *Pre-operative planning*: where a surgical plan is created based on pre-operative images and other additional information of the patient.
- *Intra-operative plan execution*: Once the patient is in the operating theatre (OT), the IGP provides assistance to the medical staff.
- *Post-operative assessment*: where images are acquired after the interventions to compare the results with the pre-operative plan.

Previous literature review reveals a lack of detailed analysis of the intra-operative phase of vascular radiology interventions. In addition, the few attempts that analyse tasks within intervention rooms are limited to time-based analysis. As described previously in the context, this thesis aims for a more comprehensive analysis and modelling of ergonomic workflow of vascular procedures with the aid of discrete event simulation techniques. With this idea, this research has three main objectives:

- First, to provide a better understanding of current scenarios of vascular image-guided procedures through workflow analysis, modelling and simulation;
- Second, to use that acquired deeper knowledge to predict the impact of protocol alterations in the scenarios studied;
- And third, to design a methodological framework to develop new protocols for the alternative use of MRI to guide vascular interventions.

To unfold these objectives, different cases of study[1] will be presented.

[1] Case study is used in this thesis as a technical term to show exemplar studies to validate the whole or parts of the methodological framework proposed.

At the same time, the following hypotheses and propositions accompany this thesis and are discussed along the results chapter and summarised in the conclusion chapter:

- DES is the appropriate technique to study workflows in image-guided procedures
- Data gathering is a critical factor for workflow analysis and modelling
- Overall procedure times are not an appropriate representation of the variability within vascular IGPs
- It is possible to implement purpose-oriented accurate mathematical models of IGPs
- Simulation can aid the prediction of the impact that different strategies can have in image-guided procedures
- Personalised 3D environment are needed in order to get the message across clinicians
- A multidisciplinary framework is needed in order to analyse and design new protocols for image-guided procedures in MRI environments
- Analysis of ergonomics constraints is important when introducing environments for IGPs

1.3. Chapter summaries

Chapter 2 gives a brief overview of the concepts, imaging modalities and modern operating rooms within interventional radiology that will be covered in this work. It reviews the literature on workflow analysis, modelling and simulation for surgical and radiology environments.

The thesis is divided now in two parts. While **Part I**, including chapters 3 to 7, presents a simulation approach to meet the needs collected from the literature in chapter 2, **Part II,** which includes chapters 8 and 9, proposes a framework for the application of physical modelling to workflow analysis.

Chapter 3 presents the simulation methodological framework. It includes an evaluation of simulation software packages to select the right tool for the research.

The framework comprises details on the data gathering and statistical analysis. It also explains how the simulating models are implemented and validated.

Chapter 4 presents the first of the cases of study of this thesis. Details of the workflow for percutaneous coronary interventions (PCIs) are analysed statistically and a discrete event simulation (DES) model is implemented for PCIs that included coronary angioplasty or stenting.

Chapter 5 describes the case of study of a multimodal imaging intervention: transarterial chemoembolization (TACE). A DES model is implemented and an optimisation-based analysis is applied to compare different alternatives to the current protocol in the pursuit of a better performance of the interventions.

Chapter 6 describes how the methodological framework for workflow modelling and simulation is applied to the case of Magnetic Resonance guided Focused Ultrasound (MRgFUS) including model validation and prediction analysis.

Chapter 7 presents preliminary results on applying the simulation model approach to a complex vascular procedure: transcatheter aortic valve implantation (TAVI). First DES model is presented and guidelines for future direction are discussed.

Chapter 8 describes a framework to apply physical modelling to study workflow for the development of new Magnetic Resonance Imaging (MRI) – guided protocols for vascular procedures.

Chapter 9 presents the results of a comparative study based on the physical model approach on the development of MRI-guided protocols for a common vascular procedure: iliac angioplasty. MRI and fluoroscopy are compared in terms of performance, user experience and ergonomics.

Chapter 10 summarises the findings of previous chapters to explain their contributions to the research hypotheses described in the first chapter. Limitations of the present study are discussed and suggestions are given for future directions and possible applications of this research.

The **Appendix** chapter at the end of this thesis presents the different sections that complement the results presented in the previous chapters. It includes relevant

information that supplements the simulation software evaluation as well as detailed material regarding the statistics calculations. In the final appendix, the logic code for the implementation of a Markov process model as part of a DES model is included to facilitate the replication of results of this thesis.

1.4. Publication list

1.4.1. Journal papers

The following papers have been published or are under peer review:

1. **Fernández-Gutiérrez F**, Barnett I, Taylor B, Houston G, Melzer A, (2013) "Framework for detailed workflow analysis and modelling for simulation of multi-modal image-guided interventions", Journal of Enterprise Information Management, Vol. 26 Iss: 1/2, pp.75 – 90
2. **R**ube MA, **Fernandez-Gutiérrez F,** Cox BF, Holbrook AB, Houston G, White RD, McLeod H, Fatahi M, Melzer A. "Preclinical feasibility of a technology framework for MRI-guided iliac angioplasty", International Journal of Computer Assisted Radiology and Surgical, August 2014 (in press)
3. **Fernández-Gutiérrez F**, Martínez S, Rube MA, Cox BF, Fatahi M, Scott-Brown K, Houston G, McLeod H, White R, French K, Gueorguieva M, Immel E, Melzer A. 'Ergonomic workflow and user experience comparative analysis of MRI versus X-Ray guided vascular interventions. Case of study: iliac angioplasty', International Journal of Computer Assisted Radiology and Surgery *(Submitted)*
4. **Fernández-Gutiérrez F**, Wolska-Krawczyk M, Bücker A, Houston G, Melzer A. 'A simulation-based workflow optimisation in a radiology department: a case of a multimodal imaging procedure', Minimally invasive therapy & allied technologies (MITAT) *(Submitted)*
5. Loeve AJ, Al-Issawi J, **Fernández-Gutiérrez F**, Lango T, Matzko M, Napoli A, Dankelman J. 'Workflow analysis and modelling of MR-guided Focussed Ultrasound', *(To be submitted)*

1.4.2. Book chapters, conferences papers and abstracts

Book chapter

1. **Fernández-Gutiérrez F**, Houston G, Elle OJ, Wolska-Krawczyk M, Orban M, and Melzer A, "Workflow Analysis, Design, Modelling and Simulation for the Multimodality Imaging Therapy Operating System (MITOS)," in Intraoperative Imaging and Image-Guided Therapy, F. A. Jolesz, Ed. New York, NY: Springer New York, 2014, pp. 325–338.

Conference papers and abstracts

1. **Fernández-Gutiérrez F**, Martínez S, Rube MA, Cox BF, Fatahi M, Scott-Brown KC, Houston GJ, McLeod H, White RD, French K, Gueorguieva M, Immel E, Melzer A. An operational comparison of MRI and X-Ray for vascular interventions. Case of study: Task and user experience analysis for iliac angioplasty. 25th Conference of the Society for Medical Innovation and Technology, SMIT 2013, Baden-Baden, Germany.
2. Loeve AJ, Al-Issawi J, **Fernandez- Gutierrez F**, Matzko M, Napoli A, Dankelman. MRgFUS workflow and bottle-necks – Preliminary results. 25th Conference of the Society for Medical Innovation and Technology (SMIT 2013), Baden-Baden, Germany.
3. **Fernandez-Gutierrez F**, Ferut J, Smink J, Houston G, Melzer A. Ergonomics for MRI guided procedures. Case of study: postural analysis for MRI scanners CARS 2013 Computer Assisted Radiology and Surgery June 26 - 29, 2013, Convention Center, Heidelberg, Germany.
4. **Fernández-Gutiérrez F**, Elle OJ, Wendt D, Melzer A, "Characterisation and simulation of TAVI procedures. Is it possible to convert to MRI guidance?" 9th Interventional MRI Symposium, 2012. Boston, USA.
5. **Fernández-Gutiérrez F**, Barclay A, Martin T, Elle OJ, Houston G, Melzer A, "Workflow for image-guided interventions: Characterisation and Validation. Towards the Integrated Imaging Operating Room of the future," 46th DGBMT Annual Conference 2012. Jena, Germany.
6. **Fernández-Gutiérrez F**, Barclay A, Martin T, Houston G, Melzer A, "Modelling and simulating MR guided workflow for endovascular and

cardiovascular procedures," 24th Conference of the Society for Medical Innovation and Technology, SMIT 2012, Barcelona, Spain.

7. **Fernández-Gutiérrez F**, Taylor B, Houston G, and Melzer A, "Building a framework for detailed workflow description for simulation of multi-modal image-guided interventions," in Proceedings of the Operational Research Society Simulation Workshop 2012 (SW12), 2012.
8. **Fernández-Gutiérrez F**, Houston G, Wolska-Krawczyk M, Elle OJ, Buecker A, Melzer A. Simulating the Imaging Operating Suite of the future. From angiography to multi-modal image-guidance: framework and pilot models. 4th NCIGT and NIH Image Guided Therapy Workshop 2011. Arlington, Virginia, United States.
9. **Fernández-Gutiérrez F**, Toomey RJ, Houston G, Wolska-Krawczyk M, Elle OJ, Buecker A, Melzer A. Computer simulation for ergonomics and workflow improvement in multi-modal image-guided interventions: a new approach. 23rd Conference of the Society for Medical Innovation and Technology, SMIT 2011, Tel-Aviv, Israel.
10. **Fernández-Gutiérrez F**, Toomey RJ, Houston G, Melzer A. Using computer simulation in workflow design and improvement in multi-modal image-guided interventions. UK Radiological Congress 2011. Manchester, UK.

Chapter 2.
Background

Contents of this chapter were published in:

Fernández-Gutiérrez F, *Houston G, Elle OJ, Wolska-Krawczyk M, Orban M, Melzer A, "Workflow Analysis, Design, Modeling and Simulation for the Multimodality Imaging Therapy Operating System (MITOS)," in Intraoperative Imaging and Image-Guided Therapy, F. A. Jolesz, Ed. New York, NY: Springer New York, 2014, pp. 325–338.*

2.1. Introduction

The following sections present an overview on image-guided techniques for vascular procedures, comprising interventional radiology and interventional cardiology. In addition, techniques for system analysis, modelling and simulation that will be covered in this text are introduced. It also presents a literature review on previous work on workflow analysis in surgical rooms and radiology environments.

2.2. Cardiovascular and interventional radiology

2.2.1. Introduction

Interventional radiology (IR) appears as an evolution of open surgery for certain procedures due to the same or better results obtained and the lower overall risks for patients. On the other hand, interventional cardiology is the part of cardiology that treats coronary artery occlusion, arrhythmias and structural heart disease through catheterisation of the heart chambers or vessels. Whereas in open surgery the physicians have direct vision and access to the area of interest, in cardiovascular and interventional radiology (CVIR), they need the aid of imaging techniques to identify the anatomical structures and to provide guidance of the instruments (Yaniv and Cleary 2006).

Nowadays, CVIR comprises a wide and evolving number of minimally invasive Image-Guided Procedures (IGP) for the diagnosis and treatment of multiple diseases (Radiology 2010). These procedures include, among others, treating diseases from the vascular, pulmonary, gastrointestinal or musculoskeletal system. Different

imaging modalities are used to carry out the interventions such as X-ray, Ultrasound (US) or Magnetic Resonance (MR). This section briefly reviews the methods, equipment and rooms used for conventional vascular interventions, which are the central focus of this research. In addition, the other focus of interest of this project, the section discusses the use of Magnetic Resonance Imaging (MRI) along with a description of the layout designs of modern operating rooms for vascular interventions.

2.2.2. Digital Subtraction angiography and angiography rooms

Digital Subtraction Angiography (DSA) is the imaging method that uses X-ray to visualise and examine the blood vessels by the injection of a radio-opaque contrast agent (commonly iodine based) (Pommi 2011). Figure 1(a) displays an example of a DSA image. In a clinical radiology department, a conventional room for DSA includes an angiographic X-ray system, a display system for image visualisation, an operating table with controls and several peripheral equipment elements (e.g. scrub trolley, bins and shelves or cupboards for device storage). Figure 1(b) shows an example on a conventional angiography room (Clinical Radiology department, Ninewells Hospital, Dundee, UK).

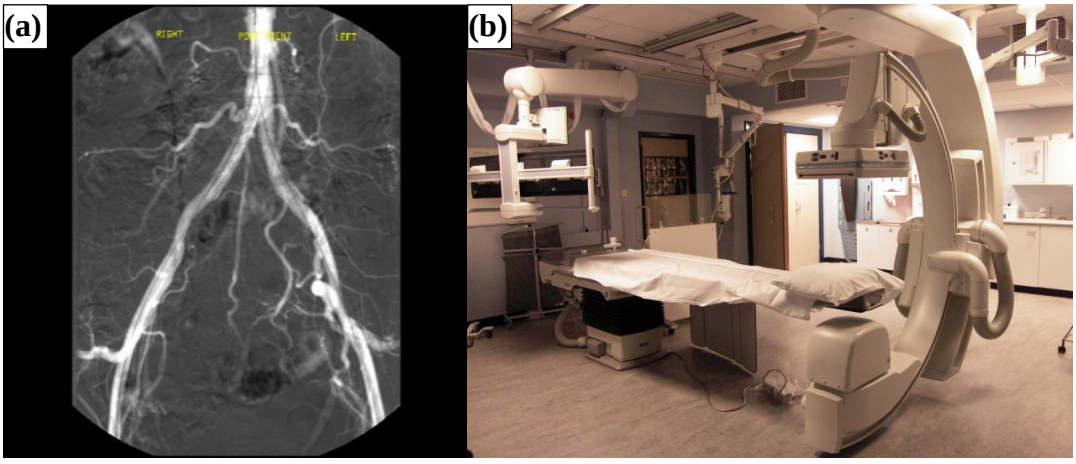


Figure 1. (a) Example of Digital Subtraction Angiography (DSA) image (iliac arteries). (b) Angiography suite at the Clinical Radiology Department at Ninewells Hospital (Dundee, UK).

The angiography system has at least an X-Ray generator and a detector, facing each other and mounted together in a C-shaped structure, which gives them their

usual name C-arm, easily identified within Figure 1(b). The C-arm can be rotated around the operating table so the images can be acquired from different angles.

IR is applied to several areas of vascular procedures, depending on the diagnosis and the therapy needs. This thesis will deal with some of the most important procedures:

- *Balloon angioplasty (PTA, percutaneous transluminal angioplasty)*: a catheter with a foldable or elastic balloon at the distal end is inserted for reopening a constricted or occluded vessel by means of inflating the balloon.
- *Stent implantation*: a stent (wire mesh or fenestrated tube) is delivered via a catheter to treat constricted or occluded vessels. Stents can be self-expanded or balloon-expanded, depending on the material and mechanism used for their deployment (Duerig and Wholey 2002).
- *Chemoembolisation*: catheter procedure for local chemotherapy and embolization (closing of a vessel) for cancer treatment. The anti-cancer drug is injected directly to the blood vessel feeding the tumour together with the embolic agent which blocks the blood supply to the tumour and at the same time, traps the drug in the tumour (Radiologyinfo.org 2013a).

One of the main advantages of DSA (and angiography in general) is that it allows real-time visualisation of the blood vessels during interventions. However, the drawback is that it is a source of radiation both for the patient and for the clinicians.

Regarding exposure levels for workers, expressed as effective dose in *mSv* (*milliSieverts*) (Radiologyinfo.org 2013b), the International Commission on Radiological Protection (ICRP) recommends a limit of 20mSv/year. Literature on coronary angiography and angioplasty procedure gives observed effective doses in patients ranging between 5 – 16.7 mSv for 8.6 – 31.5 minutes of procedure time respectively (Katritsis et al. 2000) and an average of approximately 3 mSv/year for interventional cardiologists (Chida et al. 2013; Venneri et al. 2009). Although there is no direct evidence that ionising radiation can induce cancer, radiation is one of the most studied carcinogens (Zhou 2011). There is however evidence of iodine contrast media induced nephropathy (Tavakol et al. 2012) and significant exposure to ionising radiation with an unknown but increasing lifetime risk of cancer

(Vijayalakshmi et al. 2007). Therefore, optimising time and safety of procedures to reduce radiation exposure is one of the main objectives in interventional radiology.

While patients do not wear any radiation protection in the majority of procedures, clinicians wear heavy lead aprons and badges to measure the radiation exposure (Raza 2006). In addition, lead protections are normally incorporated to the operating tables. However, the heavy weight of these lead aprons, together with the long hours standing in the interventions rooms, is responsible for most of the occupational risks for interventional radiologists (Dehmer 2006).

2.2.3. Magnetic Resonance Imaging and scanner rooms

MRI is an imaging technique used primarily in medical settings to produce high quality images of the inside of the human body. Figure 2 (a) shows an example of a MR image. Briefly, an MRI system is based on a strong static magnetic field, alternating magnetic fields gradients and a high-frequency (HF) system with transmitting and receiving coils (antennae) (Nitz 2011). The strength of the magnetic field is described in units of *Tesla* (*T*). While early MRI systems used magnets in the range of 0.1-0.2T, nowadays most hospitals work with MRI scanners with a magnetic field of 1.5 or 3T for patient diagnosis. Figure 2 (b) presents an example of an MRI scanner room at the Clinical Research Centre (CRC, Ninewells Hospital, Dundee, UK).

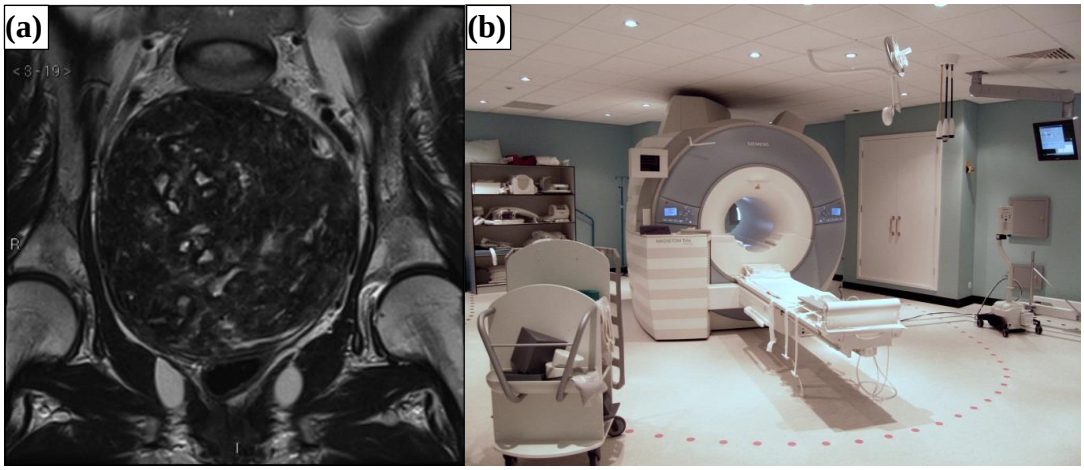


Figure 2. (a) Example of Magnetic Resonance Image (MRI) (image of pelvis showing uterine fibroid on T2 weighting). (b) MRI room at the Clinical Research Centre (CRC), Ninewells Hospital (Dundee, UK).

As well as the strength of the magnetic field, the design of the MRI scanner itself plays an important role in the room setups and in the safety and comfort of patients. Different designs for MRI scanners can be found in the market following two main configurations:

- *Close-bore scanners*: Figure 2 (b) and Figure 3 (a) illustrate two examples of close-bore scanners. In these scanners, the size of the bore is usually limited to 60cm, although modern scanners are moving to larger bore designs (e.g. 70cm, Figure 3 (a)). In addition, some companies are implementing shorter scanner models aimed to reduce the number of examinations refused due to claustrophobia.
- *Open-bore scanners*: Figure 3(b) shows an example of a *horizontal* open-bore MRI scanner from Philips Healthcare (Panorama 1T, Eindhoven, The Netherlands). These scanners were designed in a C-arm fashion, allowing better access to the patient (Wacker et al. 2005). A variation of the horizontal open-bore scanner is the *vertical* open-bore (so called mid-field system with 0.5T), first used in the late 90s but which design has been discontinued mainly due to high costs and the lower SNR (signal-to-nose-ratio) provided in comparison to high-field systems (1T or more), which makes the image resolution coarser for the same image quality. .

Figure 3. (a) 3T Wide-bore MRI scanner (Discovery, GE Healthcare, Waukesha, WI, USA). (b) 1T open-bore MRI scanner (Panorama, Philips, Eindhoven, The Netherlands).

Apart from using MRI for diagnosis, there has been an increasing interest for using MR as imaging technique for guiding interventions since the 80s (Blanco Sequeiros et al. 2005). Many characteristics such as the accurate soft tissue contrast

or the absence of ionising radiation enhance MRI as suitable modality for interventional radiology. In addition, the capabilities of MRI to acquire images in different planes without moving the patient are a great advantage when performing interventions (Gedroyc 2000).

The interventional use of MRI has influenced the design of MRI scanner rooms and the layouts of modern interventional and operating areas. With regard to MRI scanners, there are several technical solutions currently promoted (Andreas Melzer et al. 2011):

- *Conventional*: MRI installed in the operating room.
- *Ceiling mounted*: MRI mounted on a rail system in the ceiling connecting two operating rooms.
- *Adjacent MRI room*: The MRI scanner is installed next to one or more operating rooms, establishing a direct access between rooms. In this case, the patient table is moved via a floor-mounted rail system or via wheeled cradles.

Besides designing aspects, MRI rooms are different from conventional angiography rooms in a number of safety issues. Some of the most important safety concerns for both diagnostic and interventional procedures under MRI can be summarised below (Kettenbach et al. 2006; Nitz 2011):

- Attraction forces by the magnetic field
- Radio Frequency (RF) interaction with the patient's body
- RF interaction with active or passible implants
- Acoustic noise
- Switching off the magnetic field requires 30-60 sec for quenching (evaporation Helium leads to loss of superconductivity and can cause significant damage to the MRI)

These safety issues imply severe restrictions not only when designing the room, but also when operating near the scanner. Full guidelines for MR safe practise can be consulted in the *ACR (American College of Radiology) guidance document on MR safety* (Kanal et al. 2013).

2.2.4. Integrated interventional operating systems

The lower costs and better results of minimally invasive techniques are motivating the replacement of traditional open surgery for many types of IGPs (A Melzer et al. 1997). The advances in imaging information systems, and the new navigating and tracking technologies are transforming the traditional Operating Theatres (OT) and intervention rooms in a modern Multimodality Imaging Therapy Operating System (MITOS) or also known as hybrid OT (Rostenberg and Barach 2011). Many examples of these OT can be found in the literature. Focussing on hybrid OT for vascular minimally invasive procedures, there are two main approaches for the layout designs:

1. A *single hybrid operating theatre* containing all the surgical and imaging equipment;
2. A *set of adjacent rooms* directly connected allowing the transfer of the patient and/or equipment among rooms.

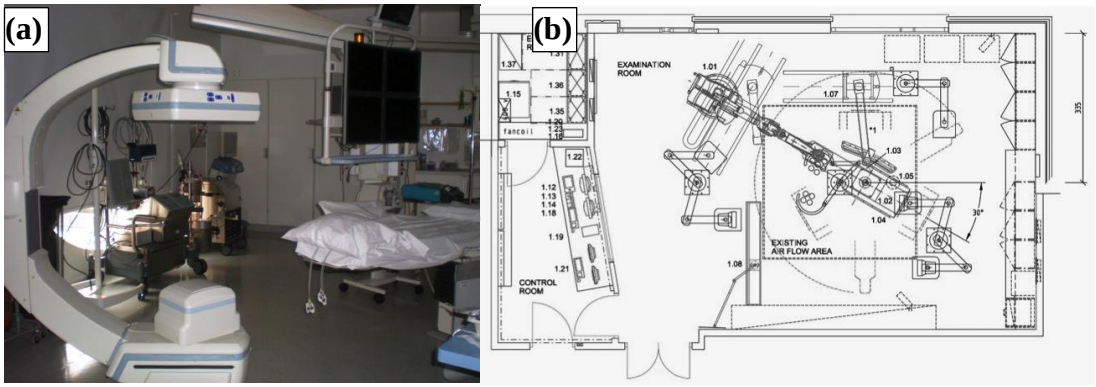


Figure 4. Hybrid Operating Room (HOR) at the Intervention Centre (Oslo University Hospital, Oslo, Norway). (a) View of the robotic C-arm, ceiling mounted screens and robotic operating table; (b) Complete layout of the operating room and control room.

As an example of the first approach, the Intervention Centre at Oslo University Hospital (Oslo, Norway) counts with a modern hybrid OT for cardiovascular procedures (see Figure 4). The facilities include a robotic mobile C-arm, ultrasound and anaesthesia equipment, heart – lung machine, ceiling mounted screens and other surgical and interventional equipment (Nollert and Wich 2009). These single rooms present many technical challenges but are increasingly common in many hospitals. These suites try to avoid some usual patient safety incidents by means of reducing

travel distances for patients and clinicians since the critical equipment is now present within the operating room. For instance, there is no need of moving the patient from an induction room to the operating room, since the anaesthesia equipment is maintained within the operating suite (Rostenberg and Barach 2011). In addition, incorporating imaging technology to the OT provides the benefits of visualisation and guidance in minimally invasive procedures without moving the patient during the intervention. The popular preference when implementing these hybrid environments is the integration of fluoroscopy with surgical equipment (Sikkink, Reijnen, and Zeebregts 2008; Kpodonu 2010). However, other approaches incorporate other imaging modalities such as MRI scanners due to the several advantages mentioned in the previous section (Bock and Wacker 2008; Schulz et al. 2004). However, in this case the whole operating room has to be equipped with non-ferromagnetic devices in order to be MRI safe thus increasing the operating costs.

Although the one-room solution is usually the less expensive option to site, the second approach offers more flexible opportunities. For example, by using separate rooms for the imaging equipment, these could be used independently for diagnosis (Gilson and Wacker 2012). There are different approaches when designing the adjacent rooms. A preferable design is to place an MRI scanner room next to an angiography/surgical room (McGee et al. 2007; Vogl et al. 2002). With this two-room layout, the patient is transferred to the MRI suite when it is required during the procedure. This configuration also allows other options where the MRI scanner can be shared between several operating rooms. This layout has been implemented in hospitals such as the Jacob Medical Center at Thornton Hospital (University of California, San Diego, CA, USA) (Lehatto and Amato 2012) or the Kokilaben Dhirubhai Ambani (Reliance) Hospital (Mumbai, India) (Kokilaben Hospital Brochure 2009). Both cases take an extra step in the design and they replace the transfer of the patient between rooms for the transfer of the MRI scanner between the rooms. These environments are equipped with a ceiling-mounted 3T MRI scanner, which can be moved between both rooms, reducing potential risks created by moving the patient during the procedures, such as brain shifts during neurosurgery or hazards related to monitoring patients under anaesthesia (Ehrenwerth et al 2009). For instance, when retrieving tumours in neurosurgery, brain shifts connected to movement of the patient between modalities can cause that the images taken prior

the treatment, before or during the intervention, to be invalid and result in errors targeting the tumour.

This philosophy is also applied to other modern environments that include multi-modal imaging modalities in a 3-room layout. This is the case of the Advanced Multimodality Image-Guided Operating (AMIGO) Suite (National Center for Image Guided Therapy – NCIGT, Brigham and Women's Hospital, Boston, MA, USA) (see Figure 5). The AMIGO suite includes a central angiography/surgical room, which is also provided with ultrasound equipment. On the left, Figure 5 shows the MRI suite with a ceiling-mounted MRI scanner, which is connected by sliding doors and can be moved to the surgical room if it is needed during the intervention. The right side of the image shows a PET/CT (Positron Emission Tomography/Computed Tomography) scanner suite that can help to localise and target viable tumour tissue before procedures or verify the completeness of surgical removal of tumours.

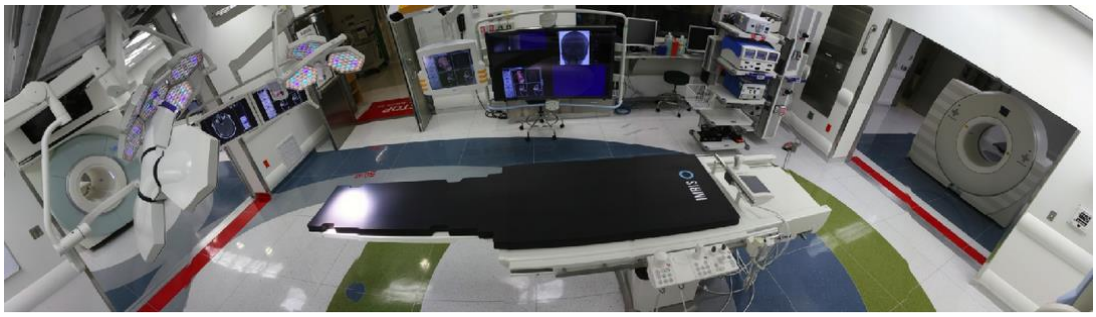


Figure 5. Advanced Multimodality Image-Guided Operating (AMIGO) Suite: 3T MRI scanner room on the left, PET/CT scanner on the right and surgical – intervention room in the middle, National Center for Image Guided Therapy (NCIGT), Brigham and Women's Hospital (Boston, MA, USA).

The MITOS at the Clinical Research Centre (CRC) at Ninewells Hospital (Dundee, UK) designed by Melzer et al. (2012) with similar idea than the AMIGO system. Figure 6 shows the plan of the CRC layout with a 3T MRI scanner room on the left and a PET/CT scanner room on the right, both connected to an central intervention room. This allows a direct transfer of the patient between the three rooms during procedures – *therapeutic workflow* (see red arrow in Figure 6). In addition, both rooms are provided with direct and independent access for diagnosis patients – *diagnostic workflow* (see blue arrows in Figure 6).

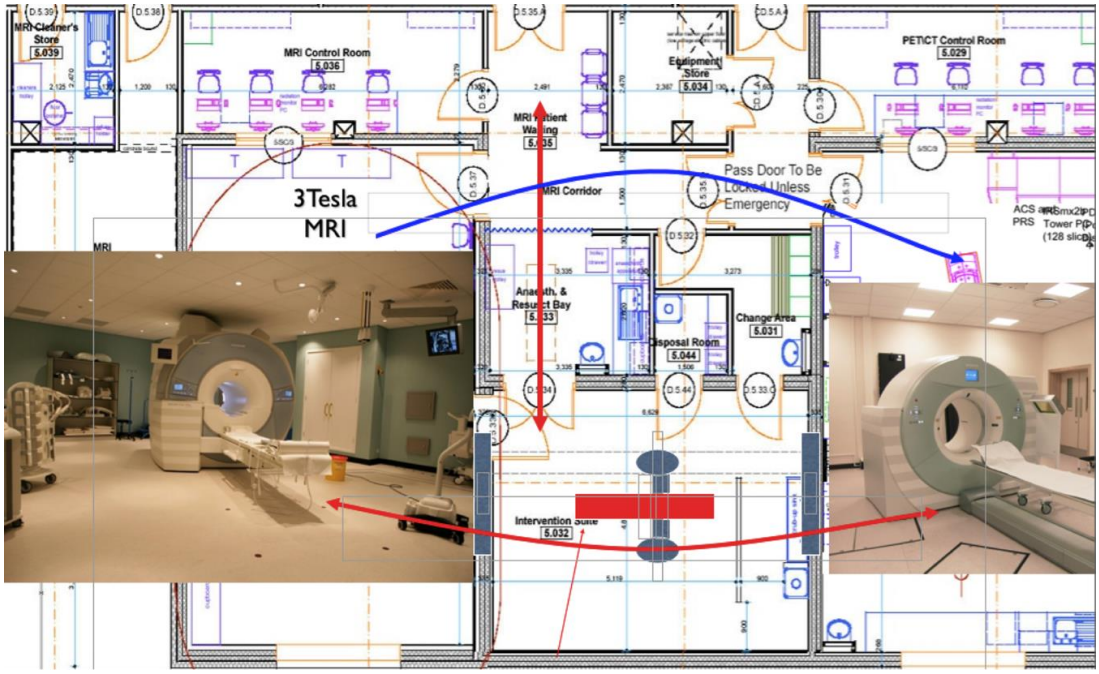


Figure 6. Clinical Research Centre (CRC) facilities at Ninewells Hospital (Dundee, UK). The layout presents a 3-T interventional MR (left) and 128-multislice interventional PET/CT (right) interconnected with a multipurpose interventional suite (diagnostic workflow: blue arrows, image-guided procedure workflow: red arrows).

2.3. System analysis, modelling and simulation

2.3.1. Introduction

This section gives essential definitions of concepts that will be used throughout the document. The different ways a system could be studied are highlighted as an important aspect that affects the research hypotheses of this thesis. In addition, the modelling techniques that are commonly used to model health environment are briefly covered which will also justify the reasons why one specific technique is preferred over other alternatives.

2.3.2. System, model and other essential definitions

Schmidt and Taylor (Schmidt and Taylor 1970) defined a *system* as *"a collection of entities, e.g. people or machines, which act and interact together toward the accomplishment of some logical end"*. The collection of entities or variables will depend on the type of system to be studied. In addition, the *state* of a system is

defined by the collection of those variables needed to describe the system at a particular time, relative to the objectives of the study (Law 2007). For example, if an emergency department was to be studied, examples of *state variables* would be the number of patients that are being attended, the number of busy medical doctors and nurses and the time of arrival of each patient at the reception desk.

Systems are usually studied in order to gain insight into the relationships of variables or to predict the performance of a system under new conditions. Experiment with the actual system can be very costly or sometimes not feasible if the system does not exist yet. For these reasons, it is usually necessary to implement and work with a *model of the system*. The Institute of Electrical and Electronics Engineers (IEEE) defines model as *"an approximation, representation or idealisation of selected aspect of the structure, behaviour, operation, or other characteristics of the real-world process, concept or system"*(IEEE Standard Computer Dictionary 1991). The model must reflect the system accurately in order to accomplish the objectives of the study. For this reason, the model needs to be validated and verified. There are several definitions for the terms *verification* and *validation* (Refsgaard and Henriksen 2004). During decades, they have been commonly differentiated as (Balci 1986)

"Model verification, to build the model right; and

Model validation, to build the right model"

For the purpose of this study, more standard definitions given by Schlesinger et al. have been adopted (Schlesinger et al. 1979). Model verification will be defined as *"ensuring that the computer program of the computerised model and its implementation is correct"*. Model validation will guarantee that *"the computerised model within its domain of applicability possesses a satisfactory range of accuracy consistent with the intended application of the model"*.

2.3.3. Physical vs. mathematical models: how to study a system.

Law (2007) discusses in the first chapter about different ways to study a system. These options are represented in Figure 7. The first decision to be made is whether it is feasible to experiment with the real system or in contrast, it is needed to

implement a model of the system. In this, experimenting with the real system (e.g. an image-guided procedure) could result in very high cost-risk situations and compromise the safety of patients and clinical staff.

However, when deciding the need of implementing a model, the next dilemma is whether to implement a *physical model* or a mathematical one. In the case of IGPs, implementing a physical model of an angiography suite to test the impact of new conditions could be very costly and time consuming. The costs can be significantly reduced when using *mathematical models*. However, recreating the system through a physical model aids the understanding of certain aspects of the system that could be missed by the use of mathematical models. Such is the case of environmental and operational limitations or other safety issues related with the procedures. Therefore, the decision of implementing a physical or mathematical model should be based on the grounds of the questions to be answered from the system.

Finally, in the case a mathematical model may be implemented, an additional step would have to be taken (see Figure 7). This extra step would occur if an *analytical* solution was found or on the contrary, it is needed to implement a simulation to find the answers. In the case of IGPs, complex relationships can be found during the workflow among clinicians, tasks, times, decision points, etc. For this reason, it is most appropriate to use *simulation*, defined in Law (Law 2007) as *"numerically exercising the model for the inputs in question to see how the effect the output measures of performance"*.

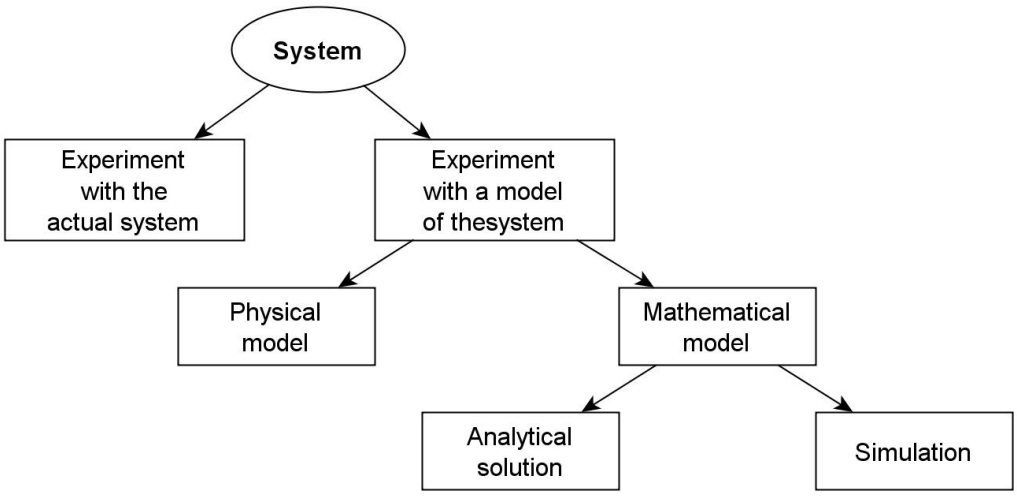


Figure 7. Ways to study a system, figure reproduced with permission from Law (2007)

2.3.4. Modelling techniques in the healthcare context

The review provided by England and Roberts (1978) reported the most common methods applied in modelling healthcare environments: regression, econometric, mathematical modelling employing queuing theory or stochastic methods, and mathematical programming. More recently, in 2011, Sobolev et al. (2011), distinguished between static and dynamic approaches, deterministic or stochastic and methods that involve discrete or continuous time. Among these techniques, Monte Carlo models, as static simulation methods and Markov chains and Discrete Event Simulation (DES) models, as dynamic approaches, are the most common used for health systems. Techniques based on Petri Nets are also widely used in modelling health systems (Zhang et al. 2009; Zoeller et al. 2006).

Monte Carlo models

Monte Carlo Models (MCM) consist of a random repetition of samples with probabilities, representing the process outcome at a particular point in time (Sobolev et al. 2011), hence the reference to the Monte Carlo Casino in Monaco and its games of luck. Figure 8 shows the schematic mechanism of MCMs to analyse uncertainty propagation by sampling an input given by a statistical distribution. The output generated can be represented by another statistical distribution with a certain reliability or with confidence intervals. There are different methods of the applying MCMs: Classical, Quantum, Integral, Simulation and so on (Sadus 2011). Within the healthcare context, MCMs are used mainly for risk assessment, prognostic and transmission models of health interventions and cost-benefit analysis of medical treatments, amongst others (Katsaliaki and Mustafee 2011).

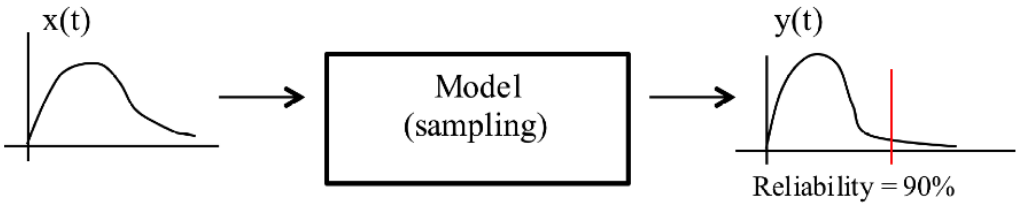


Figure 8. Schematic view of the Monte Carlo sampling method to analyse uncertainty propagation

Markov Chains

Markov Chains (MKC) are discrete-event stochastic models, where the states are defined as nodes in a graph and transitions between the states are represented by links. Markov chains, despite their usual application with discrete instants of time; can be used with a continuous time base, which means that transitions can occur at any time. Figure 9 shows an example of a graphical representation of these transitions between states in a MKC model. $P_{0,1}$ is the probability to go from 0 to 1 and $P_{1,0}$ is the probability to go back to 0. The probability to continue in the state 1 is $P_{1,1}$ and the probability of staying in the state 0 is $P_{0,0}$. These probabilities define the transition probability array P_T:

$$P_T = \begin{pmatrix} P_{0,0} & P_{0,1} \\ P_{1,0} & P_{1,1} \end{pmatrix}$$

(Eq. 2-1)

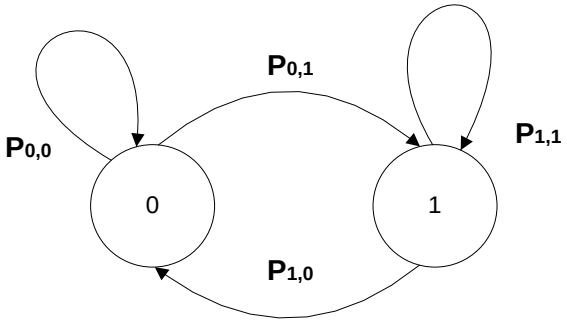


Figure 9. Example of a simple graphical representation of the transitions in a Markov Chain model, where for example, $P_{0,1}$ is the probability to go from state 0 to state 1 and $P_{1,0}$ is the probability to go from the state 1 to state 0.

One of the main properties of Markov processes is the Markov property. A stochastic process has the Markov property if the conditional probability distribution of future states of the process depends only on the present state, not on the sequence of previous events, or in other words these processes do not have memory. As a result and according to the Markov property,

$$x^{(n+1)} = x^{(n)} P_T$$

(Eq. 2-2)

Where x is a stochastic vector with the probability distributions for the states.

This property allows then the calculation of future states. As an example,

$$x^{(n+3)} = x^{(n+2)}P_T = \left(x^{(n+1)}P_T\right)P_T = x^{(n+1)}P_T^2 = \left(x^{(n)}P_T^2\right)P_T = x^{(n)}P^3$$

(Eq. 2-3)

However, this property, makes MKC not appropriate when a new state may not only depend on the previous state but also on a sequence of states that preceded it, as happens in some workflow studies. An additional limitation is the impossibility of describing interactions between concurrent processes (Sobolev et al. 2011; Wainer 2009).

Petri Nets

Petri Nets (PN) define the structure of the system using two graphical elements. The "graph's nodes or places" represent the system states, and the transitions represent the net evolution. In the example of Figure 10, L1 to L3 are the nodes and t1 to t2 are the transitions. A PN defines initially a static view of the system. To study the dynamics, the PN has to be executed and for that reason, a token is placed (black dot in the figure) on one of the nodes. During execution the token is taken from the input node to every output node (L2 and L3 in the example). Each execution of the transition is called firing the transition (Wainer 2009).

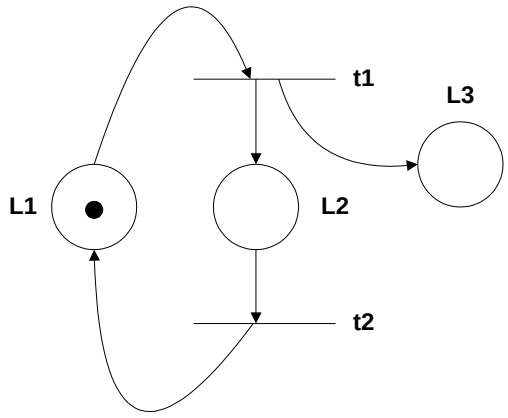


Figure 10. An example of a Petri Net graph where L1 to L3 are the nodes and t1 to t2 are the transitions.

The main drawback with PNs is that they can be very complicated to read for large and complex models as all the data has to be represented in the net. In addition, they do not define hierarchical concepts. Coloured PNs take these definitions into account by allowing tokens to carry data values (Mans et al. 2008).

Discrete Event Simulation

Discrete Event computer Simulation (DES) consists of a mathematical modelling technique that allows the building of hierarchical and modular models, from the simple to the complex. It permits the modelling of systems with a set of infinitive possible states where the new state after an event arrival can depend on previous states. The system to be modelled maintains a clock, marking timestamps throughout the event's duration. Other common components featuring the system are buffers, where components accumulate while awaiting processing, processes that perform operations, and sinks that allows the part (what we are processing) to exit the system. When modelling, data is collected on frequencies of parameters, arrival rates and process times. This information is then analysed statistically to determine the distributions that represent the groups of data that will be introduced to the simulation models. In health applications, there normally appear two types of approach. The first, called event scheduling, samples the moments when events occur from predefined distributions of times. The second approach, process interaction, describes the chronology of actions associated with the events, modelling the process as a sequence of serial and concurrent activities operating on, what some experts call, passive entities (e.g. patients or clinicians). Therefore, discrete event models are found to be appropriate for health care and are the method most used for modelling workflow in surgery (Cassandras and Lafortune 2008; Sobolev, Sanchez, and Vasilakis 2011; Wainer 2009).

Table 1 presents a summary of the classification of the modelling techniques described in this section according to their time evolution – static or dynamic – and their time base for the representation of events – discrete or continuous. The table also includes *system dynamics* as example of continuous dynamic modelling technique. System dynamics has not been contemplated in this chapter since it was considered out of the scope of this work. This modelling technique uses essentially differential equations to understand aspects of complex systems. In the context of

healthcare it is usually helpful to explain dynamics in epidemic studies (Brailsford and Hilton 2001).

Model	Static		Monte Carlo models
	Dynamic	Discrete	**Discrete Event Simulation** Markov chains Petri Nets
		Continuous	System Dynamics (Not contemplated)

Table 1. Classification of the main stochastic modelling techniques according to their time evolution (static or dynamic) and their time base for the events (discrete or continuous).

2.4. Workflow analysis, modelling and simulation in healthcare

2.4.1. Introduction

Macro- and micro-ergonomics, workflow analysis, modelling, and simulation have been used for decades in the manufacturing industry in order to optimise processes, design new layouts or modify areas to improve productivity, and explore more efficient ways in the use of human resources and equipment.

Conceptually, a hospital can be seen as a large production facility where patients enter, queue for a service and, eventually when the service is complete, are discharged or removed from the facility. This concept has been applied successfully for more than 30 years to healthcare systems.

In this section, the literature to be reviewed first is workflow analysis in operating theatres (OT), due to the similarity with interventional suites. The literature available is very extensive; therefore and for the purpose of this research the focus is on the principal factors that are involved in the operational analysis of surgical and interventional radiology procedures. Next to be examined in detail was the previous research on workflow analysis, modelling and simulation in radiology environments.

2.4.2. Workflow analysis in surgical environments

The high demand in the OTs has caused hospitals' stakeholders to become very interested in applying workflow modelling and simulation to analyse and improve their facilities. Among the approaches to analyse surgical workflow, computed-aid techniques have become very popular in the last decade. Sobolev et al (2011) presented a literature review about the use of computer simulation in surgical environments. They found 34 publications on flow simulation for surgical patients between 1957 and 2007. Since then, the number of publications has increased considerably due also to the fact that ORs together with ICUs and emergency departments are considered the most costly facilities in a hospital. For instance, the average cost per hour of a standard OT in Scotland is £1155.79 (Ramsay et al. 2012).

The approach given to the problem varies depending on different factors. One of the critical factors that determine the analysis is the amount and detail of data available. Hospitals usually hold databases with information about the operations performed. These databases are usually different for each department. In most cases, those records are usually limited to just a few metrics of the operating process such as waiting time before operating, surgery time or recovery time. The majority of these studies are focused on improving the efficiency on using the OTs and reducing waiting lists of patients, where a large amount of data is needed to find significant results (Stahl et al. 2006; Torkki et al. 2006). Some authors have dedicated most of the project period to data collection in order to have enough data to implement realistic models (Denton et al. 2007). However, in cases where a more detailed workflow description of the intervention events is needed, it is unusual to find databases available with the required information. Some authors have completed database records by interviewing experts or taking measurements (Baumgart et al. 2007). Other authors introduced new technologies in the OTs to help the data gathering. Nara et al. (2009) used an ultrasonic sensor system to localise positions of the staff during neurosurgery operations at the Tokyo Women's Medical University in Japan. Figure 11 shows the setup of the sensors in the OT and the placement of the transmitters on the clinicians without interfering in their work.

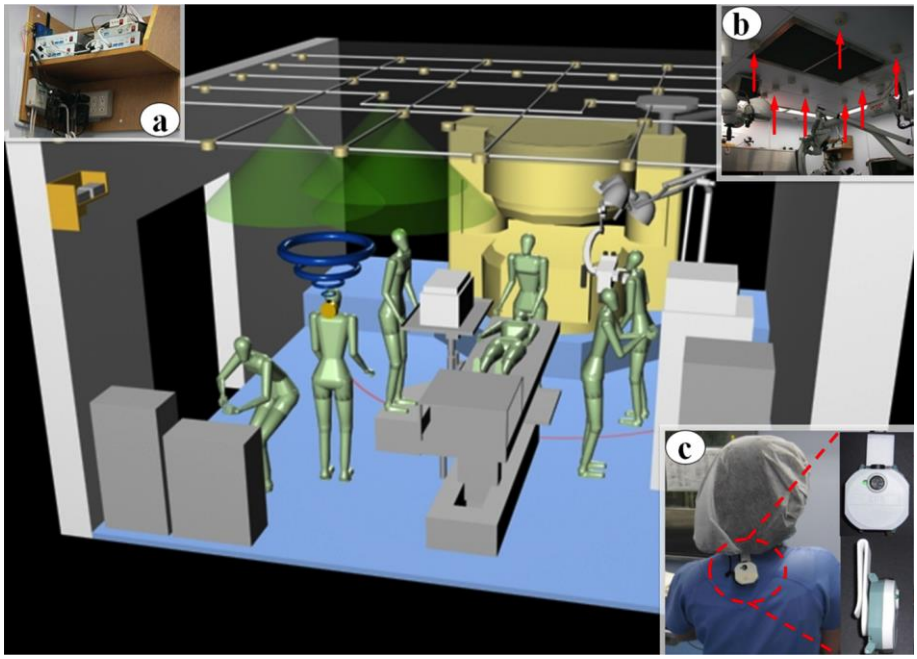


Figure 11. Ultrasonic 3D location aware system at Tokyo Women's Medical University (Japan), consisting on control units (a), receivers (b) and transmitters (c); courtesy of Nara et al. (2009).

Padoy et al. (2010) studied the feasibility of introducing a signal based modelling system able to recognise signals from the different devices used during the intervention. Thereby each device can be analysed to determine by which person and for what purpose it is being used for at discrete time steps. The information was recorded with synchronised video cameras and presented as statistical modelling for the signal and phases recognition. Gentric et al (2013) used a dedicated software to record tasks in cerebral angiographies. They divided the procedures in phases, linking instruments, actions and anatomical structure when recording the tasks. All these works mentioned agree in that obtaining sufficient information for optimal reengineering of OT management requires a systematic framework for collecting data in order to track inefficiencies in the process (Zoeller et al. 2006). In addition, safety and efficiency can be improved by objective analysis of procedures along with a detailed assessment of other components of the workspace and an examination of underlying attitudes that can contribute to medical error (Flin et al. 2006).

Another important factor in workflow modelling is the type of surgery that is being analysed. Emergency surgery cannot be scheduled in advance; therefore, other types of data are taken into account to improve workflow in the operating rooms. Some studies, such as Torkki et al (2006), reorganised the flow of patients and also

the guidance of the process redistributing tasks among the clinicians and moving phases of the operation to decrease waiting times. On the other hand, some surgical procedures have a high variability in their requirements like open cardiac surgery with an average duration of 4-5 hours. Using the hospital database to get records from years 2001 – 2003, Peltokorpi et al. (Peltokorpi et al. 2008) evaluated three different process changes for open-heart surgery: cost analysis, and underused and overused time scheduled for the surgery in the OT. The authors agreed that for a more accurate modelling to predict OT usage, the data in the hospital were limited and a specific project would be required.

Despite the limitations that appear in many studies, the effort made towards better modelling of workflow in OTs has been extended to many disciplines such as cataract surgery (Reindl et al. 2009), trauma surgery (R. a. Marjamaa et al. 2008; Torkki et al. 2006), endoscopy (Denton, Rahman, and Nelson 2007), laparoscopy (Padoy et al. 2010) and also radiology.

2.4.3. Workflow analysis, modelling and simulation in radiology environments

In 1971, Garfinkel (Garfinkel 1971) published a study about applications of computer simulation to improve patient scheduling in health systems, which included radiology as one of the highlighted fields. A year later, Jeans et al. (Jeans, Berger, and Gill 1972) presented a work about simulation on an X-Ray department in Bristol (UK). The authors studied modelled the workflow describing human resources, equipment, and arrival and waiting times, types of examinations and overall time that patients spent in the department. Their simulations evaluated workload and resources used in order to predict probable improvements achieved by trying different alternatives. In 1981, O'Kane (O'Kane 1981) provided another simulation model for an X-Ray department, introducing some new factors in the modelling such as staff breaks. The model distinguished the time of examination and the time in which the rooms or radiographers would be available for the next patient. Also taken into account was that an examination can be finished but the room might need some work before other patients can use it. In addition, the model considered the radiographers duties regarding dealing with records and checking images. Lev et

al. (Lev et al. 1976) developed a similar workflow model for scheduling process of patients. All these authors agreed that the improvements in radiology should be directed towards the optimal design of the management system and not to reducing the staff or other facilities. As mentioned in the previous section, mathematical modelling and simulation combined with measurements taken from observations allows accurate predictions when testing possible improvements. Models can contain complex logical and stochastic behaviour of the system, or interventional rooms in this context, that could be incomplete or missed when just considering the information collected through observations.

Although most of these cases modelled the system at a department level, Kapamara et al (2007) introduced elements regarding to the internal decisions for the patient treatment into the simulation model. However, this study is still incomplete as some of the parts of the treatments are judged in overall times and do not include details in the actions and decision taken by the clinicians during some parts of the procedures.

Similarly, an earlier work at the University of Applied Sciences Gelsenkirchen (Gelsenkirchen, Germany) included preliminary workflow modelling and simulation techniques in a multi-modal imaging facility comprising CT and MRI rooms in a nonclinical OT (Andreas Melzer 2003). The main objective was to test the technical feasibility of a cost-effective imaging infrastructure by diagnostic and therapeutic workflow (blue arrows and red arrows respectively in Figure 12 (a)). Figure 12 (b) illustrate a preliminary attempt of the research group using simulation for the purpose of workflow analysis at a radiology department.

The problem of improving scheduling practices, waiting times, and resource utilization has been dealt with by more refined modeling techniques for workflow simulation such as the Markov decision processes and DES (Johnston et al. 2009; Kolisch and Sickinger 2008). Other authors have focussed their work on the integration of information system in radiology departments and hospitals, including the picture archiving and communication systems (PACS) (Crowe and Sim 2009; Wendler and Loef 2001). Lindsköld et al. describe how this technique has the potential to support proper planning and use of personnel, space, and equipment resources. This study reveals however that there is a lack of studies that fully explore

simulation as a tool to facilitate changes and integration of new standards, such as DICOM (Digital Imaging and Communication in Medicine) or HL7 (Health Level Seven), and also different imaging technologies (MRI, multi-slice CT, PET/CT, ultrasound) (Lindsköld et al. 2008).

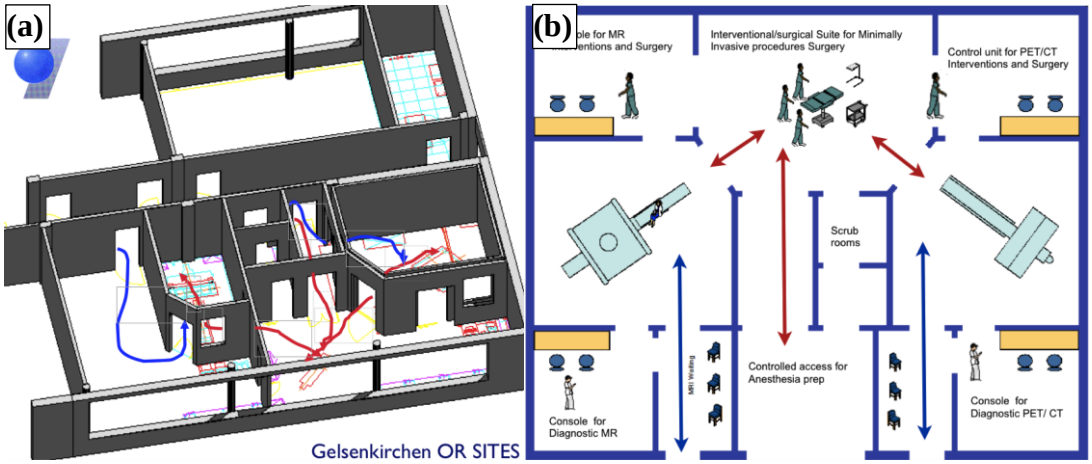


Figure 12. (a) Schematic view of the Gelsenkirchen nonclinical OT site with the differentiated diagnostic and therapeutic workflows; (b) model to simulate workflow of combination MR/CT guided surgery and interventions with diagnostic procedures. In this figure, blue arrows indicate diagnostic workflow and red arrows indicate treatment workflow.

In addition to the academic environment, global companies are working on products to facilitate and improve workflow in image-guided environments. For example, Siemens (Erlangen, Germany) has developed Dot™ (Day optimizing throughput), a software that provide an easy-to-use interface to improve examinations workflow for MRI diagnosis (Siemens 2012a). The company has also designed Symbia.net™ that intents to give a solution for acquisition, processing and integration of SPECT and CT images to give clinicians access to all patient data for a better diagnostic (Siemens 2012b). In addition, Siemens has created a software platform, Technomatix Plant Design and Optimisation, for plant design and optimisation through discrete event simulation that, although it appears to be designed for manufacturing industry, has been used successfully for modelling a radiology department (Johnston et al. 2009; Siemens 2012c). Other companies like Philips (Eindhoven, Netherlands), GE Healthcare (Milwaukee, IL, USA) or Dräger (Lübeck, Germany) provide support for room layouts and ergonomics of OTs and integration of imaging modalities to their customers to help hospital managers and

clinicians to find the right solution for their needs (Dräger 2012; GE Healthcare 2012; Philips 2012).

2.5. Summary

This chapter presented an introduction of the imaging technologies that will be covered in this thesis and a literature review on workflow analysis. The review discussed first earlier work on workflow modelling and simulation in surgical environments and then focused on radiology. Previous studies on workflow for interventional radiology did not contemplate events and decisions taken within the procedures. Although approaches to this issue can be seen in the cases of laparoscopy or trauma surgery, interventional radiology procedures are considered as blocks with an overall duration when analysing the workflow in radiology departments.

Within IGP procedures, there is a higher variability on the use of devices than in other types of surgery and therefore they need a different approach when it comes to model, analyse and simulate their workflow. This thesis presents two approaches: simulation and physical modelling. The first part describes the methodological framework developed for the application of DES to IGP and four cases where the framework was applied. The second part presents a purpose-oriented physical modelling framework for workflow analysis and comparison of MRI and fluoroscopy guided procedures based on the case of a common iliac angioplasty.

Part I:

Simulation Approach

Chapter 3.

Simulation methodological framework

Contents of this chapter appeared in:

***Fernández-Gutiérrez F**, Barnett I, Taylor B, Houston G, Melzer A, (2013) "Framework for detailed workflow analysis and modelling for simulation of multi-modal image-guided interventions", Journal of Enterprise Information Management, Vol. 26 Iss: 1/2, pp.75 – 90*

3.1. Overview of the chapter

Following methods to study a system as described in the previous section (see Figure 7), this chapter uses two methodological frameworks: the first to study the system through DES models and the second to study IGPs through workflow experiments in a simulated physical environment based on a case of study.

3.2. Simulation framework

3.2.1. Introduction

This section includes the methods used to gather and analyse the necessary data to implement the DES models. For the implementation of the DES models, it was necessary in first place to select the appropriate simulation software package. This assessment is explained below. In addition, the section describes the methodology used to model conceptually the IGP workflows and the principal details about the implementation of the DES models, as well as the mechanisms used for their validation and the output analysis.

3.2.2. Simulation software assessment

3.2.2.1. Introduction

In 2000, a survey about simulation software showed that, in the UK, simulation was applied to health systems in more than 27 per cent of the academic studies (Hlupic 2000a). Companies are increasing their use of simulation for workflow management in health care, leading to the emergence of dedicated software packages. The large variety of tools now available can make it more difficult to

decide which software is the most suitable to meet the needs of the system. Selecting a non-appropriate software package can affect negatively the workflow simulation, bringing extra costs and it may not meet the requirements of the model implementation. For this reason, it was essential to undertake an assessment of the simulation software packages existing in the market, focusing on those dedicated for DES, since it was the technique used for this research.

The next two sections describe the methodology used, together with the list of requirements requested, and the list of simulation packages with the result of the evaluation process. Finally, since it is an important part of this research, the selected simulation package is presented.

3.2.2.2. Methodology for simulation software evaluation

The evaluation of DES software packages was based on a general method for software described by Jadhav and Sonar (2009):

1) Determine the need for acquiring the software and preliminary research of availability of suitable software in the market;
2) Shortlisting of candidates;
3) Eliminate candidates that do not have required features;
4) Evaluate remaining packages (for example, through the ranking and testing of trial versions);
5) Negotiate a contract with specifications such as price, licenses, functional specification and maintenance;
6) Acquire the software.

This method can be applied to any type of software but it does not establish the features we should require for the simulation software. In the survey conducted by Hlupic in 2000, the authors studied the main limitations and the main features requested by the users. The users gave more importance to the flexibility and compatibility with other types of software packages, along with being easy to learn and with good visual facilities. In addition, Hlupic presented in 1999 an evaluation framework of simulation software for general purpose, giving a list of features divided into several groups of criterion (Hlupic et al, 1999). More recently, Swain

and MacGinley (2009) analysed a number of simulation software packages with an updated list of features, including some of those indicated by Hlupic (2000b).

Apart from these general characteristics, it was essential to add specific features and requirements to accomplish the objectives of this research project. Table 2 presents the detailed list of criteria analysed grouped by type. Each feature was given a score from 1 to 5, where 1 meant *"not important"* and 5 meant *"very important"* criterion. In addition, a classification in the context of the derived criteria for the simulation software evaluation was provided. This classification indicated whether a particular feature was provided with the package or whether the software required a particular feature in a high, medium or low degree.

Criteria type	Criteria	Score	Classification
Software features	System requirements: operating system, RAM, space on disk	2	High Medium Low
	Run time debug	4	Provided Not provided
	Output analysis (information can be collected after the simulation)	5	Possible Not possible
	Real time viewing	5	Possible Not possible
	Support/training/Maintenance/documentation	5	Provided Not provided
	Price	4	High Medium Low
	Error reporting	4	Provided Not provided
	Graphical model implementation	4	Possible Not possible
	Model building using programming/access to programmed modules/	5	Possible Not possible
	CAD drawing import/adequate library provided	5	Provided Not provided
	Code reuse	4	Possible Not possible
	Animation	3	Possible Not possible
	Experimental design	3	Possible Not possible
	Statistical facilities	2	Provided Not provided
	Model packaging	3	Possible Not possible
	Micro-ergonomics design	4	Possible Not possible
	Interface user friendly	3	Easy/Average/ Difficult
	Input data import	4	Possible

Criteria type	Criteria	Score	Classification
			Not possible
	Model optimisation	3	Possible Not possible
Analysis functionality included	Partial and total times	5	Provided Not provided
	Costs: total, operation, resources	3	Possible Not possible
	Resources under-utilised time	4	Provided Not provided
	Entity Activity: Number of entities that exit the system after simulation time/Number of entities remaining in the system after simulation time/Average time in the system for an entity/Average time that an entity spent travelling between locations/Average time waiting for a resource or other entity/Average time in operation/Average time waiting for a location to have available capacity/Number of entities that failed to arrive at a specific location due to insufficient capacity	5	Provided Not provided
	Variables changed during simulation: total of times the value was changed/average time per change/current value/average, max and min value the variable had	5	Provided Not provided
	Location analysis: percentage of occupation by an entity/idle time/number of entities processed/number of entities remaining after simulation time/average time of travelling for a resource between locations	5	Provided Not provided
	Scheduling: entities/locations/resources	5	Provided Not provided
	Micro-ergonomics: postural and biomechanical analysis of single and grouped activities/ anthropomorphic constraints implementation/device handling analysis	4	Possible Not possible

Table 2. List of features and requirements analysed grouped by criteria and type. Each criterion was given a score from 1 to 5, where 5 meant "very important", and classification for the software evaluation in the context of the derived criteria.

3.2.2.3. Results of simulation software evaluation

Following the steps indicated in the previous section, a initial list of simulation software packaged was prepared using two main sources, Internet and publications, using terms as *simulation software package*, *discrete event simulation software*, *simulation software healthcare, workflow simulation software* or *simulation software operating room*. In the second phase, a short list of 13 simulation software packages was selected:

- Analytica by Lumina Decision System Inc

- AnyLogic by XJ Technologies
- Arena Simulation Software by Rockwell Automation
- Delmia by Dassault Systemes
- Emergency Department Simulator by ProModel
- ExtendSim Suite by Imagine That Inc
- Flexsim HC by Flexsim Software Products Inc
- MedModel Optimization Suite by ProModel
- Micro Saint Sharp by Alion Science and Technology, MA & D Operation
- Simcad Pro-Patented Dynamic Process Simulator by CreateASoft Inc
- Simio by Simio LLC
- SIMUL8 Professional by SIMUL8
- Witness by Lanner Group Limited

The third phase of the evaluation was performed using the information facilitated on the respective vendors' websites. Appendix A encloses the contact information for all vendors. In cases where the website did not facilitate all the information indicated in Table 2, for instance in the case of Flexsim HC or Delmia Quest, the vendors were contacted to complete the assessment through a questionnaire. Table 3 shows a summary of this evaluation with some of the key differences among the software packages. At this point, only the software features were taken into account as it was agreed that the functionality criteria would be more appropriately evaluated testing the demo versions in the next phase of the evaluation. Appendix B presents the rest of features evaluated. This assessment was completed on December 2010; therefore the current software versions might be different.

After this first evaluation and with a look to the high-scored software features from Table 2, five of the simulation software packages were selected: Delmia, ExtendSim, Flexsim HC, Medmodel and Micro Saint Sharp. These packages were then tested through demo versions or online demonstrations done by the vendors in the cases where the demo version was not possible to obtain. Through the demo versions, several aspects were evaluated such as user interface, flexibility on changing the scenarios, facility to import and export data, price or the robustness. In addition, it was taken into account the capability of the software to provide the functionality indicated in Table 2.

Software package	Real time viewing	Model building using programming	CAD import/ library	Animation	Experimental design/ Model optimisation	Micro-ergonomics design
Analytica	Not possible	Possible	Not provided	Not possible	Not possible	Not possible
AnyLogic	Possible	Possible	Provided	Possible[b]	Possible	Not possible
Arena	Possible	Possible	Provided	Possible[b]	Possible	Not possible
Delmia	Possible	Possible	Provided	Possible	Possible	Possible
Emergency Department Simulator	Possible	Not possible	Not provided	Not possible	Possible	Not possible
ExtendSim	Possible	Possible	Provided	Possible	Possible	Not possible
Flexim HC	Possible	Possible	Provided	Possible	Possible	Not possible
MedModel	Possible	Possible	Provided	Possible[b]	Possible	Not possible
Micro Saint Sharp	Possible	Possible	Provided	Possible	Possible	Possible[c]
Simcad	Possible	Possible	Provided	Possible	Possible	Not possible
Simio	Possible	Possible[a]	Provided	Possible	Possible	Not possible
SIMUL8	Possible	Possible	Provided	Possible[b]	Possible	Not possible
Witness	Possible	Possible	Provided	Possible[b]	Possible	Not possible

Table 3: Simulation software packages evaluation summary

After the experience with the different demo versions, Delmia resulted as the most suitable simulation software package to fulfil the objectives of the project. In order to understand better the implementation process of the models, the main features and parts of the software package are described in the next section.

3.2.2.4. Delmia: main features and 3D library

The two packages used with the academic version of Delmia (Dassault Systèmes S.A., Vélizy-Villacoublay, France) were Quest for workflow modelling and simulation and human ergonomics simulator. Quest offers a 3D environment for process flow simulation, analysis and optimisation. The human ergonomics package allows having life-like human models to simulate tasks and analyse postures for a better understanding of the activities that are being performed. Although Delmia is a general purpose software oriented mainly to the manufacturing industry, numerous examples can be found where Delmia has been used for workflow analysis in health care systems such as the trauma operating unit of the Helsinki University Central Hospital or the trauma orthopaedic department at the Skaraborg Hospital in Sweden (Marjamaa et al, 2008; Moris 2010).

Delmia Quest

The Quest interface has three different parts (see Figure 13):

- A graphical user interface (GUI) where the models are visually programmed.
- A control area with all the menus.
- A view area that has all the buttons to navigate through the GUI.

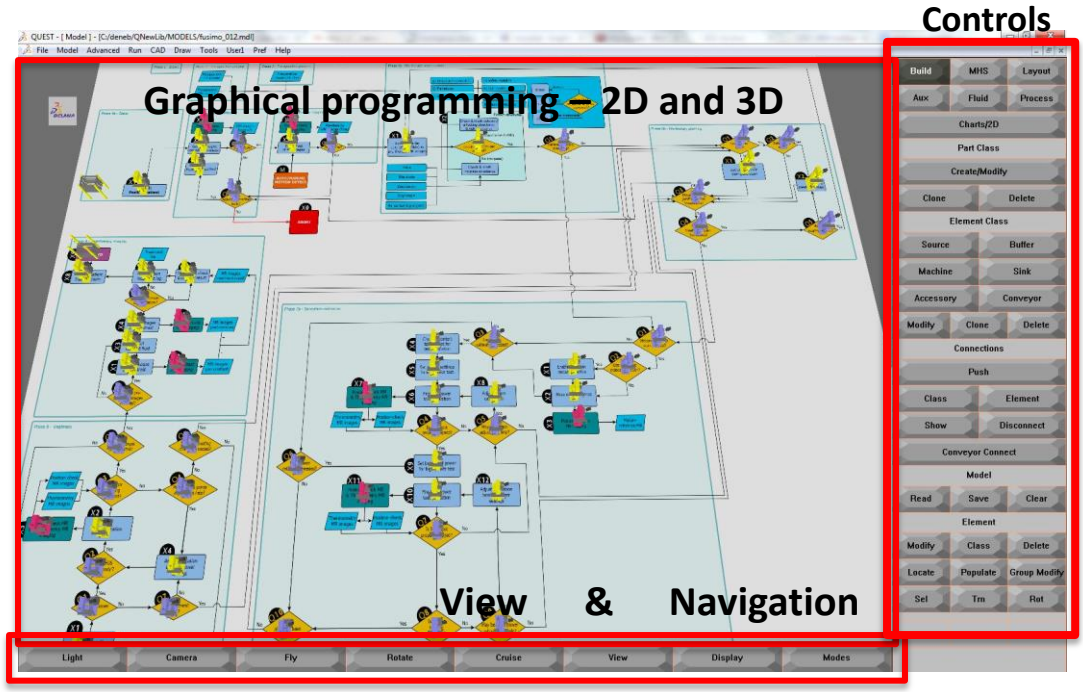


Figure 13. Delmia Quest interface. Labels are provided for graphical programming interface and controls, view and navigation menus.

With regards of the DES models implementation, Quest is divided into three main sections or worlds:

- *Model world*. This part contains the menus for the graphical implementation of the models.
- *Simulation world*. This unit comprises the controls to run the simulations and to compile the logics that are programmed in separate files.
- *CAD world*. This section has the necessary menus and features to read and alter 3D objects for the models libraries.

The first thing to notice when opening the Quest software is the terms used in the menus and control buttons. Since Quest was oriented primarily to the manufacturing industry, we find terms such as machines, parts, labours or buffers. Figure 14 shows an example of these control buttons. Once the principles of Quest programming are understood, this terminology can be translated into clinical environment without major problems. The main elements that we need to take into account when modelling are translated as follows:

- *Parts*. A part is anything that enters the system and it is processed before it is dismissed. Here, the *patient* is then our part. The patient is who enters our model (e.g. intervention room or radiology department), receives a service (e.g. intervention or diagnosis) and is dismissed.
- *Machines*. Any element that processes a *part*. This could be represented by the operating table or the MRI scanner where the patient is placed for diagnosis or as part of the intervention.
- *Labours*. These elements are the human resources needed to perform a service inside our system: interventional radiologists, nurses, surgeons or radiographers.
- *Source/Sink*. These are simply elements that as indicated in the introduction (see section 2.3.4) help when modelling the logics: how the parts/patients enter and leave the system.
- *Buffer*. In general terms, a buffer is placed whenever there is a potential waiting area for parts before they are processed by an element. For example, in a clinical environment it can be a waiting room before the patients go to the scanner room as we might have patients arriving at a higher rate than they are served by the MRI scanner.
- *Process*. Quest defines process as "what happens to a part as it moves through an element". Any activity or decision that requires certain time or logic would be programmed here as a process. If the process is simple it can be defined simply through the GUI, in the case where the logic is more complex, *"user functions"* would be needed. These functions are programmed in separate files in a proprietary Simulation Control Language (SCL). These user functions are linked to the corresponding element using the control menus in the GUI.

- *Accessory*. These are elements created to enhance the graphical representation of the system, e.g. cupboards, desks, surgical lights, etc. Some of these accessories aid also the model implementation. For instance, adding walls and doors as accessories in the model would facilitate the reconstruction of paths for clinicians and patients amongst the rooms.

Further information about Quest can be found at Quest manual distributed with the software (2006).

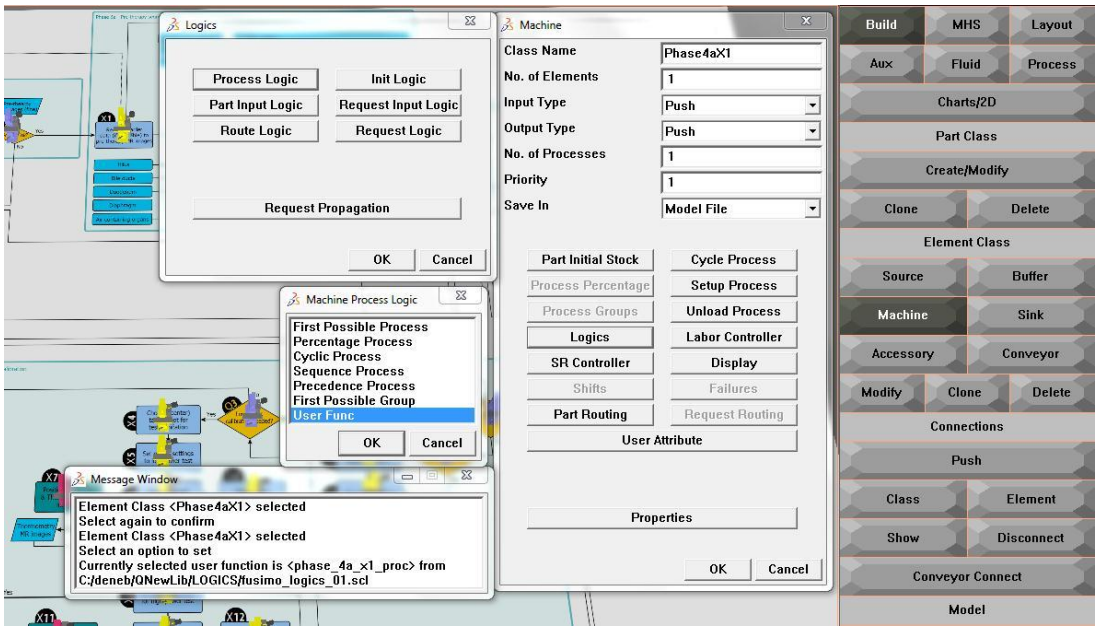


Figure 14. Detail of Delmia Quest interface and menu samples.

Due to the nature of Quest, the libraries available for the implementation of DES models are oriented to industrial environments. Therefore, it was necessary to create an additional library with the elements needed to create virtual imaging operating rooms.

Google 3D Warehouse (http://sketchup.google.com/3dwarehouse/, accessed 03/03/2014) offers 3D models under a royalty-free license unless otherwise stated in the individual models. With these premises, a library was created with a list of objects including different types of operating tables, surgical lights and screens, X-Ray equipment and MRI scanners. More than 50 objects were incorporated to the Quest standard library. In order to be able to incorporate these models into Quest, it was necessary to convert their format. The 3D warehouse objects can be open and

modified using Sketchup (http://www.sketchup.com/intl/en/ index.html, accessed 03/03/2014). Sketchup v7 and a free plugin – under General Public License (GPL) – were used to convert the 3D objects into STL (Stereo Lithography) format, which can be open in Quest. Figure 15 shows an example of a Sketchup model – (a) – of an MRI scanner with the corresponding STL version – (b) – of the same model in Delmia Quest CAD world. When converting to STL, the models lose their colour and some other minor features but keep their dimensions and external aspect. The CAD world in QUEST allows adding colours and minor modifications to the 3D objects but everything is subjected to some limitations on the new STL format.

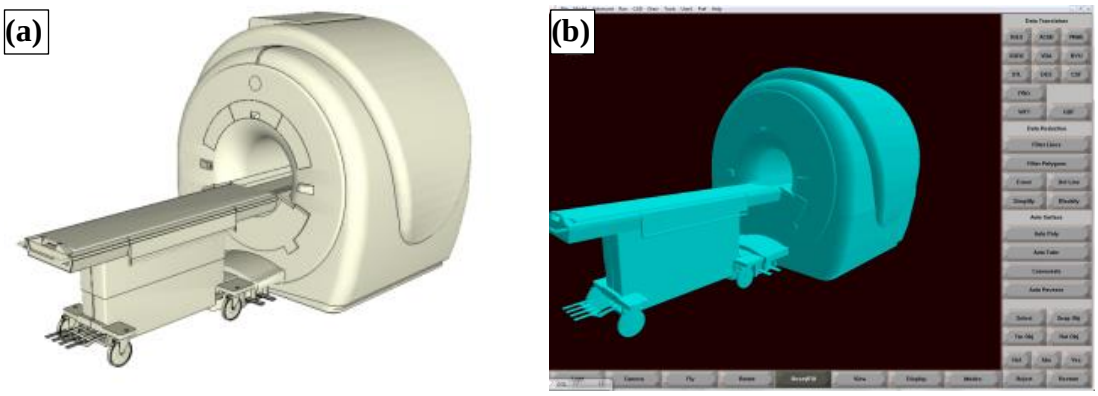


Figure 15. (a) 3D model of an MRI scanner with table in Sketchup v7, (b) 3D model converted into STL format and incorporated into Delmia Quest through the CAD world.

Another important part of the virtual environment was the design of the layouts. As mentioned above, adding walls and doors to the 3D environment would aid when describing paths for clinicians and patients in the model. Here, the rooms were designed to scale using Sweet Home 3D (http://www.sweethome3d.com/, eTeks, Paris, France), an interior design application under GPL. Sweet Home 3D can read a layout plan through and image. Then, the user can draw walls, doors and windows using this plan. Finally a 3D object, readable by Sketchup, is created with the real dimensions to scale. Figure 16 illustrates an example using Sweet Home 3D, the layout plan of the radiology department at Homburg – Saarland University Hospital (Homburg, Germany). The 3D object can be added to the Quest library as explained previously.

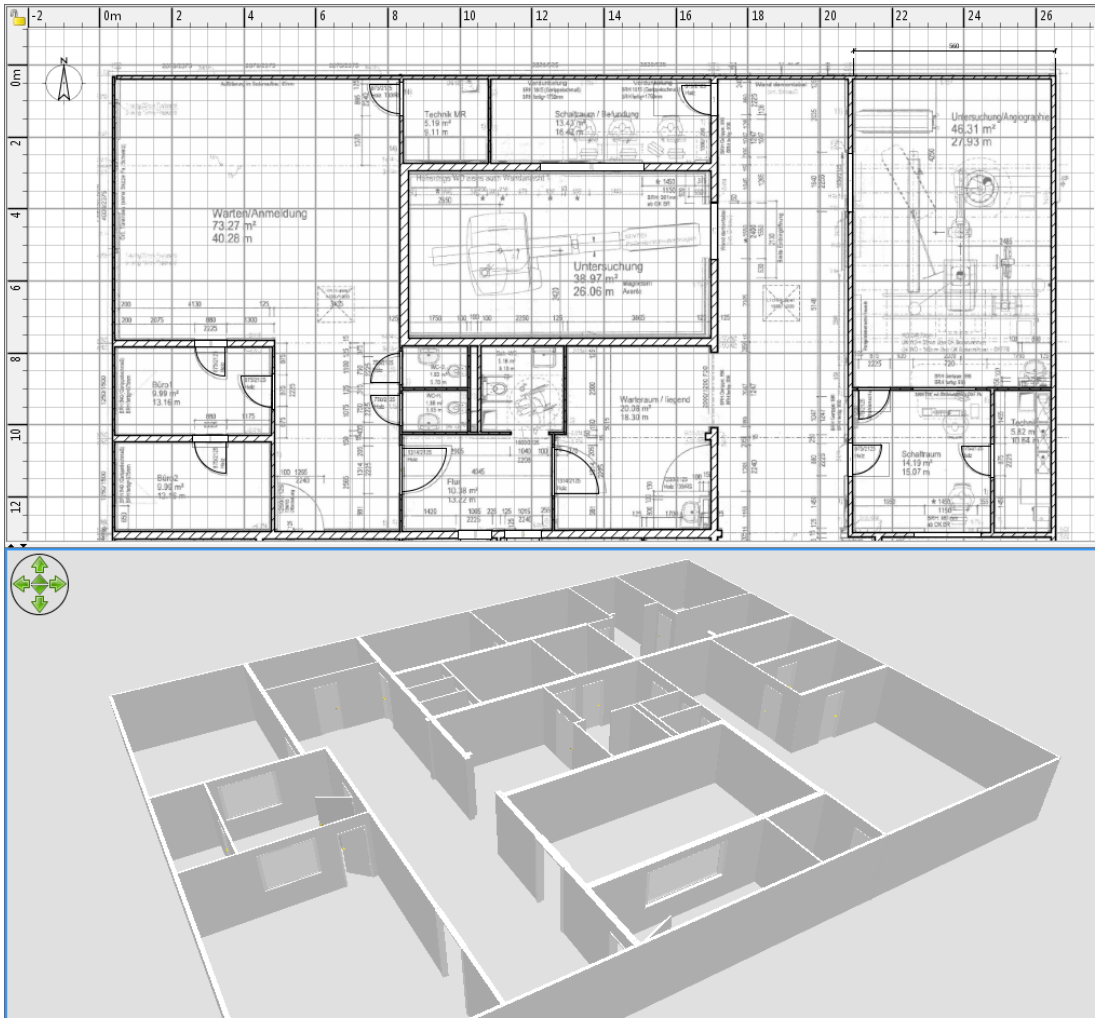


Figure 16. 2D and 3D view of the radiology department at Homburg Saarland Hospital (Homburg, Germany) created to scale using Sweet Home 3D (eTeks, Paris, France).

Delmia V5R20 for Human Ergonomics Design and Analysis

Delmia for Human Ergonomics is a modelling tool used to create, validate and simulate digital human manikins or models (DHM) in a virtual environment to analyse human interaction and worker process. Delmia Human uses NIOSH (National Institute for Occupational Safety and Health) 91 equations (Waters et al. 1993) and RULA (Rapid Upper Limb Assessment) for posture and activity analysis (McAtamney and Nigel Corlett 1993).

Delmia Human allows importing CAD (Computer aided design) elements from multiple formats. Figure 17 shows the GUI interface of Delmia Human. The control menus for the interface and the RULA analysis are highlighted. The vision window

gives an indication of what the manikin is *"seeing"* during an activity. RULA for ergonomics posture analysis is detailed in a subsequent section.

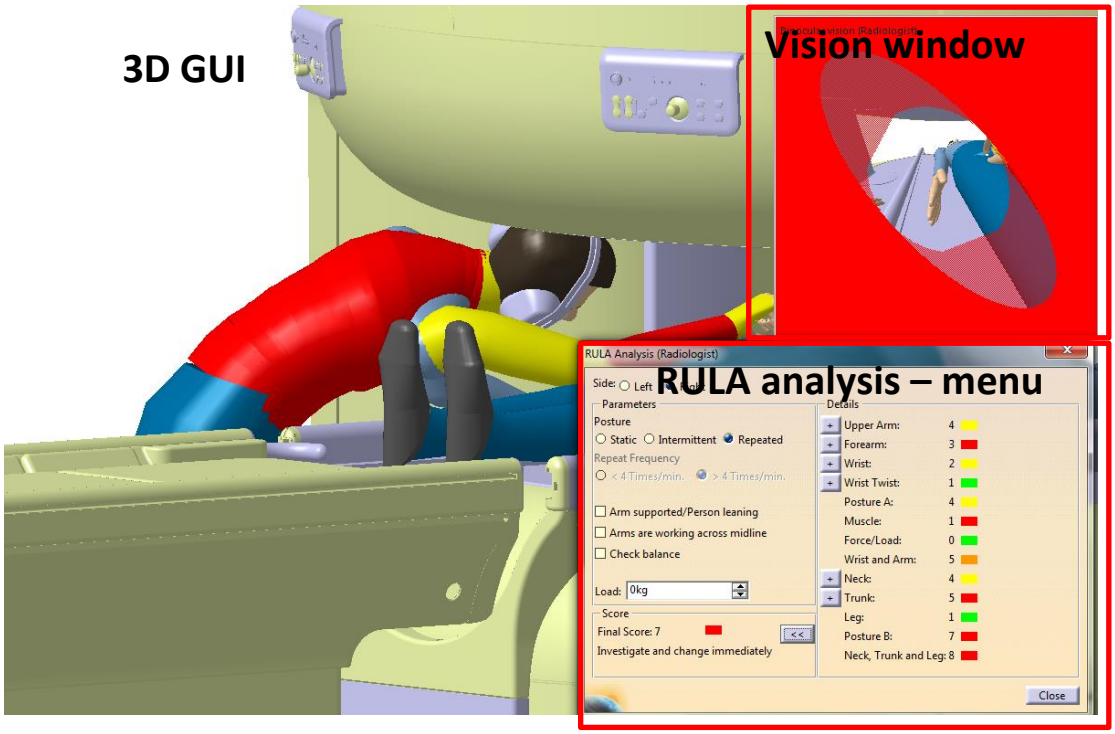


Figure 17. Delmia V5R20 for Human Ergonomics Design and Analysis graphical user interface (GUI). To illustrate the RULA analysis menu and result windows, the GUI shows a 50th percentile human-like manikin in standard position operating inside an open-bore MRI scanner model (Panorama 1T MRI, Philips, Eindhoven, The Netherlands).

3.2.3. Data gathering and analysis for DES simulation

3.2.3.1. Data collection

Padoy et al. (2010) showed how an extensive analysis of minimally invasive surgery could help in order to meet future requirements in terms of ergonomics and operability. The authors based their study on laparoscopic surgery using statistical modelling and monitoring the use of devices during interventions. However, this approach would only in part be suitable for image-guided interventions due to the greater variety of different instruments involved. Cannulae, energetic probes, catheters, guide wires, introducers, vascular implants, monitoring devices, etc. feature multiple types, sizes and shapes. The devices are selected according to the kind of procedure, indication, the patient's personal characteristics, and the type of imaging that is needed. In addition, although the use of some of these devices is

planned ahead of the intervention, it was observed that, in multiple cases, extra devices not projected were utilised. In some cases, these other devices were stored in adjacent rooms. Some other times, nurses prepared a range of devices since the true size needed was still uncertain from the pre-images. Then, some of these devices remained unused after the intervention. These reasons make recording the use of devices very complicated. This hazardous situation makes it difficult and time consuming to track projected devices would therefore result in incomplete datasets.

Therefore and due to the nature of this study, the data collection was done manually, attending the interventions in most of the cases, as the detailed data required was not usually available in databases. Several centres collaborated in the data collection:

- Clinical radiology and cardiology departments at Ninewells Hospital (Dundee, UK)
- Radiology Department at Homburg – Saarland University Hospital (Homburg, Germany)

Data set	Description
Patient Data	Gender
	Age
	Height
	Weight
Procedure details	Name
	Previous similar interventions
	Images used prior the intervention
Staff	Role
	Number
	Sterilized
	Experience
Supplies	Type
	Model
	Manufacturer
Event log	Time
	Summary
Contrast agent	Contrast details
	Total amount
	Comments
X-Ray dose	Emitted dosage
	Absorbed dosage
	Dosage period
Complication	Time

Data set	Description
	Summary of complication
	Other comments

Table 4. Data collection template

Table 4 presents the type of data collected from the institutions mentioned. The data set was mutually agreed after attending several interventions and with the collaboration of clinical staff from different radiological suites. Templates for data collection were designed based on the records collected in the cardiology department in Ninewells Hospital (Dundee, UK). The cardiology department maintains a proprietary database and a dedicated technician stores information such as indicated in Table 4 during interventions. In this case, data could be collected from their database after printing and anonymising the patient sensitive information. In the rest of cases, data was collected manually.

Figure 18. Screenshots of MIDAS (Medical Interventional Data Analysis System) website: (a) shows a partial view of a completed record and (b) the analysis web page with a graph.

The records collected were transferred into a database using a web application for the gathering. The web application, called MIDAS (Medical Interventional Data Analysis System) is in its second major revision (http://midas.heroku.com/, accessed 03/03/2014). Although the original idea of designing a web application for the data gathering is part of this thesis, the implementation of this website was carried out in

first instance under a master project in Applied Computing at University of Dundee. Further description can be found in Appendix C.

3.2.3.2. Data input analysis for DES

Once the data is gathered, probability and statistics analyses are needed before implementing the DES model. A crucial part of that analysis is to choose the input probability distributions for the models. The use of the mean or inappropriate distributions can lead to error in the output and to bad decisions when testing for alternative protocols. These distributions are used to generate random samples during the simulations of the time-based parts of a procedure such as task durations or patient arrivals.

Task or arrival times behave as random variables, which can be described by their probability distribution. EasyFit (http://www.mathwave.com/, Dnepropetrovsk, Ukraine), distribution fitting software, was used to analyse statistically the times collected per case of study. The analysis consisted on a description of the main features of the samples collected (mean, standard deviation, maximum and minimum value, among other parameters) and a probability distribution fitting process. In order to calculate the fitted distributions, it was assumed that the distributions have a finite lower bound fixed to 0 as all time-based records collected are positive. To find the best-fitted distribution, two criteria were used:

1. The no rejection of the null hypothesis (the data follow a specific distribution) in the Anderson-Darling Goodness-Of-Fit (GOF) test (level of the test $\alpha = 0.05$). This test is designed to detect discrepancies in the tails of the dataset and is more powerful in this sense that other GOF tests (Stephens 1974). The test implemented in EasyFit uses the same critical values for all distributions, using the approximation formula:

$$A^2 = -n - \frac{1}{n}\sum_{i=1}^{n}(2i-1)\cdot\left[lnF(X_i) + ln\left(1 - F(X_{n-i+1})\right)\right]$$

(Eq. 3-1)

Where X is an IID (Independent and identically distributed) random variable, F is the cumulative distribution function and n is the sample size.

If the test statistic, A^2, is greater than a critical value given by the level of the test, then the hypothesis is rejected.

2. In case of rejection of the null hypothesis, the data is examined in order to characterise the records with the most appropriate statistical distribution. In this case, descriptive statistics such as mean, variance, median and skewness are taken into account. In addition, (probability – probability) P-P and (quantile – quantile) Q-Q plots are considered[2] to select the fitted distribution. In case of several statistical distributions resulted appropriate to represent the data, the selection is based on experience based literature (Law 2007).

3.2.4. Conceptual modelling

In the study by Aguilar-Savén (2004), the author states that to implement the right model, it is essential to understand the purpose of the analysis and to know the tools and techniques for process modelling. Conceptual modelling prior to implementation of the workflow model facilitates that understanding and re-engineering of the processes. The level of granularity chosen is also important for the modelling. Studying actors, tasks, decision points as well as static or dynamic aspects of the systems may be needed (Jannin and Morandi 2007). However, choosing the right technique is a complex task due to the large range of approaches. Flow charts, data flow diagrams, role activity diagrams (RAD), Petri nets (PNs), Unified Modelling Language (UML) or Soft Systems Methodology (SSM) are just some of the most common used.

The level of detail required for the modelling of workflows of IGP may include the possibility to indicate roles and interactions between them, simplicity, and the capability to show decision points and sub-activities. Consequently, a combination of flow diagrams and RAD was selected among the techniques to model the process flows and the interactions among clinicians in the different phases of the procedures.

In Patel (2000), the author demonstrated how RADs can be applied to activities of health care organisations such as the National Health System (NHS, UK),

[2] The (probability-probability) P-P plots are graphs where the empirical cumulative distribution function (CDF) is plotted against the theoretical CDF. The (quantile-quantile) Q-Q plots are graph with the observed data values are plotted against the theoretical (fitted) distribution quantiles.

contributing to a better understanding of the processes and determination of information requirements. This method takes into account the roles and interactions happening during the process, in contrast to PNs or flow charts. In addition and in contrast to UML, RAD gives a view of the whole process in a unique diagram and it has a well-defined and documented notation, unlike SSM (SPRINT 2009).

Other studies on workflow of radiology departments used flow diagrams or PNs for the conceptual modelling (Johnston et al. 2009; Zhang et al. 2009). However, they did not represent staff roles or detailed events during interventions, which is essential to achieve the objectives of this project. A combination of both types of diagrams to model image-guided workflow results in a better-balanced solution for understanding the process at a glance and at the same time provides a flexible tool to facilitate the re-engineering process of the workflow. Figure **19** shows the legends and graphic symbols that will be used in the flow diagrams and role activity diagrams designs for the conceptual modelling.

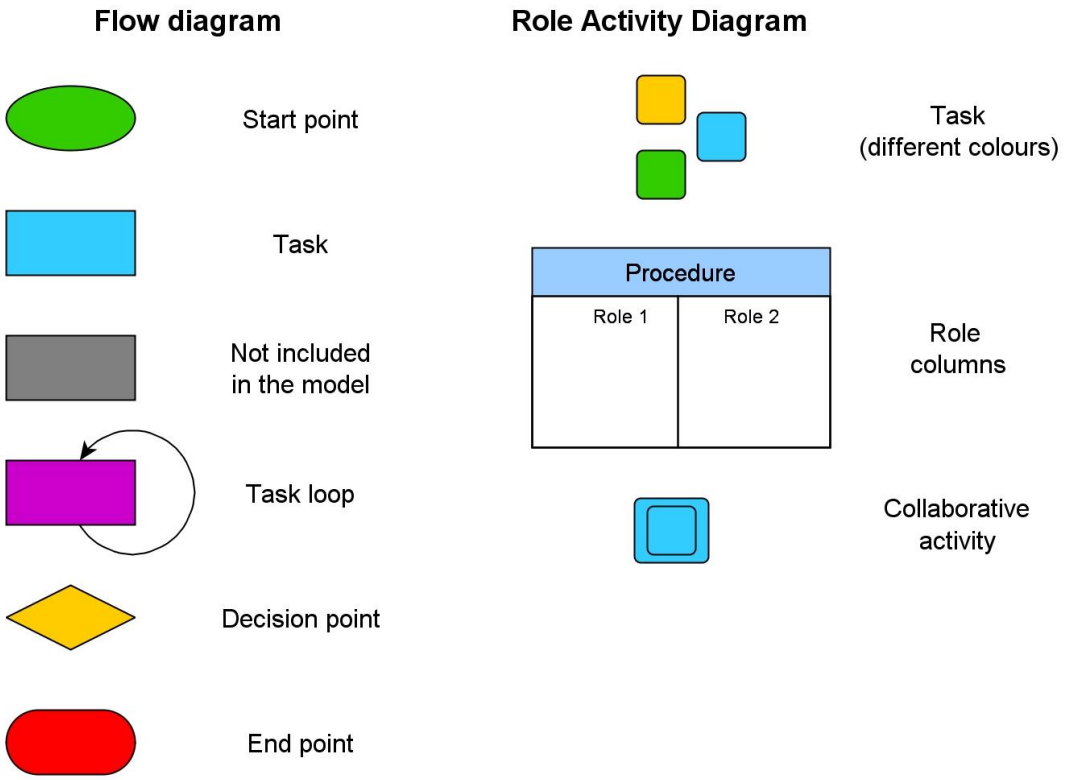


Figure 19**. Legend for symbols and graphic styles used on the flow diagrams and Role Activity Diagrams (RAD) of the conceptual models.**

3.2.5. Models implementation

Implementing a simulation model that accurately represents the real system is one of the most challenging problems when analysing a system. One of the factors that need to be considered is the level of detail needed, which would be given by the conceptual model previously designed.

Another factor is the quality of data collected to describe the model. As it was mentioned in *Section 3.2.3*, it is essential to select the appropriate statistical distribution for the time-based actions of the system. However, this is also subjected to the amount of data available. Unless historical data is available, the collection of data can be very time consuming depending on the level of detail needed. Simulation, by generating random samples, allows the use of additional techniques to deal with the absence of data. One of these approaches is the use of the triangular distribution to model actions or task where there is no data or just a few records (Santibáñez et al. 2009; Liebsch 2003). In this case, experienced clinicians or so called subject-matter experts (SMEs) are asked about estimations for the minimum, maximum and most-likely (*mode*) times to perform a particular task (Law 2007; Alexopoulos and Goldsman 2010). These values, *a*, *b* and *m* respectively, are the parameters describing the triangular distribution used as input for the simulation model in the absent of sufficient data. Once the triangular distribution is described, it can be used to generate random samples for the times to perform the task from which we did not have records. An example of a triangular distribution function shape can be seen in Figure 20. Although, the use of triangular distributions is still a subjective method to deal with absence of data, it has been successfully used to deal with variability in health systems such as emergency departments (Ahmed and Alkhamis 2009)or hospital wards (Worthington et al. 2010), when data was not available for certain processes.

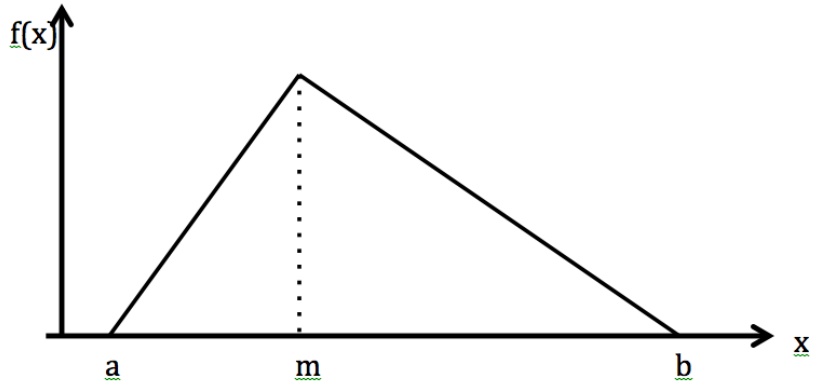


Figure 20. Triangular distribution where a, b and m are the minimum, maximum and mode values.

In addition, modelling correctly the decision points plays an important role in the implementation process. The decisions will be specified by probabilities of taking one path or another in the model logic. Calculating these probabilities is then critical and depends also in the quality of the collected data. As well as for the time-based information, the SMEs are asked when little or no data is available. Furthermore, these probabilities may not remain static during the simulations, being necessary to model dependencies on previous events. The way these dependencies are modelled will be subjected to each case.

Besides these factors, the objectives of the simulating study will affect how the model is built. Therefore, the description of the implementation process will be given for each singular case in the next chapters.

3.2.6. Validation and verification

Once implemented, the models need to be verified and validated following the definitions given in *Section 2.3.2*. The verification and validation processes were done following the methodology suggested by Law (2007), Nakayama (2006) and Sargent (2011), involving several tests done over the conceptual modelling, the computer programming and implementation phase and the operational validation.

For the conceptual model validation, constant communication and reports were exchanged among the different partners involved. The flow diagrams were re-designed several times during this phase. Trace methods and animations, embedded

in Delmia Quest, were used during the programming phase in order to debug the logic implemented.

The operational behaviour was validated following several steps: animation, expert validation, event validity and variability analysis. For the variability analysis, the simulating models were compared with the real system following the method for the Behrens-Fisher problem (Scheffé 1970), for an unknown ratio of variance, using the Welch confidence interval (CI):

$$\bar{X}_1(n_1) - \bar{X}_2(n_2) \pm t_{f,1-\alpha/2}\sqrt{\frac{S_1^2(n_1)}{n_1} + \frac{S_2^2(n_2)}{n_2}}$$

(Eq. 3-2)

Where $\bar{X}_1(n_1)$, $S_1^2(n_1)$ and $\bar{X}_2(n_2)$, $S_2^2(n_2)$ are the means and variances of the two systems (real world and model) with n_1 and n_2 samples, respectively; and $t_{f,1-\alpha/2}$ is the Student-t for 100(1-α) CI and f – degrees of freedom, calculated by

$$f = \frac{\left[S_1^2(n_1)/n_1 + S_2^2(n_2)/n_2\right]^2}{[S_1^2(n_1)/n_1]^2/(n_1-1) + [S_2^2(n_2)/n_2]^2/(n_2-1)}$$

(Eq. 3-3)

In this study, we used a 90% confidence interval.

3.2.7. Simulation and output analysis

3.2.7.1. Output data analysis

A number of key performance indicators (KPIs) were defined per case of study and used to evaluate the outcome of the simulations. CIs for these KPIs were calculated using the same number of simulations (replications) necessary to validate the model (same number needed for the Welch CI).

To calculate these CI, let *X* be the measure for the duration of an event in seconds. Then, X_j is the mean of the observations of that measure for the *jth* replication. Given the conditions above for the simulations, $X_1, X_2, \ldots, X_n$ *(j=1, 2, …, n)* will be the IID

random variables with $E(X_j) \approx \mu$ and $\bar{X}(n)$, an approximately unbiased point estimator for μ. Then, the $100(1-\alpha)\%$ confidence interval for μ is given by:

$$\bar{X} \pm t_{(\alpha/2,n-1)}\sqrt{\frac{S^2}{n}}$$

(Eq. 3-4)

Where $\bar{X}$ is the global mean and S^2 is the sample variance,

$$\bar{X} = \sum_{j=1}^{n} \frac{X_j}{n}, S^2 = \sum_{j=1}^{n} \frac{(X_i - \bar{X})^2}{n-1}$$

(Eq. 3-5)

And $t_{(\alpha,n-1)}$ is the number such that for the *t-Student* distribution with $n-1$ degrees of freedom, $P(t_{n-1} \geq t_{(\alpha,n-1)}) = \alpha$.

Summaries of the output analysis are shown in the following chapter for each case.

3.2.7.2. Optimisation analysis

Ranking and selection (R&S) methods are commonly used in simulation-based optimisation analysis. These methods compare a number of alternatives and select the best of those scenarios based on previously defined KPIs. As a proof of concept, this thesis will present in a posterior chapter the use of an R&S method, together with the framework for analysis and modelling of IGPs.

There are many R&D methods for selection of the best alternative proposed in the literature. Bechhofer (1954) proposed one of the first ones for known common or equal variances for the different alternatives considered. Later on, Paulson (1964) described an R&S method for when the variances are unknown but they can be assumed to be common. Zinger and St. Pierre (1958) proposed a method for known but unequal variances. Dudewicz and Dalal (D&D) (1975) developed a R&S method that does not assume the variances are known. In addition, this method does not assume equal variances for the different alternatives. Assuming known or similar

variances might be unrealistic when simulating real systems. A comprehensive description of other R&S methods can be found in Kiekhaefer (2011).

The high-variability observed when modelling IGPs makes the D&D method appropriate to study these systems since variances are not known a priori and cannot be assumed to be equal. The D&D method involves "two-stage" sampling for each of the alternatives (systems) to be analysed. Firstly, $n_0 > 2$ replications per system have to be done. According to the literature, it is recommended to choose a starting number between 10 and 30. For this study, $n_0 = 20$ was chosen arbitrarily. For each system, means, $\bar{X}_i^{(1)}(n_0)$, and variances are calculated for each KPI that wants to be used to assess the system. Then N_i, number of samples, is calculated for the "second-stage" for the system i as follows

$$\boldsymbol{N_i = max\left\{n_0 + 1, \left\lceil \frac{h_1^2 S_i^2(n_0)}{(d^*)^2} \right\rceil \right\}}$$

(Eq. 3-6)

Where the symbol $\lceil x \rceil$ means the smallest integer that is greater than or equal than the real number x, $S_i^2(n_0)$ is the variance of the system i, $d^* > 0$ is the smaller actual difference between the means of the systems that we care about detecting and h_1 is a constant dependent on n_0, the number of alternatives being evaluated and the least probability that assures selecting the best system. This probability was established to 90%. The h_1 value for this study was obtained from the tables in (Dudewicz et al, 1975). Parameters are adjusted depending on the system and the case of study.

Next, $N_i - n_0$ more replications were calculated for each system, calculating the new sample means $\bar{X}_i^{(2)}(N_i - n_0)$. Then, weights are defined as

$$\boldsymbol{W_{i1} = \frac{n_0}{N_i}\left[1 + \sqrt{1 - \frac{N_i}{n_0}\left(1 - \frac{(N_i - n_0)(d^*)^2}{h_1^2 S_i^2(n_0)}\right)}\right]}$$

(Eq. 3-7)

And $W_{i2} = 1 - W_{i1}$. Then, the weighted sample means are calculated

$$\widetilde{\boldsymbol{X}}_{\boldsymbol{i}}(\boldsymbol{N}_{\boldsymbol{i}}) = \boldsymbol{W}_{\boldsymbol{i1}}\overline{\boldsymbol{X}}_{\boldsymbol{i}}^{(\boldsymbol{1})}(\boldsymbol{n}_{\boldsymbol{0}}) + \boldsymbol{W}_{\boldsymbol{i2}}\overline{\boldsymbol{X}}_{\boldsymbol{i}}^{(\boldsymbol{2})}(\boldsymbol{N}_{\boldsymbol{i}} - \boldsymbol{n}_{\boldsymbol{0}})$$

(Eq. 3-8)

Finally, the alternative with smallest $\tilde{X}_i(N_i)$ for each KPI is selected.

3.3. Summary

This chapter described the methodological framework proposed to apply DES to analyse and model IGPs workflow. In addition, Delmia Quest and Human Ergonomics software package is presented after comprehensive assessment of simulation platforms available in the market. The simulation framework consisted in detailed guidelines over five blocks need for analysing, modelling and simulating IGPs workflow: data collection and input analysis, conceptual modelling, model implementation, validation and verification, and simulation and output analysis. The following chapters present three cases of vascular IGPs where the simulation framework was applied. Chapter 6 shows how the methodology can be extended for its application to non-vascular procedures with a case based on MRgFUS interventions.

Chapter 4.
Results: Case study of percutaneous coronary interventions

4.1. Background of the case

Percutaneous coronary intervention (PCI) is a minimally invasive vascular procedure used to open obstructed coronary arteries to improve blood circulation of the heart muscle. It is usually implemented when coronary artery bypass surgery may be too dangerous for the patient and in more than half of the patients needing revascularisation (Grech 2003).

In 2007, the European Society of Cardiology published a report about PCIs across Europe based on data up to 2004. When comparing records from 2003, there was an increase of 11% for coronary angiographies while the number of PCIs increased 20%. In case of coronary stenting, the increment was even higher with 22% more procedures compared to 2003. However, the report also observed that the cardiac catheterisation facilities per million inhabitants in Europe remained unchanged (2.6) between 2003 and 2004 (Cook et al. 2007). This highlights the importance of improving the efficiency in the performance of PCIs in order to handle their predicted increasing demand.

A simulating study for PCIs was conducted in collaboration with the Cardiology Department at Ninewells Hospital (Dundee, UK). During this work, feedback was collected and discussed with the clinical team, especially with Prof Dr Graeme Houston (consultant interventional radiologist) and Dr Thomas Martin (consultant interventional cardiologist) at Ninewells Hospital. PCIs were selected to be studied because they are well-established procedures and they are broadly standardised. In first instance, an overview of PCIs is presented based on data collected at the cardiology department. Then, a deeper analysis was performed covering angioplasty and stenting PCIs – treatment PCIs. This analysis included times and probabilities associated to relevant events within treatment PCIs and resulted in the implementation of a DES model, which particularities are explained. This model was

then validated and the main results are discussed in the last section. This analysis is shown as a proof of concept to understand the performance of PCIs. The knowledge gained about the activities and decisions taken during the interventions can be used to improve the throughput of cardiology suites (also known as *cath labs*).

4.2. Overview analysis of the PCIs records

4.2.1. General information analysed

Anonymised data was extracted from the cath lab existing database. In total, 125 consecutive records (4 weeks) were collected, 83 corresponding to diagnostic procedures and 42 to treatment (angioplasty or stenting) PCIs. Out of all the treatment interventions, 14 were elected patients, 25 were follow-on patients and 3 were emergency patients. In average, a diagnostic procedure took 27:55 (01:34) and a treatment 59:10 (04:35) (times expressed in MEAN (SE) and min:sec). Figure 21 displays the differences between the total duration for diagnostic and treatment PCIs. The box plot shows how diagnostic PCIs, despite some singular cases represented by the outliers in the graph, have less intrinsic variability than the treatment procedures. The two far outliers for diagnostic PCIs correspond to a case where the procedure was not successful after several tries of the cardiologist to access the circumflex coronary artery; and a case where the X-Ray equipment failed. In the other single outlier, much closer to the box, the evaluation of the left ventricular function seemed to have taken longer than average but no other complication was observed from the records.

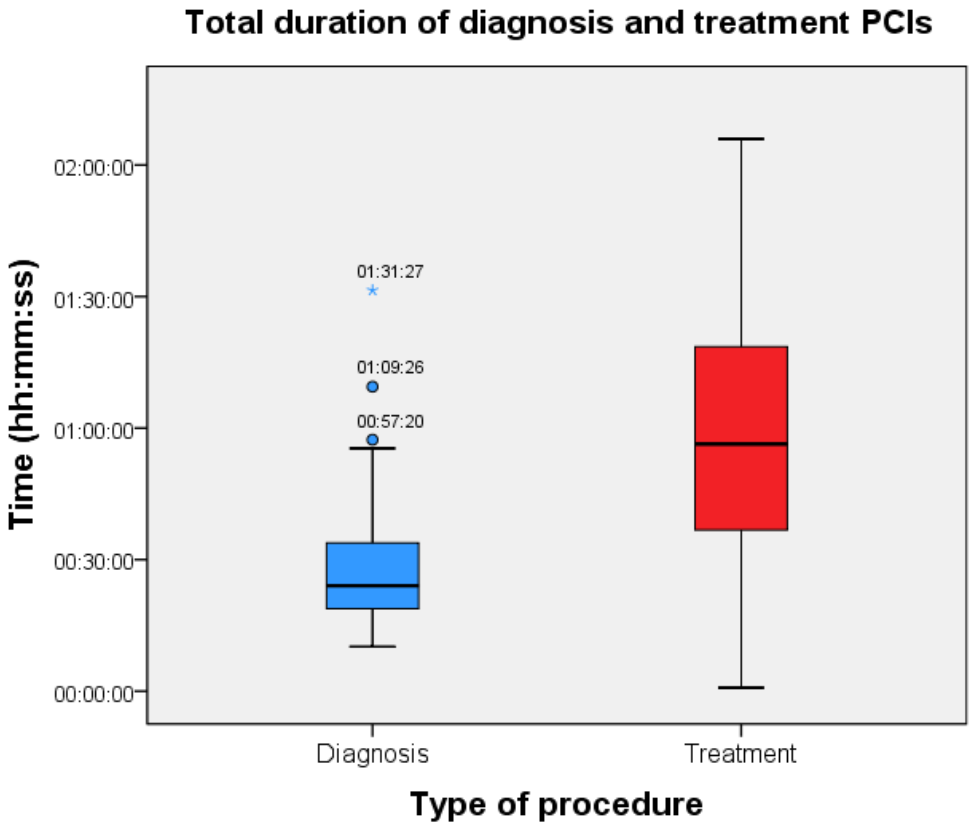


Figure 21. Box plot of total duration (hh:mm:ss) per purpose of PCI – diagnostic and treatment.

In the case of the PCIs that involved stenting, two different approaches were distinguished: the pre-dilatation approach, where a balloon was used before a stent implantation, and the direct approach, where the stent was applied directly without a balloon dilatation. Six records were collected with the direct approach and 30 with the pre-dilatation approach. The direct approach took on average 44:15 (05:31) and the pre-dilatation approach took 1:02:20 (05:35). Figure 22 shows the higher variability in procedural time with the pre-dilatation approach.

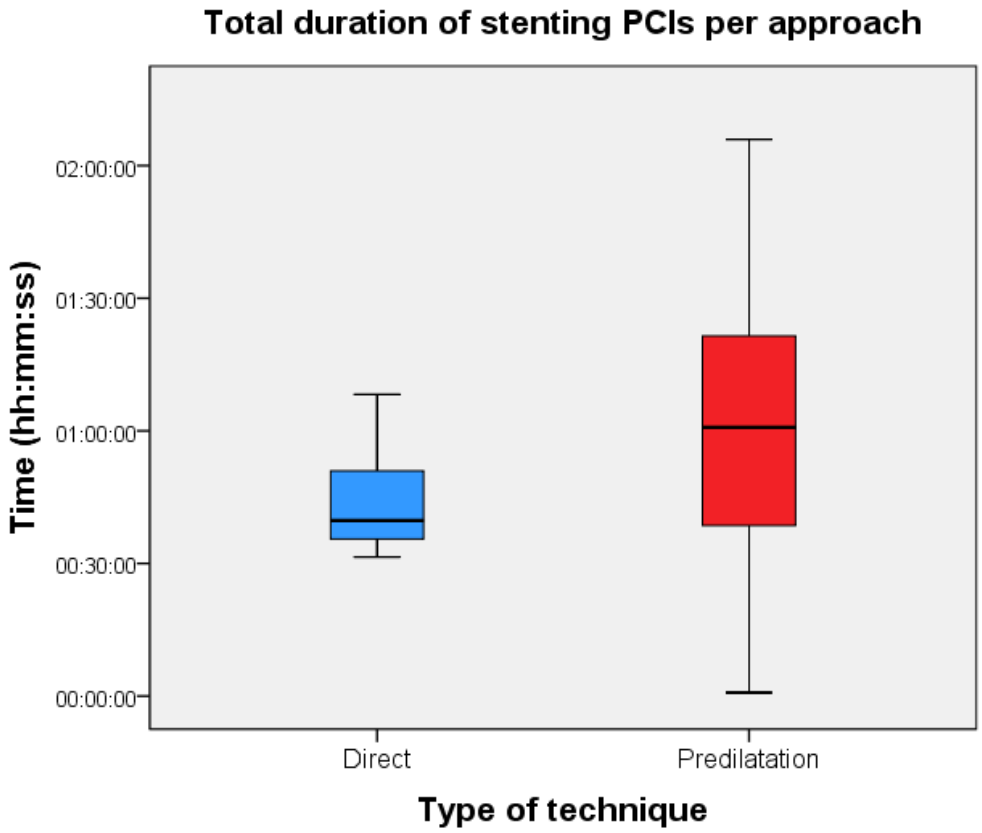


Figure 22 Box plot of the duration for stenting PCIs divided by technique used – Direct and pre-dilatation approach.

4.2.2. Cath lab times analysed

Time between procedures

In addition to the procedural times, the time between procedures was measured. Although this time does not appear in the records, according to the cardiologists collaborating in the study, it could be estimated from the records by calculating the time from when a procedure finished until the next one started. This time includes: time for taking the previous patient out of the room, time for cleaning and preparation for the next patient, patient interview (including consent) and preparation of the new patient for the subsequent intervention. Figure 23 presents the average time in between procedures categorised per weekday. Although slight variations can be observed in the figure, no statistically significant difference was found (one-way ANOVA test applied, CI = 95%).

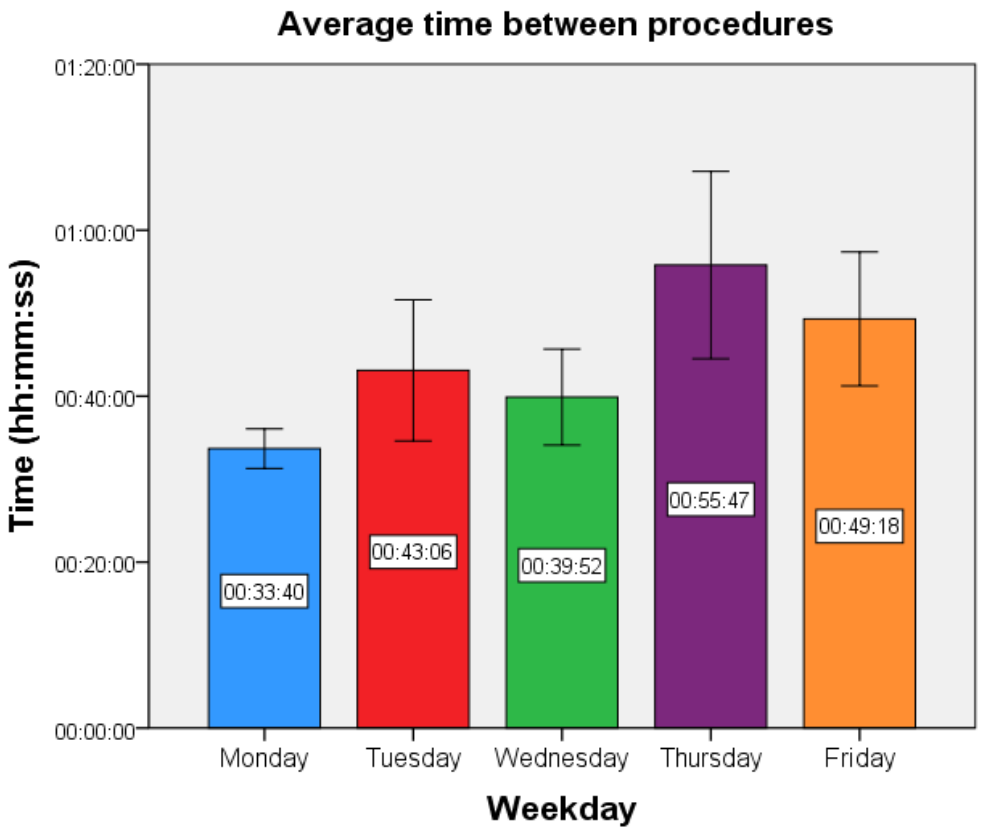


Figure 23. Average duration between procedures shown per weekday

Time to first patient

In a usual schedule, a working day in the cath lab would start at 9:00am. That is also the time at which the first patient is scheduled. However, the interventions are likely to start later due to room and equipment setup times. It was of interest to calculate the time between the first patient appointment and the start of the intervention. This would enable a better understanding about the average working routine in the department. Figure 24 shows this time distribution. An average time of 39:21 (06:09) was observed. The times varied from 08:43 – 1:47:20 (minimum – maximum). The records did not provide an explanation or indication for the causes of the two substantial outliers in the graph.

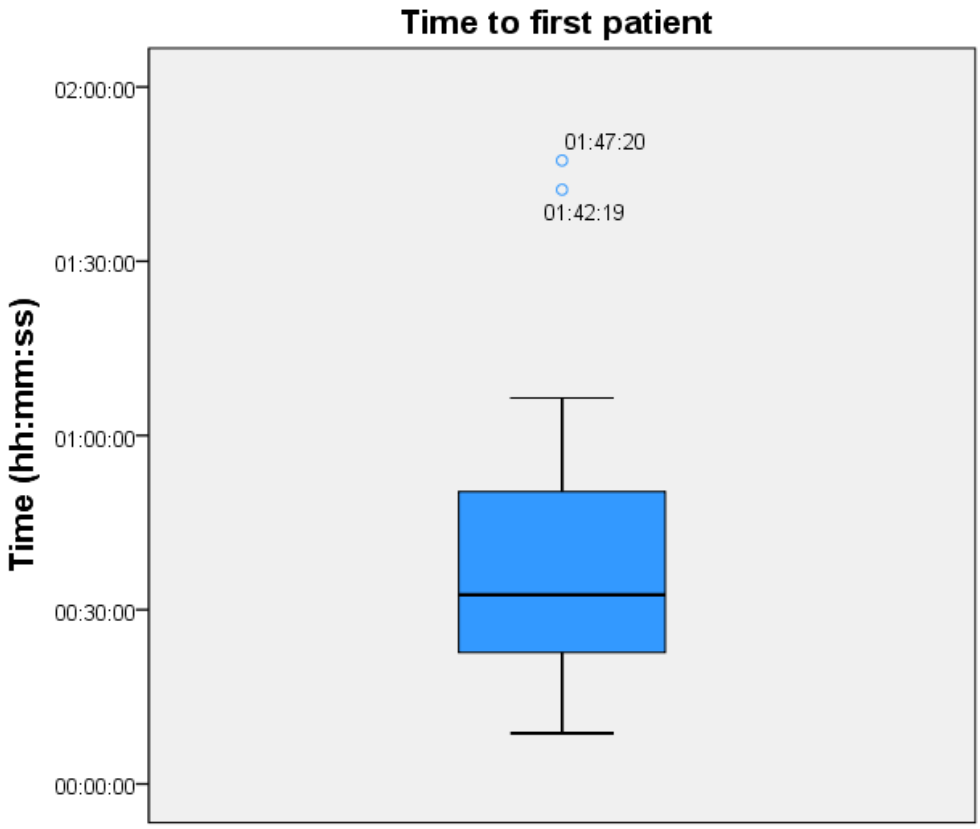


Figure 24. Distribution for the times calculated until the start of the first PCI

4.3. Workflow analysis for angioplasty and stenting PCIs

An overall analysis of PCI records confirmed an expected higher variability present in angioplasty and stenting procedures. Therefore, a deeper analysis of these interventions (42 records) was carried out following the framework described for the DES model implementation.

Figure 25 shows the proposed conceptual workflow representing angioplasty and stenting PCIs. This flow diagram was designed through careful analysis of the collected records and real-life observations of PCIs in the cardiac department. Figure 26 shows the RAD with the interactions among clinicians during angioplasty and stenting PCIs.

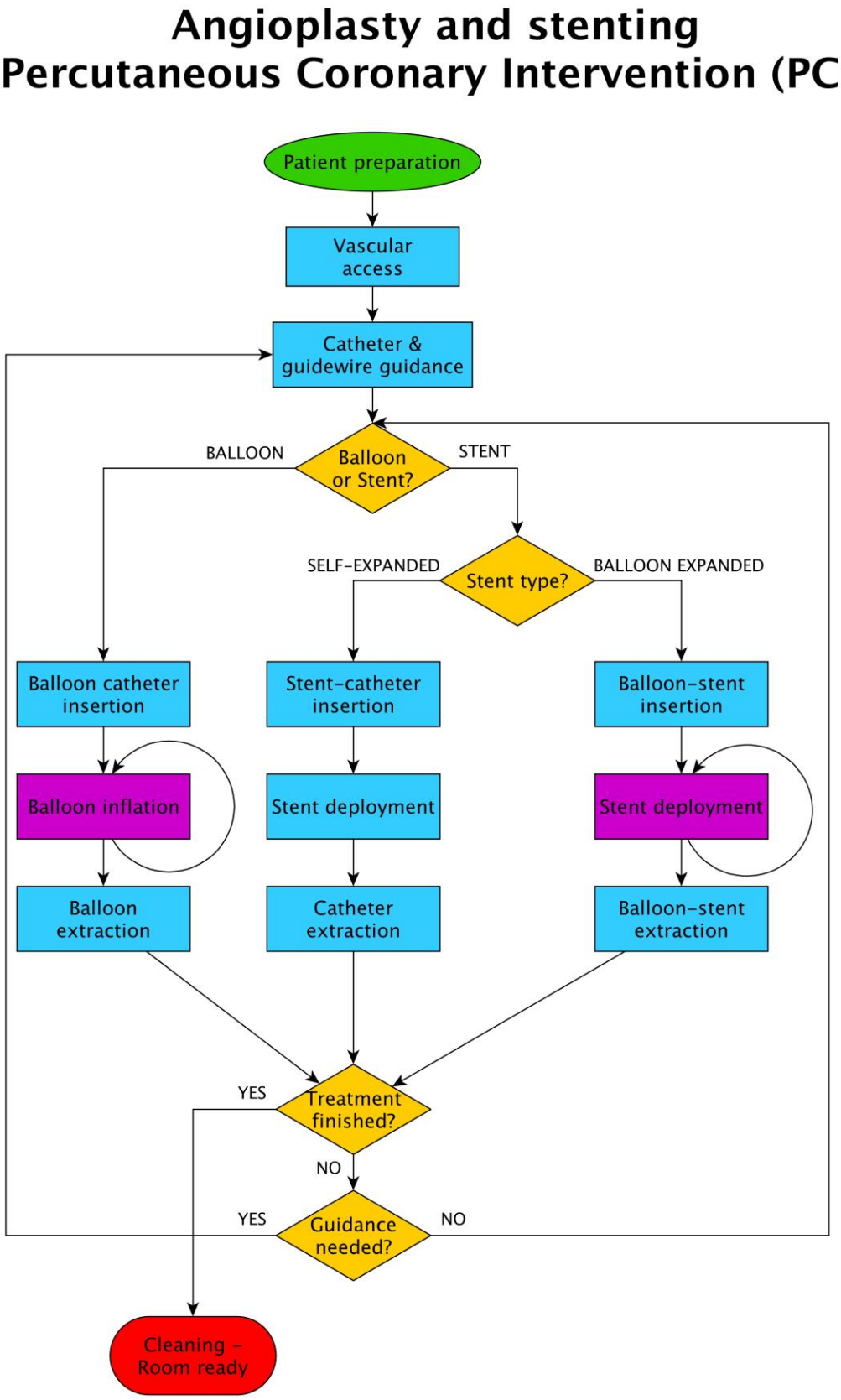


Figure 25 Proposed conceptual workflow for angioplasty and stenting PCI procedures

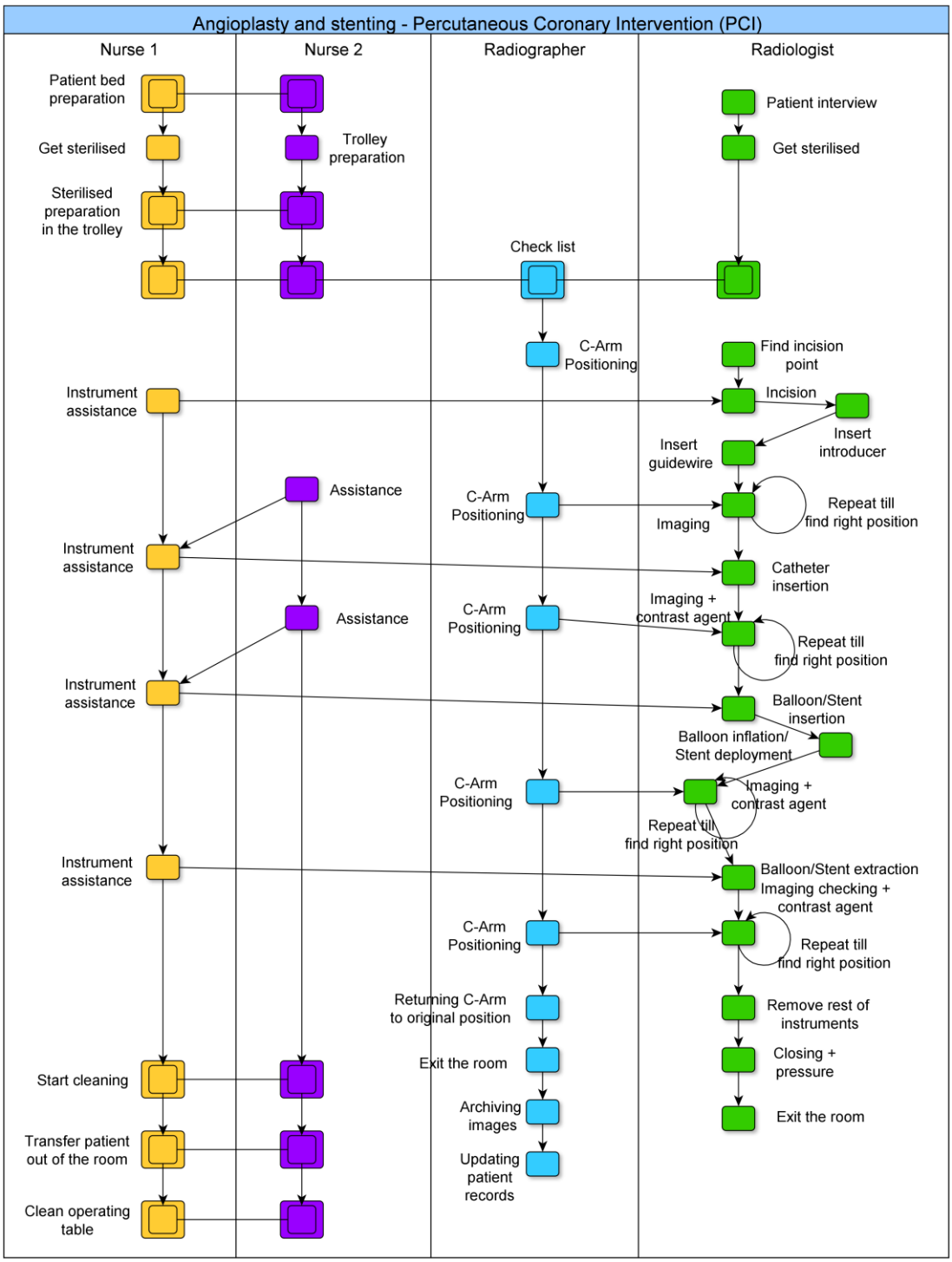


Figure 26 Proposed role activity diagram to show interactions among clinicians for angioplasty/stent implantation PCIs

Relevant phases, highlighted in the diagrams, were analysed. Results of descriptive statistics of these phases are shown in Table 5. It was not possible to distinguish between the phases of balloon or stent insertion, inflation or deployment and extraction for all the records. Either some of the intermediate tasks were missing

or some tasks were double recorded, being then impossible to distinguish which was the valid record. In addition, no significant difference was found between the times for balloon or self-expanded stent deployment (T-Test for independent samples applied, CI = 95%). In these cases, to keep the consistency among all the data, it was agreed to consider these phases together and rename them as *"single balloon angioplasty"* in the case of the balloon catheter procedure and *"single stent implantation"* for both self-expanded and balloon-expanded stent deployment. The "*single guidance*" event, or "*catheter and guidewire guidance*" in Figure 25, is defined for each time there was an exchange of catheter(s) and guidewire (s) to reach the area to treat.

Event	Mean (min)	Std. Dev (min)	Median (min)	Q1 (25%) (min)	Q3 (75%) (min)
Preparation	13.02	4.73	11.75	10.23	13.88
Access	4.15	6.30	2.28	0.44	5.21
Single guidance (exchange of catheter and guidewires in between treatments)	9.86	7.68	8.40	4.40	13.02
Single balloon angioplasty	3.98	1.69	3.71	2.76	4.89
Single stent implantation	4.38	2.43	3.75	2.49	5.60
Room ready time	9.01	0.66	8.87	8.47	9.57

Table 5. Standard descriptive analysis of the duration (in minutes) of the events collected for 42 angioplasty and stenting PCI procedures. Statistics include mean, standard deviation, median and Q1 and Q3 quartiles[3].

The next step in the data analysis was to fit the statistical distributions to the data shown in Table 5 in order to fit the DES model. To illustrate the process as it is explained in *Section 2.2.3*, the fitting of "*single guidance*", which is defined above, is presented in more detail. Durations of "single guidance" were calculated from the 42 treatment PCIs records collected. They were fed into EasyFit and fitted into several continuous statistical distributions with the restrictions of lower bound fixed to 0 and $\alpha = 0.05$ for the Anderson-Darling GOF test. With this condition, a gamma

[3] Quartiles divide a rank-ordered dataset into four equal parts. Q1 is the middle value for the first half of the ordered dataset and Q3 is the middle value for the second half. Q1 and Q3 define the interquartile range which is a measure of the variability of the dataset.

distribution was chosen, ranked as best fit by the GOF test. Figure 27 shows how the fitting looks like graphically when compared to the histogram of the data. Scale – β – and shape – α – parameters, describing the specific gamma distribution fitting the data, are also given by EasyFit (Law 2007).

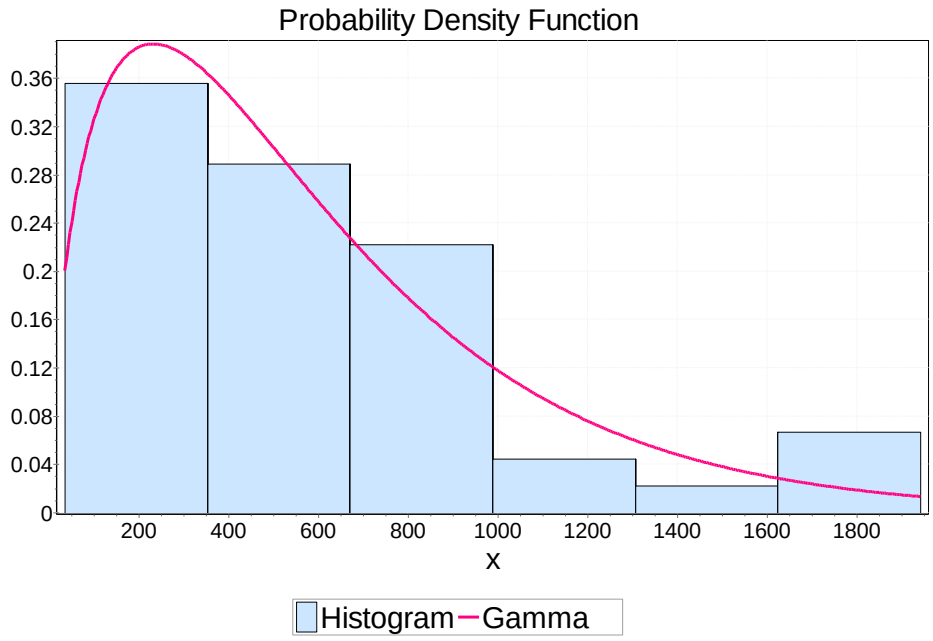


Figure 27. Example of distribution fitting for the "*single guidance*" event with the EasyFit software. Histogram of the durations collected and curve of the probability distribution function fitted are shown.

Table 6 shows the rest of probability distributions fitted to the events indicated in Table 5. These were calculated through EasyFit following the indications in *Section 2.2.3* for data analysis. Information about the distribution curves and data histograms can be seen in Appendix D.

4.4. Model implementation

Figure 25 and Figure 26 were used to implement the logic for angioplasty and stenting PCIs DES model. Although the logic seemed to be simple at first sight, the analysis revealed several particularities that will be described below. The assumptions and approaches taken were validated during the simulation analysis and will be discussed in the last section of the chapter.

Event	Distribution	Parameters (sec)
Preparation	Lognormal	μ = 6.62, σ = 0.27 Mean (± SD) = 776.18 (± 216.59)
Access	Gamma	α = 0.43, β = 573.11
Single guidance	Gamma	α = 1.65, β = 358.66
Single Balloon Angioplasty	Gamma	α = 5.52, β = 43.20
Single Stent implantation	Lognormal	μ = 5.45, σ = 0.48 Mean (± SD) = 260.8 (± 133.91)
Room ready time	Erlang	m = 183, β = 2.94, (Mean=538.87)

Table 6. Statistical distributions of the events collected for PCIs interventions, where α and σ are the shape parameters, and β and μ are the scale parameters of the distribution functions

Number of treatments

Observations revealed that patients could have more than one single treatment ("*single balloon angioplasty*" or "*single stent implantation*") during one intervention. The number of single treatments varied from 1 to 9 with a mode = 3[4]. This number was also modelled with EasyFit software using the discrete distribution fitting option. Figure 28 shows the histogram and the Poisson distribution ($parameters: \lambda = S^2 = 3.4242\ and\ mode = 3$) that was selected as the best fit to represent the sample data. Although the Poisson distribution rejected the A-D GOF for α = 0.05, it did not rejected it for α = 0.02 and 0.01. Therefore it was still decided to be used for representation of the data (see *Section 2.2.3*). This distribution was added to the model and was sampled at the beginning of each simulation in order to collect all the variability of cases.

[4] Where mode is the statistical value defined as the value that appears more often in the dataset. In this context it would be the more likely (often) number of treatments that a patient may have

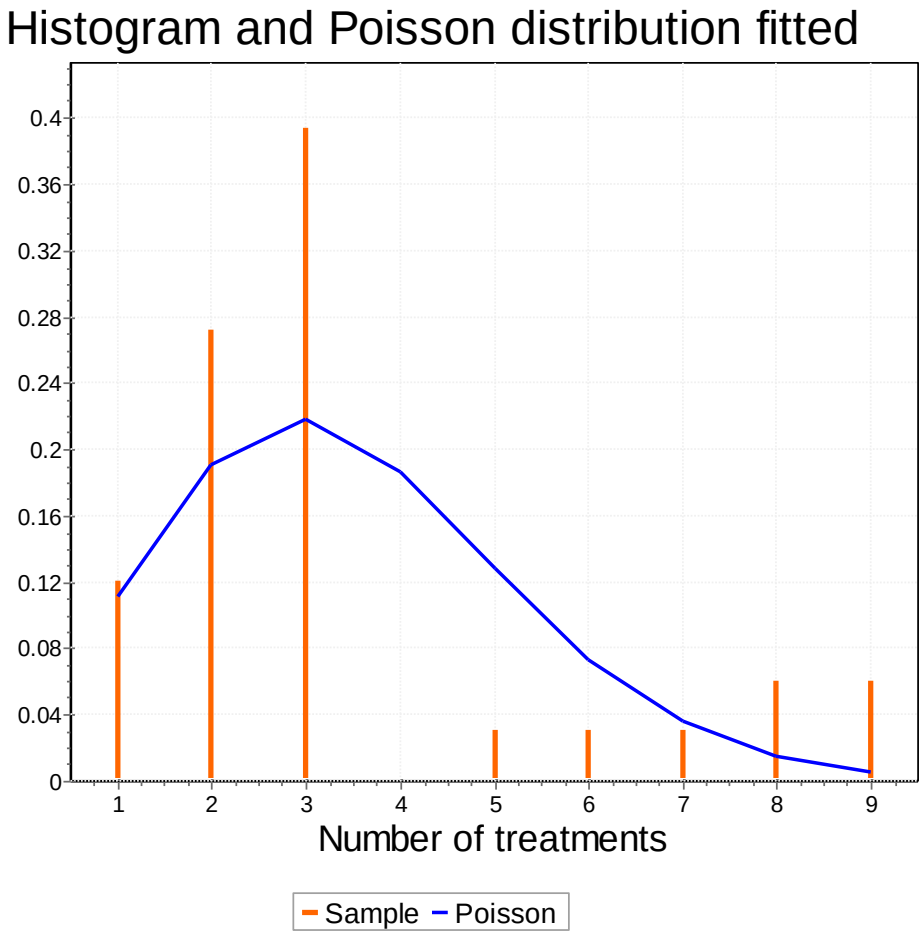


Figure 28 Histogram and Poisson distribution for the number of single treatments (angioplasty or stenting) performed on a patient during a PCI. In the diagram, frequency indicates the probability of having a particular number of treatments. The frequencies take values from 0 to 1 instead of using probability percentages, e.g. having 3 treatments during a single procedure has a frequency of 0.39, which means a probability of 39%.

Probability for angioplasties and stenting

When studying the decision points shown in Figure 25, different probabilities of treatments by angioplasty or stenting were observed. These probabilities changed depending on the previous treatment given to the patient. For instance, in 81.82% of the cases the cardiologist performed a balloon angioplasty in the first place, representing stenting without a previous angioplasty only in 18.18% of the cases studied. After this, treatment finished in 66.66% of the cases that had a stent implantation, while treatment continued for the cases that had a balloon angioplasty in first place. The full probability tree observed from the records collected is shown

in Appendix D. However, the sample size (42 records) is not large enough to give an exact estimation of these probabilities for all the cases. In this case, MKC was used as first approximation to model these probabilities (see *Section 2.3.4*).

The initial probabilities are given by the state vector P_0 = (0.8182, 0.1818), indicating as mentioned, that initially 81.82% of the cases had an angioplasty, while the rest had a stenting procedure. Then, the transition probability array is given by:

$$P_T = \begin{matrix} \\ Balloon \\ Stent \end{matrix} \begin{matrix} \begin{matrix} Balloon & Stent \end{matrix} \\ \begin{pmatrix} 0.1852 & 0.8148 \\ 0.5 & 0.5 \end{pmatrix} \end{matrix}$$

P_T defines the probabilities of having an angioplasty or stenting, depending on the previous case. For instance, having had an angioplasty, the probability of having a stent implantation next is 81.48%.

Case: Several areas to treat

Several cases needed an exchange of catheters and guidewires after a treatment. Since, no further information was available about the reason for this extra guidance times, this was modelled as a new area to be treated. In this case, a simpler approach was chosen and direct probabilities were calculated:

- Guidance needed after first treatment = 30.3% of the cases
- Guidance needed after second/third/etc. treatment = 6%

Heparin/Medicine ingestion/injection effect

Several notes were found on the data about the injection of heparin or ingestion of other medications such as Diazemuls or Nitrocene. All these procedures had a time noted and this time was modelled on EasyFit as Gamma distribution (α = 1.3937, β = 224.7).

This injection/ingestion of these medications could take place at the beginning of the procedure (6% of the cases), after the vascular access (78.8%), before the treatments (54.5%), or at the end of a procedure (21.2%). These probabilities were calculated and were implemented in the model logics. A patient could have several injections during the whole procedure.

Pauses

Although there were pauses during most of the procedures according to interviews with clinicians, only in 15% of the cases, there were identified in the records. These cases might be due a particular complication during the procedure but this cannot be confirmed with the current data available. Nevertheless, this pause, in the 15% of the cases, was modelled with a Gamma distribution ($\alpha = 3.65$, $\beta = 73.14$) and was also included also in the model. It was assumed, for simplicity in the logic implementation that the pause would be taken before a treatment, which was observed in most of the cases. Figure 29 shows the DES model of the Cath lab in Ninewells Hospital (Dundee, UK) implemented in Delmia Quest. For this model, a standard staff team was included – cardiologist, radiographer, circulating nurse and scrub nurse – and interactions were programmed as indicated in the RAD diagram of Figure 26.

Figure 29 DES model in Delmia Quest of the Cath Lab (Ninewells Hospital, Dundee, UK)

4.5. Validation and verification of the PCI model

For validating and verifying the model implementation, the indications given in *Section 3.2.6* were followed, particularly considering the following:

- Operational behaviour through animations

- Event validity, where the recurrences (loops) were checked accordingly to the real data. For instance, most likely number of treatments, probabilities of having an angioplasty or stenting, etc.
- Internal validity. The Welch CI was calculated for the total duration of the procedure, comparing the simulating model with the historical data collected, obtaining a CI of [634.83, -153.27]. The given Welch CI was calculated executing 100 simulations with different random seeds, each of them with 30 patients. Since this confidence interval contains zero, the model is validated as a good representation of the real system.

4.6. Discussion

The overall analysis of PCIs revealed in first some interesting findings. Figure 21 shows that while the duration of the diagnostic procedures is quite homogenous (despite some outliers), the duration of the treated patients has a higher variability. It might not be advisable therefore to model angioplasty and stenting PCIs with traditional statistical tests based on the assumption of normally distributed population. This supports the hypothesis of using advanced modelling techniques such as DES and more refined statistical analysis to understand this variability and investigate the impact of new policies or approaches to optimise efficiency when performing these procedures. With particular focus on the treatment PCIs, previous studies have already shown how the direct approach can save costs, radiation exposure and procedure times (Martínez-Elbal et al. 2002; Lozano et al. 2004). This has also been confirmed by the present work. However, these studies consider only average overall times of both cases. In addition, it can be observed in Figure 22, how procedures with the pre-dilatation approach have a more disperse distribution. This could lead to wrong considerations if a potential analysis was done to improve efficiency in the cardiology department.

Only one paper was found on the use of DES in cardiovascular processes. Pirolo et al (2009) presented a simulation model to improve throughput in a cath lab. Authors accurately represented the complexity of load fluctuations due to unscheduled emergency patients or bottlenecks when transferring patients, among other reasons. However, the procedures within the cath lab were again only

represented with average times in this study. Complex high-level models like the presented by Pirolo et al. could benefit from models like the one introduced in this chapter, which represent a closer approximation of real angioplasty and stenting PCIs.

However, there are some limitations of the present study that shall be further investigated in order to gain accuracy and knowledge of this particular case study. For instance, the analysis included information about delays before treating the first patient. According to the records, nothing was annotated regarding the large delays found in two cases. Furthermore, times shown in Figure 23 indicate that the average duration between procedures is remarkably long. However, information about these times was not available in the database from which the datasets were retrieved. Nevertheless, cardiologists experience suggests that the sources of delays are complex and multi-factorial and might involve the support teams work pattern: nurses, technicians and radiographer. Further investigation would help to detect and identify the potential causes for the delays before first procedures and for the duration between procedures. As a potential solution the impact of adding further staff could be investigated. In addition, simpler approaches were chosen when dealing with surgical pauses or extra guidance time in between single treatments. Current records do not provide the reasons for the pauses or whether the multi-treatments were performed in different arteries or they were done for the same lesion. Collection of further and more detailed data could help to clarify these points. Nevertheless, a model should always be implemented to answer the questions of the stated problem. Simpler models, designed with elements relevant to the modelling objectives, are quicker to implement and easier to interpret (Kotiadis and Robinson 2008). Besides, the assumptions of using these simpler approaches in this study as well as the use of Markov process to model the decision points were proven valid through the simulation analysis and the Welch CI.

4.7. Summary

In conclusion it was shown how DES techniques can be applied to model angioplasty and stenting PCIs as suggested in Chapter 3 in order to obtain satisfactory and valid results that are important to cardiology teams.

Chapter 5.
Results: Case study of transarterial chemoembolisation

Contents of this section are included in:

Fernández-Gutiérrez F, Wolska-Krawczyk M, Bücker A, Houston G, Melzer A. 'A simulation-based workflow optimisation in a radiology department: a case of a multimodal imaging procedure', Minimally invasive therapy & allied technologies (MITAT) (Submitted)

5.1. Background to the case

Hepatocellular carcinoma (HCC) represents more than 90% of liver cancers, being these the sixth most common cancers, with more than 700 thousand new cases every year worldwide (European Association for the Study of the Liver 2012). Transarterial chemoembolisation (TACE) is the recommended palliative therapy in the intermediate stage of HCC without extrahepatic spread or vessel invasion (Bruix and Sherman 2011). The procedure is characterised by a slow injection in the tumour area of a chemotherapeutic agent and oily emulsion of iodinated contrast agent, which has a temporary embolic effect. This leads to tumour necrosis due to clotting of smaller tumour feeding vessels and results in delivery of the chemotherapeutic agent solely to the HCC with relatively low systemic effects. The unexpected vascular supply of neoangiogenesis of the liver tumour may however hamper TACE success and the unselective application of the chemoembolic agents may contribute to treatment-related liver failure (Llovet et al. 2008; Takayasu et al. 2006). Complications derived from this prompted the intervention team of the clinic of diagnostic and interventional radiology in Saarland Medical Centre (Homburg, Germany) to investigate whether MR angiography, after transcatheter intraarterial contrast agent application offers the possibility to identify the treated liver parenchyma. The hypothesis was that this method could allow visualisation of potentially new vascularisation or newly formed metastases or not perfused areas, which would suggest the tumour supplies from another, extrahepatic collateral vessel. Hence, the interventional radiologist could change the primary therapy

position of the catheter before the final treatment, which may be significant for optimal tumour targeting.

In addition, it is important to treat the tumour selectively and not the whole liver at once. Patients with HCC require further treatment when new or residual disease is detected, so-called TACE on demand (Ernst et al. 1999). This was the case of the majority of the patients included in the study carried out by the clinic. The follow up was scheduled every 4 to 8 weeks; hence patients were treated with TACE in those intervals. Before additional chemoemobolisation sessions, liver function tests and a complete blood count were also performed again to ensure that the patient was still an appropriate candidate for the study. It is needed to mention that for the patients participating in the cohort study, HCC had been diagnosed with MRI in 21 of the cases, with CT in 5 and with a biopsy with 1 patient. The follow-up was performed with MRI in all cases.

However, this new protocol was more time consuming than the original procedures, resulting large waiting times when transferring the patient to the MRI area at the existing infrastructures. Waiting times are a common problem in healthcare environments when high demanded shared facilities within the department are involved (Granja et al., 2010; Torkki et al., 2006). In these cases, simulation techniques such as DES help to identify bottlenecks in order to understand and improve clinical protocols (Katsaliaki and Mustafee 2011). Recent studies in radiology departments support the application of simulation to improve machine usage and reduce waiting times for patients (Nickel and Schmidt 2009), scheduling policies (Johnston et al, 2009) and radiotherapy planning process (Kapamara et al, 2007; Werker et al, 2009). Up to now, studies have examined departments at various levels of complexity. Johnston et al. (2009) and Werker et al. (2009), for example, classified different patient types but did not apply optimisation analysis to compare workflow alternatives as Granja et al. (2010) or Nickel and Schmidt (2009) did. In their studies, they modelled decision points and variability at department level not optimising procedures themselves. From the author best knowledge, statistical methods to aid decisions towards selecting the best alternative have not been use in this context.

This chapter presents a DES model of a TACE as multimodal image-guided procedure, involving MR and CT. Multilevel information about diagnostic and interventional patients was combined to gather the inherent variability of intraprocedural phases. The model was implemented through real data collected during procedures, as well as using information gathered from questionnaires in collaboration of the interventional radiology team at Saarland Medical Centre. Data was collected by by Dr Malgorzata Wolska-Krawczyk (interventional radiologist in training). The model validation was done with the aid of local interventional radiologists in Homburg Saarland Medical Centre Dr Arno Bücker and Dr Malgorzata Wolska-Krawczyk and the scenarios considered for the optimisation analysis were discussed with the clinical team. The scenarios were assessed defining a set of key performance indicator (KPI) and using a statistical ranking and selection procedure for simulation optimisation. The purpose of the study was to improve the current workflow by means of detecting bottlenecks and minimising waiting times without having a negative impact in the current MRI throughput.

5.2. Data collection and statistical analysis

5.2.1. The multimodal imaging TACE new protocol

The clinic of diagnostic and interventional radiology in Saarland Medical Center (Homburg, Germany) is equipped with a 1.5T wide bore (70cm) MR scanner (Magnetom AERA, Siemens, Erlangen, Germany). The scanner room is placed across the angiography suite, separated by a 3.7m wide corridor. The angiography suite is provided with a sliding door to facilitate the transport of patients.

The TACE procedure begins in the angiography suite with local anaesthesia applied to the disinfected groin of the patient. Then the right femoral artery is punctured by the Seldinger technique followed by catheter guidance to the hepatic artery and in some cases its subsegment arteries (cannulation). At this moment, DSA is performed to confirm the correct therapy position of the catheter. As part of the new protocol developed in the department, the patient is then prepared for transfer to the MRI suite by removing all metal and non-MR compatible objects from the angiography table. Once in the MRI suite, the patient is moved over a rolling slide board to the MR table. The patient, already draped in sterile fashion at the beginning

of the procedure, is covered with additional sterile drapes and then the MR coil is placed on top to avoid contamination of the puncture site. An sterile plastic tube with a contrast agent (Gadolinium, Dotarem Guerbet, Villepinte, France), previously prepared before the procedure, is connected to the distal part of the catheter. The patient is provided with noise protection earmuffs and an emergency bell. Once inside the MRI scanner, an MR angiography is performed to confirm the position of the catheter. Afterwards, the patient is transferred back to the angiography. In case the MR reveals that repositioning of the catheter is needed, this is done under fluoroscopic guidance (cannulation). Then, the chemotherapy is applied via catheter in the therapy position. Finally, the catheter and sheath are removed and the access is closed using an angio-seal closure system.

Large delays were observed when transferring the patient from the angiography suite to the MRI scanner room due to the high demand of MR imaging in the hospital. Data from MRI patients was incorporated to the study at a later stage in order to study ways to reduce these waiting times.

5.2.2. Data collection

Records of 59 TACE interventions were collected and submitted via the MIDAS website (http://midas.heroku.com) (see Appendix C for further information). Data included the information detailed in Table 4. Table 7 presents the significant events registered per TACE intervention together with their average (standard error) duration in minutes.

Information corresponding to MRI diagnosis times was gathered through a questionnaire completed by the MRI department clinical team at Homburg Saarland University Hospital. Table 8 contains information about minimum, maximum and most likely time of the most common MRI diagnostic procedures performed in the hospital. The times collected for the MRI diagnostic procedures included the positioning of the patient and scanning times. The preparation of the patient for the MRI was set to 10min. An extra 5min was considered to model the time needed to dismiss the patient from the MRI scanner room.

Event	Mean (SE) (min)	Distribution	Parameters
Access	7.55 (2.39)	Lognormal	$\mu = 1.70$ $\sigma = 0.74$
Cannulation	42.22 (2.82)	Gamma	$\alpha = 3.87$ $\beta = 10.91$
Transfer to MRI suite	11.09 (0.94)	Lognormal	$\mu = 2.22$ $\sigma = 0.62$
MRI diagnosis sequences	16.02 (0.84)	Lognormal	$\mu = 2.71$ $\sigma = 0.36$
Transfer to angio suite	9.15 (0.83)	Gamma	$\alpha = 2.08$ $\beta = 4.40$
Cannulation after MRI	19.21 (3.81)	Lognormal	$\mu = 2.34$ $\sigma = 1.22$
Chemoembolisation	26.38 (2.29)	Lognormal	$\mu = 3.08$ $\sigma = 0.62$

Table 7. Descriptive statistics and statistical distributions of the events collected for TACE interventions, where the times are expressed in minutes, α and σ are the shape parameters, and β and μ are the scale parameters of the distribution functions. Cannulation, as indicated in the previous section means cannulation of the vessel with a catheter and it is used as "Cannulation after MRI" when repositioning of the catheter was needed.

Type of MRI procedure	Minimum (min)	Maximum (min)	Most Likely (min)
Knee	20	60	30
Pelvis	40	60	45
Wrist	20	60	45
Whole Body	60	180	120
Neck	43	65	52
Angiography Abdomen	12	20	15
Angiography Pelvis and Lower Extremities	15	55	30
Cardiac	50	75	65
Thigh	35	115	65
Arthography Hip	40	60	42

Table 8. Procedure times gathered for the most common diagnostic procedures at the MRI department (Homburg Saarland University Hospital, Homburg, Germany).

5.3. Model implementation

Figure 30 represents the conceptual workflow used to implement the logic for the DES model. The model reads a proposed schedule of patients based on one TACE patient and seven MRI-diagnostic patients. Depending on the type of patient, this is

sent to the angiography room or the MRI suite. MRI patients will be waiting in the waiting area in case the MRI suite is occupied. Once the MRI suite is available and the room has been cleaned, the patient is prepared and proceeds for the MRI scanning. The TACE patients, once ready to be transferred, would wait on the operating table if the MRI was occupied. All these waiting times were collected during the simulations.

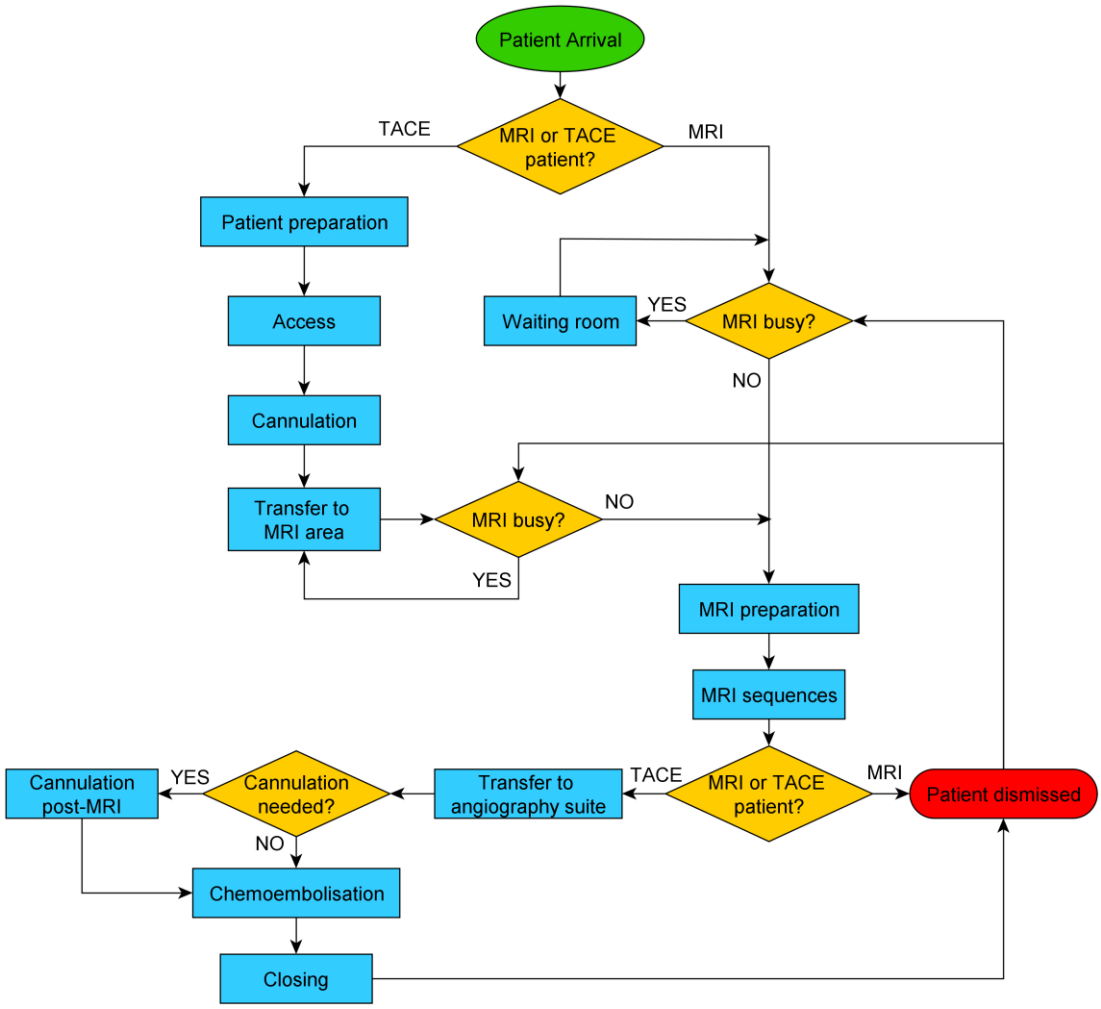


Figure 30 Conceptual workflow of the patients around the MRI area. Two groups are distinguished: patients for the TACE interventions[5] and the MRI diagnostic patients at the clinic of diagnostic and interventional radiology in Saarland Medical Center (Homburg, , Saarland, Germany).

[5] TACE patients considered in this diagram and consequently in the design of the model are referred to the patients attending the TACE intervention. TACE patients attending to routine MRI scanner scheduled another day prior to the TACE procedure are not considered. The radiology clinic at Saarland Medical Centre counts with several MRI facilities. Therefore there would be multitude of patients for MRI scanning in other rooms. For the purpose of this study, only the MRI room in the proximity of the angiography suite is considered and for illustration purposes, patients attending only MRI are just label as "MRI patients".

As input for the simulating model, times collected for the TACE events were fitted into the corresponding statistical distributions using the software package EasyFit. The results are presented in Table 7 with their correspondent event. The Anderson-Darling GOF test ($\alpha = 0.05$) was used to determine the best distribution fitting. The MRI diagnosis data set (see Table 8) was modelled using triangular distributions as explained in *Section 3.2.5*.

Figure 31 shows a screen capture of the DES model implemented in Delmia Quest. The model includes the angiography suite and MRI scanner room layouts at scale, together with their respective control rooms and a waiting area for patients.

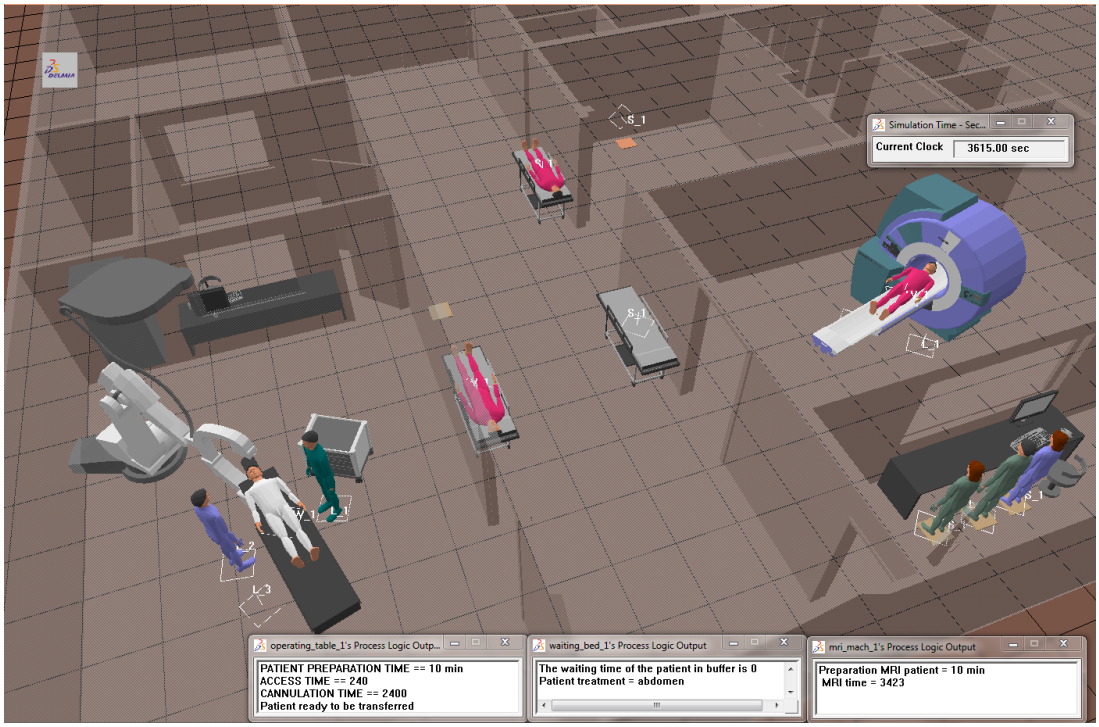


Figure 31 Screenshot during simulation of the DES model for TACE interventions and MRI patients implemented in Delmia Quest. The 3D environment corresponds to the facilities at the department of Radiology, Saarland Medical Centre (Homburg, Saarland, Germany). Note: the beds in the corridor are only used to collect the waiting times due to limitations in Delmia for this purpose. They do not represent the real waiting areas at the radiology department.

5.4. Validation and verification

Table 9 presents the Welch 90% CIs, given by Eq. 3-2, calculated for each of the events recorded for the TACE procedure when compared with the real system. Since each CI interval contains zero, the DES model of the TACE procedure results a valid

representation of the real system (see *Section 3.2.6*). Unfortunately, no data was available to compare the complete model including the diagnostic MRI patients with the real world situation so this part was uniquely validated through the clinical team.

Events	Welch 90% CI (sec) [max,min] (sec)
Access	[85.09, -149.89]
Cannulation	[485.92, -221.92]
Transfer to MRI suite	[111.99, -145.59]
MRI diagnosis sequences	[39.26, -150.86]
Transfer to Angiography suite	[64.76, -147.56]
Cannulation after MRI	[789.48, -41.88]
TACE	[113.50, -419.50]
DynaCT	[24.55,-42.56]

Table 9. Welch 90% confidence intervals for the event in the TACE procedure when compared with the real system

5.5. Simulation-based optimisation analysis

In agreement with the clinical team, 14 scenarios were formulated for the optimisation analysis. These scenarios were defined depending on three different factors:

- **Arrival time for the TACE patient**: first time in the morning (9am) or in the afternoon (12am).
- **Interarrival time for the patients**: scheduling patients every hour or scheduling patients based on the most likely procedural duration. For this last case, an average time for preparation of 15 minutes was added in conjunction with the clinicians' experience.
- **Duration of the MRI diagnosis**. Three categories were defined: short procedure (duration less than 45 min), medium procedure (between 45 and 60 min) or long procedure (more than 60 min and less than the upper limit given for the defined MRI procedures in Table 8).

Table 10 shows the fourteen scenarios defined for the study, which were tested and analysed in the model. The rest of scenarios resulting from the combination of the factors mentioned above were discarded in agreement with the clinical team.

TEST	TACE patient		Inter-arrival time		Duration MRI patients	
	Morning	Afternoon	Most likely time	Every Hour	Short first	Large first
1	X		X		X	
2	X			X	X	
3	X		X			X
4	X			X		X
5	X		X		Alternating short/long	
6	X			X	Alternating short/long	
7	X		X		Organising 3 blocks: Block 1: Procedures ≤ 45min Block 2: Procedures ≤ 60min Block 3: Procedures > 60min	
8		X	X		X	
9		X		X	X	
10		X	X			X
11		X		X		X
12		X	X		Alternating short/long	
13		X		X	Alternating short/long	
14		X	X		Organising 3 blocks: Block 1: Procedures ≤ 45min Block 2: Procedures ≤ 60min Block 3: Procedures > 60min	

Table 10. Scenarios (tests) studied during the simulation analysis.

The optimisation process consisted in simulating these scenarios and measuring three KPIs per scenario:

- **Overtime work**; defined as the difference between the 8h (usual working time agreed) and the overtime worked due to the length of the procedures.
- **Average waiting time**; defined as the average time that a patient needed to wait to start the procedure (TACE or MRI).
- **Waiting time in angio suite**, defined as the average time that a TACE patient needed to wait for the MRI to be available.

Following the optimising simulation method described in *Section 3.2.7*, the weighted means were calculated for each scenario and for each of the KPIs considered. Regarding the parameters for the D&D method, $d^* = 300\,seg$ (5min) was chosen for the cases of the waiting times in angio suite (TACE patients) and waiting area (MRI diagnostic patients) and $d^* = 600\,seg$ (10min) for the overtime work.

Table 11 shows the results of applying the D&D method for the average waiting time. As mentioned in *Section 3.2.7.*, the initial number of replications was set to 20 (n_0=20). The results of the first-stage of simulations are then given in the $\bar{X}_i^{(1)}(n_0 = 20)$ and $S_i^2(n_0 = 20)$ (mean and variance calculated by Eq.3-5) columns of Table 11. $S_i^2(n_0 = 20)$, h_1=3.37, calculated from tables in Dudewicz et al (1975) with number of scenarios 14, n_0=20 and probability of getting the best system 90%; and d^* are used to calculate the total sample size N_i given by Eq. 3-6. Then (N_i – 20) additional replications are made for the second stage, e.g. 81 for scenario 1, 101 for scenario 2, etc.; and the $\bar{X}_i^{(2)}(N_i - n_0)$ are calculated as shown in the next column of Table 11. Finally, the weights W_{i1} and W_{i2} are calculated using Eq. 3-7 for each scenario and the weighted sample means $\tilde{X}_i(N_i)$.

i	$\bar{X}_i^{(1)}(n_0 = 20)$	$S_i^2(n_0 = 20)$	N_i	$\bar{X}_i^{(2)}(N_i - n_0)$	W_{i1}	W_{i2}	$\tilde{X}_i(N_i)$
1	2659.2	641275.6	81	2685	0.26	0.74	2678.3
2	1294.4	793370.9	101	1029.3	0.24	0.76	**1091.8**
3	2852	827479.5	105	2370.9	0.22	0.78	2476.7
4	5068.0	728295.3	92	5253.2	0.23	0.77	5210.4
5	2520.5	1021205	129	2713.1	0.17	0.83	2680.9
6	4138.9	470874.4	60	4035.3	0.38	0.62	4074.7
7	2823.5	808040.8	102	2748.6	0.20	0.80	2763.8
8	1938.9	566470.3	72	1782.4	0.32	0.68	1831.9
9	1362.3	87462.49	21	935.4	1.15	-0.15	1428.3
10	2225.6	1336427	169	2462.8	0.13	0.87	2431.2
11	4914.9	711166.4	90	5146	0.24	0.76	5089.4
12	2348.4	933096.3	118	2380.1	0.19	0.81	2374.1
13	3783.9	930951.9	118	2741.8	0.19	0.81	2944.6
14	1650.6	351590.9	45	1758.7	0.50	0.50	1704.2

Table 11. Two-stage means, variances, replications and weighted means calculated per alternative for the average waiting time (in seconds) (see *Section 3.2.7.2* for explanation of parameters).

Scenario 2 (see Table 10), which has the smallest weighted mean, gave the best performance, while the worst-case scenario was scenario 4. For the rest of KPIs, comparative results of the weighted means are also shown graphically in Figure 32. For the 'waiting time in angio' the best result was obtained also with the scenario 2, while alternative 4 gave again the maximum value for the weighted mean. In the case of 'overworked time', several scenarios gave similar results. The absolute minimum was in the scenario 14 and the worst-case was scenario 9. Table 12 shows

the 90% CI calculated by Eq. 3-4 for the KPIs times in minutes. Scenarios that gave the best, second best and worst cases are highlighted.

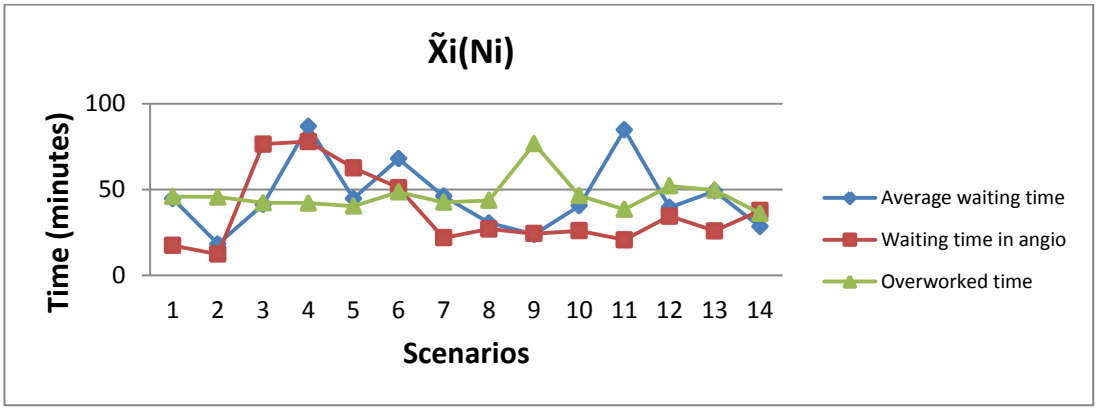


Figure 32. Weighted means ($\tilde{X}_i(N_i)$) calculated for each scenarios for the three key performance measures considered.

KPI	*1*	*2*	*4*	*9*	*11*	*14*
Overworked time (min)	**[42, 32]**	[57, 47]	[50, 40]	[86, 78]	[49, 38]	[49, 39]
Average waiting time (min)	[47, 43]	**[20, 17]**	[91, 87]	[25, 23]	[88, 83]	[32, 29]
Waiting time in angio suite (min)	[19, 14]	**[12, 9]**	[90, 79]	[26, 21]	[24, 19]	[38, 31]

Table 12. KPIs and the respective 90% CI [max, min] for their times (minutes) for all the scenarios that gave the best, second best and worst cases. For each case, the 90% CI corresponding to the best alternative is shown in bold and underlined font.

Data from patients waiting in the angio suite to be transferred to MRI during the TACE procedures was gathered as part of the study. It was observed that in the 71.19% of the cases, patients had to wait an average of 20 (± 20) minutes, with a maximum waiting time of 80 minutes. This was due to MRI being occupied for diagnostic patients. The optimisation analysis has shown that with scenario 2, which would be to schedule TACE patients as first appointment and scheduling MRI patients every hour with short diagnostic procedures first, would reduce the waiting times in angio by a 48.74% in average. According to this alternative, the overall waiting time for MRI diagnostic patients could be estimated to be minimum within the 90% CI of [20, 17] (min).

5.6. Discussion

MRI environments appear to be one of the most in demand resources in hospitals. Several studies agree that improving the planning of MRI processes will reduce waiting times (Barter et al., 2009; Otsubo et al., 2011). Additionally, there are numerous efforts on introducing MRI as part of therapeutic procedures as well in diagnosis (Blanco Sequeiros et al. 2005; Krombach 2012). Simulation based analysis can be a powerful tool for an optimal integration of MRI-guided or multi-image guided procedures in the already saturated radiology departments. By the implementation of a DES model, several scenarios, previously discussed with the clinical team involved in the study, were simulated to study the impact of different policies. An optimisation algorithm was used to select the best option for three KPIs, also agreed with the clinicians. This algorithm suggested a scenario (number 2 in Table 10) for with a 48% average lower waiting time for TACE patients. This choice would also be optimal to minimise the waiting times for MRI diagnostic patients. However, the algorithm estimates another scenario (number 1) as the best option for minimising overtime work. A comparison between the simulating results for overworked time and average waiting time for MRI patients with the real system was not possible since such information was not recorded at the moment of the study.

These results are likely to be discussed at clinic of diagnostic and interventional radiology in Saarland Medical Center. The adoption of any of these alternatives will depend on the feasibility of its implementation with the resources available. If any of these alternatives were adopted, it would then be possible to validate the predicted improvements. In this case, it would be beneficial to collect detailed information about patient preparation and cleaning times that are now only estimations based on the clinicians' experience.

5.7. Summary

This chapter presented a simulation optimisation framework to model and improve a current multi-imaging guided intervention protocol by taking into account the intrinsic variability within the procedures. The work was based on the particular case of a new multi-imaging protocol for TACE procedure. This study highlighted

some of the difficulties when introducing multi-image guided interventions in clinical radiology departments such as long waiting times resulting in an inefficient use of human and material resources. The optimization-based simulation analysis was used to predict the impact of several alternative scenarios. The results that were predicted to reduce patient waiting time by as much as 48% were presented to the clinical team and the feasibility to implement an optimal alternative policy are considered within the clinic.

Chapter 6.
Extending the framework to non-vascular IGPs: MRgFUS

Contents of this section are included in:

*Loeve AJ, Al-Issawi J, **Fernández-Gutiérrez F**, Lango T, Matzko M, Napoli A, Dankelman J. 'Workflow analysis and modelling of MR-guided Focussed Ultrasound', (To be submitted)*

6.1. Introduction to the chapter

This chapter presents a simulation model developed to predict the impact on potential improvements in workflow for MRgFUS procedures. These improvements are designed under the framework of a European project: the FUSIMO (Patient specific modelling and simulation of focused ultrasound in moving organs) European project (http://www.fusimo.eu/, accessed 21/02/2014), which is introduced in the first part of the section.

The simulation model was implemented according to the methodological framework introduced in chapter 3 for modelling vascular image-guided procedures through discrete-event simulation. MRgFUS is an excellent example of integration of imaging techniques and represents a modern form of MR image-guided treatment of solid organ tumours. Due to its inherent nature of computer control, it was selected as a suitable case study for validation of the new methodological framework. The data gathering and conceptual modelling of MRgFUS procedures were carried out by other researchers within the FUSIMO consortium. Therefore, it was decided to treat these results in this separate chapter, clarifying and differentiating the contribution of this author and the other researchers participating in the workflow analysis within FUSIMO.

6.2. The FUSIMO project background

Over the last two decades, MRI-guided Focused Ultrasound (MRgFUS) surgery has become an attractive non-invasive alternative to treat benign and malignant tumours. MRgFUS has been already approved by the U.S. Food and Drug

Administration (FDA) for uterine fibroid treatment and pain palliation of metastatic bone cancer; and is in ongoing clinical or pre-clinical trial for the treatment of breast, liver, prostate and brain cancer (F. a Jolesz 2009; Hynynen 2010).

In FUS, the acoustic energy that propagates through the tissue is concentrated into a focal point and transforms to thermal energy. The temperature rises in the focal volume and this results in thermal ablation with subsequent necrosis of cells inside the focus while the surrounding tissue remains at normal body temperature (Fischer, Gedroyc, and Jolesz 2010). MRI is a valuable option for the target definition, the treatment planning and closed-loop control of the acoustic energy deposition. In addition, MRI can generate accurate, near real-time temperature maps with high spatial and temporal resolution. Such thermal feedback can facilitate treatment monitoring, since it allows an immediate evaluation of the temperature in the targeted area and can minimise the risk of thermal rise in the adjacent tissues (Hokland et al. 2006; Sapareto and Dewey 1984; Viola Rieke and Butts Pauly 2008).

There have been attempts for treatment of liver tumours with MRgFUS in pre-clinical (F. A. Jolesz et al. 2004; Kopelman et al. 2006) and a few clinical trials (Gedroyc 2007; Okada, Murakami, and Mikami 2006). Despite the potential benefits of MRgFUS, there are two major challenges in liver MRgFUS treatment that remain to be overcome: the presence of the ribcage surrounding the liver, and the organ motion due to respiration. The ribcage bone structure would absorb the ultrasound beam, affecting the treatment. For that purpose, there has been research involving multiple-element ultrasonic transducers, which can "switch-off" elements that sonicate on ribs (Civale et al. 2006; Quesson et al. 2010). The respiratory motion can shift the target tumour and can also induce motion artefacts in the MR and temperature maps (de Senneville, Mougenot, and Moonen 2007). Voluntary breath-holding or gating techniques have been suggested to patients to avoid movement (Suramo, Paivansalo, and Myllyla 1984). Other techniques, involving reference-less MR thermometry and steering of the FUS beam have also been applied to compensate for the motion (V Rieke, Kinsey, and Ross 2007; Holbrook et al. 2014).

The FUSIMO project aims to develop, implement and validate a multi-model for moving abdominal organs, i.e. liver and kidney for MRgFUS surgery. In addition, FUSIMO intends to develop technology likely to be applied during MRgFUS

interventions in parallel to an existing FUS software system. A detailed workflow model based on DES was developed to estimate the benefits that FUSIMO technology may have in MRgFUS procedures (particularly on moving abdominal organs).

The following section presents the data collection and the conceptual modelling carried out by dr. ir. Arjo Loeve, postdoctoral researcher at Delft University of Technology (TUDelft, Delft, the Netherlands) in collaboration with other centres within the FUSIMO consortium. Then and as part of the contribution of this thesis to the FUSIMO project, the probability distribution analysis over the gathered data is presented. The later sections explain the implementation of the particularities of the simulation model, followed by the validation process and a description of the simulation analysis. A summary of the conclusions of this study is presented in the last section.

6.3. Conceptual model, data collection and statistical analysis

This model was designed through observations on MRgFUS interventions performed with the Exablate system 2100/ONE (Insightec Ltd, Haifa, Israel) at the Amper Klinikum (Dachau, Germany). The workflow consists of 11 main phases. Figure 34 shows the diagram with the current workflow and the different phases. Only phases from 4a to 9 are included in the simulation model, since phases 1 to 3 – *Intake*, *pre-operative imaging* and *planning* – correspond to the pre-operative part of the procedure. These phases are briefly described below for clarification:

- *Phase 4a – Setup*: Preparation of the MRI-room.
- *Phase 4b – Patient positioning*: The patient is positioned on the MRI-table such that there is an acoustic window (free field of view) for the FUS transducer on the region of treatment.
- *Phase 5 – Pre-therapy imaging*: high-resolution MR images are obtained to be used during the treatment.

- *Phase 6a – Pre-therapy segmentation*: Relevant structures are marked on the MR images to indicate areas to treat and to be avoided (e.g. neighbouring healthy tissue or sensitive organs).
- *Phase 6b – Pre-therapy planning*: The target volumes are filled automatically or manually with the planned sonications. The number of sonications may vary depending on the procedure and the patient condition.
- *Phase 7a – Sonication calibration*: Calibration of the FUS transducer and system to assure proper predictions of US propagation.
- *Phase 8 – Treatment*: Planned sonications are done one by one. In this phase, there might be adjustments on the plan or individual sonications.
- *Phase 9 – Post therapy imaging*: After completing the treatment, contrast MR images are obtained to assess the treatment outcome. Data are exported and the patient is taken out of the room.

A legend explaining the use of symbols and graphics for better interpretation of Figure 34 is shown in Figure 33. Both diagrams are courtesy of dr. ir. Arjo Loeve and FUSIMO project (Loeve et al. 2013).

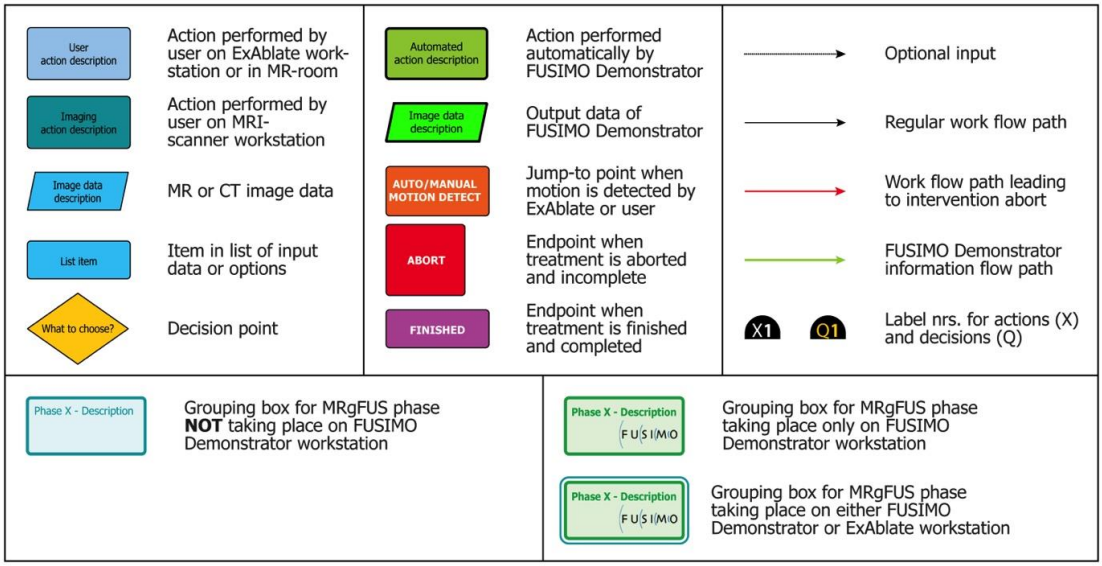


Figure 33 Legend for symbols and graphic styles used in MRgFUS conceptual model diagram.

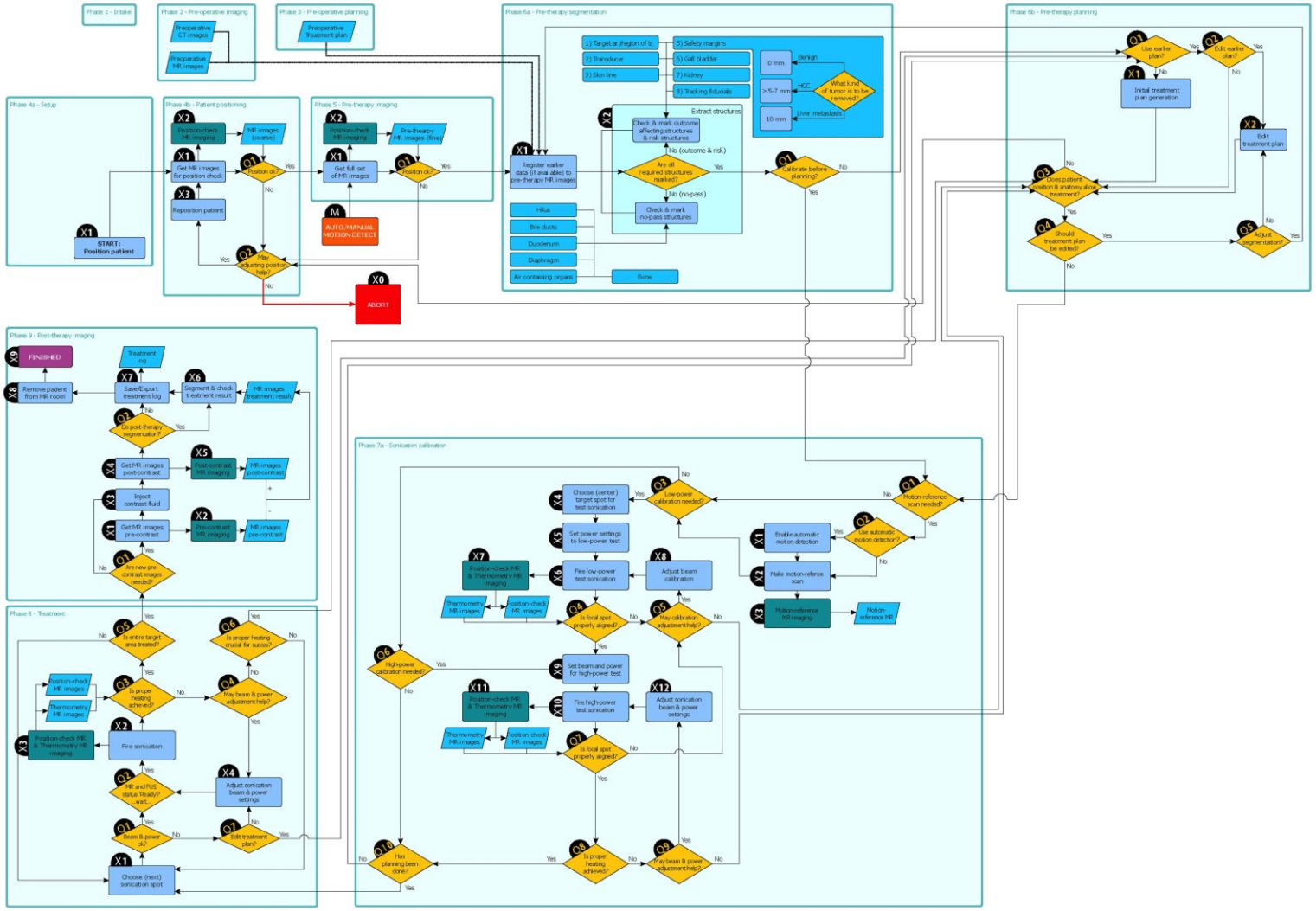


Figure 34 Conceptual model of the MRgFUS procedure current workflow designed through observations of FUS procedures (courtesy of dr. ir. Arjo Loeve, TUDelft, Delft, the Netherlands).

Records of six procedures were collected from the FUS centre in the Amper Klinikum. Table 13 presents standard descriptive analysis for significant events (actions and decision points) within the procedures. The duration times for the rest of events included in Figure 34 but not shown in Table 13 were considered 0 (e.g. instant decision or action with no relevant duration) or were estimated by the two experienced clinicians participating in the study. This information was collected through a questionnaire (see Appendix F). This questionnaire was also focused on identifying the most likely behaviour of the workflow for critical decision points as support for the small number of records available.

Events			Mean (SE) (sec)	Max (sec)	Min (sec)	75% (Q3)	25% (Q1)
Phase	Action	Decision					
4a	X1		531.33 (172.4)	1311	120	830.25	257.25
4b	X1		80.38 (25.05)	339	7	84.5	30
	X3		74.25 (27.96)	196	1	166.25	16.25
		Q1	15.25 (3.94)	47	1	19.75	6.25
		Q2	142.17 (69.58)	405	8	327	11
5	X1		480.29 (70.39)	1320	151	628.5	222.5
		Q1	27.2 (7.87)	50	1	40.5	12.5
6a	X2		333.33 (78.48)	1206	32	447	110
	X3		6.29 (1.94)	13	2	12	2
7a	X4		6.17 (2.83)	20	2	9.5	2
	X5		23.20 (8.87)	55	1	40	9
	X6		101.73 (11.65)	152	47	137	59
	X7		65.62 (9.80)	84	17	84	37
	X8		16.6 (7.26)	43	3	31	3.5
	X9		45.29 (18.75)	133	4	90	5
	X10		70.5 (5.76)	83	49	83	58
	X11		61.17 (5.92)	89	50	68.75	51.5
		Q1	13 (4.31)	38	2	18.75	2.75
		Q4	14.33 (8.37)	53	1	29	1
8	X1		33.41 (1.45)	159	1	38.25	15
	X2		57.88 (0.67)	173	6	66	52
	X3		44.33 (0.67)	156	2	51	38
	X4		32.09 (10.33)	116	1	35	11
		Q1	10.59 (0.81)	132	1	11	2
9	X1		555.40 (134.16)	1065	318	820.5	354.5
	X3		116 (13.83)	142	50	139	98
	X4		376.33 (35.92)	518	268	440	310.75
	X8		444.17 (143.0)	1130	204	609.5	209.25

Table 13. Statistical descriptive analysis for the different stages collected for the MRgFUS procedures. The corresponding events labels for *phase*, *action* and *decision* can be identified in Figure 34.

Probability distributions for data presented in Table 13 were calculated using EasyFit and the A – D GOF test following indications from *Section 3.2.3.2*. As in the

previous cases, it was assumed that distributions had a finite lower bound fixed to 0. For those cases that rejected the null hypothesis, descripted statistics were used as explained in *Chapter 2*. Table 14 presents the probability distributions and their parameters for each action and decision point measured. Distribution curves and corresponding data histograms can be seen in Appendix D.

6.4. Model implementation and validation

The simulation model was implemented in Delmia Quest, using the statistical distributions of Table 14 and the information collected from the questionnaires as inputs.

Event			Distribution	Parameters
Phase	Action	Decision		
4a	X1		Lognormal	μ = 6.02, σ = 0.73 Mean (± SD) = 538.17 (± 454.27)
	X1		Lognormal	μ = 3.95, σ = 0.95 Mean (± SD) = 80.159 (± 93.683)
	X3		Gamma	α = 0.88, β = 84.25
		Q1	Gamma	α = 1.25, β = 12.21
		Q2	Lognormal	μ = 4.00, σ = 1.54 Mean (± SD) = 178.77 (± 559.12)
5	X1		Lognormal	μ = 5.97, σ = 0.63 Mean (± SD) = 480.24 (± 336.86)
		Q1	Triangular	m = 30, a = 0, b = 58.36
6a	X2		Lognormal	μ = 5.44, σ = 0.92 Mean (± SD) = 350.83 (± 404.99)
	X3		Gamma	α = 1.51, β = 4.17
7a	X4		Lognormal	μ = 1.44, σ = 0.79 Mean (± SD) = 5.80 (± 5.43)
	X5		Gamma	α = 1.37, β = 16.95
	X6		Triangular	m = 152, a = 0, b = 152
	X7		Weibull	α = 1.28, β = 78.86, γ = 0 Mean (± SD) = 73.05 (± 57.44)
	X8		Gamma	α = 1.05, β = 15.86
	X9		Lognormal	μ = 3.09, σ = 1.33 Mean (± SD) = 52.81 (± 116.17)
	X10		Gamma	α = 24.96, β = 2.82
	X11		Gamma	α = 17.80, β = 3.44
		Q4	Gamma	α = 1.13, β = 11.45
		Q8	Lognormal	μ = 1.53, σ = 1.62 Mean (± SD) = 17.20 (± 61.37)
8	X1		Lognormal	μ = 3.18, σ = 0.82 Mean (± SD) = 33.82 (± 33.12)
	X2		Gamma (*) Reject hypothesis on A-D	α = 16.44, β = 3.52
	X3		Gamma (*) Reject hypothesis on A-D	α = 9.76, β = 4.54
	X4		Lognormal	μ = 2.88, σ = 1.26 Mean (± SD) = 39.40 (± 77.55)

Event			Distribution	Parameters
Phase	Action	Decision		
		Q1	Lognormal (*) Reject hypothesis on A-D	μ = 1.67, σ = 1.12 Mean (± SD) = 9.98 (± 15.92)
9	X1		Lognormal	μ = 6.22, σ = 0.42 Mean (± SD) = 550.61 (± 241.78)
	X3		Gamma	α = 11.72, β = 9.89
	X4		Gamma	α = 18.29, β = 20.58
	X8		Lognormal	μ = 5.90, σ = 0.58 Mean (± SD) = 433.32 (± 276.65)

Table 14. Statistical distributions and parameters corresponding to each stage collected, where α, m and σ are the shape parameters, and β and μ are the scale parameters, where (*) means that the null hypothesis was rejected but that distribution was selected based on P-P curves and previous literature experience.

In addition to the statistical distributions, the simulating model gathered a number of features to represent the MRgFUS current behaviour in decision points:

"Instant" decisions and actions

As mentioned, there were a number of actions and decisions points which duration was collected as zero. These are represented as empty functions in the DES logic so their execution does not affect the posterior time analysis. This also makes the programming more flexible in case additional data are collected in the future.

Static decision points

A decision point was defined as static when the probability of taking one or the other *branch* did not depend on the number of times that the decision point was executed with the same patient (number of times that the flow passes for that decision point). These probabilities were simply programmed using *if-then-else* statements and were based on the data collected or clinical experience.

Dynamic decision points

A decision point was defined as dynamic when the probabilities of taking one or other branch changed depending on the number of times that the decision point was executed. Since the sample size is not large enough to make an exact estimation on these probabilities, a MKC model was used for this purpose in the same way it was used for the PCI model (Sirl 2005) (see Appendix E for further details on the Markov chain routine used).

Number of sonications

As mentioned, the number of sonication may vary from one patient to another. Judging for the records collected, it was appreciated that some procedures were significant shorter than others. While *short* procedures had a mean of 39 sonications, the *long* procedures had 107 sonications in average. For the simulation study it was decided to consider both type of procedures with a 50% of probability of having either a short or a long procedure. The number of possible sonications was modelled with a Poisson distribution. In 50% of the simulations, a short procedure with a mode of 39 sonications and in the other 50% a Poisson distribution with a mode of 107, indicating a long procedure.

Figure 35 shows the implemented simulating model of the current MRgFUS workflow.

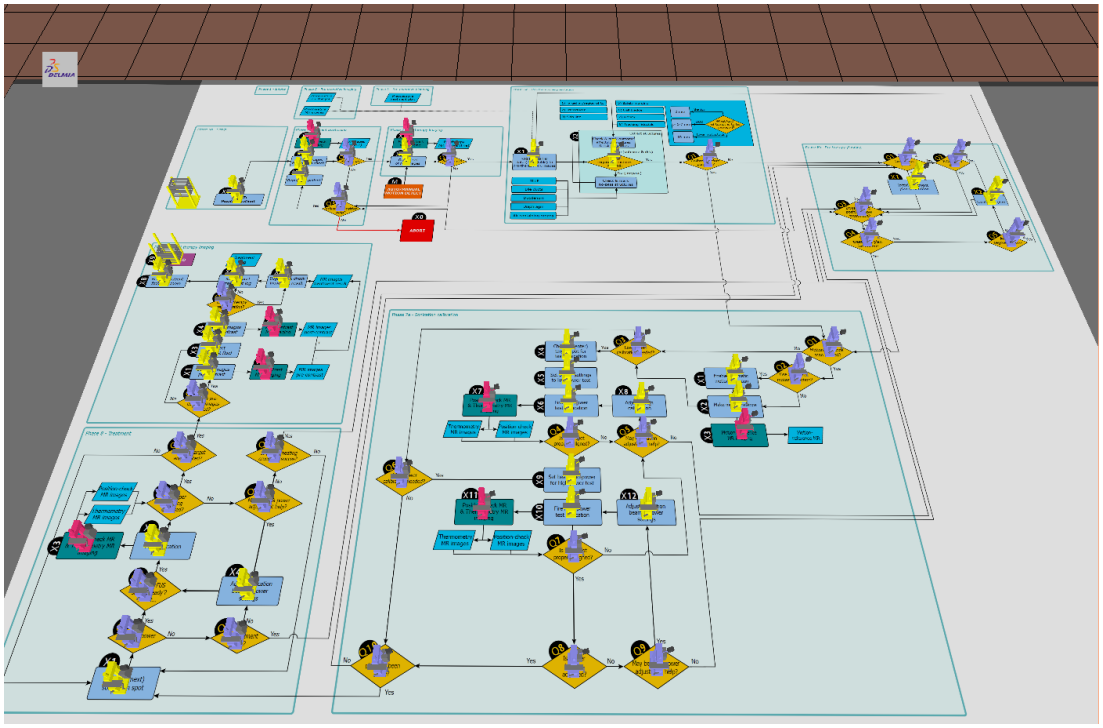


Figure 35 MRgFUS workflow model implemented in Delmia Quest ((Dassault Systèmes S.A., Vélizy-Villacoublay, France).

For validating the model implementation, several indications were followed as indicated in chapter 2:

- Operational behaviour through animations
- Event validity, where the recurrences (loops) were checked accordingly to the real data.
- Internal validity: Welch 90% CI was calculated for the total duration of the procedure, comparing the simulating model with the historical data collected. The large number of stages/decision points and the limited number of records precludes testing test the validity per stage.

To calculate the Welch 90% interval, series of simulations were run: 100, 300, 1000 and 3000 simulations, each simulation containing 30 patients. The number of patients per simulation was taken arbitrary but taking the suggestions given in the software package's manual for statistical calculations. The CI was calculated for the series until finding an interval that would include zero, necessary condition to validate the model in comparison with the real system. The Welch 90% CI resulted [1064.131, -4227.93] and was found when running 3000 simulations, each simulation with 30 patients.

6.5. Simulation analysis

The simulation study compared in first place the relation between motion and procedure duration for the current MRgFUS workflow:

- *Motion relation.* Motion is defined as organ motion that would require making new imaging, having to adjust segmentations and adapt treatment plans. If motion is not detected, it can cause the tissue outside the treatment area to be ablated. The simulation study predicted the effect from the case of *no-motion* up to a 90% motion occurrence (motion alert in 90% of all sonications) in steps of 10% of motion occurrence.

Taking into account the motion occurrence situation, the model was used to simulate the impact in the workflow of new and improved future versions:

- *Automated Segmentation.* This would mean that delineation of risk structures, skin and no-pass zones for instance, and the placement of motion detection fiducials would be done fully automatic by the software instead of manually by the user (radiologist). The effect on procedure durations for all previously

simulated motion occurrence percentages of having automated segmentation was predicted by reducing the times in phases (6a and 9) in which segmentation times are involved.

- *Automated Sonication.* The effect on procedure durations for all previously simulated motion occurrence percentages of having automated sonication was predicted by reducing waiting times around Phase 8Q2 and eliminating Phase 8X4 (see Figure 34), since the system would continuously adapt the sonication parameters to improve the sonication settings and automatically move through the entire treatment area.
- *Combined effect.* The effect on procedure durations of a combination of both the automated segmentation and sonication was predicted for all previously simulated motion occurrence percentages.
- *95% Motion Compensation.* This situation combines all the above mentioned improvements and adds the motion compensation technology. The motion compensation technology includes both tracking of and compensating for organ motion as well as using selectively disabled transducer elements. The situation was modelled by assuming that 95% of all motion occurrences can be successfully dealt by the FUSIMO system. For instance, if there is a 70% probability of detecting motion for each sonication, and the new FUSIMO workflow would be able to compensate the motion for 95% of those cases, the net probability of motion would be 3.5% resulting from $\{[0.7 - (0.7 * 0.95)] * 100\}$. In summary, this motion compensation technology would reduce the number of motion occurrences that actually become problematic and therefore, decreasing the procedural time.

The analysis of each scenario kept the same conditions as when calculating Welch 90% CI, performing 3000 simulations, each simulation with 30 patients.

When analysing the effect of increasing the probability of motion detection, the average duration of the procedure goes from 3h56m45s in case of no motion, up to 256h05m33s in the case of 90% of motion, which means an increase of more than 6390% when motion is detected in the 90% of the sonications.

Figure 36 presents the average MRgFUS procedure duration (in hours) of a procedure for each of the scenarios mentioned above with relation to the increased

probability of motion detection. The figure shows the exponential increase of time related with the increase of probability of motion for the majority of the scenarios. The graph indicates that automating the segmentation decreases the duration in a higher degree that only automating the sonication. This decrease is more noticeable when increasing the motion detection probability and when combining the two effects. In the case of *automated segmentation*, the duration decreased from a 2% in the case of no motion detected up to a 24% in when detecting motion in a 90% of the sonications. In the case of automating the sonication, the effect of this scenario in the duration of the procedure decreases with the probability of motion detection, from 15% in the no motion case to 4% in 90% motion detection case. When combining both scenarios, the average duration of the procedure decreased from 17% in the case of no motion, up to a 28% in the case of 90% motion detection.

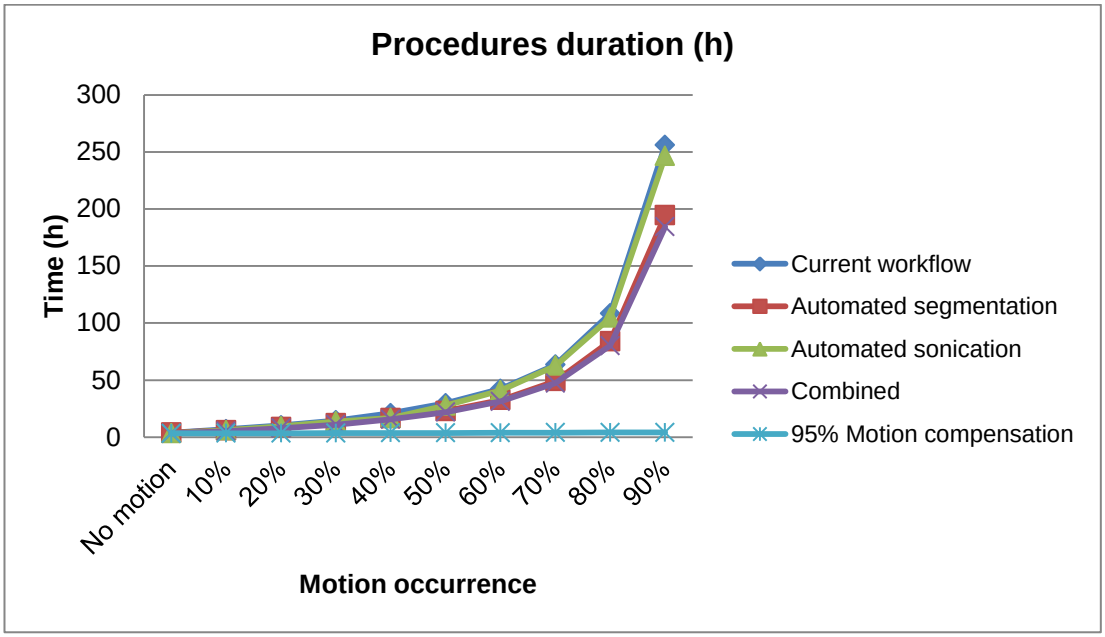


Figure 36 Impact that different scenarios has in the duration (in hours) of the MRgFUS procedures against the probability of having motion per sonication. The five scenarios considered are: current MRgFUS workflow, automated segmentation, automated sonication, combined effect (automated segmentation + automated sonication) and 95% motion compensation effect (motion compensation + combined effect of automated segmentation and sonication).

Finally, when combining the effects of automating the segmentation and the sonication with the motion compensation, the figure shows how the duration of the procedures remains considerably stable with an increase of only the 24% between

the cases of "*no motion*" and 90% of motion detection. In the case of 90% of motion detection per sonication, the added effects of motion compensation and combined effect of automated segmentation and sonication can decrease the duration on a 98.4% with respect to the current workflow, allowing for a 4h:04m:22s procedure as it can be observed in Table 15. Table 15 also shows the average total duration in hh:mm:ss format for each of the rest scenarios considered.

	Total procedure duration (hh:mm:ss)									
	No motion	**10%**	**20%**	**30%**	**40%**	**50%**	**60%**	**70%**	**80%**	**90%**
Current workflow	03:56:45	06:48:59	10:10:23	14:39:24	20:56:13	29:32:55	42:10:04	63:28:37	108:21:01	256:05:33
Autom. segm.	03:52:10	05:59:30	08:38:49	12:00:17	16:40:37	22:50:56	32:35:48	49:09:45	84:00:58	194:29:01
Autom. sonic.	03:21:20	05:59:36	09:26:59	13:44:34	16:40:37	27:41:52	40:59:21	62:31:33	104:42:21	246:25:26
Combined effect	03:17:07	05:13:34	07:53:59	10:59:04	15:30:15	21:50:03	31:17:41	47:19:09	80:06:40	184:22:10
95% Motion comp. + Comb. effect	03:17:07	03:21:23	03:25:29	03:30:23	03:37:23	03:42:48	03:47:01	03:51:31	04:02:49	04:04:22

Table 15. Total average duration (hh:mm:ss) of MRgFUS procedures for each analysed case: current MRgFUS workflow, automated segmentation, automated sonication, combined effect (automated segmentation + automated sonication) and 95% motion compensation effect (including the combined effect of automated segmentation and sonication).

6.6. Discussion

Results showed that performing MRgFUS on moving abdominal organs is currently very time consuming without FUSIMO technology including motion compensation. Future FUSIMO software applications used in parallel with existing software are likely to reduce the impact of organ motion during the treatment, therefore decreasing procedural times. This simulation analysis compared the outcome of the addition of FUSIMO technology to the current MRgFUS workflow by quantifying the relation between motion and procedure duration. This analysis was done in stages to understand the effect of the individual planned improvement.

Predictive analysis allowed calculating realistic expectations of the impact of new and improved versions of the workflow on procedural times. Discrete event

simulation provides therefore a useful and flexible tool when studying systems that do not exist yet in the real world.

Although the current simulation model only contemplates information from the Amper Klinikum, the conceptual workflow model was designed taking into account observations from other centres, e.g. Policlinico Umberto I, Sapienza-University of Rome (Italy). Further analysis could be done in order to compare variables from different centres and how changes in the protocols may affect the overall outcome.

6.7. Summary

This chapter showed how a simulation framework proposed in chapter 2 could be applied to non-vascular IGPs, such as MRgFUS. Very little modifications were done over the original framework. For instance, RADs were not used since the process flow is done mostly by one person (radiologist) so it was considered unnecessary to include them in the description of the conceptual workflow. Simulation was used to predict the impact of planned modifications to the MRgFUS workflow. The results will help the development team of FUSIMO technology to show how their technology could make MRgFUS procedures more efficient without losing efficacy in the treatment.

Chapter 7.
Preliminary results modelling complex vascular procedures: TAVI

7.1. Introduction

Previous chapters presented two cases using the simulation approach to study relatively common vascular interventions. Although these procedures can present complications linked to the condition of the patient, they are performed by small teams, usually composed by an interventional radiologist or cardiologist, one or two nurses and a radiographer. In some cases, a training radiologist participates also during those interventions.

As seen in the introduction, the advances in imaging technology and the design of the new hybrid operating systems allow the performance of more complex image guided procedures. These procedures usually involve large teams and numerous and heterogeneous high technology equipment in the room. An example of these procedures is the transcatheter aortic valve implantation (TAVI) procedure. TAVI is a minimally invasive procedure where a replacement heart valve is delivered via a catheter using one of the following access methods:

- *Transfemoral*: the catheter is inserted in the upper leg
- *Transapical*: the valve is delivered through the wall of the heart
- *Direct aortic*: through a minimally invasive surgical incision into the aorta
- *Subclavian*: the access is beneath the collar bone

Since 2002, when the first TAVI procedure was performed in Europe, this technique is becoming more popular when dealing with operative high-risk patients (Ferrari and von Segesser 2010). TAVI procedures usually involve a large team including interventional radiologists, cardiac-thoracic surgeons, anaesthesiologists, nurses and radiographers. With such a heterogeneous team, planning and training are very important parts to achieve an efficient performance.

The methodological framework presented in this thesis for the use of DES can be applied also to analyse and model workflow for the complex procedures. First version of a simulated model was implemented with data gathered at the Hybrid Operation Room at the Interventional Centre (IC) at Oslo University Hospital (Oslo, Norway). Several members of the IC and Oslo University Hospital participated in this study given expert feedback on design and implementation of the model including mainly: cardiac surgeon Dr Gry Dahle, IC researchers Karl Oyri and Dr Ole Jacob Elle and senior radiographer Hilde Sofie Korslund. Preliminary results are presented in the next section. The limitations of this study and some proposed guidelines to continue this work are given in the last section of the chapter.

7.2. Preliminary results: transfemoral TAVI

7.2.1. Data analysis and conceptual workflow

Records of 6 TAVI procedures performed with the *transfemoral* approach were collected through observations at the IC. Three records were recorded personally attending interventions at the IC. The rest were collected by a medical student at the IC who was provided with a template to collect the information indicated in Table 4. These procedures had an average duration of 3:13:00 (00:09:37) in hh:mm:ss. Table 16 presents the initial statistical analysis over these records.

Events	Mean (SE) (min)	Max (min)	Min (min)	Distribution	Parameters
Other preparation for the patient	17.83 (3.71)	30	7	Gamma	$\alpha = 3.85$ $\beta = 277.79$
Anaesthesia induction (general or local)	47.83 (3.73)	65	38	Erlang	$m = 27$ $\beta = 104.57$
Transoesophageal echocardiography	16.5 (3.22)	25	5	Gamma	$\alpha = 4.37$ $\beta = 226.55$
Right femoral access	20 (2.87)	28	10	Gamma	$\alpha = 8.06$ $\beta = 148.8$
Ventricular pacing	17.83 (1.98)	30	7	Lognormal	$\mu = 5.53$ $\sigma = 0.64$
Left femoral access	4.83 (0.17)	5	4	Gamma	$\alpha = 140.17$ $\beta = 2.07$
Catheter and guidewire guidance	25.83 (8.61)	61	5	Gamma	$\alpha = 1.50$ $\beta = 1032.5$
Balloon placement/inflating/ext	7.83 (2.07)	17	3	Lognormal	$\mu = 5.99$ $\sigma = 0.55$

Events	Mean (SE) (min)	Max (min)	Min (min)	Distribution	Parameters
raction					
Valve implantation (self and balloon expanded)	11.67 (2.04)	20	5	Gamma	$\alpha = 5.43$ $\beta = 128.91$
Screening-contrast test post-treatment	4 (1.12)	9	1	Gamma	$\alpha = 2.10$ $\beta = 114$
Closing	11.67 (1.82)	19	7	Gamma	$\alpha = 6.85$ $\beta = 102.17$
Patient Ready (Awakening - Out of room)	17.83 (2.94)	30	7	Gamma	$\alpha = 7.46$ $\beta = 158.24$

Table 16. Descriptive statistics and statistical distributions fitted for the events collected of TAVI procedures (femoral approach), where α, m and σ are the shape parameters, and β and μ are the scale parameters.

Figure 37 illustrates the conceptual model of TAVI workflow, designed through the observations and with the significant phases taken into account in this preliminary study, already indicated in Table 16. First of all, the patient is prepared in the operating table. This preparation includes several steps that at this moment are considered as a total time. Then, depending on the critical state, the patient is induced under general anaesthesia or under a deep sedation. After that, an endoscopic ultrasound probe is introduced through the patient's oesophagus, to evaluate the heart through ultrasound (transoesophageal echocardiogram). The patient may also be connected at any time to a heart-lung machine for external support in an emergency case. After that, surgeons make two incisions: on the right femoral access to place a ventricular pacemaker and on the left femoral artery, another access used to insert the heart valve after an angioplasty. These phases can be split into several small steps; some of them are executed in parallel by different members of the team. Some of these steps are indicated in grey in the figure but are not taken into account for this first model.

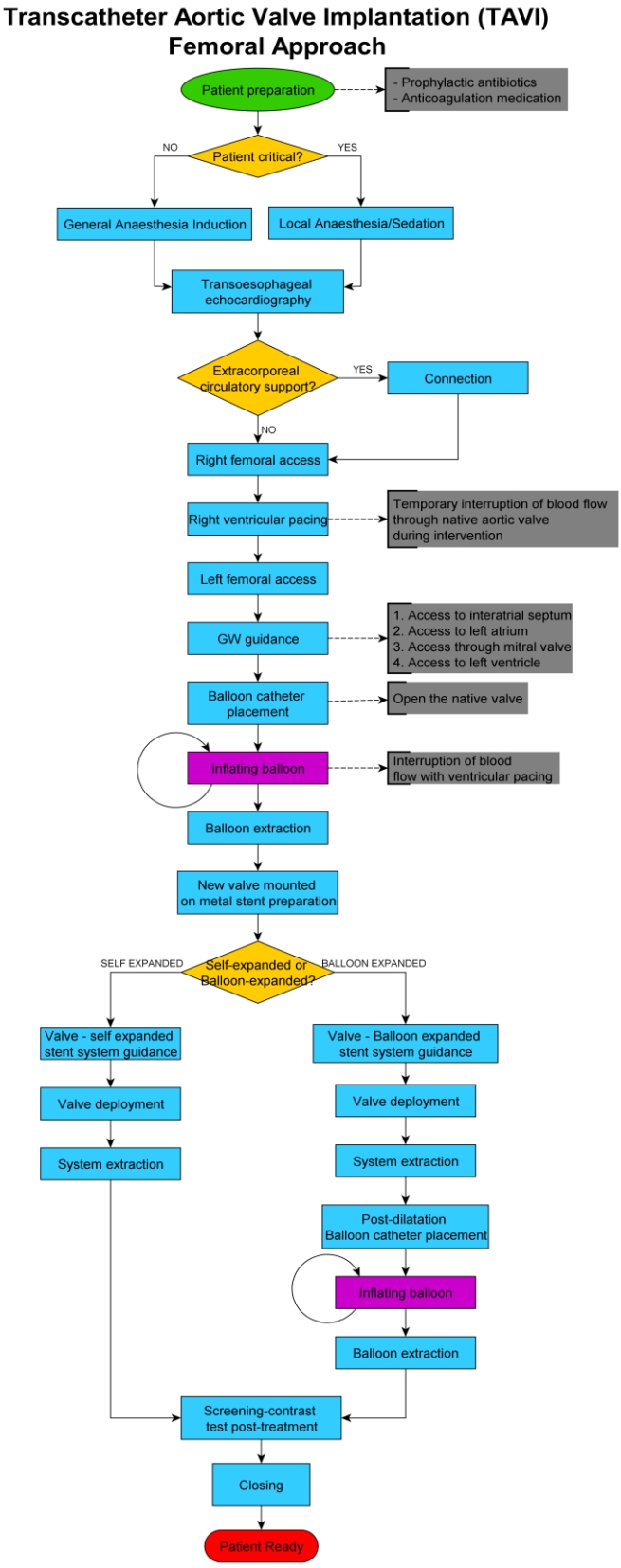


Figure 37 Conceptual model designed from the observations on TAVI procedures (femoral approach). Grey areas indicate features that are not contemplated in current version of the model.

7.2.2. Simulation model

A first version simulation model of the hybrid operation room at the IC was implemented in Delmia Quest. Statistical distributions for the different events according to Table 16 were used as inputs for the DES model. Figure 38 shows a capture of this model with a team of 8 clinicians, although the number of people involved during a real TAVI at the IC can vary from 8 to 15 staff members including surgeons, interventional cardiologists, nurses, radiographers, anaesthesiologists and perfusionists.

Following the established framework, a preliminary simulation analysis was done based on 100 replications (simulations), each of them with 30 patients. The Welch 90% CI for the total duration (in min) resulted [18.67, -20.16], validating then this first version of this model when compared against the real system.

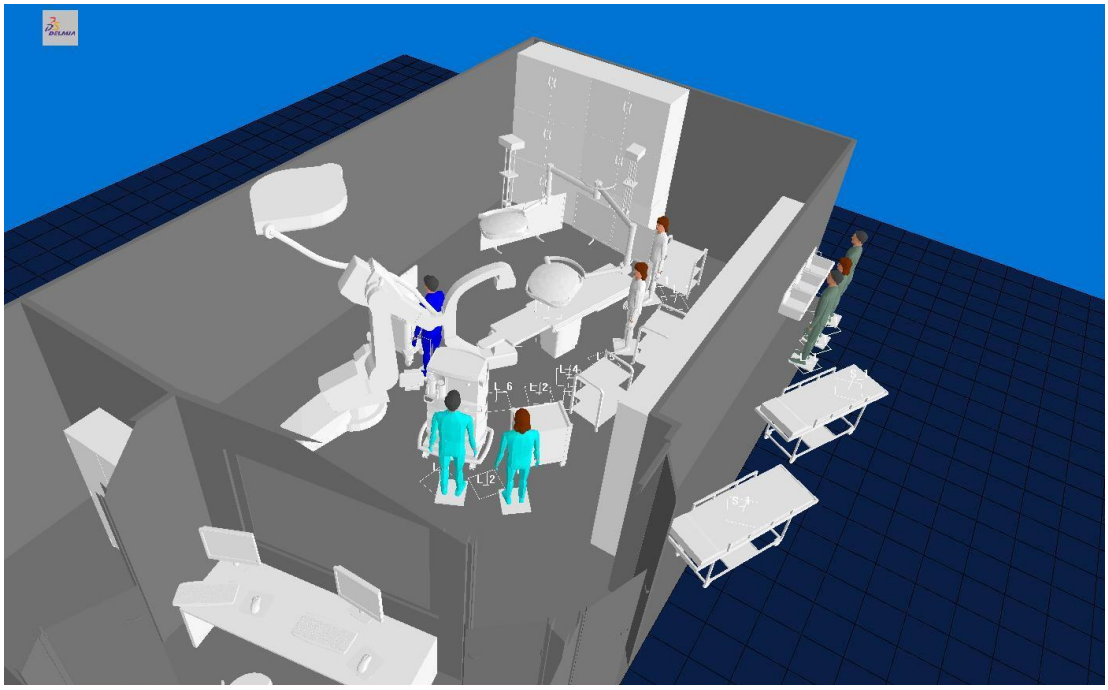


Figure 38. DES model of a TAVI procedure at the hybrid operation room at the Interventional Centre (Oslo University Hospital, Oslo, Norway)

7.3. Discussion

TAVI procedures involve a complex collaboration within the operating room. In addition, several of the tasks are also performed in parallel, fact that is not

contemplated in the current version of the model. Moreover, feedback from clinicians involved in the preliminary study suggested that current defined events should be divided in subtasks, some of them already indicated in Figure 37 (see areas in grey), in order to implement a higher fidelity simulation model. However, observations might not be sufficient to collect this type of information. The suggestion would be to include a multi-video recording system in the operating room so precise records can be captured.

Despite the observed limitations, clinicians agreed on the potential usability of the DES model to compare cost-efficiency between the different TAVIs approaches. A brief review on literature suggests an increasing interest on analysing costs of TAVIs procedures (Fairbairn et al. 2013; Murphy et al. 2013). A detailed workflow model could provide a deeper understanding of these procedures to aid efficiency and cost optimisation.

In the particular case at IC, clinicians identified other potential uses, such as medical training. The presence of a large and heterogeneous team in the OT arises many challenges when identifying team collaborative tasks and when training new staff members on new high-tech facilities. A DES model that contemplates the clinical interactions with the OT may help during the training.

In analogy to the study of fluoroscopy versus MRI – Chapter 8 –, the framework can be also applied in the future to support the design and development of MR-guided TAVI procedures (Andreas Melzer et al. 2014).

7.4. Summary

This chapter presented the preliminary results of the first version DES model of TAVI interventions based on data collected at Oslo University Hospital. Although the model was built around the femoral approach, it could be easily adapted for the other approaches (transapical, aortic or subclavian). This shows how the simulation framework could is adaptable to complex IGPs. However, a higher complexity increases the complexity of the data collection. This makes data collection challenging, requires more time and demands thoroughly planning.

Part II:
Physical Modelling Approach

Chapter 8.

Physical modelling framework for comparative workflow analysis

Contents of this and the following chapter are included in:

Fernández-Gutiérrez F, Martínez S, Rube MA, Cox BF, Fatahi M, Scott-Brown K, Houston G, McLeod H, White R, French K, Gueorguieva M, Immel E, Melzer A. 'Ergonomic workflow and user experience comparative analysis of MRI versus X-Ray guided vascular interventions. Case of study: iliac angioplasty', International Journal of Computer Assisted Radiology and Surgery (submitted)

8.1. Introduction

As seen in *Section 2.3.3*, implementing a physical model is purpose-oriented, aimed to simulate the environment of the real system. Therefore, in order to facilitate the understanding of the framework designed to analyse IGPs workflows using physical models, this section presents the case of use of a comparative workflow analysis of a fluoroscopic and MRI-guided iliac angioplasty on a vascular phantom. The physical environment was prepared using the facilities at the Institute for Medical Science and Technology (University of Dundee, Dundee, UK).

This case study has been developed in collaboration with the Centre for Psychology in the School of Social and Health Sciences at the University of Abertay Dundee (Dundee, UK). Prof Ken Scott-Brown and Dr Santiago Martínez provided support during the design of the experiments and contributed with their experience in the analysis of the protocols from the user experience perspective. Members of the MRI team at IMSaT also collaborated during the preparation of the configurations considered for the study. Specifically, PhD student Martin Rube, research assistant Mahsa Fatahi and research associate Dr Ben Cox from the MRI team at IMSaT prepared balloons, devices, communications and phantom for the experimental setup. Further details can be found at Rube et al. (2014).

As it will be explained in the next section, three clinicians with different levels of experiences participated in the experiments: Dr Graeme Houston (GH), Dr Richard White (RW) and Dr Benjamin Cox (BC). Helen McLeod, researcher at IMSaT and nurse with experience in imaging environments through attendance of several

interventions at the Clinical Radiology department in Ninewells Hospital, assisted the clinicians during all experiments.

8.2. Case study: Fluoroscopic vs. MRI-guided iliac angioplasty

MRI – guided vascular interventions could be a favourable alternative to the conventional fluoroscopic guidance due to added diagnosis value of having a high soft tissue contrast without exposing patients and clinicians to ionising radiation (Krombach 2012). However, MRI environments present operational challenges that need to be addressed in order to make MRI guided procedures comparable to fluoroscopy in terms of safety efficiency and efficacy and to make them acceptable for clinical practice. Much of the current published research has focused on overcoming technical limitations and safety issues (Bock and Wacker 2008; Kos et al. 2008). In addition, concerns on the potential longer procedural times have been reported in previous studies (Saborowski and Saeed 2007; Wacker et al. 2005).

Two studies have been conducted in the field of interventional radiology. Johnson et al. (2006) presented a cognitive task analysis on several fluoroscopy-guided procedures in order to incorporate the acquired knowledge to better simulate models for training. Van Herzeele et al. (2008) applied this concept to a simulator for fluoroscopic treatment of iliac stenoses, comparing trainees and experts. Both studies agreed on the importance of cognitive task analysis as a training method for the development of new protocols.

However, the MRI context is substantially different from angiography suites in terms of patient access, equipment, and physical space available for clinicians as well as significant image acquisition and visualisation differences. Cue retrospective protocol analysis (CPRA) allows for the participant to engage in the primary task without the distraction of concurrent commentary, and includes information that may be subconscious during the primary task and therefore, difficult or impossible to collect with a questionnaire or a conventional question and answer interview (van Gog et al. 2005).

MRI environments for endovascular procedures create other challenges such as the potential occupational hazards that clinicians may face during interventions. In this regard, one important factor to be considered is the risk of a musculoskeletal injury, which in radiology environments can be related to multiple factors such as computer-related activities but also can be suffered while handling patients or standing for long periods of time while wearing the protective lead aprons (Brusin 2011). In addition, uncomfortable postures during the work activity can cause fatigue, pain and reduce concentration, thereby increasing medical errors and the risk for the patient (Harisinghani et al. 2004; García-Lallana et al. 2011). Recent studies highlight the importance of ergonomic analysis when designing new imaging environments for vascular procedures (Sikkink et al. 2008; Rostenberg and Barach 2011). Restricted access to the patients and limited space in the scanner rooms are some of the considerations when analysing ergonomics in MRI suites. However, despite increasing interest in ergonomics in radiology environments, only few authors go beyond suggestions or guidelines to provide a deeper analysis of the environments. Moreover, most analyses are focussed mainly on diagnostic workspaces and on the correct postures for the workstation utilisation (Brusin 2011; Harisinghani et al. 2004; Goyal, Jain, and Rachapalli 2009).

8.3. Environmental setup

As mentioned, the interventions were performed at IMSaT imaging facilities. These installations include an angiography suite and an adjacent MRI scanner room, both connected through sliding shielded doors. The angiography suite accommodates a DSA unit (OEC 9900 Elite, GE Medical Systems, Waukesha, WI, USA). The MRI room is equipped with a 1.5T MRI scanner (Signa HDxt, GE Medical Systems, Waukesha, WI, USA). The transfer between modalities is enabled by the use of a mobile table with radiolucent sliding tabletop (MR surgical suite GE Medical Systems and Maquet, Rastatt, Germany) (see Figure 39a).

In addition to the standard control console for the MRI scanner, another workstation was installed with a real-time MRI software framework (RTHawk, Version 0.9.28, HeartVista, Inc., Los Altos, CA, USA). RTHawk is a flexible research real time MRI software framework that allows the generation of new pulse

sequences and the dynamically change of major aspects of data acquisition on the fly (Santos et al. 2004). Both workstations were in communication via Gigabit Ethernet and were connected via optical fibre cables (M1-1000, Opticis, Sungnam City, Korea) to a shielded 40" LCD monitor (Multeos 401, NEC Corporation, Tokyo, Japan) to display the MR images inside the MRI scanner room (see Figure 39 b).

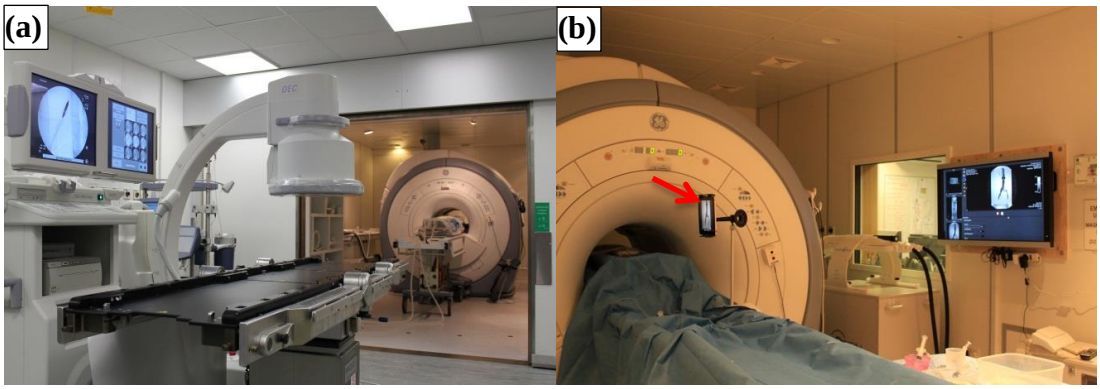


Figure 39. (a) View of the angiography suite connected by sliding door to the MRI suite, (b) MRI suite with the intervention physical layout: a 40" LCD in-room shielded monitor and iPad attached to MRI table (red arrow).

A wireless network was installed in the MRI scanner room with a modified router (DIR615, D-Link, Taipei, Taiwan) with one antenna being positioned in the magnet room and the other one outside the Faraday cage providing a stable network connection throughout both areas. The wireless network enabled the location of three IP webcams in different positions with respect to the MRI scanner: right, left, and in-bore (models M1011w and M1031w, Axis Communications, Lund, Sweden) (Figure 40a-c). Radiologists participating were provided with recording spectacles (PivotHead, models Durango Chameleon and Recon Black Jet frames with no lenses fitted, Cape Evolution Ltd, Greenwood Village, CO, USA) for a first-person experience evaluation (Figure 40d).

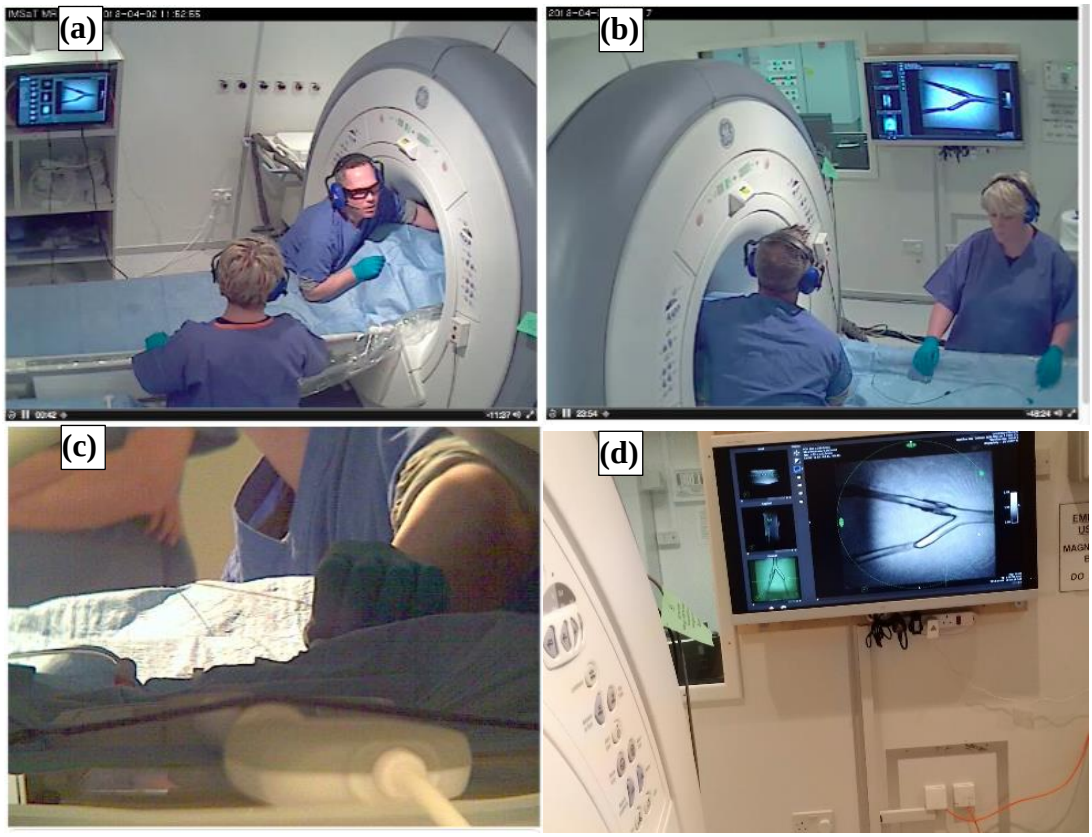


Figure 40. Perspectives of the cameras arranged in the MRI suite during the interventions: (a) right, (b) left, (c) bore, (d) first-person.

In addition, an MRI-safe wireless in-room operator control system based on mobile touchscreen devices (iPad 1, Apple Inc., Cupertino, CA, US) was implemented as part of the experimental setups evaluated. Physician and operator used a second tablet device (iPad 3, Apple Inc., Cupertino, CA, US) and Bluetooth earphones (Calisto B70, Plantronics, Santa Cruz, CA, USA) for communication during the procedures. The earphones were positioned under the noise protection earmuffs.

The experimental setups were all conducted on an arterial vessel phantom (see Figure 41) consisting of linked femoral, abdominal and thoracic module (L-F-S-Left-003, A-S-N-001, T-R-N-020, Elastrat, Sarl, Switzerland). The phantom was connected to a heart-lung machine (HL-30, Maquet, Rastatt, Germany), customising one HL-30 D150 pump to mimic (pulsatile) physiologic flow. A permanent introducer sheath (12F) was inserted into the femoral artery to facilitate access and exchange of devices during the interventions.

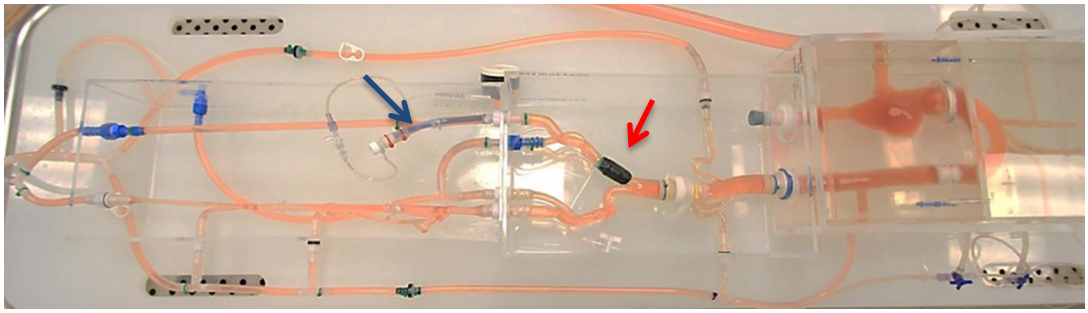


Figure 41. Fully perfused thorax to above the knee vascular phantom (Elastrat, Sarl, Switzerland). Blue arrow indicates the 12F sheath introducer used for permanent access. Red arrow indicates a neonatal pressure cuff (SoftCheck Neonatals, Statcorp Medical, Jacksonville, FL, USA) that was attached to the right common iliac artery to mimic a stenosis.

Commercially available non-braided balloon catheters (5F PTA Balloon catheter, Workhorse II, AngioDynamics, Lathan, NY, US) were customised by attaching a resonant circuit 5mm distally to the inflatable balloon (Burl, Coutts, and Young 1996). Each resonant circuit was tuned to 63.8 MHz (the proton Larmor frequency at 1.5T) in 0.9% saline solution.

8.4. Methodology

Procedure

A total of 43 uncomplicated percutaneous transluminal angioplasties of the iliac artery (PTA-IA) were performed in the phantom (9 under fluoroscopy and 34 under MRI guidance). The aims were: 1) to identify and evaluate the procedural differences between a fluoroscopy-guided and an MRI-driven procedure; and 2) analyse the potential effects on the performance and clinical experience during vascular interventions.

A standard protocol for PTA-IA, followed in the Clinical Radiology department in Ninewells Hospital (Dundee, UK) was adapted for the experiments. Observations of real iliac angioplasty procedures were carried out at the angiography suites and the corresponding information detailed in Table 4 was collected during the interventions. The records were used in the conceptual designed of the adapted PTA-IA protocol with is shown in Figure 42(a).

Figure 42(b) presents the alternative protocol proposed for the MRI-guided procedures, which significant phases were intentionally designed to be similar to the fluoroscopy driven procedure for better acceptance by the clinicians. Some stages were not taken into account in the study for practical reasons (in grey in the figure), such as consideration of total arterial occlusion or tasks related to the preparation of the phantom.

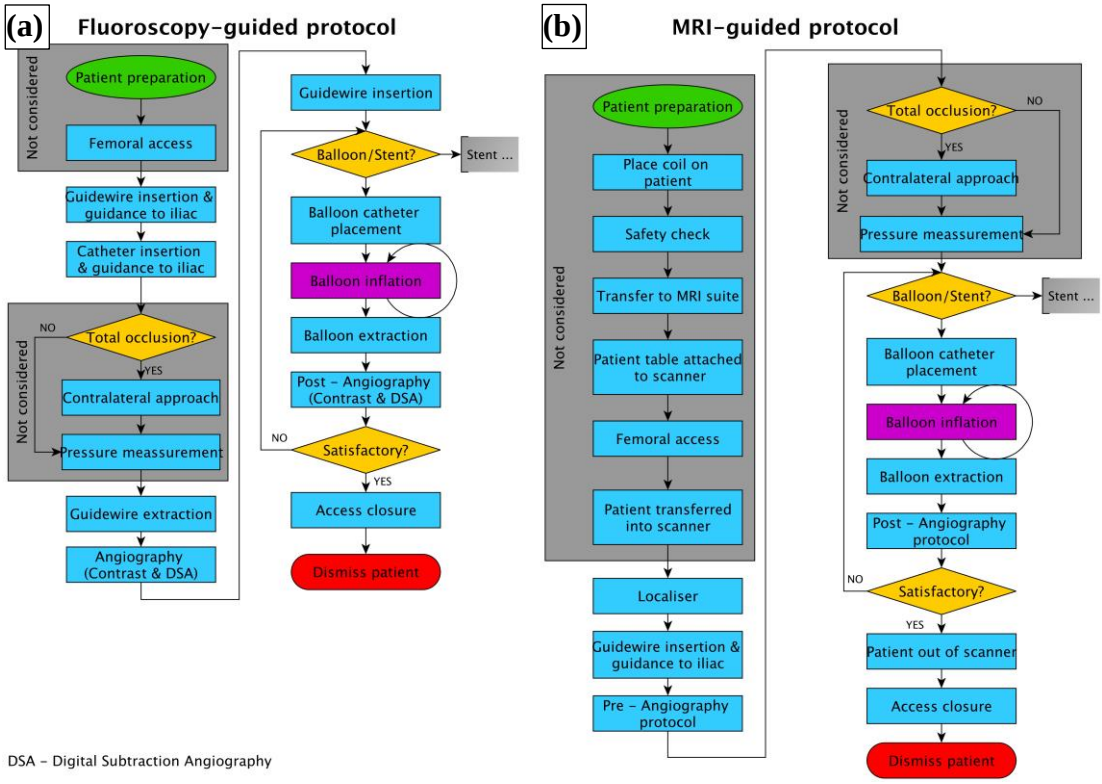


Figure 42. (a) PTA-IA for the iliac artery under fluoroscopy and under MRI guidance (b) followed during the experiments. The grey areas indicate the tasks that are not considered for the study.

Clinicians

Three clinicians with different levels of expertise participated in the experiments:

- GH, senior interventional radiologist (consultant) with more than 20 years of experience in vascular procedures.
- RW, final-year specialty trainee interventional radiologist (3 years' experience in vascular procedures).
- BC, trainee physician with no experience in clinical interventional radiology.

While GH and BC were both familiar with MRI environments and the facilities prior to this study, RW had no previous experience in MRI.

Methodology

Each clinician (GH, RW and BC) performed three repetitions (nine in total) of PTA-IA under fluoroscopy guidance following the adapted protocol presented in Figure 42(a). Times were collected for the durations of the significant phases indicated in the figure. This protocol was established as baseline for the operational comparison with the MRI environment.

To prepare the MRI environment for the comparative analysis, a pilot study was performed with the participation of all three clinicians. A total of 16 MRI guided PTA-IA were performed during this pilot study. Qualitative feedback was requested on six different configurations for the MRI suite. Table 17 shows the summary of these configurations. The changes considered in the setups consisted of: varying the workstation controlling the scanner (RTHawk or Standard Interface – GE iDrive); varying the in-room visualisation equipment; and whether or not the Bluetooth earphones for communication between the scanner and control rooms were used.

Configuration	Communication with Control Room	Workstation	Visualisation
I - GEScreenBT	Bluetooth	Standard	In-room monitor
II - GEiPadBT			iPad
III - RTScreenBT		RTHawk	In-room monitor
IV - RTiPadBT			iPad
V - GEScreen	None	Standard	In-room monitor
VI - RTScreen		RTHawk	In-room monitor

Table 17. MRI configurations evaluated

The clinicians' report requested after the pilot study highlighted the need for communication between the clinician inside the scanner room and the controller inside the control room during the procedures. Following this feedback, only four configurations incorporating the preferred two-way voice communication (i.e. Bluetooth earphones) – I to IV in Table 17–, were taken forward in a second block of experiments under MRI guidance.

Due to limited clinicians' availability, only GH and BC participated in this second block of experiments, where times were collected for the MRI-guided procedure stages. Also, additional information was compiled such as discussions between the teamwork and any difficulty found with the vascular model or the devices.

All procedures were audio-visually recorded from two personal perspectives: a third-person perspective with 4 cameras, one positioned on a tripod to record the fluoroscopic guided interventions and 3 IP cameras (see Facilities and equipment) for the MR-guided procedures, placed as explained in the previous section; and a first-person perspective with high definition (HD; considered conditionally MRI-safe) recording spectacles worn by each clinician.

Cued retrospective protocol analysis

A CRPA was carried out with clinicians GH and BC, who completed all sets of experiments in fluoroscopy and MRI. The CRPA analysis included interviews and analysis of their commentary gathered while viewing their own audio-visual recordings obtained during interventions (see Figure 43). Oral descriptions were recorded from the clinicians when they simultaneously were visualising their own operation in first-person (i.e., HD spectacles camera) and third-person perspectives (i.e., front, rear and bore). In total, 4 perspectives were concurrently shown (see Figure 40) in one large screen (3200 x 1200 resolution with a length of 5.7 metres). The clinicians' viva voice and the visualised material were recorded.

As an additional information gathering exercise, the participants engaged in CRPA wore a head mounted iView-X HED eye movement recording device (SensoMotoric Instruments GmbH (SMI), Warthestraße, 21D-14513, Teltow, Germany) which is indicated in Figure 43 by the red cursor. This system allows for free head movement during commentary and records the eye gaze position at 30Hz frequency with an accuracy of 0.5 degrees of visual angle. A 5-point calibration protocol was conducted to ensure accurate recordings by ensuring participants look at each corner of the monitor and the centre while the experimenter registers eye position on the associated iView software. The resulting recordings provide a first person perspective video with overlaid gaze cursor. This is then used by the experimenter in the review of the CRPA to inform the viewer of the gaze associated

with individual elements of the task. CRPA recordings of these tasks were reviewed to identify the factors that influenced the performance of the procedures, both for MRI and fluoroscopy guidance.

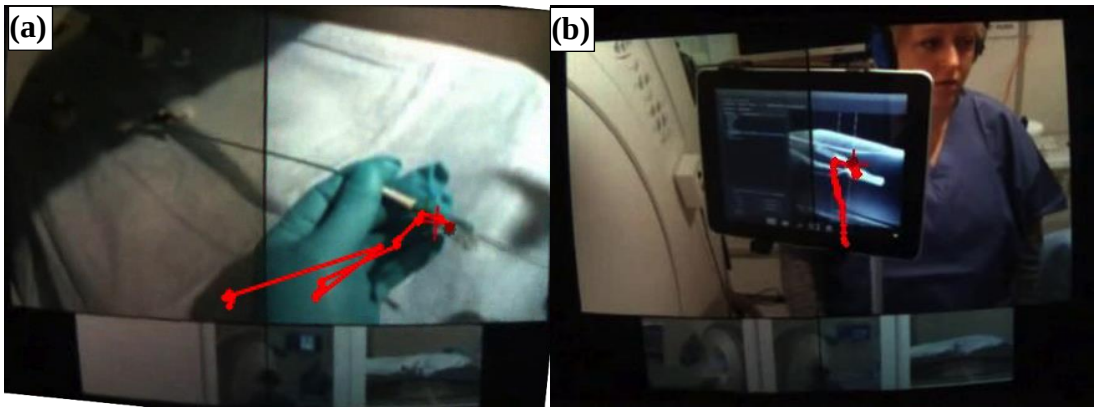


Figure 43. CRPA interviews with clinicians. Figure (a) and (b) illustrate the first and second person perspectives (lower part of the images) with overlaid gaze cursor. This red cursor shows the location of the eye gaze on the image for the current location and the previous 0.25 of a second.

8.5. Statistical analysis

The generalised estimating equations (GEE) method for repeated measures was used to analyse the complete dataset after the second block of experiments (Ballinger 2004). GEE provides a robust analytic tool when variables might not be normally distributed and there could be a correlation between subjects. For the purpose of this research and following the literature, gamma distribution was assumed for the tasks completion times (Law 2007). In addition, first-order autoregressive correlation was considered as a robust design measure for the GEE analysis.

During the experimentation, values of several variables were unavailable (13.5% of the total values collected) due to the restricted availability of the clinicians. Due to the low number of repetitions for each configuration (n = 2 or 3 depending on the case) and that the data was missing completely at random (MCAR), multiple imputation (MI) method was used to generate the missing values (Ibrahim et al. 2005; He 2010). Five imputed datasets were created using the fully conditional specification approach in IBM SPSS v21.0.0 (New York, USA) (van Buuren 2007).

This approach uses all variables as possible predictors for the MI analysis, including the ones that do not have missing values. The rest of parameters are as follows:

- *Method*: Markov chain Monte Carlo. Maximum iterations = 10.
- *Constraints*: Minimum = 0, maximum cases draws = 50, maximum parameter draws = 50.

Results using MI were compared repeating the analysis without the imputed data to test the robustness of the analyses.

8.6. Ergonomic analysis

CRPA interviews and the multi-video recordings were used to identify clinical perceptions about postures in the MRI environment. A RULA (Rapid Upper Limb Assessment) analysis was implemented over the positions identified (McAtamney and Nigel Corlett 1993) using DHM models in Delmia for Human Ergonomics Design and Analysis software module.

The RULA risk analysis gives scores from 1 (the posture is acceptable) to 7 (changes are required immediately). This global score is calculated by taking two groups of posture scores. The first group – posture A in Figure 44– is calculated based on individual scores for the upper arm, lower arm, wrist and wrist twist posture, and also considering the muscle use and force scores. The second group – posture B in Figure 44 – is obtained from individual scores for the neck, trunk and legs, together with the corresponding effect of the muscles and forces required to maintain the posture. A score of '1' is given to a posture of a segment when the risks factors present are minimal. Then, points are added when the segment reaches particular angles. An example of how the points are calculated is shown in Figure 45. To interpret these scores, the RULA analysis provide a colour coding for 6 of the 13 individual scores: green for scores of 1-2, yellow for 3-4, orange for 5-6 and red for 7. Interpretation of these values is given in Table 18. Details of how this is provided within the Delmia environment is shown in Figure 46.

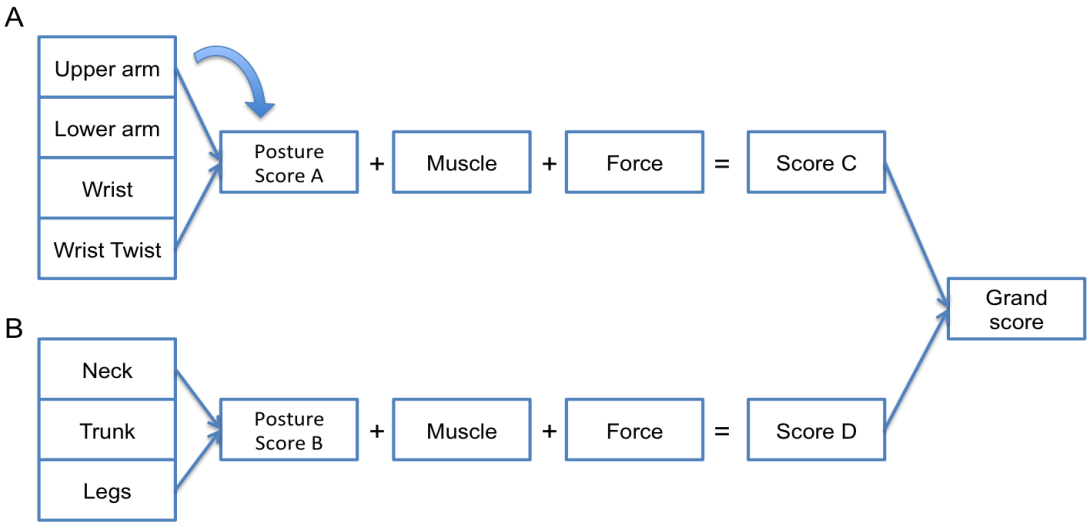


Figure 44. Diagram showing how the global or grand score is calculated from the grouped scores in A and B.

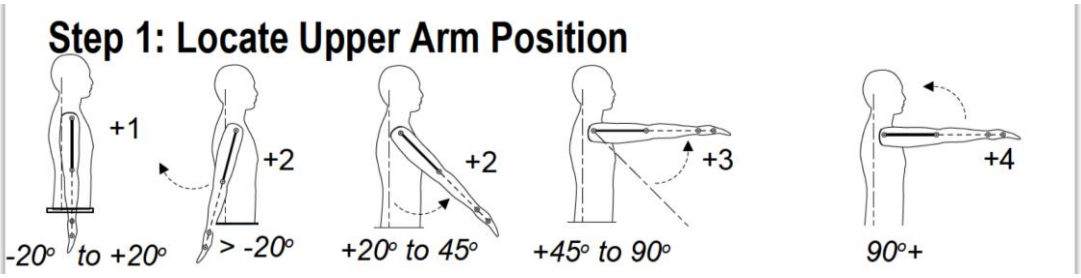


Figure 45. Upper Arm posture score calculation

Action Level	RULA score	Interpretation
1	1-2	The person is working in the best posture with no risk of injury from their work posture
2	3-4	The person is working in a posture that could present some risk of injury from their work posture, and this score most likely is the result of one part of the body being in a deviated and awkward position, so this should be investigated and corrected
3	5-6	The person is working in a poor posture with a risk of injury from their work posture, and the reasons for this need to be investigated and changed in the near future to prevent an injury
4	7+	The person is working in the worst posture with an immediate risk of injury from their work posture, and the reasons for this need to be investigated and changed immediately to prevent an injury

Table 18. RULA scores classification and interpretation

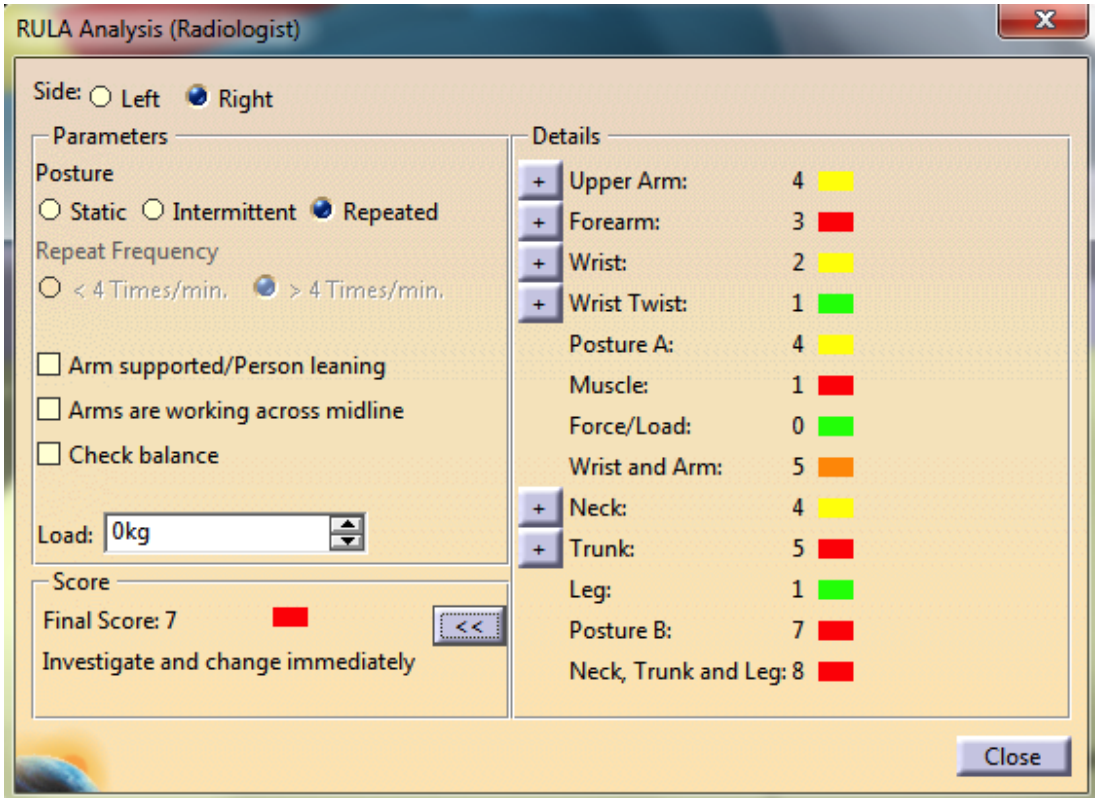


Figure 46. Detail of menu for RULA risk analysis on Delmia for Human Ergonomics Design and Analysis. General parameters regarding the posture are set on the left side of the menu, which shows also the global score. Current scores for postures A and B are given colour labelled on the right side of the menu.

To perform the analysis, simulated 3D environments were implemented using a 50th percentile male manikin (173.cm height and 76.20 Kg weight (Woodson et al., 1992)) as DHM. A comparison was done to measure the effect that different scenarios might have in the defined postures. The usual posture adopted by clinicians in angiography suites, which also corresponds with the initial defined position (further referred as position 1), was set as the baseline to compare with the MRI scenarios. The analysis made a distinction on the type of evaluated activity: static (position held for more than one minute); intermittent (position held less than one minute) or repeated (position repeated a minimum of three times during the activity).

In the first instance, the RULA analysis was applied to the postures on the 3D model of a 1.5T Signa MRI scanner (GE Healthcare, Waukesha, WI, USA) with a 60cm diameter bore, as also used for the clinicians during the experiments. The output was compared to a simulation on a 70cm wide bore 3T Discovery MRI scanner (GE Healthcare, Waukesha, WI, USA) and a 1T open bore Panorama MRI

scanner (Philips, Eindhoven, The Netherlands) (see Figure 3 (a) and (b)). A simple scale CAD model of the 1.5T Signa MRI scanner was implemented by IMSaT student Christoph Boerzsoenyl. CAD scale models of the Discovery and Panorama were kindly provided by GE Healthcare and Philips respectively. In addition, three more scenarios were compared to improve the comfort of postures during interventions; firstly, to measure the effect of integrating an arm-supporting device; secondly, to study the impact of an adjustable platform for personalised height and finally a combination of both previous scenarios.

8.7. Summary

This chapter presented a framework to design a purpose-oriented physical model to analyse and compare workflow for fluoroscopy and MRI-guided vascular procedures. The case was based on the study of iliac angioplasty and described four blocks in which the framework is divided. Firstly, the environmental setup is presented, including the description of the devices used and the angiography and MRI rooms. Then, the methodology is explained, which includes the protocols that were tested, the clinicians that participated as well as the configurations that were evaluated quantitatively (time-based analysis) and qualitatively, through the CRPA. The third block presents the statistical analysis over the data collected and the last block describes how an ergonomic analysis was performed in a simulation using RULA analysis in Delmia Human and Ergonomics simulated environment. The next chapter presents the results obtained in these four blocks and discuss the main findings.

Chapter 9.

9.1. Results: Fluoroscopy versus MRI – an iliac angioplasty case studyIntroduction

Section 2.3 presented a framework to use a purpose-oriented physical model to compare vascular IGPs workflows based on the case study of a common iliac angioplasty. Results of the comparison of fluoroscopy versus MRI guidance are presented in this chapter to validate the framework for developing novel procedures. The results are divided in three parts: time-based task analysis, cognitive and user experience analysis and ergonomic evaluation of the MRI environment for interventions. The significant findings are discussed in the last section.

9.2. Task analysis

In total, 43 procedures were recorded, 9 under fluoroscopy and 34 under MRI guidance. As mentioned in *Section 8.4*, 16 MRI-guided procedures were performed during the pilot study. Table 19 presents the total procedure times for the 9 fluoroscopy interventions and the 18 MRI-guided PTA-IA collected during the second block of experiments. The procedure times are shown in minutes and per configuration per clinician. The mean total duration was 12.08 (0.95) (mean (standard error - SE) minutes (min) per procedure.

Configuration	Total duration per clinician (Mean (SE)) (min)		Total Duration (Mean (SE)) (min)
	Clinician GH	Clinician BC	
Fluoroscopy (baseline)	7.47 (0.77)	9.53 (1.08)	8.49 (0.75)
I - GEScreenBT	17.82 (0.96)	18.36 (0.94)	18.09 (0.57)
II - GEiPadBT	16.37 (0.14)	18.43 (1.66)	17.19 (0.73)
III - RTScreenBT	7.32 (0.07)	9.39 (0.72)	8.56 (0.64)
IV - RTiPadBT	7.71 (1.17)	11.25 (0.13)	9.48 (1.13)

Table 19. Total procedure times in minutes for fluoroscopy guided procedures and MRI configurations evaluated (see Table 17) during the second block of sessions. All the times are expressed in mean (standard error).

The overall performance of clinician GH was significantly ($p<0.001$) faster than clinician BC, taking the first one an average of 11.43 (1.43) min versus the 12.74 (1.27) min of clinician BC. When comparing the different configurations of MRI guidance versus the standard fluoroscopy protocol, the GEE analysis revealed significant difference ($p<0.05$) when the MRI standard control console was used (GEScreenBT and GEPadBT in Table 17), and also when the RTHawk control console was used together with the iPad (RTiPadBT in Table 17). There was no significant difference in the overall performance of the standard fluoroscopy protocol (8.49 (0.75) min) when compared with the RTHawk control console using the LCD in-room monitor (8.56 (0.64) min).

Table 20 also shows an overall better performance using RTHawk, comparable to the times obtained with the standard protocol. As indicated in the physical modelling framework, RTHawk allows changes between pulse sequences and parameters during the intervention on the fly, which avoids delays. In addition, the user interface can be designed in terms of controls and views for the radiologists needs.

In addition, a more detailed analysis of the differences between clinicians and configurations for the stages indicated in Figure 42 was performed, with the ones considered more relevant for the study reported here. The treatment phase was defined from the moment the balloon catheter was inserted until the moment the balloon was extracted after inflation. For these stages, performance of clinicians GH and BC were compared during the fluoroscopy procedure and the MRI-guided configurations. Configurations II – GEiPadBT and IV – RTiPadBT were significantly different when compared with the performance under fluoroscopic guidance. As seen in Table 20, in GEiPadBT times were on average faster (3.14 (0.28) min) than in fluoroscopy (3.63 (0.27) min), while RTiPadBT took longer (4.25 (0.45) min). However, it can be seen that although GEiPadBT was slightly faster than the X-Ray procedure for the treatment times, overall GEScreenBT and GEiPadBT were slower than the others (see Table 19). This is explained when looking at the pre- and post-angiography times (see Table 20). In GEScreenBT and GEiPadBT, these phases took significantly ($p < 0.01$) longer than in the fluoroscopically guided procedure. On the contrary, in RTScreenBT and RTiPadBT, these times were similar.

Configuration	Treatment (Mean (SE)) (min)	Pre-angiography (Mean (SE)) (min)	Post-angiography (Mean (SE)) (min)
Fluoroscopy (baseline)	3.63 (0.27)	1.71 (0.24)	1.94 (0.25)
I – GEScreenBT	3.23 (0.25)	6.28 (0.05)	5.61 (0.11)
II – GEiPadBT	3.14 (0.28)	6.00 (0.14)	5.70 (0.31)
III – RTScreenBT	3.33 (0.35)	1.34 (0.18)	1.72 (0.17)
IV - RTiPadBT	4.25 (0.45)	1.38 (0.01)	1.47 (0.04)

Table 20. Average durations per configuration for the phases of treatment, pre-angiography and post-angiography protocols.

9.3. Cognitive and user experience analysis

Figure 47 provides an overview of the factors most frequently discussed by clinicians GH and BC during the interviews. The importance level of these factors was classified qualitatively by the number of times they were referred to during the interviews and is graphically indicated by the size of the particular bubble with their name in the figure. In addition and for clarity, they were primarily grouped according to their nature: communication; visualisation and ergonomics. The diagram also shows the hierarchical dependency within the groups (black arrows) and the interrelations among factors from different groups (red arrows). In a general evaluation of the groups, communication appeared as the most important factor during all procedures, followed by visualisation. Ergonomics inside the room was important for the clinicians but in a lower degree. Specifically within the groups, communication with the control room was given a higher importance than the communication inside the room. In the same way, clinicians considered that the visualisation of devices was critical during the procedures. Moreover, the type of screen played an important role. To a lower degree, the clinicians considered that the acquisition of MRI images should be improved as appreciative differences were encountered when compared to DSA. By contrast, the clinicians mentioned the importance of the temporal and spatial resolution of interventional MRI images, but rated these sufficient with the current MRI pulse sequences used in the proposed protocol (Rube et al. 2014).

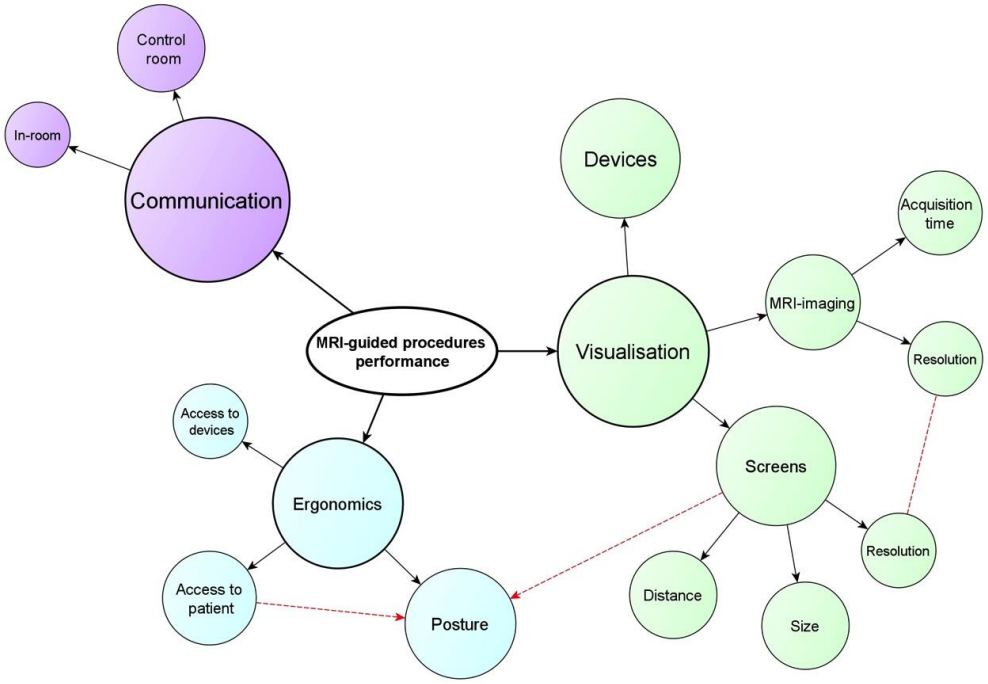


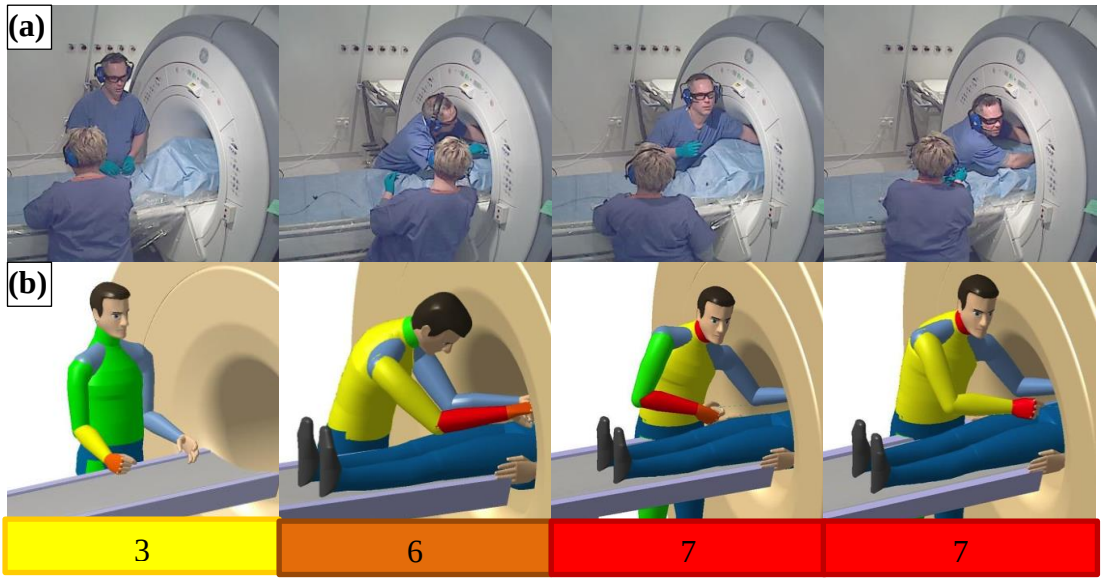
Figure 47. CRPA diagram illustrating main factors that affect an intervention according to the feedback of the clinicians. The size of a bubble represents the importance level given by the clinicians during the interviews: A larger bubble means higher importance. Black arrows represent the hierarchy within a group. A red arrow indicates an interrelation between factors of two different groups.

9.4. Ergonomic analysis

The information gathered by the multiple video recordings showed that clinicians maintained ergonomically disadvantageous postures while carrying out the procedures under MRI in comparison with the performance in the angiography suite. Clinicians explicitly confirmed that these postures were uncomfortable during the CRPA interviews. As a result, a pilot ergonomic assessment of the MRI environment for IGP was carried out using the RULA analysis (see *Section 8.6*).

Four key positions were identified as being repeatedly adopted by the clinicians during the MRI-guided procedures: one ‘rest’ position (position 1) and three operating positions (positions 2 – 4). As mentioned in *Section 8.6*, the analysis was applied to 3 MRI scanners: 1.5T Signa MRI scanner with 60cm diameter bore, 3T Discovery MRI scanner with a 70cm bore and the 1T open bore Panorama MRI scanner.

Figure 48 and Figure 49 show the RULA analysis applied to the three types of MRI scanners considered. Figure 48 displays in the first row (a) screenshots of clinician BC during an MRI-guided procedure holding positions 1 to 4 defined for the analysis. Below, rows (b) and (c) show the corresponding DHMs for two of the MRI scanners considered, 1.5T GE Signa and 3T GE Discovery. The DHM scenario for the 1T open bore Panorama MRI scanner is shown separately in Figure 49 due to the notable differences on shape of the scanner and to give a better perspective of the postures. For the scenario with the open bore Panorama MRI scanner, it was not possible to obtain real video images of an MRI-guided intervention. Images of interventional radiologists using the open bore Panorama MRI scanner, courtesy of Prof. Ulf Teichgräber at Charité Berlin (Berlin, Germany), were used for this purpose (see Figure 50). For this particular case, postures 3 and 4 are considered the same as the screen used for the navigation would be likely to be on the other side of the scanner which does not happen with the close bore scanners (see Figure 50(a)). Below all virtual environments, RULA global scores are given for each posture position. Posture 1 was considered static, posture 2 was considered intermittent and the rest were considered repeated. The scores show very small differences between the postures held using all scanners and indicate that positions 2 – 4 are ergonomically not acceptable for day-to-day practice.



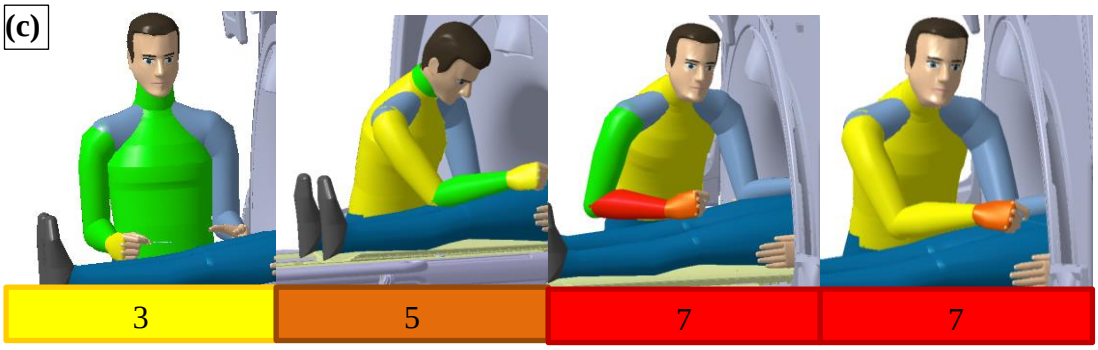


Figure 48. Screenshot of key postures 1 – 4 defined during a MRI-guided procedure for clinician BC (first row (a)), equivalent postures modelled in Delmia V5R20 for the 1.5T GE Signa MRI scanner (second row (b)) and the 3T GE Discovery MRI scanner (third row (c)) (GE Healthcare, Waukesha, WI, USA). Below the virtual environments, global scores given by the RULA analysis are shown.

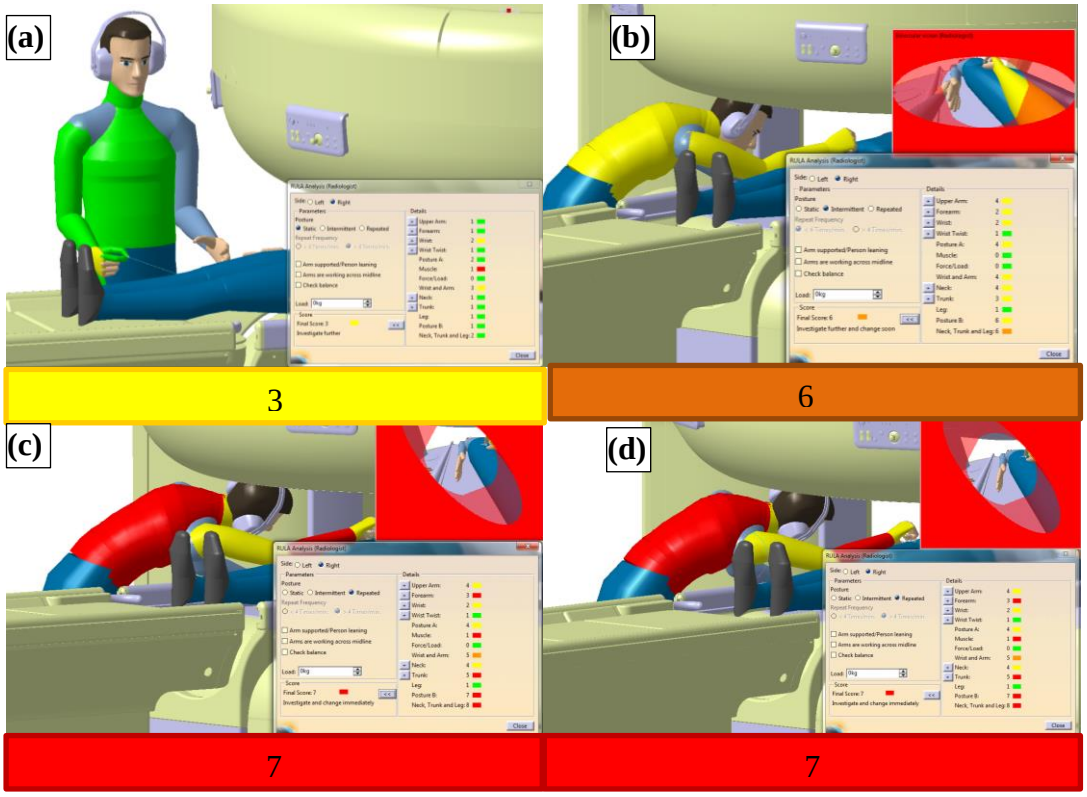


Figure 49. RULA analysis applied to the 1T open bore Panorama MRI scanner (Philips, Eindhoven, The Netherlands); (a) to (d) in the figure correspond to defined postures 1 to 4, respectively. Below the virtual environments, global scores given by the RULA analysis are shown.

Figure 50. Interventional radiologists using the 1T open bore Panorama MRI scanner. Images courtesy of Prof. Ulf Teichgräber at Charité Berlin (Berlin, Germany).

The results regarding the second part of the ergonomic analysis are shown in Table 21. This table compares the RULA global scores for the initial test with the three alternatives scenarios considered: adding an arm-support, an adjustable height platform and a combination of both. The arm-support can be added in the Delmia RULA context menu as virtual feature to provide support to the lower arm segment, from the elbow to the wrist. With an adjustable height platform, the height of the manikin was reduced until a comfortable position for the lower back was found, resulting in a deduction of -10cm for the manikin measures.

	1.5T GE Signa (60cm bore)				3T GE Discovery (70cm bore)				1T open bore Philips Panorama			
	Initial	Arm-Support	Height platform	Combined effect	Initial	Arm-Support	Height platform	Combined effect	Initial	Arm-Support	Height platform	Combined effect
Posture 1	3	3	3	3	3	3	3	3	3	3	3	3
Posture 2	6	6	5	4	5	4	3	3	6	6	6	5
Posture 3	7	6	3	3	7	6	3	3	7	7	7	6
Posture 4	7	6	6	5	7	6	3	3	7	7	7	6

Table 21. RULA global scores obtained for the additional tests: added arm-support, adjustable height platform and a combination of the two factors for all three MRI scanners considered.

Results show a slight improvement for postures 2 and 3 for all types of scanners when adding the arm-support. However, for posture 4, this improvement is only appreciable for the Signa and Discovery MRI scanners. When adjusting the virtual height platform to the recommended height, the improvement was substantial for all postures in the case of the Discovery MRI scanner. This was less significant in the case of the Signa scanner and only posture 3 got notably improved. The same results were noted when combining the arm-support with the height platform effect for both

closed bore scanners. In the case of the Panorama MRI scanner, adding the height platform or both, arm-support and height platform, did not introduce any significant improvement in the postures.

9.5. Discussion

The time-based task analysis revealed that it is possible to reduce the duration of a PTA-IA procedure under MRI guidance to the usual duration under fluoroscopy. Since several scenarios in MRI were considered for the study, it was possible to identify which elements played an important role during the performance. During the first block of sessions, overall times collected for MRI revealed that the total duration of the procedures using the standard control console with no communication system installed between the control room and the scanner room, took up to 5 times more than using the RTHawk system with communication. When the Bluetooth communication was established, the duration of the procedures using the standard control console in MRI (GEScreenBT and GEiPadBT) took still on average more than twice the length of the fluoroscopy-guided procedure. When using the RTHawk as a control console (RTScreenBT and RTiPadBT), the times were comparable to the fluoroscopy protocol. One of the factors that affected more drastically was the better performance for the phases of pre and post-angiography, which were up to 6 times shorter when using RTHawk than when the standard console was used. In addition, the advantage that RTHawk offers of choosing and changing sequences on the fly, gave more flexibility to the technician in the control room to provide requested images, avoiding some delays during the real-time guidance. However, these times did not take into account several important stages of the usual angioplasty procedure, as indicated in Figure 42. These stages, mostly regarding the preparation of the patient prior the intervention, would add between 5-10 minutes to the overall duration and should be considered in future investigations. During patient preparation, the equipment available and personnel training are some of the main factors to analyse. A dedicated interventional coil prototype “DuoFlex Coil Suite” (MR Intruments Inc., Mineapolis, MN, USA) (Rube et al. 2014) was used during these experiments. Other approaches, such as the use of integrated surface coils for the MRI tables should be investigated. Although, the preparation time for MRI might be potentially longer than in fluoroscopy (as it includes the

correct placement of the radiofrequency coil), recent studies have shown how acceptable times can be achieved. Takahara et al. (2010) presented a time-efficient whole-body MRI examination protocol with an average (± SD) extra time for coil positioning and re-positioning of 2 min 41.4s (± 15.3s), using for this purpose a whole-body surface coil. In this regard, appropriate training of the intervention team plays an essential role (Kettenbach et al. 2006). When using the iPad as a visualisation device, times were slightly longer in the case of RTiPadBT configuration (4.25 (0.45) min for treatment phase) but shorter in the case of GEiPadBT. This can be explained by the lack of familiarity that the clinicians had with this device (using it for the first time), since RTScreenBT and RTiPadBT configurations were tested before GEScreenBT and GEiPadBT configurations. As was reported during the interviews, clinicians detected a small delay (approximately 1-2 seconds) between the operational handle of the devices in the phantom and the refresh of the images shown on the iPad screen. This delay is likely to be caused by a network problem in the MRI environment setup and a more direct connection to control the MRI is being investigated for the IMSaT team.

The performance analysis was supplemented by the CRPA methodology, which provided the capture of all the experimental learning and observation data from the clinician in an unbiased and unobtrusive method. By withholding commentary until the task is completed, it removed the risk of contamination of thought and action by concurrent protocols (which are problematic in an MRI scanner). The offline analysis of video evidence allowed for the capture of procedural expertise through the viewing of video. By creating a multiplex to view both first and third person perspectives, the capacity of CRPA was maximised. In addition, the results of this study raised the possibility of establishing the optimal form of video demonstration for novice clinical staff, which could be investigated as a future application. By manipulating the expertise level of the clinician, the speed of the video and rapidity of the procedure itself, it can be determined whether the best demonstrator is an expert working normally, or some other form of elaborated or exaggerated demonstration. Recent work in more general tasks - such as small object lifting with fingertips - raises an intriguing possibility that it might be more informative to view novice as well as expert behaviour. In a series of experiments, Buckingham and colleagues (Buckingham et al. 2013) presented participants with a cube-lifting task

and provided training with videos of accurate (expert) behaviour or erroneous lifting behaviour (from novices when weights were uncertain). When they measured the accuracy of the lifting using a biomechanical feedback register, they found better performance for participants who had viewed novice error-prone lifts involving over- and underestimation. This poses the question as to what would constitute the best form of demonstration: error free expert learning or some combination of expert and novice tuition? Perhaps viewing mistakes helps the observer appraise the parameters of the task at hand, in which case these can highlight potential errors that may then be avoided with proactive behaviour.

By contrast to this study, previous studies used multi-video recordings in fluoroscopic interventions to evaluate intraprocedural decision making (Duncan, Kline, and Glaiberman 2007; Beta et al. 2009). They focussed on task analysis from the third-person perspective, not taking advantage of first-person experience nor paying attention to how the limitations in the environment affect the performance.

As anecdotal reports, one of the operators had had previous microdiscectomy and open operative repair of femoroacetabular impingement (i.e. back and hip surgery) for which good posture is advised. Far from anecdotes, the prevalence of low back injuries is a significant concern within the clinical community. Back pain appears as a psychological stressor, leading to medical errors and thereby compromising patient safety. In addition, it has a considerable impact on medical and legal costs (Klein et al. 2009; Mohseni-Bandpei et al. 2011). Therefore, the design of an efficient operational protocol in a new environment should be accompanied with a study of the ergonomic constraints of the workplace. The study presented took one of the most important constraints, which is clinician posture during the procedure, and quantified it with regards to the stress it causes on the body segments and the muscle work needed to maintain that position (McAtamney and Nigel Corlett 1993). Results from the MRI environment indicated that the rooms should be adjusted for its use as interventional facility. However, the DHM simulation results advised that the adjustments should be customisable depending on the clinician anthropomorphic features (e.g. height, weight, age). Further analyses should follow this work with volunteers from different percentiles of the population. It could be beneficial to perform a less subjective ergonomic analysis, placing sensors in the body during the

interventions to record precise parameters of the held postures. Recent similar approaches in this regard have been done to assess surgeons' positions during laparoscopy procedures (Pérez-Duarte et al. 2014; Kramp et al. 2014).

9.6. Summary

This chapter described a systematic framework to observe, analyse and assess operational protocols for vascular image-guided procedures. This multidisciplinary framework allowed an integral comparison between a conventional protocol under fluoroscopy and a new one under MRI guidance. In addition, several scenarios were analysed in order to identify key factors for the development of efficient and safe clinical protocols. In contrast to other similar studies, this comparison was undertaken looking at multiple key factors to performance at the same time: cognitive load, user experience and ergonomics. This approach could provide information about relationship between those factors that has not been considered before.

Chapter 10.
Conclusions and future work

10.1. Introduction

This final chapter summarises the major findings already discussed in chapters from 4 to 7 and 9 for each use case. It discusses how these results match the research hypotheses and propositions established in the first chapter. In addition, general limitations of the present research work are presented, together with suggestions for its improvement. In the last section, the chapter presents some potential applications and possible future work.

10.2. Conclusions over research hypotheses and propositions

Hospitals are facing an increasing demand for vascular IGPs due to their many benefits for patients. Moreover, the appearance of new imaging technologies, which need to be integrated in the current radiology environments or require the design of new interventional suites, makes essential the development of efficient workflows.

This thesis presented a methodological framework to analyse and model the intra-operative phase of vascular interventions through two approaches: using discrete event simulation and using a physical simulated environment. Four case studies illustrated the successfully application of this framework: two common vascular procedures, e.g. PCIs and iliac angioplasty, and a multi-modal image-guided vascular procedure, e.g. TACE. The fourth case shows that the methodology can be extended to other non-vascular multi-modal image guided procedures, e.g. MRgFUS interventions. In addition, preliminary results are shown for the case of a complex IGP, e.g. TAVI procedure in which a larger interdisciplinary team is usually involved.

The DES models have been effectively used also to make predictions and compare alternatives to current protocols in the TACE and MRgFUS interventions.

Results have also proved that average procedure durations are not an appropriate characterisation for radiology interventions due to the stochastic nature of actions and decisions within the procedures.

Delmia Quest for the model implementation allowed for a modular flexible programming by making possible to re-use of code structures from one model to another. This shortened the programming time considerably when implementing alternatives to current scenarios. Moreover, during the development of the simulation models, it was observed that clinicians responded more positively when there was a graphical representation of the procedures. Conceptual flow diagrams and animations in 3D environments helped to engage clinicians during the research. The participation of clinicians played an important role for the data gathering and the validation process, both aspects very closely related. High-fidelity information was essential for the models implementation. Failing in collecting critical information could result in a non-reliable model. In this sense, questionnaires and continuous communication with clinicians were carried out throughout the development process, facilitating the validation of the simulation models. For instance, clinicians' expert knowledge was fundamental to complement information for those cases where data was not available or few records were collected. In these cases, their advice was used to design triangular distributions for procedure events when corresponding times were missing or incomplete.

Although DES models showed to be useful to analyse and improve the performance in IGPs, certain aspects such as the clinicians' experience, understood as their perception of the interventional environment, can be easily missed when translating standardised protocols from traditional angiography rooms into new interventional imaging environments. In this respect, the use of a purpose-oriented physical simulated environment brought new insights to understand workflow in vascular image-guided procedures by comparing operational differences under fluoroscopy and MRI. A multi-perspective framework was proposed to design an MRI protocol for uncomplicated vascular procedures. In contrast to other studies found in the literature, this methodology combined a time-based performance evaluation, cognitive assessment of the protocol and ergonomic analysis of the environment. A case study of iliac angioplasty was used to evaluate this approach

and results were presented in Chapter 9. Results indicated that it could be possible to perform MRI-guided vascular procedures close in duration and operation to standard fluoroscopic guided interventions. The qualitative assessment of the clinical experience, presented through a CRPA, showed the importance and the need of an integral and multi-directional framework in the development of operational protocols for vascular IGPs, especially when they are developed for new technology challenging imaging environments. Aspects as ergonomics, communication and visualisation where highlighted by clinicians during the CRPA evaluation. The methodology presented could aid the design of more efficient and safer procedures.

10.3. Limitations of present research work

Although some limitations have already been discussed particularly at the end of each case study, this section discusses below general drawbacks of the present research study and some suggestions on how they could be improved.

Analysing detail aspects of IGP workflows required the collection of large and heterogeneous information within the procedures. Table 4 showed the type of data intended to be collected in each procedure. However, as mentioned, this information was not usually available and had to be collected by attending the procedures in most of the cases. Collecting records by hand for specific procedures was very time consuming and needed the collaboration of clinical staff members during the data collection. As a result, datasets were not always complete and non-homogeneous terminology was used. Some measures could be taken in the future to prevent these limitations. For instance, video recording could have compensated the missing information from the live observations. This is a costly and technical demanding setup and would require ethical approval by the hospital that should be in place at the start of the project; otherwise the data collection could be delayed by four or six month in average. In addition, it would be advisable to use or develop an electronic application that could allow collecting data using a common and homogenous terminology for all vascular procedures. These applications have been used before to record other types of surgical procedures. For example, the Surgical Workflow Editor developed by the University of Leipzig (Neumuth et al.) can be used to define specific ontological concepts regarding to particular surgical procedures that would

be used in the data collection, obtaining as a result homogenous datasets differentiated only by the type of the procedures that are defined in the application.

The data collection also revealed an additional limitation when using the physical simulated environment: the learning curve. After the first pilot study, clinicians were familiar with the environment and with the protocol. Since the experiments were prepared for uncomplicated interventions, this resulted in an expected better performance in the repetitions per configuration analysed. In order to study further this phenomenon, a suggestion could be to recruit more users with different level of experience in interventional radiology and to perform more repetitions. In addition, it could be interesting to see the effect that the videos from different perspectives recorded for the CRPA may have in that learning curve. This could be done for example by dividing the users in two groups: a group that would watch a third-user perspective video (Figure 40(a)) and another group watching the first-user perspective video prior to the experiments (Figure 40(d)).

10.4.Potential applications and future work

10.4.1. Perspectives for workflow analysis and simulations used for in regulative procedures

Medical devices approval is based on safety and effectiveness. In 2005, the FDA highlighted how training physicians through simulated procedures was likely to be considered as a key factor in medical devices regulation (Cavanaugh 2005). In 2013, the FDA gave approval for Elyria-based Surgical Theatre for their platform for cerebral and spine pre-surgery simulation (http://www.surgicaltheater.net, access on the 21/02/2014). This interactive platform allows for planning procedures and developing additional cases from pre-loaded ones. Similar initiatives can be found in the Center for Integration of Medicine and Innovative Technology (CIMIT, Boston, USA, http://www.cimit.org/programs-simulation.html, accessed on the 21/02/2014). CIMIT provides simulation-based training approaches for clinical workflows in, for instance, trauma or minimally invasive surgical environments.

Simulation appears also as a flexible and efficient tool for risk management by allowing reducing medical errors, testing case scenarios and training in

complications management (Caroll and Messenger 2008). In addition, some authors are developing the so-called patient-specific simulation. These models based on accurate data can help by determining tailored medical treatments aiding clinician in the decision-support process (Sadiq et al. 2008).

10.4.2. Comprehensive ergonomic analysis

Chapters 8 and 9 presented a pilot study on radiologist's postures during MRI-guided interventions. The RULA analysis was proved to be a valid method to assess the impact of the postures that clinicians hold during IGPs. In this present work, postures were measured through videos and images taken during the procedures and therefore they contained certain subjectivity. To ovoid this issue, further research could be done using sensors placed in the areas of interest of the body, for instance arms, low part of the back and head. This would allow an objective recording of the postures. Some studies have successfully applied body sensor to record surgeon's positions and movements during procedures (Kramp et al. 2014; Pérez-Duarte et al. 2014).

In addition, to perform a more comprehensive ergonomic analysis, it would be advisable to measure postures using volunteers from different genders and levels of experience with different anthropometric features (height and weight). Moreover, a comparative analysis could be done between the postures in traditional angiography suites and in MRI rooms. In this case and since angiography tables can be rotated, it could be interesting to find out if left-handed vs. right-handed people adds new constraints in the MRI environment, which is more restrictive. On the other hand, it would be necessary to add, in the case of angiography suites, how the use of lead aprons affects the joints when they are worn for long periods.

10.4.3. Modelling multimodal imaging environments

As mentioned in the introduction, new multi-modal imaging operating suites are being designed in response to the higher demand on minimally invasive surgery. The AMIGO system at Brigham and Women's Hospital (Boston, MA, USA) or MITOS at the Clinical Research Centre at Ninewells Hospital (Dundee, UK) are some examples of these suites. However, these facilities are very costly and therefore, they

should be used in the most efficient and cost-effective way possible. Simulation can be used for planning improved workflow and help clinicians to deliver the best care.

Simulation-based medical education can help preparing clinicians with the professional skills and knowledge needed in these new challenges environments. Simulators have shown in last reports to be superior to traditional clinical medical education in achieving specific skill acquisition goals (McGaghie et al. 2010). Several approaches for the use of simulators in minimally invasive environments confirm that is possible to transfer skills learned on a simulator to real operations, resulting in error reduction, improving patient safety and shortening of procedural operating time (Schreuder et al. 2011).

Some studies have also explore pattern recognition as tools to improve efficiency in surgical environments, including IGPs (Nara et al. 2011). A system able to capture workflow trajectories could help in the standardisation of procedures in new multi-modal operating rooms such as the mentioned above, e.g. AMIGO and MITOS. The system presented by Nara et al. used data mining techniques to post-process the workflow patterns and acquire knowledge of the workflow that could support decisions of staff about managing resources. These tools together with comprehensive DES modelling could aid the design of new image-guided protocols.

Basic versions of DES models have been implemented for the MITOS CRC and IMSaT facilities. These models could be used as test benches for testing multi-modal image-guided protocols. Figure 51 shows the DES model of the CRC imaging facilities. This 3D environment has been implemented at scale and equipped with the fundamental resources and logic skeleton to facilitate the process programming. In a similar way, Figure 52 presents the DES model of IMSaT MRI area, which is also provided with a combined surgical and angiography suite. This model is already in a more advanced development stage since basic logics for image-guided procedures have been included for testing. This simulation model has been provided with real-time annotations to identify the task that is being executed at every moment, which can make easier the understanding and use of the model in a clinical environment. Real-time annotations of procedural and task times, resource utilisation percentage, etc. could be helpful during medical training.

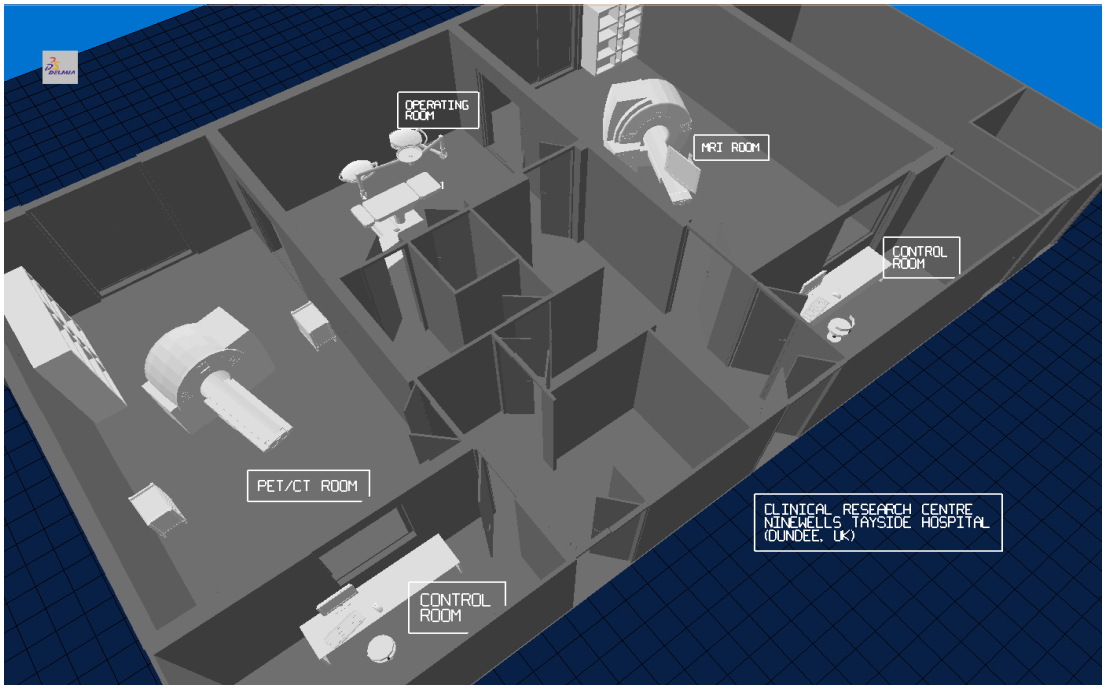


Figure 51. DES model of the MITOS at the Clinical Research Centre (CRC) imaging facilities (Ninewells Hospital, Dundee, UK).

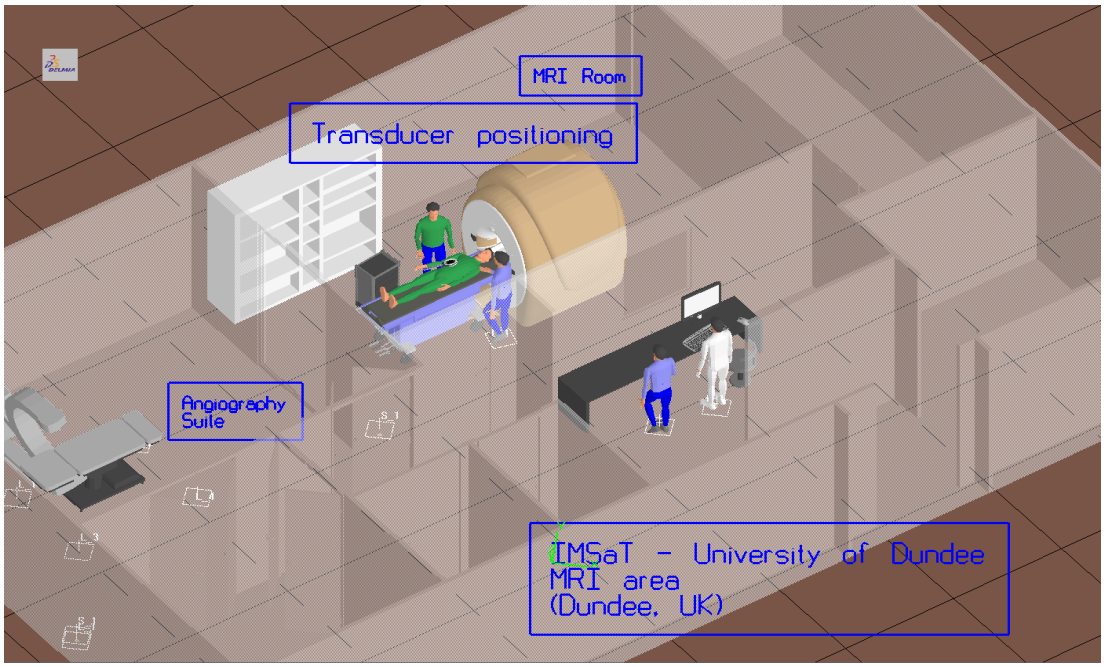


Figure 52. DES model of the imaging facilities at the Institute for Medical Science and Technology (IMSaT, University of Dundee, Dundee, UK).

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Appendix A: Vendors' list

This appendix presents the contact information of the simulation software vendors evaluated:

Alion Science and Technology,
MA&D Operation
4949 Pearl East Circle, Suite 200
Boulder, CO 80301 USA
303-442-6947
303-442-8274
IPME_support@alionscience.com,
microsaintsharp@alionscience.com
www.alionscience.com
www.maad.com

CreateASoft, Inc
3909 75th Street, Suite 105
Aurora, IL 60563 USA
630-428-2850
630-963-3755
info@createasoft.com
www.createasoft.com

Dassault Systemes
10, Rue Marcel Dassault
78140 Vélizy-Villacoublay
FRANCE
Tel: + 33 1 61 62 61 62
Fax: + 33 1 70 73 43 63
http://www.3ds.com/

Flexsim Software Products, Inc.
1577 North Technology Way
Orem, Utah 84097 USA
801-224-6914
801-224-6984
rogerh@flexsim.com
www.flexsim.com

Imagine That Inc.
6830 Via Del Oro, Suite 230
San Jose, CA 95119 USA
408-365-0305
408-629-1251
info@extendsim.com
www.extendsim.com

Lanner Group Limited
The Oaks
Clews Road
Redditch, Worcestershire
B98 7ST, UK
+44 (0) 1527 403400
info@lanner.co.uk
www.lanner.co.uk

Lumina Decision Systems, Inc
26010 Highland Way
Los Gatos, CA 95033 USA
650-212-1212
650-240-2230
sales@lumina.com
www.lumina.com

ProModel Corporation
7540 Windsor Drive, Suite 300
Allentown, PA 18195
610-391-9700
610-391-9709
saleshelp@promodel.com
www.promodel.com

Rockwell Automation
2100 Corporate Drive, Suite 550
Wexford, PA 15090
(+1) 724-741-4000
(+1) 724-741-4001
arena-info@ra.rockwell.com
www.arenasimulation.com

Simio LLC
504 Beaver Street
Sewickley, PA 15143
412-528-1576
412-253-9378
info@simio.biz
www.simio.biz

SIMUL8 Corporation
225 Franklin Street, 26th Floor
Boston, MA 02110 USA
800-547-6024
800-547-6389
support@SIMUL8.com
www.SIMUL8.com

XJ Technologies
AnyLogic North America
9 Ramsey Rd.
Lebanon, NJ 08833 USA
908-236-6283
908-292-1129
grivas@anylogic.com
www.anylogic.com

Appendix B: Simulation software evaluation summary

This appendix presents the complete results of the simulation software packages indicated in Section 1 of Chapter 3. Table 22 shows the features evaluated for those simulation software packages that were not shortlisted. Access to some of the features was not possible for some of the packages. Nevertheless, these packages were removed from the list for other more significant reasons indicated in Table 3 (see section 3.2.2.3). Table 23 shows the summary of the total features evaluated on the shortlisted simulation software packages.

Criteria	Analytica	AnyLogic	Arena	Emergency Department Simulator	Simcad	Simio	SIMUL8	Witness
System requirements	Low	Medium	Medium	Low (limited to certain OS[1])	Low	Medium	Low	Low (limited to certain OS[1])
Run time debug	Not provided	Provided	Provided	Provided	Provided	Provided	Provided	Not provided
Output analysis	Possible	Possible	Possible	Possible	Possible	Possible	Possible	Possible
Real time viewing	Not possible	Possible	Possible	Possible	Possible	Possible	Possible	Possible
Support/training/Maintenance/ documentation	Provided	Provided	Provided	Provided	Provided	Provided	Provided	Provided
Error reporting	Provided	Provided	Provided	Provided	Provided	Provided	Provided	Provided
Graphical model implementation	Possible	Possible	Possible	Possible	Possible	Possible	Possible	Possible
Model building using programming	Possible	Possible	Possible	Not possible	Possible	Possible[a]	Possible	Possible
CAD drawing import/ adequate library provided	Not provided	Provided	Provided	Not possible	Provided	Provided	Provided	Provided
Code reuse	Possible	Possible	Possible	Possible	Possible	Possible	Possible	Not known
Animation	Not possible	Possible[b]	Possible[b]	Not possible	Possible	Possible	Possible[b]	Possible[b]
Experimental design	Not possible	Possible	Possible	Possible	Possible	Possible	Possible	Possible
Statistical facilities	Provided	Provided	Provided	Provided	Provided	Provided	Provided	Provided
Model packaging	Possible	Possible	Possible	Possible	Possible	Possible	Possible	Not known

Criteria	Analytica	AnyLogic	Arena	Emergency Department Simulator	Simcad	Simio	SIMUL8	Witness
Micro-ergonomics design	Not possible	Not possible	Not possible	Not possible	Not possible	Not possible	Not possible	Not possible
Input data import	Possible	Possible	Possible	Possible	Possible	Possible	Possible	Possible
Model optimisation	Possible	Possible	Possible	Possible	Possible	Not known	Possible	Possible
Notes: [a]Limited features to add restrictions to interactions among entities; [b]limitations for the 3D environment; [1]OS: Operating System								

Table 22. Summary of features evaluated for those software packages that were not shortlisted

Criteria	Delmia	ExtendSim	Flexsim HC	Medmodel	Micro Saint Sharp
System requirements	Medium (limited to certain OS[1])	Low	Low (limited to certain OS[1])	Medium (limited to certain OS[1])	Low
Run time debug	Provided	Provided	Provided	Provided	Provided
Output analysis	Possible	Possible	Possible	Possible	Possible
Real time viewing	Possible	Possible	Possible	Possible	Possible
Support/training/Maintenance/documentation	Provided	Provided	Provided	Provided	Provided
Price	Low	Medium	High	Low	Low
Error reporting	Provided	Provided	Provided	Provided	Provided
Graphical model implementation	Possible	Possible	Possible	Possible	Possible
Robustness	High	High	High	High	High
Model building using programming	Possible	Possible	Possible	Possible	Possible
CAD import/ library	Provided	Provided	Provided	Provided	Provided
Code reuse	Possible	Possible	Possible	Possible	Possible
Animation	Possible	Possible	Possible	Possible[b]	Possible
Experimental design	Possible	Possible	Possible	Possible	Possible
Statistical facilities	Provided	Provided	Provided	Provided	Provided
Model packaging	Possible[c]	Possible	Possible[c]	Possible	Possible
Micro-ergonomics design	Possible	Not possible	Not possible	Not possible	Possible[c]
Interface user friendly	Average	Average	Easy	Average	Easy
Input data import	Possible	Possible	Possible	Possible	Possible
Model optimisation	Possible[c]	Possible	Possible[c]	Possible[c]	Possible[c]
Partial and total times	Provided	Provided	Provided	Provided	Provided
Costs: total, operation, resources	Possible	Possible	Possible	Possible	Possible
Resources under-utilised time	Provided	Provided	Provided	Provided	Provided
Entity Activity	Provided	Provided	Provided	Provided	Provided
Variables changed during simulation	Provided	Provided	Provided	Provided	Provided
Location analysis	Provided	Provided	Provided	Provided	Provided
Scheduling: entities/locations/resources	Provided	Provided	Provided	Provided	Provided
Micro-ergonomics	Possible	Not possible	Not possible	Not possible	Possible[c]
Notes: [a]Limited features to add restrictions to interactions among entities; [b]limitations for the 3D environment; [c]separate package; [1]OS: Operating System					

Table 23. Summary of features evaluated for the shortlisted software packages

Appendix C: MIDAS - Medical Interventional Data Analysis System

The MIDAS (Medical Interventional Data Analysis System) was implemented in first place by the student Mr Bruce Taylor for the award of an MSc degree in Computer Science in 2011 (University of Dundee, Dundee). A later version was developed by the freelance programmer Iain Barnett as a voluntary collaborator. The web site was designed to facilitate the data gathering by potential collaborators. Implementing a software application instead a web-interface was considered but rejected due to some disadvantages such as possible incompatibility among operating systems and probable restrictions on the installation in certain computers (for example in hospitals). The web site is compatible with any browser, it does not need any further installation in the computer and the versions are maintained by the administrator of the server so all the users will have access to the current version at the same time.

The website has two different interfaces depending on the user profile. It can be access by a normal user or an administrator user, who has access to the statistical analysis page. The administrator is the only that can approve new users and delete/modify records.

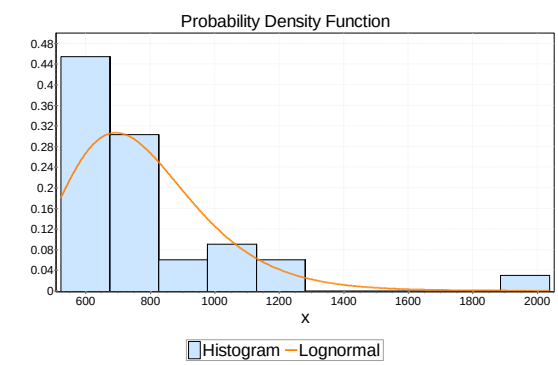
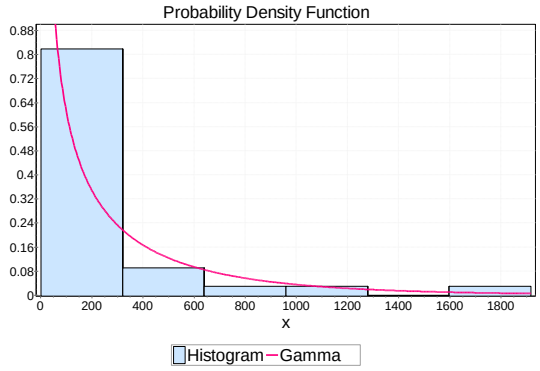
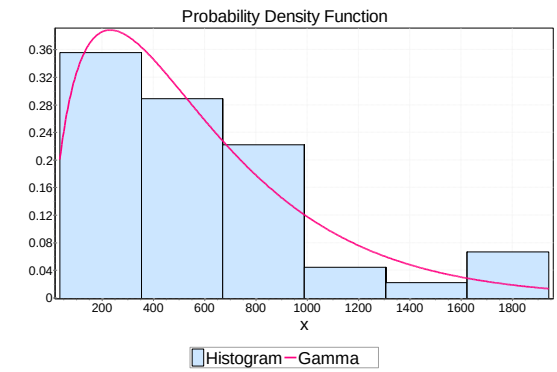
The website has three main tabs:

- *Account*. It stores profile information and allows changing the password.
- *Data*. It accesses the data submission form and the previous submitted records. The form has been designed to resemble the template for manual collection of the data so that can be more familiar to the users. Other adds-in are validation of data during the submission and auto complete feature in most of the form fields.
- *Admin*. This tab only exists for the administrator user. It controls the records of other users and gives access to the analysis page. The preliminary version of the analysis page shows the mean and the standard deviation of a set of timings associated with an interval indicated by the user. A graph provides a quick visual tool of the range

of timings associated with that interval. This version also allows selection of procedure by type, to filter that dataset by type of device used.

Appendix D: DES model statistics

D.1. PCI

Event	Distribution	Parameters	Histogram/Density Function
Preparation	Lognormal	μ = 6.62 σ = 0.27 Mean (± St Dev) = 776.18 (± 216.59)	
Access	Gamma	α = 0.43 β = 573.11	
Single guidance	Gamma	α = 1.65 β = 358.66	

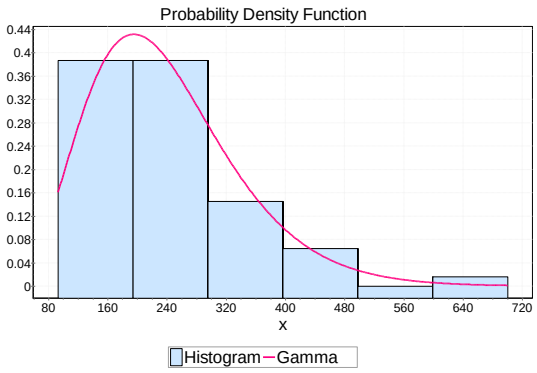
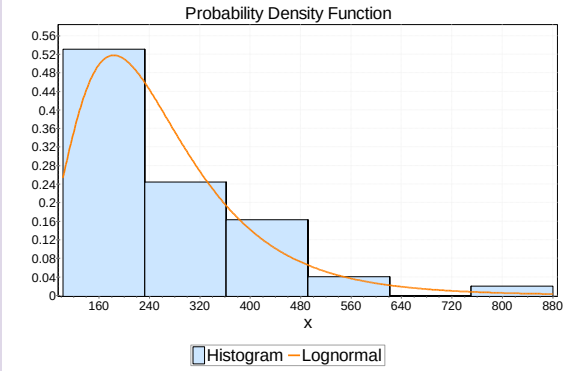
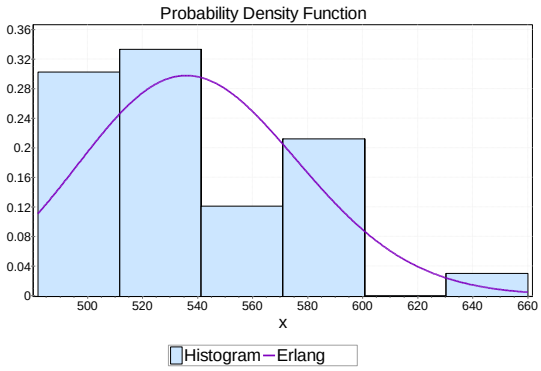
Event	Distribution	Parameters	Histogram/Density Function
Single balloon angioplasty	Gamma	α = 5.52 β = 43.20	
Single stent implantation	Lognormal	μ = 5.45 σ = 0.48 Mean (± St Dev) = 260.8 (± 133.91)	
Room ready time	Erlang	m = 183 β = 2.94 (Mean=538.87)	

Table 24. Statistical distributions, parameters and histogram for significant events analysed for treatment PCIs.

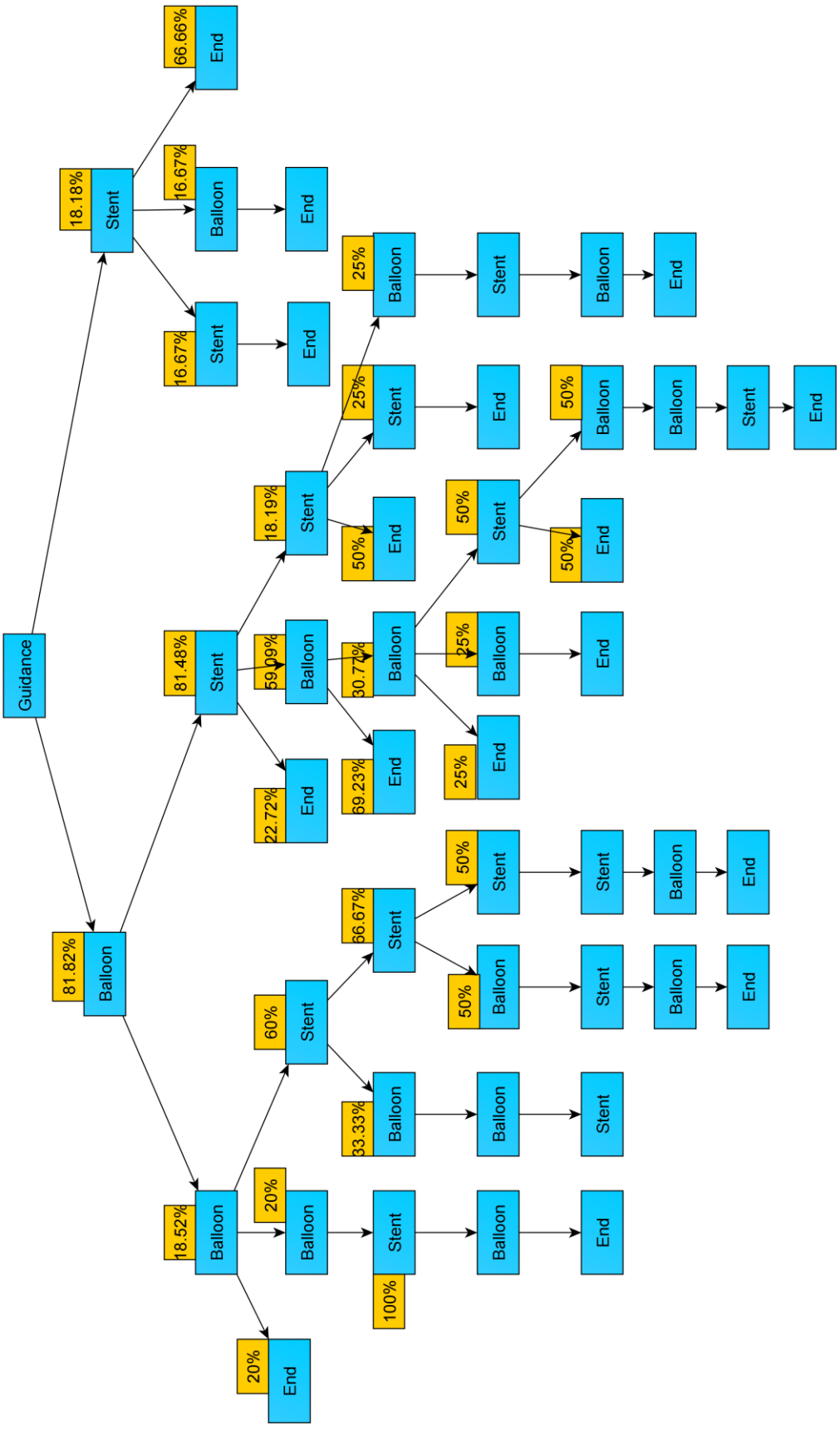
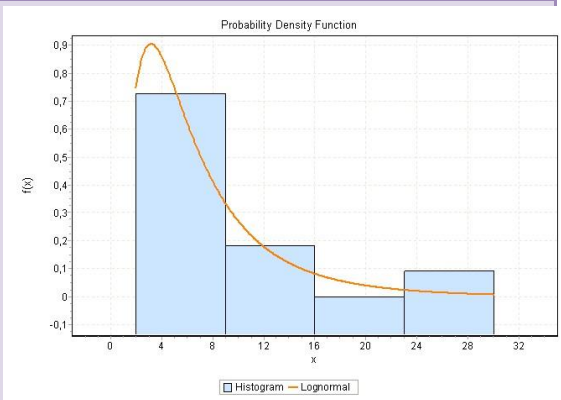
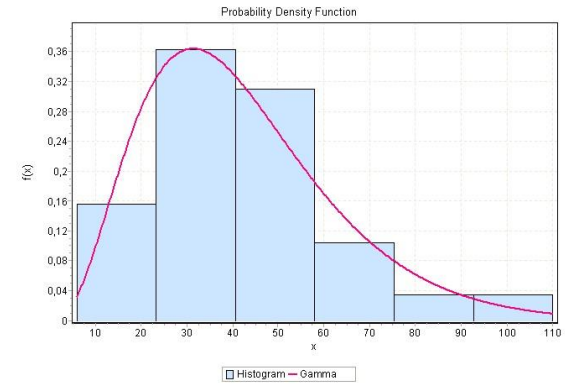
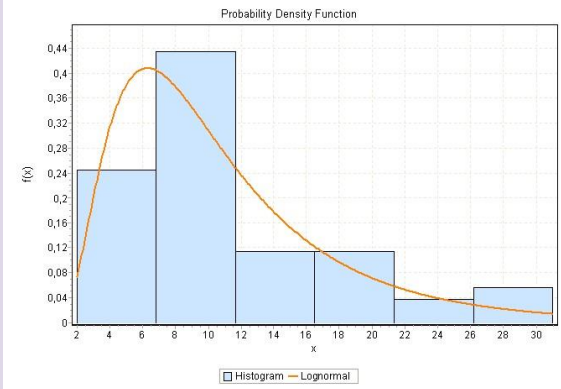
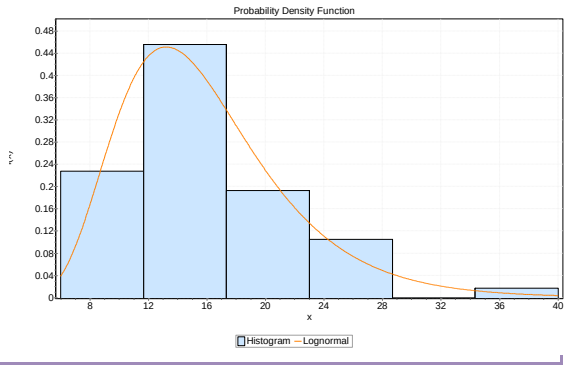


Figure 53. Probability tree of single treatments (angioplasties and stenting) PCIs

D.2. TACE

Event	Distribution	Parameters	Histogram/Density Function
Access	Lognormal	μ = 1.70 σ = 0.74 (Mean = 7.22, Std Dev = 6.18)	
Cannulation	Gamma	α = 3.87 β = 10.91	
Transfer to MRI suite	Lognormal	μ = 2.22 σ = 0.62 (Mean = 11.21, Std Dev = 7.67)	
Time in MRI	Lognormal	μ = 2.71 σ = 0.35 (Mean = 15.98, Std Dev = 5.87)	

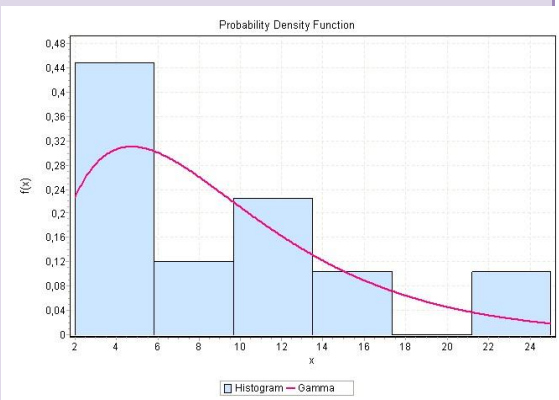
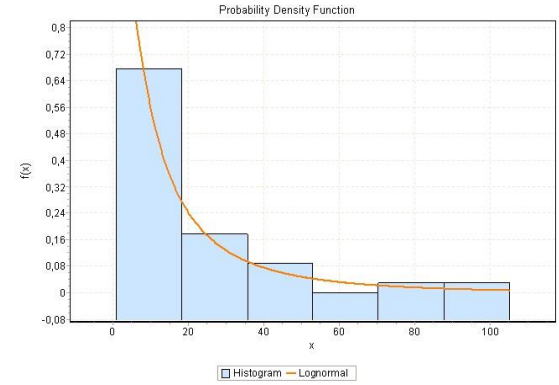
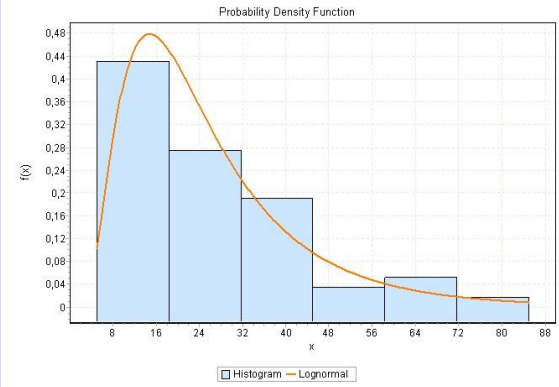
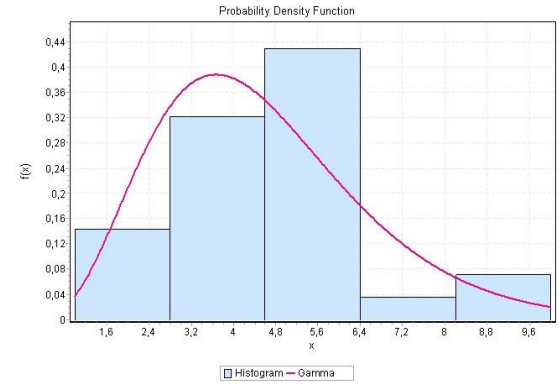
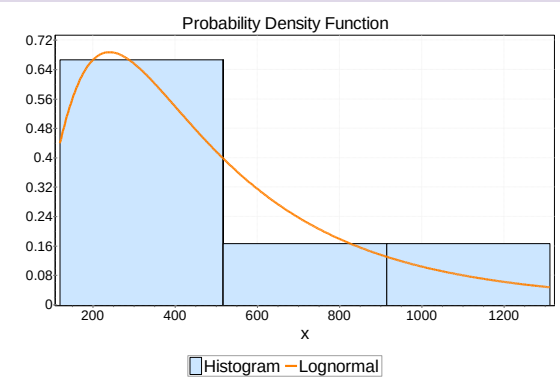
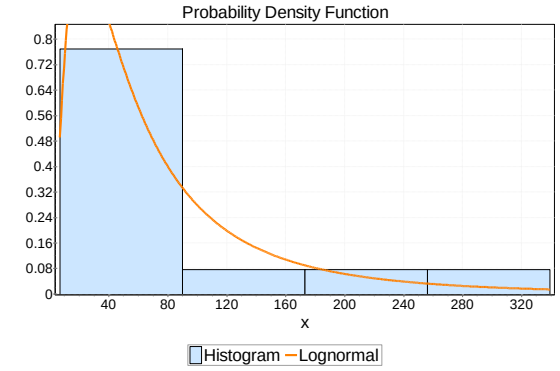
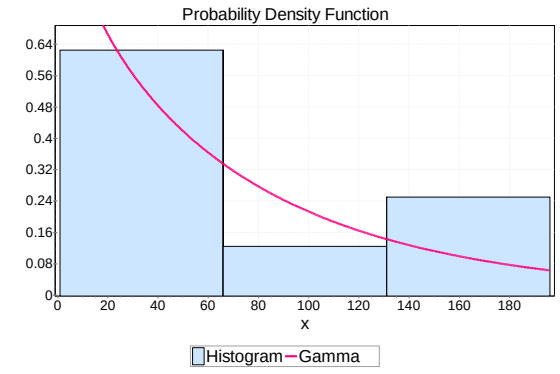
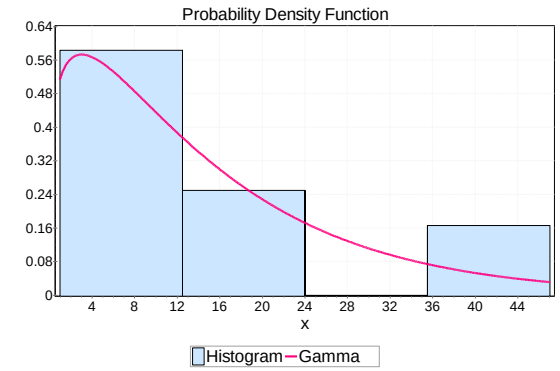
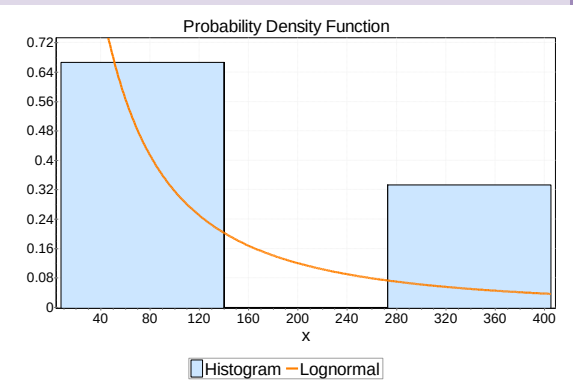
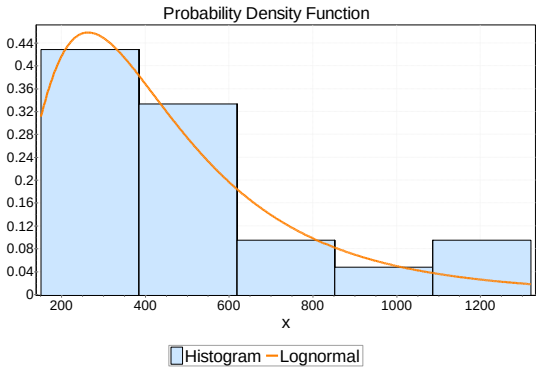
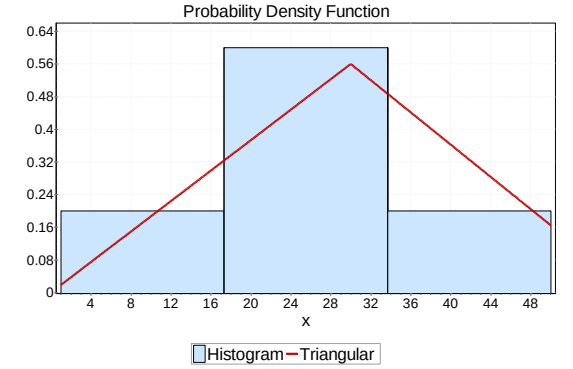
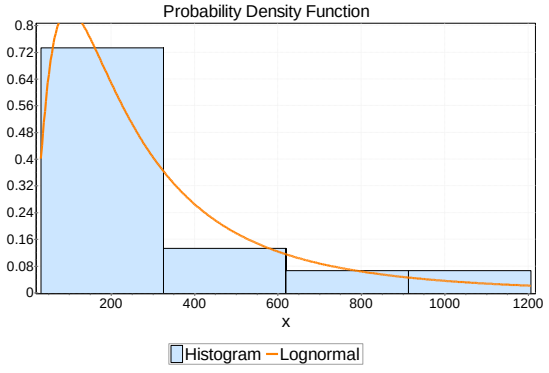
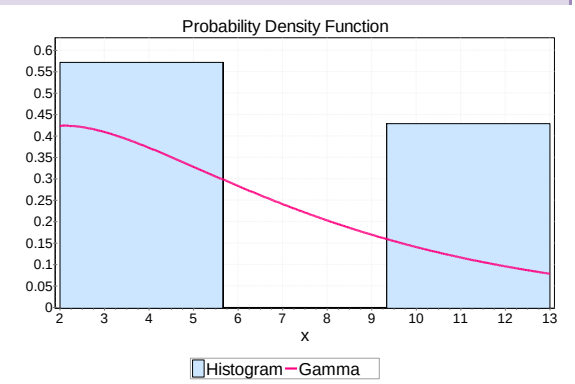
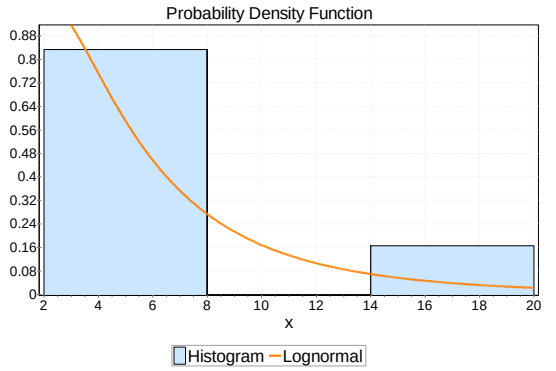
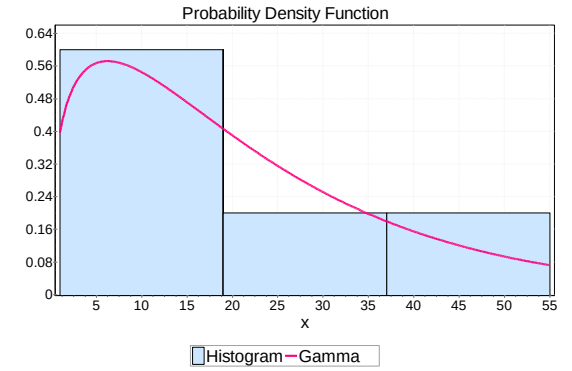
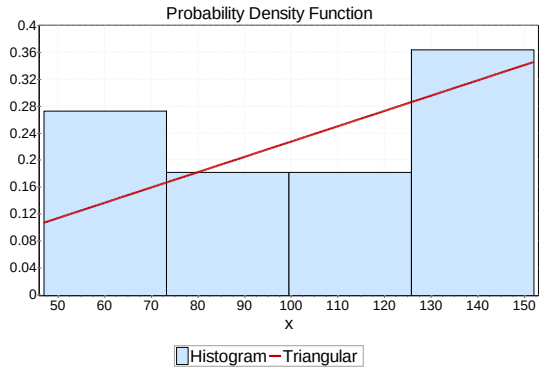
Event	Distribution	Parameters	Histogram/Density Function
Transfer to Angiography suite	Gamma	α = 2.08 β = 4.40	
Cannulation after MRI	Lognormal	μ = 2.34 σ = 1.22 (Mean = 21.98, Std Dev = 40.86)	
Chemoembolization	Lognormal	μ = 3.08 σ = 0.62 (Mean = 26.38, Std Dev = 18.07)	
DynaCT	Gamma	α = 5.09 β = 0.90	
Where α and σ are the shape parameters, and β and μ are the scale parameters			

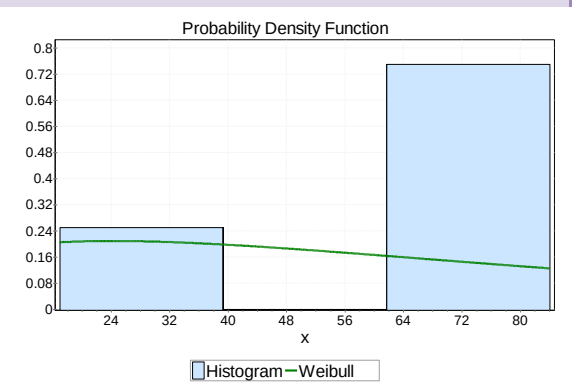
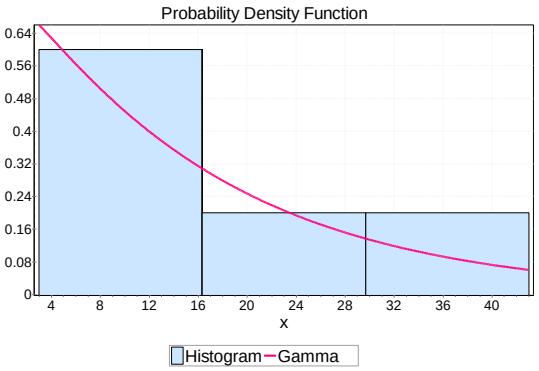
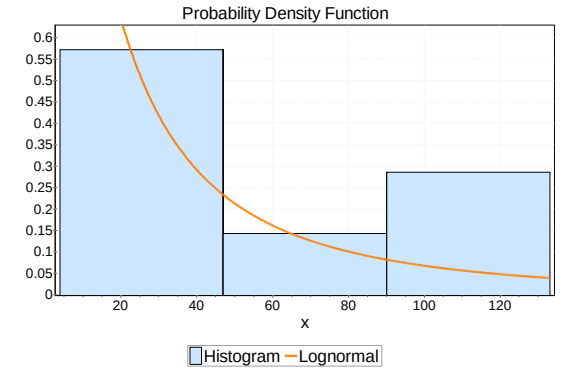
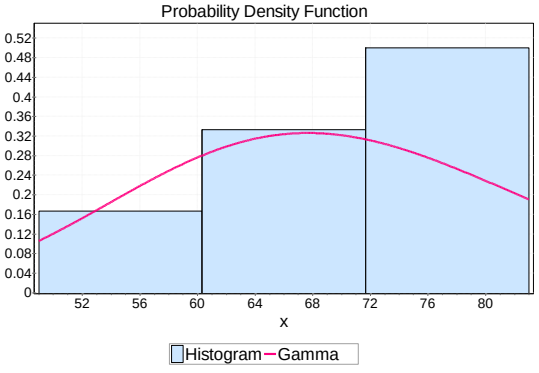
Table 25. Statistical distributions, parameters and histogram for significant events analysed for TACE procedures

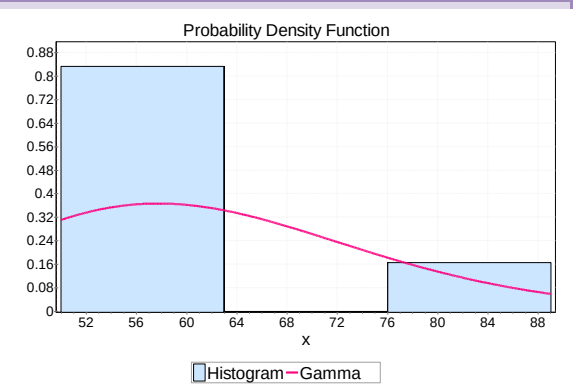
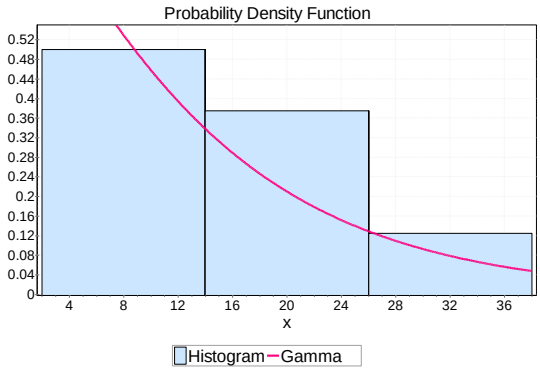
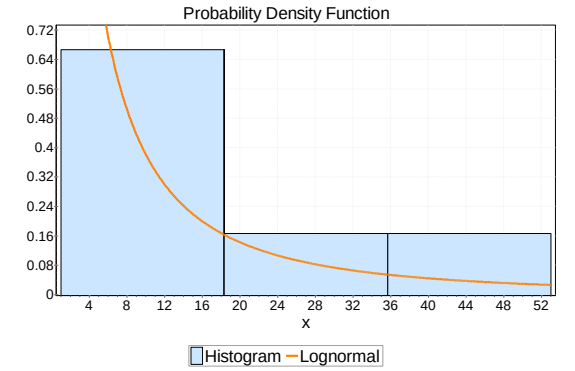
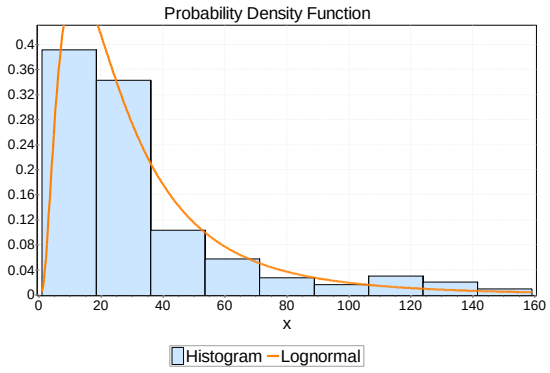
D.3. MRgFUS

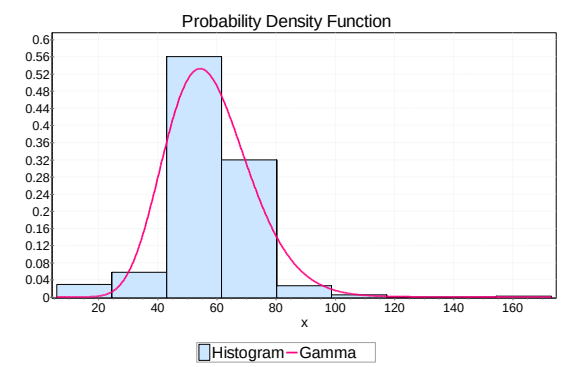
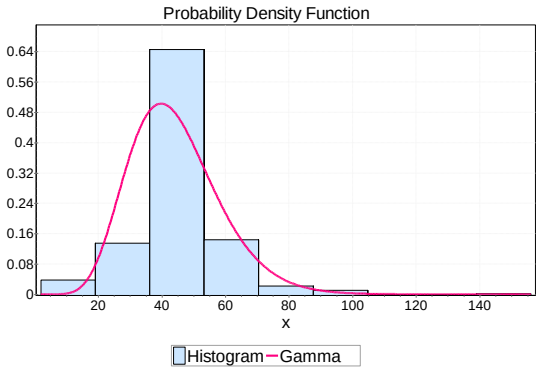
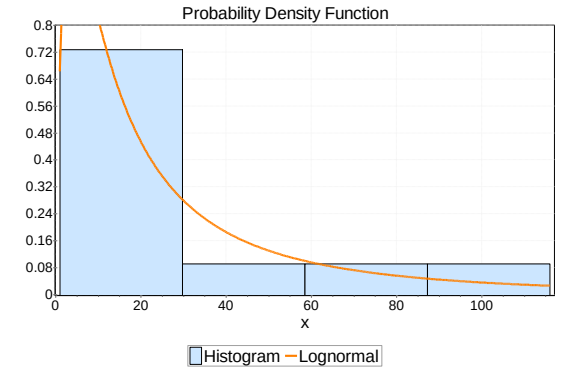
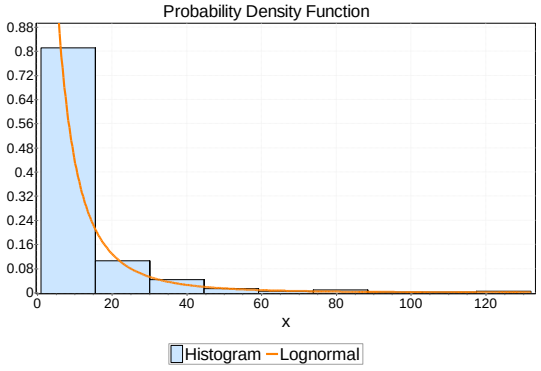
Event			Distribution	Parameters	Histogram/Density Function
Ph.	**Act.**	**Dec.**			
4a	X1		Lognormal	μ = 6.02 σ = 0.73 Mean (± St Dev) = 538.17 (± 454.27)	
4b	X1		Lognormal	μ = 3.95 σ = 0.95 Mean (± St Dev) = 80.16 (± 93.68)	
4b	X3		Gamma	α = 0.88 β = 84.25	
4b		Q1	Gamma	α = 1.25 β = 12.21	

Event			Distribution	Parameters	Histogram/Density Function
Ph.	Act.	Dec.			
4b		Q2	Lognormal	μ = 4 σ = 1.54 Mean (± St Dev) = 178.77 (± 559.12)	
5	X1		Lognormal	μ = 5.97 σ = 0.63 Mean (± St Dev) = 480.24 (± 336.86)	
5		Q1	Triangular	m = 30 a = 0 b = 58.36	
6a	X2		Lognormal	μ = 5.44 σ = 0.92 Mean (± St Dev) = 350.83 (± 404.99)	

Event			Distribution	Parameters	Histogram/Density Function
Ph.	Act.	Dec.			
6a	X3		Gamma	α = 1.51 β = 4.17	
7a	X4		Lognormal	μ = 1.44 σ = 0.79 Mean (± St Dev) = 5.80 (± 5.43)	
7a	X5		Gamma	α = 1.37 β = 16.95	
7a	X6		Triangular	m = 152 a = 0 b = 152	

Event			Distribution	Parameters	Histogram/Density Function
Ph.	Act.	Dec.			
7a	X7		Weibull	α = 1.28 β = 78.86 γ = 0 Mean (± St Dev) = 73.05 (± 57.44)	
7a	X8		Gamma	α = 1.05 β = 15.86	
7a	X9		Lognormal	μ = 3.08 σ = 1.33 Mean (± St Dev) = 52.81 (± 116.17)	
7a	X10		Gamma	α = 24.96 β = 2.82	

Event			Distribution	Parameters	Histogram/Density Function
Ph.	Act.	Dec.			
7a	X11		Gamma	α = 17.80 β = 3.44	
7a		Q4	Gamma	α = 1.13 β = 11.45	
7a		Q8	Lognormal	μ = 1.53 σ = 1.62 Mean (± St Dev) = 17.20 (± 61.37)	
8	X1		Lognormal	μ = 3.18 σ = 0.82 Mean (± St Dev) = 33.82 (± 33.12)	

Event			Distribution	Parameters	Histogram/Density Function
Ph.	Act.	Dec.			
8	X2		Gamma (*) Reject hypothesis on A-D	α = 16.44 β = 3.52	
8	X3		Gamma (*) Reject hypothesis on A-D	α = 9.76 β = 4.54	
8	X4		Lognormal	μ = 2.88 σ = 1.26 Mean (± St Dev) = 39.40 (± 77.55)	
8		Q1	Lognormal (*) Reject hypothesis on A-D	μ = 1.67 σ = 1.12 Mean (± St Dev) = 9.98 (± 15.92)	

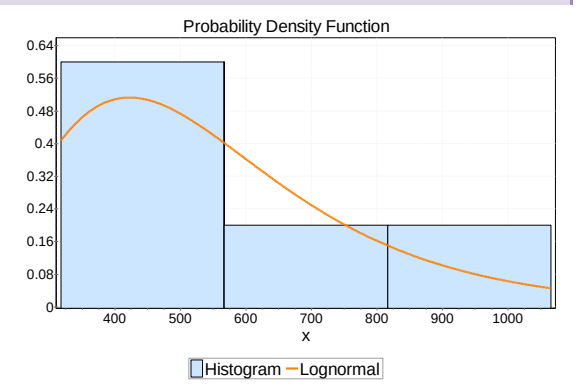
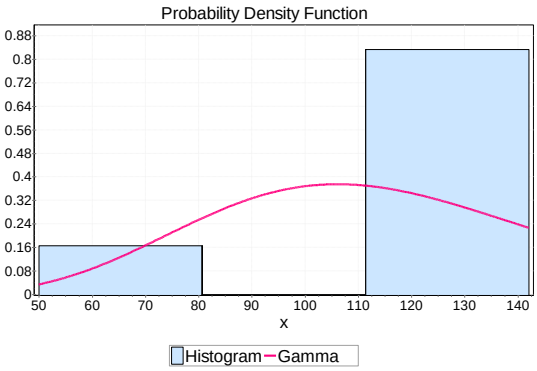
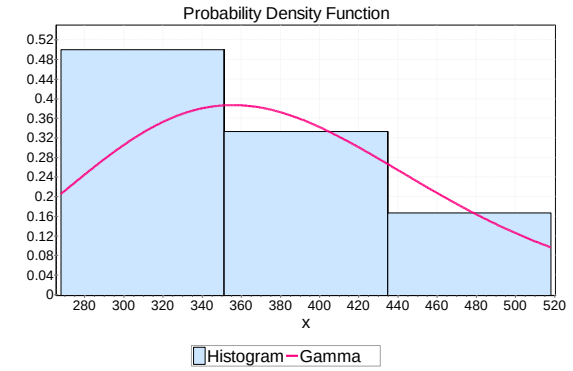
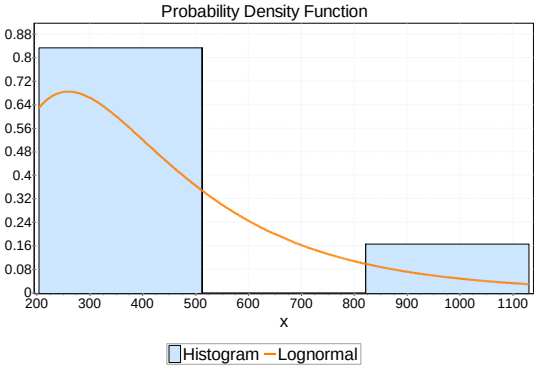
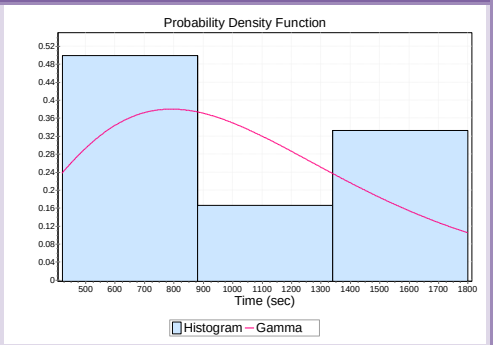
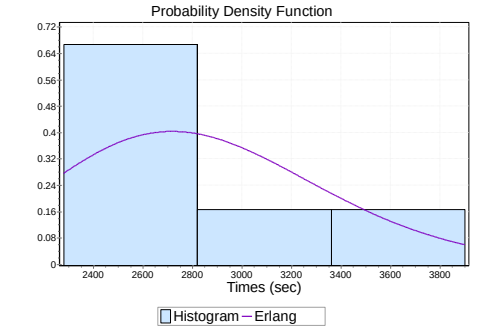
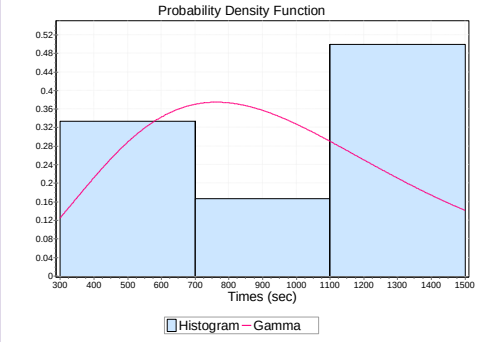
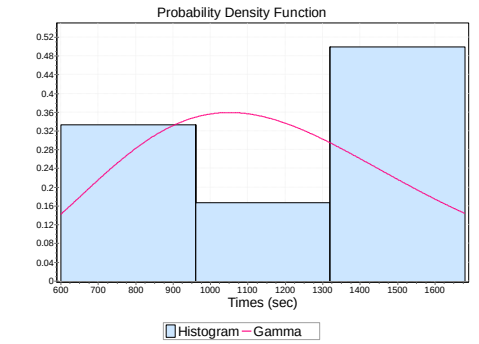
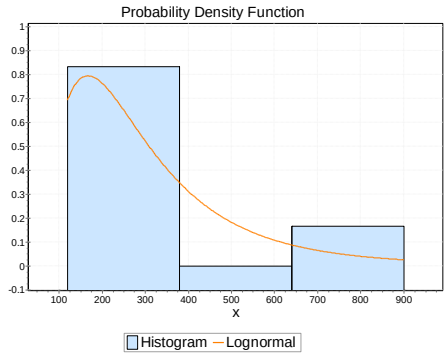
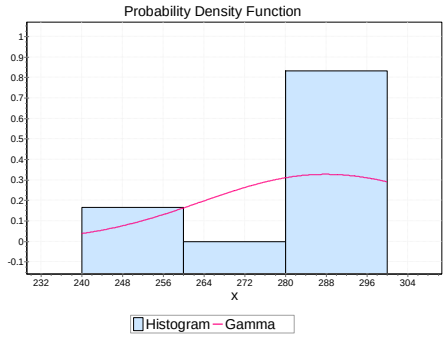
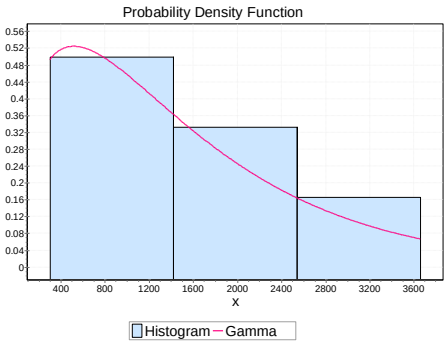
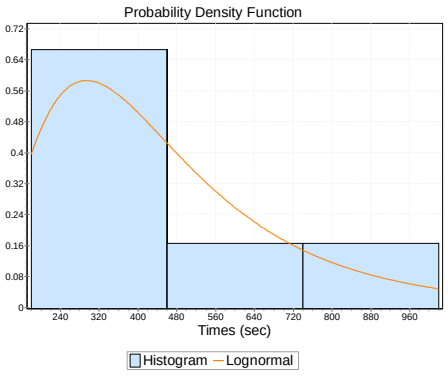
Event			Distribution	Parameters	Histogram/Density Function
Ph.	Act.	Dec.			
9	X1		Lognormal	μ = 6.22 σ = 0.42 Mean (± St Dev) = 550.61 (± 241.78)	
9	X3		Gamma	α = 11.72 β = 9.89	
9	X4		Gamma	α = 18.29 β = 20.58	
9	X8		Lognormal	μ = 5.90 σ = 0.58 Mean (± St Dev) = 433.32 (± 276.65)	

Table 26. Statistical distributions, parameters and histogram for significant events analysed for MRgFUS procedures

D.4. TAVI

Event	Distribution	Parameters	Histogram/Density Function
Other preparation for the patient	Gamma	α = 3.85 β = 277.79	
Anaesthesia induction (general or local)	Erlang	m = 27 β = 104.57 (Mean=2823.4)	
Transoesophageal echocardiography	Gamma	α = 4.37 β = 226.55	
Right femoral access	Gamma	α = 8.06 β = 148.8	

Event	Distribution	Parameters	Histogram/Density Function
Ventricular pacing	Lognormal	μ = 5.52 σ = 0.64 Mean (± St Dev) = 307.73 (± 217.45)	
Left femoral access	Gamma	α = 140.17 β = 2.07	
Catheter and guidewire guidance	Gamma	α = 1.50 β = 1032.5	
Balloon placement/inflating/extraction	Lognormal	μ = 5.99 σ = 0.55 Mean (± St Dev) = 467.81 (± 280.79)	

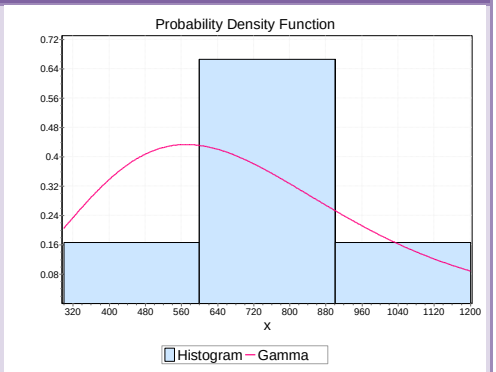
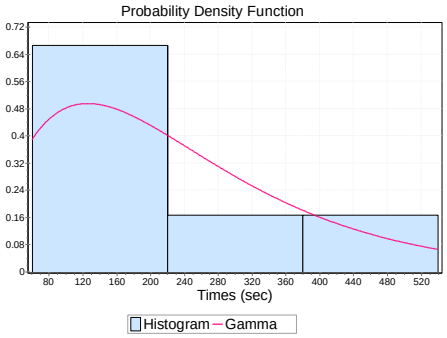
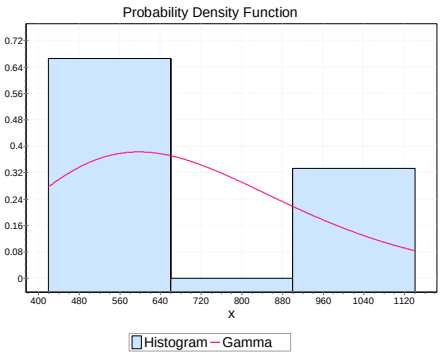
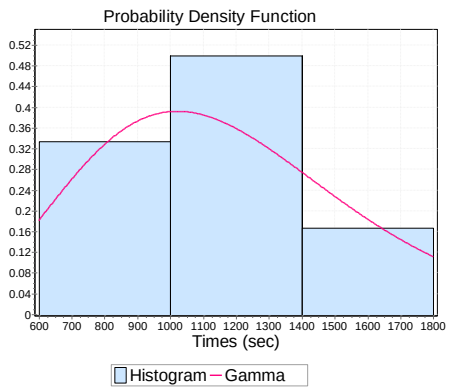
Event	Distribution	Parameters	Histogram/Density Function
Valve implantation (self and balloon expanded)	Gamma	α = 5.43 β = 128.91	
Screening-contrast test post-treatment	Gamma	α = 2.10 β = 114	
Closing	Gamma	α = 6.85 β = 102.17	
Patient Ready (Awakening - Out of room)	Gamma	α = 7.46 β = 158.24	

Table 27. Statistical distributions, parameters and histogram for significant events analysed for TAVI procedures

Appendix E: Probability assessment questionnaire for MRgFUS workflow analysis

Filled out by: **Intervention type:**	**LIKELIHOOD** **0 – Very unlikely / 10 – Very likely**	**IMPACT** **0 – Very low impact / 10 – Very High impact**
Phase 4b – Patient Positioning		
1. Position adjustments will not help and treatment cannot be started (4b-Q2)		
Phase 6a – Pre-therapy planning		
2. During planning, it appears that the patient position does not allow treatment (6a – Q3)		
Phase 7a – Sonication calibration		
3. Focal spot is not properly aligned after LOW-POWER test sonication (7a – Q1)		
4. Focal spot is not properly aligned after HIGH-POWER test sonication (7a – Q3)		
5. Treatment cannot be completed due to not achieving proper focal spot alignment with low power calibration adjustment (7a – Q6 – Q2)		
6. Treatment cannot be completed due to not achieving proper focal spot alignment with high power calibration adjustment (7a – Q6 – Q5)		
Phase 8 - Treatment		
7. The plan cannot be completed due to not reaching adequate heating of a target spot that is accessible by the sonication beam. (8 – Q3)		

Appendix F: Markov routine code

```
routine routine_markov_chain(par_init_array: array [2] of real; par_trans_array: array[x_dimension, y_dimension] of real; par_state: integer) : real

    var
        int_var: integer
        prob_int: real
        V_state: array[2] of real
        Aux_array: array[x_dimension, y_dimension] of real
        Pt_aux_array: array[x_dimension, y_dimension] of real

    begin

        ---- Initiate Pt_aux to Identity so the state=1 gives just the Transition matrix
```

```
Pt_aux_array[0,0]=1
Pt_aux_array[0,1]=0
Pt_aux_array[1,0]=0
Pt_aux_array[1,1]=1
int_var=1
----- We evaluate the correct state for the markov chain

--write('par_init_array[0]= ', par_init_array[0], ' ', 'par_init_array[1]= ', par_init_array[1], cr)

while(int_var<=par_state) do


Aux_array[0,0]=Pt_aux_array[0,0]*par_trans_array[0,0]+Pt_aux_array[0,1]*par_trans_array[1,0]

Aux_array[0,1]=Pt_aux_array[0,0]*par_trans_array[0,1]+Pt_aux_array[1,0]*par_trans_array[1,1]

Aux_array[1,0]=Pt_aux_array[1,0]*par_trans_array[0,0]+Pt_aux_array[1,1]*par_trans_array[1,0]

Aux_array[1,1]=Pt_aux_array[1,0]*par_trans_array[0,1]+Pt_aux_array[1,1]*par_trans_array[1,1]

    --write('Aux_array[0,0]= ', Aux_array[0,0], ' ', 'Aux_array[0,1]= ', Aux_array[0,1], ' ',
'Aux_array[1,0]= ', Aux_array[1,0], ' ', 'Aux_array[1,1]= ', Aux_array[1,1], cr)

Pt_aux_array=Aux_array
    --write('Pt4bd1_aux_array[0,0]= ', Pt_aux_array[0,0], ' ', 'Pt4bd1_aux_array[0,1]= ',
Pt_aux_array[0,1], ' ', 'Pt4bd1_aux_array[1,0]= ', Pt_aux_array[1,0], ' ', 'Pt4bd1_aux_array[1,1]= ',
Pt_aux_array[1,1], cr)
int_var=int_var+1

endwhile


--write('state= ', state_number, cr)
    --write('Pt[0,0]= ', Pt_aux_array[0,0], ' ', 'Pt[0,1]= ', Pt_aux_array[0,1], ' ', 'Pt[1,0]= ',
Pt_aux_array[1,0], ' ', 'Pt[1,1]= ', Pt_aux_array[1,1], cr)

--- We calculate the new state vector
V_state[0]=(par_init_array[0]*Pt_aux_array[0,0]+par_init_array[1]*Pt_aux_array[1,0])
V_state[1]=(par_init_array[0]*Pt_aux_array[0,1]+par_init_array[1]*Pt_aux_array[1,1])

--write('V_state[0]= ', V_state[0],' ', 'V_state[1]= ', V_state[1], cr)

prob_int = V_state[0]

return prob_int
end
```