Grant agreement for: Collaborative project*

Annex I - "Description of Work"

Project acronym: RASimAs

Project full title: " Regional Anaesthesia Simulator and Assistant "

Grant agreement no: 610425

Version date: 2013-09-24

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A1:
Project summary

Project Number [1]	610425	Project Acronym [2]	RASimAs

One form per project

General information			
Project title [3]	Regional Anaesthesia Simulator and Assistant		
Starting date [4]	01/11/2013		
Duration in months [5]	36		
Call (part) identifier [6]	FP7-ICT-2013-10		
Activity code(s) most relevant to your topic [7]	:		
Free keywords [8]	Regional Anaesthesia, Nerve Block, Virtual model, Regional Anaesthesia Simulator, Regional Anaesthesia Assistant,		

Abstract [9]

Regional anaesthesia (RA) has been used increasingly during the past four decades. This is addressed to the perceived advantages of reduced postoperative pain, earlier mobility, shorter hospital stay, and significantly lower costs. The performance of regional anaesthesia necessitates blocking the peripheral nerves by local injection of anaesthetic. Clinically this is achieved by the insertion of the injection needle close to the peripheral nerve, which is visualized with ultrasound and the proximity of the needle to the nerve is assessed with an electric nerve stimulator. However, it is a subtle technique and requires good theoretical, practical, and non-cognitive skills to allow trainees to achieve confidence in performing regional anaesthesia and to keep complications to a minimum. Current training methods for regional anaesthesia include cadavers, video teaching, ultrasound guidance, and simple virtual patient modelling. These techniques have limited capabilities and do not consider individual anatomy. The Virtual Physiological Human (VPH) creates the possibility to generate patient-specific computer models and apply them to RA procedures. The goal of this project is to increase the application, the effectiveness and the success rates of RA and furthermore the diffusion of the method into a broader clinical use through the development
of patient-specific VPH models for anaesthesia. We aim at developing two independent but complementary systems, one system for training and one for guidance: a patient-specific Regional Anaesthesia Simulator (RASim) enhanced with ultrasound guidance and a Regional Anaesthesia Assistant (RAAs), which will assist the physicians to localize the nerve during the actual procedure. The RASimAs project will combine both, offering the possibility of training in the regional anaesthesia technique during the training phase of the physician and providing assistance during the clinical application of regional anaesthesia at later stages.

A2:
List of Beneficiaries

Project Number [1]	610425	Project Acronym [2]	RASimAs

List of Beneficiaries

No	Name	Short name	Country	Project entry month[10]	Project exit month
1	UNIVERSITAETSKLINIKUM AACHEN	UKA	Germany	1	36
2	RHEINISCH-WESTFAELISCHE TECHNISCHE HOCHSCHULE AACHEN	RWTH	Germany	1	36
3	BANGOR UNIVERSITY	Bangor	United Kingdom	1	36
4	UNIVERSITY COLLEGE CORK, NATIONAL UNIVERSITY OF IRELAND, CORK	UCC	Ireland	1	36
5	UNIVERSIDAD REY JUAN CARLOS	URJC	Spain	1	36
6	FOUNDATION FOR RESEARCH AND TECHNOLOGY HELLAS	FORTH	Greece	1	36
7	INSTITUT NATIONAL DE RECHERCHE EN INFORMATIQUE ET EN AUTOMATIQUE	INRIA	France	1	36
8	ZILINSKA UNIVERZITA V ZILINE	UNIZA	Slovakia	1	36
9	KATHOLIEKE UNIVERSITEIT LEUVEN	KU Leuven	Belgium	1	36
10	STIFTELSEN SINTEF	SINTEF	Norway	1	36
11	SENSEGRAPHICS AB	SG	Sweden	1	36

A3:
Budget Breakdown

Project Number [1]	610425	Project Acronym [2]	RASimAs

One Form per Project

Participant number in this project [11]	Participant short name	Fund. %[12]	Ind. costs[13]	Estimated eligible costs (whole duration of the project)					Requested EU contribution
				RTD / Innovation (A)	Demonstration (B)	Management (C)	Other (D)	Total A+B+C+D	
1	UKA	75.0	T	1,100,630.00	0.00	103,840.00	0.00	1,204,470.00	929,312.00
2	RWTH	75.0	T	297,840.00	79,200.00	83,200.00	0.00	460,240.00	346,180.00
3	Bangor	75.0	T	223,353.00	0.00	0.00	0.00	223,353.00	167,514.00
4	UCC	75.0	T	179,200.00	0.00	0.00	0.00	179,200.00	134,400.00
5	URJC	75.0	T	237,889.00	56,870.00	0.00	0.00	294,759.00	206,851.00
6	FORTH	75.0	A	290,212.00	20,196.00	0.00	0.00	310,408.00	227,757.00
7	INRIA	75.0	S	284,233.00	25,184.00	0.00	0.00	309,417.00	225,766.00
8	UNIZA	75.0	T	91,360.00	12,160.00	0.00	0.00	103,520.00	74,600.00
9	KU Leuven	75.0	T	187,200.00	0.00	0.00	0.00	187,200.00	140,400.00
10	SINTEF	75.0	A	572,790.00	185,214.00	1,500.00	0.00	759,504.00	523,699.00
11	SG	75.0	T	338,240.00	183,040.00	0.00	0.00	521,280.00	345,200.00
Total				3,802,947.00	561,864.00	188,540.00	0.00	4,553,351.00	3,321,679.00

Note that the budget mentioned in this table is the total budget requested by the Beneficiary and associated Third Parties.

*** The following funding schemes are distinguished**

Collaborative Project (if a distinction is made in the call please state which type of Collaborative project is referred to: (i) Small of medium-scale focused research project, (ii) Large-scale integrating project, (iii) Project targeted to special groups such as SMEs and other smaller actors), Network of Excellence, Coordination Action, Support Action.

1. Project number

The project number has been assigned by the Commission as the unique identifier for your project, and it cannot be changed. The project number **should appear on each page of the grant agreement preparation documents** to prevent errors during its handling.

2. Project acronym

Use the project acronym as indicated in the submitted proposal. It cannot be changed, unless agreed during the negotiations. The same acronym **should appear on each page of the grant agreement preparation documents** to prevent errors during its handling.

3. Project title

Use the title (preferably no longer than 200 characters) as indicated in the submitted proposal. Minor corrections are possible if agreed during the preparation of the grant agreement.

4. Starting date

Unless a specific (fixed) starting date is duly justified and agreed upon during the preparation of the Grant Agreement, the project will start on the first day of the month following the entry info force of the Grant Agreement (NB : entry into force = signature by the Commission). Please note that if a fixed starting date is used, you will be required to provide a detailed justification on a separate note.

5. Duration

Insert the duration of the project in full months.

6. Call (part) identifier

The Call (part) identifier is the reference number given in the call or part of the call you were addressing, as indicated in the publication of the call in the Official Journal of the European Union. You have to use the identifier given by the Commission in the letter inviting to prepare the grant agreement.

7. Activity code

Select the activity code from the drop-down menu.

8. Free keywords

Use the free keywords from your original proposal; changes and additions are possible.

9. Abstract

10. The month at which the participant joined the consortium, month 1 marking the start date of the project, and all other start dates being relative to this start date.

11. The number allocated by the Consortium to the participant for this project.

12. Include the funding % for RTD/Innovation – either 50% or 75%

13. Indirect cost model

A: Actual Costs
S: Actual Costs Simplified Method
T: Transitional Flat rate
F :Flat Rate

Workplan Tables

Project number

610425

Project title

RASimAs—Regional Anaesthesia Simulator and Assistant

Call (part) identifier

FP7-ICT-2013-10

Funding scheme

Collaborative project

WT1
List of work packages

Project Number [1]	610425	Project Acronym [2]	RASimAs

LIST OF WORK PACKAGES (WP)

WP Number [53]	WP Title	Type of activity [54]	Lead beneficiary number [55]	Person-months [56]	Start month [57]	End month [58]
WP 1	Project Management	MGT	1	22.00	1	36
WP 2	Technological Environment	RTD	6	63.00	1	24
WP 3	Patient-Specific Virtual Models	RTD	7	72.00	1	36
WP 4	RASimAs Components	RTD	5	110.00	1	27
WP 5	RASimAs Prototype	DEM	10	52.00	10	36
WP 6	RASimAs Evaluation	RTD	9	63.00	20	36
WP 7	Regulatory Affairs and Quality Assurance	RTD	1	46.00	1	36
WP 8	Dissemination & Exploitation	RTD	1	35.00	1	36
			Total	463.00		

WT2:
List of Deliverables

Project Number [1]	610425	Project Acronym [2]	RASimAs

List of Deliverables - to be submitted for review to EC

Delive-rable Number [61]	Deliverable Title	WP number [53]	Lead benefi-ciary number	Estimated indicative person-months	Nature [62]	Dissemi-nation level [63]	Delivery date [64]
D1.1	Periodic Activity Report 1	1	1	3.00	R	PU	12
D1.2	Periodic Activity Report 2	1	1	3.00	R	PU	24
D1.3	Periodic Activity Report 3	1	1	3.00	R	PU	36
D1.4	Final Report to the Commission	1	1	4.00	R	PU	36
D1.5	Periodic Financial Report 1	1	1	3.00	R	PU	12
D1.6	Periodic Financial Report 2	1	1	3.00	R	PU	24
D1.7	Periodic Financial Report 3	1	1	3.00	R	PU	36
D2.1	User Specifications Report	2	4	4.00	R	CO	3
D2.2	Reference Architecture Plan	2	6	14.00	R	CO	6
D2.3	Data Storage Component, incl. report	2	6	15.00	O	CO	9
D2.4	Integrated Platform (inital), incl. report	2	6	15.00	P	PU	14
D2.5	Integrated Platform (final), incl. report	2	6	15.00	P	PU	24
D3.1	Toolkit for Pose Transforms of VPH Models, incl. report	3	5	14.00	O	CO	15
D3.2	Patient-Specific Dataset Library, incl. report	3	1	16.00	O	CO	18
D3.3	Physics-based models for Body Torso, Upper	3	7	30.00	O	PU	18

WT2:
List of Deliverables

Delive-rable Number [61]	Deliverable Title	WP number [53]	Lead benefi-ciary number	Estimated indicative person-months	Nature [62]	Dissemi-nation level [63]	Delivery date [64]
	and Lower Extremities, incl. report						
D3.4	Toolkit for Integration of Patient-Specific Data and Physics-Based Models into VPH Models, incl. report	3	6	12.00	O	CO	20
D4.1	Haptic Feedback Components, incl. report	4	5	25.00	O	CO	24
D4.2	Tool-Tissue Interaction Models, incl. report	4	7	22.00	O	CO	24
D4.3	Ultrasound Simulation Components, incl. report	4	2	27.00	O	CO	24
D4.4	Training Functions of Simulator, incl. report	4	5	22.00	O	CO	27
D4.5	Guidance System Specifications	4	10	14.00	R	PU	27
D5.1	RASim Specifications	5	11	10.00	R	CO	12
D5.2	RASim Prototype, incl. report	5	10	11.00	P	PU	24
D5.3	RAAs Specification	5	11	10.00	R	CO	27
D5.4	RAAs Prototypes, incl. report	5	10	11.00	P	PU	27
D5.5	RASimAs Revised Specification	5	10	10.00	R	CO	27
D6.1	SOP for RASim-Guided Training of Physicians	6	1	21.00	R	PU	27

WT2:
List of Deliverables

Delive-rable Number [61]	Deliverable Title	WP number [53]	Lead benefi-ciary number	Estimated indicative person-months	Nature [62]	Dissemi-nation level [63]	Delivery date [64]
D6.2	SOP for RAAs-Guided Application of RA	6	9	21.00	R	PU	30
D6.3	Ethic and Regulatory Approvals	6	1	21.00	O	RE	30
D7.1	Quality Assurance Plan (QA-Plan)	7	1	4.00	R	CO	3
D7.2	Technical Files	7	1	5.00	R	CO	27
D7.3	Clinical Trial Protocol	7	1	5.00	R	PU	27
D7.4	Patient Informed Consent Form	7	1	4.00	R	PU	27
D7.5	eCRF & EDC System, incl. report	7	1	7.00	O	PU	24
D7.6	Investigator's Brochure (IB)	7	1	8.00	R	PU	24
D7.7	Annual Ethics Report 1	7	1	4.00	R	PU	12
D7.8	Annual Ethics Report 2	7	1	4.00	R	PU	24
D7.9	Annual Ethics Report 3	7	1	5.00	R	PU	36
D8.1	Project Website continuously updated, journalistic descriptions of the project, press releases, video and other media	8	1	5.00	O	PU	2
D8.2	Dissemination Plan	8	1	5.00	R	RE	6
D8.3	IPR Directory	8	1	6.00	R	CO	36
D8.4	Exploitation Plan 1	8	10	6.00	R	RE	12
D8.5	Exploitation Plan 2	8	10	6.00	R	RE	24

WT2:
List of Deliverables

Delive-rable Number [61]	Deliverable Title	WP number [53]	Lead benefi-ciary number	Estimated indicative person-months	Nature [62]	Dissemi-nation level [63]	Delivery date [64]
D8.6	Press release about project results; film or photos about using project technology	8	1	1.00	O	PU	30
D8.7	Final Report on Dissemination and Exploitation	8	10	6.00	R	RE	36
			Total	463.00			

WT3:
Work package description

Project Number [1]	610425	Project Acronym [2]	RASimAs

One form per Work Package

Work package number [53]	WP1	Type of activity [54]	MGT
Work package title	Project Management		
Start month	1		
End month	36		
Lead beneficiary number [55]	1		

Objectives

Project management of RASimAs is designed as effective and efficient framework for all partners from multidisciplinary institutions to ensure a proper accomplishment of all scientific tasks and objectives. The WP “Project Management” encompasses the financial, administrative, contractual, and ethical components during the entire project period. Clearly structured management procedures are defined for the implementation of RASimAs:

- Establish an appropriate liaison with the EC for financial administration and reporting;
- Establish and maintain a common understanding within the interdisciplinary team by fostering the exchange of project related information;
- Supervise and monitor the implementation and project progress according to the scheduled work plan with its tasks, deliverables and milestones;
- Assure high-quality documentation of projects’ results in accordance with the reporting periods;
- Organize meetings of the consortium at all stages and provide minutes and documentation;
- Oversee ethical issues and gender equity during the entire project duration.

The WP 1 is to ensure the realisation of all tasks and objectives on time and within the budget with transparency at all stages of the project and a high-quality outcome.

Description of work and role of partners

Task 1.1 Project Administration & Management (Task Leader: UKA-IMI)
Ensuring the compliance with the provisions of the Commission (Grant Agreement and Annexes) the Coordinator
(supported by the Project Manager) is responsible for all contractual work and provisions of the European Commission for RASimAs. A specific project management infrastructure will be set up based on the web-based open source software Collabtive (http://collabtive.o-dyn.de/) for project tracking and the open source TRAC system (http://trac.edgewall.org/) for issue tracking. The project management software will support adequate communication for the Consortium members and set up the knowledge management. The project manager provides guidelines and templates at all stages of the project according to the provisions of the European Commission. A timely review of the scheduled deliverables and milestones will allow an efficient implementation of the project as well as concrete options for adjustments of management procedures. The project manager collects and compiles the scientific reviewed project findings and results for progress and activity reports. All meetings of the Consortium (kick-off, mid-term and final) and the Steering Committee will be scheduled, prepared and organised by the Project Manager. Minutes will be distributed in a timely manner to all respective participants and safeguarded. All information on project results as well as on financial reports will be reflected in the final report.

Task 1.2 Financial Administration (Task Leader: RWTH-EU-PM)
The Coordinator will establish an appropriate liaison with the European Commission and the financial procedures
within the Consortium and prepares the financial reports for the project. RWTH-EUPM assists with the timely distribution of the EC Contribution to all beneficiaries and will monitor and control the transfers and accounting on a regular basis. Cost statements and cost certificates from each partner will be collected

and controlled in order to prepare and submit the financial reports to the Commission. In order to monitor the expenditures, the individual partner administrative documents and statements will be collected by the half-time of the reporting periods. To ensure transparency of financial issues, the costs of each beneficiary will be monitored and appropriately stated, that during all stages of the project runtime information on the finance of RASimAs is available.

Person-Months per Participant

Participant number [10]	Participant short name [11]	Person-months per participant
1	UKA	12.00
2	RWTH	10.00
	Total	22.00

List of deliverables

Delive-rable Number [61]	Deliverable Title	Lead benefi-ciary number	Estimated indicative person-months	Nature [62]	Dissemi-nation level [63]	Delivery date [64]
D1.1	Periodic Activity Report 1	1	3.00	R	PU	12
D1.2	Periodic Activity Report 2	1	3.00	R	PU	24
D1.3	Periodic Activity Report 3	1	3.00	R	PU	36
D1.4	Final Report to the Commission	1	4.00	R	PU	36
D1.5	Periodic Financial Report 1	1	3.00	R	PU	12
D1.6	Periodic Financial Report 2	1	3.00	R	PU	24
D1.7	Periodic Financial Report 3	1	3.00	R	PU	36
		Total	22.00			

Description of deliverables

D1.1) Periodic Activity Report 1: A periodic report within 60 days from the end of each reporting period will be provided. It will include an overview, including a publishable summary of the progress of work towards the objectives of the project, including achievements and attainment of any milestones and deliverables identified in Annex I. [month 12]

D1.2) Periodic Activity Report 2: A periodic report within 60 days from the end of each reporting period will be provided. It will include an overview, including a publishable summary of the progress of work towards the objectives of the project, including achievements and attainment of any milestones and deliverables identified in Annex I. [month 24]

D1.3) Periodic Activity Report 3: A periodic report within 60 days from the end of each reporting period will be provided.It will include an overview, including a publishable summary of the progress of work towards the objectives of the project, including achievements and attainment of any milestones and deliverables identified in Annex I. [month 36]

D1.4) Final Report to the Commission: In addition to the periodic report for the last period of the project, a final report will be submitted, within 60 days after the end of the project. [month 36]

D1.5) Periodic Financial Report 1: In order to monitor the expenditures, the individual partner administrative documents and statements will be collected by the half-time of the reporting periods. To ensure transparency of financial issues, the costs of each beneficiary will be monitored and appropriately stated, that during all stages of the project runtime information on the finance of RASimAs is available. [month 12]

D1.6) Periodic Financial Report 2: In order to monitor the expenditures, the individual partner administrative documents and statements will be collected by the half-time of the reporting periods. To ensure transparency of financial issues, the costs of each beneficiary will be monitored and appropriately stated, that during all stages of the project runtime information on the finance of RASimAs is available. [month 24]

D1.7) Periodic Financial Report 3: In order to monitor the expenditures, the individual partner administrative documents and statements will be collected by the half-time of the reporting periods. To ensure transparency of financial issues, the costs of each beneficiary will be monitored and appropriately stated, that during all stages of the project runtime information on the finance of RASimAs is available. [month 36]

Schedule of relevant Milestones

Milestone number [59]	Milestone name	Lead beneficiary number	Delivery date from Annex I [60]	Comments

WT3:
Work package description

Project Number [1]	610425	Project Acronym [2]	RASimAs

One form per Work Package

Work package number [53]	WP2	Type of activity [54]	RTD
Work package title	Technological Environment		
Start month	1		
End month	24		
Lead beneficiary number [55]	6		

Objectives

In close interaction with WP3, WP4, and WP5, this work package supports the development of the targeted platforms by addressing:
- identified key-features of RA simulation and assistance
- reference architectural plan for RASimAs
- model and data repository development
- integrated technological environment including appropriate interfaces and computational resources

Description of work and role of partners

Task 2.1 System Specifications (Task Leader: UCC)
Based on the current standard of RA, we focus on conventional as well as US-guided RA procedures, characterize procedural errors associated with both types of RA, and specify key features of both, the training system assistance device. The specifications include (i) conceptual and technical specifications of the RASim system and (ii) conceptual and technical specifications of the RAAs system. This task will match the aforementioned specifications and requirements to the relevant software tools and systems that are already available from the members of the Consortium in order to identify an efficient and as seamless as possible integration strategy.

Task 2.2 Reference Architecture (Task Leader: FORTH)
Technological reference architecture for subsequent implementation and integration of the different modules/ services is developed. The RA specification will provide software architecture design patterns to effectively guide and support the construction of coherent, consistent and interoperable service-oriented architecture (SOA)-based systems and services. Particular emphasis will be given to the definition of appropriate interfaces among the modules to enable interoperability. Central to this technical architecture will be the data repository (task 2.3) for the management of the patient specific data (the magnetic resonance imaging (MRI) and magnetic resonance angiography (MRA) data, the Ultrasound (US) measurements, the segmentation results for the physiological node, etc.) as well as the information needed for the training module of the system. In addition to the functional aspects, the designed architecture should support certain qualities for the system, such as the confidentiality, security, audit control, and availability of the data, the real time communication needs, the run time monitoring and reporting, etc. Finally this task will define certain deployment options and distributed or centralized software organization strategies. In order to define an implementation and component integration plan, in this task also relevant existing standards with impact on the system will be identified, analysed, and selected. Such standards range from the architecture definition process (e.g. the ISO/IEC/IEEE 42010:2011, Systems and software engineering — Architecture description) to the concrete implementation technologies (e.g. Web/REST services and the DICOM standard for imaging data and X3D for 3D geometry). This task, being the architecture definition and component integration venue, will serve as a guide for the integration of the corresponding systems.

Task 2.3 Information Storage (Task Leader: FORTH)
The objective of this task is the implementation of system's data repository, the definition of its interfaces, and the selection of the relevant data storage and communication standards based on the managed information. Much of the data gathered in this project will be in the form of medical images, obtained through techniques such as (MRI), (MRA) data and (US) data. The DICOM format is used throughout the medical imaging community

as a standard for such data, with data being stored in PACS servers within the clinical environment. In order to conform to these standards and to ensure interoperability with the imaging and modeling tools in RASimAs, we will develop an imaging data component using a PACS server as backend image storage. This will address the needs of model development in WP3. The DICOM format links a great deal of metadata alongside images – the use of a PACS backend will ensure that this metadata is also stored alongside the medical images. We will also explore the use of cloud storage to store DICOM metadata and enable sharing it with applications that aren't necessarily DICOM clients. In order to assist the RA simulation components a number of post-processing results (e.g. annotations, segmentation results of organ structures), will also be stored next to the corresponding patient image data. The MedX3D extension of the ISO standard X3D established a link between DICOM data and n-dimensional geometry data and will be used for this purpose.

Task 2.4 Integrated Platform (Task Leader: FORTH)
The orchestration and automation of a series of processing tasks (e.g. data access segmentation, registration and fusion) are an essential component for the realization of the project's RA simulators. The aim of this task is to deliver an intuitive user level application where data delivering consortium members are able to discover the most applicable tools for analyzing the data at hand, combine these tools into data flows and pipelines, and furthermore to keep an archive of their data processing pipelines, which can be shared and reused by other users. As an end user application, this environment requires the delivery of a user interface that builds upon the tool/model repositories and the domain specific metadata for the efficient discovery of analysis tools and their successful integration. The final result will be the integrated RASimAs platform and will allow the partners to contribute imaging data from different modalities, e.g., MRI and US as well as model data, e.g., surface geometry, tetrahedral meshes and other multi-dimensional parameters for simulation.

Task 2.5 Image Processing Library (Task Leader: UKA-IMI)
The Consortium unifies academia and industry of different background, all of which have outstandingly contributed to the state-of-the-art in their respective fields. The delivered impact, however, is developed using different technological platforms, algorithms, and interfaces. This task aims at unifying those environments, interfacing them, and providing model-based tool for segmentation, registration and rendering. It is not intended, however, to develop novel approaches in the field of image processing.

Person-Months per Participant

Participant number [10]	Participant short name [11]	Person-months per participant
1	UKA	19.00
2	RWTH	3.00
3	Bangor	2.00
4	UCC	3.00
5	URJC	5.00
6	FORTH	11.00
7	INRIA	2.00
8	UNIZA	6.00
10	SINTEF	4.00
11	SG	8.00
	Total	63.00

WT3:
Work package description

List of deliverables

Delive-rable Number [61]	Deliverable Title	Lead benefi-ciary number	Estimated indicative person-months	Nature [62]	Dissemi-nation level [63]	Delivery date [64]
D2.1	User Specifications Report	4	4.00	R	CO	3
D2.2	Reference Architecture Plan	6	14.00	R	CO	6
D2.3	Data Storage Component, incl. report	6	15.00	O	CO	9
D2.4	Integrated Platform (inital), incl. report	6	15.00	P	PU	14
D2.5	Integrated Platform (final), incl. report	6	15.00	P	PU	24
		Total	63.00			

Description of deliverables

D2.1) User Specifications Report: WP 2.1 will describe the essential components of procedural performance within peripheral nerve block, characterise errors associated with nerve block performance and define the assessment metrics which may be used to assess procedural performance. User needs with respect to both training in, and performance of, peripheral nerve block will be identified. Both outputs will be used to inform the system specifications and design for subsequent work packages. [month 3]

D2.2) Reference Architecture Plan: This deliverable will shed light on the RASimAs technological reference architecture that will guide the subsequent implementation and integration of the different modules/services to be developed. [month 6]

D2.3) Data Storage Component, incl. report: This deliverable will report on the implementation of system's data repository, the definition of its interfaces, and the selection of the relevant data storage and communication standards based on the managed information. [month 9]

D2.4) Integrated Platform (inital), incl. report: This deliverable will initially report on the RASimAs integration environment for orchestration and automation of a series of processing tasks (e.g. data access segmentation, registration and fusion), essential for the realization of the project's RA simulators. [month 14]

D2.5) Integrated Platform (final), incl. report: This deliverable will report on the completed RASimAs integration environment for orchestration and automation of a series of processing tasks (e.g. data access segmentation, registration and fusion), essential for the realization of the project's RA simulators. [month 24]

Schedule of relevant Milestones

Milestone number [59]	Milestone name	Lead benefi-ciary number	Delivery date from Annex I [60]	Comments
MS1	RASimAs integrated platform initial demonstration	6	14	

WT3:
Work package description

Project Number [1]	610425	Project Acronym [2]	RASimAs

One form per Work Package

Work package number [53]	WP3	Type of activity [54]	RTD
Work package title	Patient-Specific Virtual Models		
Start month	1		
End month	36		
Lead beneficiary number [55]	7		

Objectives

For the creation of the Patient-Specific Virtual Models an essential task is the modelling nerves from a biomechanical and electrical standpoint. For the multi-physics modelling the Open Source “SOFA framework” is used and a key element of this modelling is to account for the impact of soft tissue deformation onto the nerve location, as well as the definition of tissue characteristics for electric impulse propagation (task 4.2), which can lead to a nerve stimulus. The aim is that the models include anatomical and mechanical properties of the tissues, as well as computational models compatible with real-time simulation. Patientspecific data will be inferred from various imaging modalities. Models created in this WP will be used as components for the RA simulator and for the RAAs system in WP4.

Description of work and role of partners

Task 3.1 Data Acquisition & Management (Task Leader: UKA-IMI)
All necessary imaging data sets for the development of the anatomical model will be acquired, including individual (MRI), (MRA) data and (US) data. These data-sets will be pre-processed and archived in the data repository developed in WP2. Another focus will be on standard model data such as the Human Anatomy Collection from Zygote that will be merged to enhance the resulting patient-specific descriptions. These data will be used in the following WPs for the model development and will be available to all involved participants. As a result, the key sub-tasks are:
- Identification of the most suitable techniques and requirements for the imaging modalities;
- Develop registration techniques for multi-modality data fusion;
- Analyze anatomical and physiological variability across patients;
- Build an atlas based on the various datasets;
- Assess the resulting model(s) within a clinical environment.

Task 3.2 Anatomical Modelling (Task Leader: UKA-IMI)
Anatomical models of upper body torso, upper and lower extremities will be developed based on the data sets created in Task 3.1. Segmentation algorithms will be developed and existing VPH toolkits will be used in order to extract the different tissue classes. These classes will include skin surface, muscle, fat, vessels, bone and nerves. Particular attention will be given to generating geometrical models that meet the requirements of the computational models that will rely on this data. Surface meshes will be compatible with collision detection methods, and will allow for the generation of finite element models. Nerves, which are not sufficiently visible in conventional imaging modalities, will be modelled using a template approach (based on a hierarchical tree data structure). Anatomical landmarks extracted from MRI data will be used as functional nodes. Mechanical data from Task 3.1 will be associated with the anatomical representations, so it will provide localized, patient-specific, material properties within their anatomical context.

Task 3.3 Mechanical Modelling (Task Leader: INRIA)
Using models from Task 3.2 and data from Task 3.1, biomechanical models of the different tissue classes will be developed. Soft tissue modelling will rely on the finite element method, using approaches that have already demonstrated their potential for accurately representing tissue deformation while remaining compatible with real-time computation. Such approaches involve for instance the co-rotational method, allowing for large displacements. Total Lagrangian methods, using hyper elastic materials, will also be investigated. Particular attention will also be given to the relationship between tissue deformation and the underlying nerve

physiology. This will be done using a multi-physics approach, as already demonstrated in the context of cardiac electrophysiology.

Task 3.4 Physiological Modelling (Task Leader: BANGOR)
This task will essentially address the problem of modelling nerves from an electro-physiological standpoint. This multi-physics modelling will be addressed using the Open Source SOFA framework. A key element of this modelling will be to account for the impact of soft tissue deformation onto the nerve location. Also, different variations in physiological anatomy will be taken into account.

Task 3.5 Model Integration (Task Leader: FORTH)
The Model Integration will integrate all various components of the model already developed. An environ-ment for this function will be created, including the anatomical and the mechanical properties of the individual classes. The model integration will be based on the abstraction of the participating models as reusable software components that exchange standardized data through well-defined communication channels. The component models will therefore be orchestrated so as to support the high level integration thereof, and a web based orchestration environment will be developed to facilitate the linking of models and data.

Task 3.6 Subject Posing (Task Leader: URJC)
In this task, algorithms will be adopted and developed that allow to transform the integrated subject-specific data into poses that are used for RA, because the gantry-based imaging (i.e., CT, MRI) is usually performed in a subject posing that is different to the patient positioning when applying RA.

Person-Months per Participant

Participant number [10]	Participant short name [11]	Person-months per participant
1	UKA	16.00
3	Bangor	18.00
5	URJC	4.00
6	FORTH	18.00
7	INRIA	14.00
9	KU Leuven	2.00
	Total	72.00

List of deliverables

Delive-rable Number [61]	Deliverable Title	Lead benefi-ciary number	Estimated indicative person-months	Nature [62]	Dissemi-nation level [63]	Delivery date [64]
D3.1	Toolkit for Pose Transforms of VPH Models, incl. report	5	14.00	O	CO	15
D3.2	Patient-Specific Dataset Library, incl. report	1	16.00	O	CO	18
D3.3	Physics-based models for Body Torso, Upper and Lower Extremities, incl. report	7	30.00	O	PU	18
D3.4	Toolkit for Integration of Patient-Specific Data and Physics-Based Models into VPH Models, incl. report	6	12.00	O	CO	20

WT3:
Work package description

List of deliverables

Delive-rable Number [61]	Deliverable Title	Lead benefi-ciary number	Estimated indicative person-months	Nature [62]	Dissemi-nation level [63]	Delivery date [64]
		Total	72.00			

Description of deliverables

D3.1) Toolkit for Pose Transforms of VPH Models, incl. report: Software and detailed specification designed to enable the VPH models to be positioned and moved between the various poses needed during the procedure. [month 15]

D3.2) Patient-Specific Dataset Library, incl. report: The deliverable will be composed of several personalized imaging data (CT, MRI, MRA, US), organized by parameters such as body region and patient describing parameters such as age, gender, weight, and size of the person. The different modalities will be registered in geometry with respect to the Zygote data. This allows enrichment and completion of the resulting patient-specific models. [month 18]

D3.3) Physics-based models for Body Torso, Upper and Lower Extremities, incl. report: This deliverable will integrate results from all work packages, and will demonstrate functional models for body torso, upper and lower Extremities. The main functionalities of this model will be tissue deformation and physiological response. The deliverable will be implemented using the SOFA and H3D software platforms. [month 18]

D3.4) Toolkit for Integration of Patient-Specific Data and Physics-Based Models into VPH Models, incl. report: This deliverable is the toolkit for integrating the anatomical and the mechanical models and individualize each integrated model with patient-specific data. [month 20]

Schedule of relevant Milestones

Milestone number [59]	Milestone name	Lead benefi-ciary number	Delivery date from Annex I [60]	Comments
MS2	Final version of patient-specific library released	7	18	

WT3:
Work package description

Project Number [1]	610425	Project Acronym [2]	RASimAs

One form per Work Package

Work package number [53]	WP4	Type of activity [54]	RTD
Work package title	RASimAs Components		
Start month	1		
End month	27		
Lead beneficiary number [55]	5		

Objectives

WP 4 is defined to develop the RASim and the RAAs system. Based on the user needs and specifications (task 2.1), the RAAs system specifications and requirements have been defined. In comprehensive interaction of software developers and clinician, all specifications will be classified into “critical” and “desirable”. The thus agreed set of specifications needs to be transferred into functional requirements and software design. The design choices and consequences thereof will be communicated to all medical partners of the Consortium, preferably in a joint meeting which results in a thoroughly discussed and agreed final design. The interactive virtual reality (VR)-based training simulator will offer both types of techniques for locating the desired nerve: electrical stimulation and ultrasound-guidance. The algorithms in the tasks related to the RAsim system will be implemented or interfaced to the Open Source H3D software, which will be the foundation for the RASim prototypes in WP5.

Description of work and role of partners

Task 4.1 Haptic Feedback Development (Task Leader: URJC)
It is necessary to develop haptic rendering algorithms that can provide users with an intuitive interaction during the simulated palpation and needle and ultrasound probe steering procedures; the quality of the force feedback provided in RASim is essential for allowing trainees to develop skills which can be transferred to real surgical environments. In particular, special attention will be devoted to ensure that the haptic feedback has the required degrees of realism and stability.

Task 4.2 Tool Tissue Interaction Modelling (Task Leader: INRIA)
The main goal of this task is the construction of the simulator core. For this purpose it will be necessary: (i) to develop appropriate collision detection, contact response and soft tissue deformations algorithms, (ii) to provide mechanisms for these algorithms to incorporate the patient-specific virtual model and data described in WP3, (iii) to integrate the modules meeting the overall simulator design specifications. This research line will be driven by the following key factors: the performance of these algorithms for meeting the real-time needs of the simulator, the requirement to work on patient-specific data and the interaction between the haptic rendering algorithms and the soft-tissue model. The electrical stimulus simulation also is integrated in this task.

Task 4.3 Ultrasound Simulation (Task Leader: RWTH-VR)
The ultrasound module will be fully developed within this task. There are two main techniques for guiding physicians during the nerve location phase, based on electrical stimulation and ultrasound guided procedures. Currently, there is no agreement on which technique is best, the choice depends on specific preferences and infrastructure of the different anaesthesia departments (furthermore, some physicians combine both techniques). In consequence, RASim will let trainees choose between both methods; the previous work performed by RWTH, INRIA, SG and URJC in ultrasound simulation will be invaluable in this respect.

Task 4.4 Training Function Development (Task Leader: URJC)
Virtual Reality resources will be exploited to provide supportive information to guide the training process, whereas formative and summative feedback will be supplied before, during, and at the completion of the tasks. This feedback will be used by trainees and physicians for self-directed learning and training, detection of errors and weak points, and study of the learning curve. Trainees will evolve from simple tasks involving basic competencies, to more complex tasks that will prepare them to perform RA procedures in real settings. Therefore, the training function will allow the repetition of tasks, with the necessary feedback to guide the trainee

towards expertise by means of deliberative practice. To facilitate the training function and to accommodate the results of this task a dedicated courseware system will be interfaced with the simulator.

Task 4.5 Real-Time Model Processing (Task Leader: SINTEF)
A major task will be the real-time registration of the models obtained from the imaging data and preprocessing with the real patient, such that the accuracy is within an acceptable range for the intervention. This will require research on adequate markers (visible in scan and comfortable for the patient) research on camera's (sensitivity) and optimal 3D-positioning of markers and camera's. Furthermore, the algorithms for (i) real-time processing and registration of the US data, (ii) segmentation and registration of the blood
vessels and the nerves, (iii) automatic localization of the nerve on the ultrasound images, and (iv) navigation feedback, estimation of the proximity of the needle to the target nerve will be integrated in the real-time framework.

Task 4.6 Intra-Procedure Guidance Development (Task Leader: SINTEF)
The guidance function of the RAAs system will be developed in this task. Based on the localization estimation provided by the algorithm developed in task 4.5, a function will be developed that provides guiding indications to the user. The guiding rules will be based on the anatomical model and the US data and the goal will be to minimize the needle proximity to the target nerve. It should be investigated whether haptic guidance is desirable and feasible here and to what extent.

Person-Months per Participant

Participant number [10]	Participant short name [11]	Person-months per participant
2	RWTH	23.00
3	Bangor	5.00
5	URJC	25.00
6	FORTH	10.00
7	INRIA	13.00
8	UNIZA	6.00
10	SINTEF	15.00
11	SG	13.00
	Total	110.00

List of deliverables

Delive-rable Number [61]	Deliverable Title	Lead benefi-ciary number	Estimated indicative person-months	Nature [62]	Dissemi-nation level [63]	Delivery date [64]
D4.1	Haptic Feedback Components, incl. report	5	25.00	O	CO	24
D4.2	Tool-Tissue Interaction Models, incl. report	7	22.00	O	CO	24
D4.3	Ultrasound Simulation Components, incl. report	2	27.00	O	CO	24
D4.4	Training Functions of Simulator, incl. report	5	22.00	O	CO	27
D4.5	Guidance System Specifications	10	14.00	R	PU	27

WT3:
Work package description

List of deliverables

Delive-rable Number [61]	Deliverable Title	Lead benefi-ciary number	Estimated indicative person-months	Nature [62]	Dissemi-nation level [63]	Delivery date [64]
		Total	110.00			

Description of deliverables

D4.1) Haptic Feedback Components, incl. report: This demonstrator will contain all the software modules that will be developed to provide the system with haptic feedback. The haptic modules will support simulations of palpation and needle steering procedures. [month 24]

D4.2) Tool-Tissue Interaction Models, incl. report: This deliverable will consist in a set of optimized algorithms for collision detection, contact response and soft tissue deformations. These algorithms will be implemented as modules within the SOFA framework, and will allow personalization based on patient-specific data. [month 24]

D4.3) Ultrasound Simulation Components, incl. report: This deliverable consists of the software modules for the simulation of Ultrasound imaging of body structures with the necessary realism and level of detail to allow training of regional anesthesia procedures. The components will utilize the datasets in deliverable D3.1 and provide interfaces to interact with other simulation components. [month 24]

D4.4) Training Functions of Simulator, incl. report: Task 4.4 will make use of the technology developed in Tasks 4.1, 4.2 and 4.3 to provide trainees and physicians with supportive information for self-directed learning and training. D 4.4 will implement assessment and feedback mechanisms to guide the training process, as well as a dedicated courseware system. [month 27]

D4.5) Guidance System Specifications: The achievable guidance specifications of the regional anaesthesia assistant system (RAAs) , with respect to accuracy, sensitivity, navigation feedback and haptic guidance. [month 27]

Schedule of relevant Milestones

Milestone number [59]	Milestone name	Lead benefi-ciary number	Delivery date from Annex I [60]	Comments
MS3	Haptic rendering algorithms, simulator core, and ultrasound module developed	5	24	
MS4	Training courseware developed; RAA system specification released	5	27	

WT3:
Work package description

Project Number [1]	610425	Project Acronym [2]	RASimAs

One form per Work Package

Work package number [53]	WP5	Type of activity [54]	DEM
Work package title	RASimAs Prototype		
Start month	10		
End month	36		
Lead beneficiary number [55]	10		

Objectives

Within this work package (Lead: SINTEF), the RASimAs prototype is developed, which includes the definitions and systems previously defined in WP2-4. The prototype consists of two individual parts for the simulator (RASim) and the assistant system (RAAs).

Description of work and role of partners

Task 5.1 RASim System Integration (Task Leader: SG)
All of the simulator functions will be integrated using the Open Source Software H3D as a central engine and combined within a prototype unit. This task is focused on the software components and will include the haptic input/output, the tool-tissue interaction, simulation of the guidance procedures and the training module. Special care will be devoted to the integration of the haptic rendering algorithms with the tool-tissue interaction module, in order to reach the project specifications in terms of accuracy and speed of the haptic response. This task will need a number of activities such as (i) system architecture, (ii) component integration, (iii) system optimization and (v) technical evaluation.

Task 5.2 RASim Portable Prototype (Task Leader: SG)
The task focuses on the development of a working prototype used in clinical trials (WP6). The project will require the development of 3 portable system stations, which will be transferred or directly integrated within the facilities of the 3 testing institutions, and additional units to be used by the developers, The combination of hard- and software will lead to the prototype of the simulator. This will be a four-stage process consisting of the following steps (i) hardware acquisition and modification, (ii) hardware and software integration, (iii) system tests and evaluation, and (iv) final system design.

Task 5.3 RAAs System Integration (Task Leader: SINTEF)
All the methods developed in task 4.5 and task 4.6 will be integrated to a single system. A prototype system will be developed with respect to the user needs and specifications according to WP2 and WP6T1. Emphasis should be put on the user interface here. The system should be easy to use, OR-compatible, fitting the expectations of the user and should not interfere with other necessary tasks of the user. To start we will build a flexible set-up with relatively easy interchangeable components. There will be a continuously back and forth switching between this task and tasks 4.5-4.6 to ultimately obtain an optimum configuration.

Task 5.4 RAAs Portable Prototype (Task Leader: SINTEF)
Hardware and software is combined to prototypes that can be used in the clinical applications of WP 6. This requires the addition of the guidance function in the portable system stations developed in Task 5.2, following the same workflow process.

Task 5.5 Support & Improvement (Task Leaser: SINTEF)
The prototypes will be tested at the medical partners for RA education and practice. There will be a continuous user-centred development cycle taking care of feedback from evaluation results in order to ultimately obtain an optimum configuation.

WT3:
Work package description

Person-Months per Participant

Participant number [10]	Participant short name [11]	Person-months per participant
2	RWTH	9.00
5	URJC	8.00
6	FORTH	3.00
7	INRIA	3.00
8	UNIZA	4.00
10	SINTEF	9.00
11	SG	16.00
	Total	52.00

List of deliverables

Delive-rable Number [61]	Deliverable Title	Lead benefi-ciary number	Estimated indicative person-months	Nature [62]	Dissemi-nation level [63]	Delivery date [64]
D5.1	RASim Specifications	11	10.00	R	CO	12
D5.2	RASim Prototype, incl. report	10	11.00	P	PU	24
D5.3	RAAs Specification	11	10.00	R	CO	27
D5.4	RAAs Prototypes, incl. report	10	11.00	P	PU	27
D5.5	RASimAs Revised Specification	10	10.00	R	CO	27
		Total	52.00			

Description of deliverables

D5.1) RASim Specifications: This deliverable consists of a specification of the system architecture documented with UML diagrams and text. Based on this, there will be also a first prototype of the simulator with limited functionality and clearly defined interfaces to modules that are developed in WP5 for the next deliverable D.5.2. [month 12]

D5.2) RASim Prototype, incl. report: This deliverable is a successor of the prototype of D.5.1 with extended functionality and results in three portable test systems that will be used for evaluation. Furthermore, a public report will describe those prototypes functionality in text and photos for press release and documentation. [month 24]

D5.3) RAAs Specification: The requirement specifications of the RAAs based on the guidance system specifications and user needs. [month 27]

D5.4) RAAs Prototypes, incl. report: RAAs Prototype hardware and software to be tested and evaluated in the clinics (WP6) [month 27]

D5.5) RASimAs Revised Specification: Adjustments on previously defined specifications coming from the clinical evaluation and leading to improvements of the prototype. [month 27]

WT3:
Work package description

Schedule of relevant Milestones

Milestone number [59]	Milestone name	Lead benefi-ciary number	Delivery date from Annex I [60]	Comments
MS5	RASim function available on the portable prototypes	10	24	
MS6	RAAs function available on the portable prototypes	10	27	

WT3:
Work package description

Project Number [1]	610425	Project Acronym [2]	RASimAs

One form per Work Package

Work package number [53]	WP6	Type of activity [54]	RTD
Work package title	RASimAs Evaluation		
Start month	20		
End month	36		
Lead beneficiary number [55]	9		

Objectives

This work package focuses on the evaluation of the RA Simulator and RA Assistant. Evaluations will take place at three different study sites (UKA-DA, UCC, KUL). Evaluation will be performed in controlled clinical trials to obtain most reliable results. This WP also aims at proving the usefulness of (patient-specific) VPH models in health care.

Description of work and role of partners

Task 6.1 RASim Experts Assessment (Task Leader: UCC)
In a first step, the cognitive walkthrough method will be used to identify usability issues on different RA locations. Next, experts in the field of anaesthesia will perform the evaluation on different nerve blocks. Three experts from each participating medical partner institution will carry out this study. The approach used is to match recreated sensations (e.g., insertion of the needle through skin or fascia) with experts' perceptions of the equivalent clinical events. In dependency of the identified problems, the simulator will be modified and further developed to enhance realistic RA-simulation. Subsequently the same experts will evaluate the simulator again (iterative development approach). This process will be repeated to achieve a high level of expert consistency and reliability.

Task 6.2 RASim Evaluation Design (Task Leader: UKA-DA)
In this task, the RASim system will be evaluated in a setting comparable to a controlled clinical trial, where a group of novices trained with the system competes against a group of novices that were trained conventionally, i.e., without the RASim portable system. 15 first year anaesthetics trainees (total of 45 trainees) from all three contributing medical institutions will participate in this randomized prospective trial. This task will deliver all instructions, guidance, and measurements in written form.

Task 6.3 RASim Evaluation Conduction (Task Leader: UKA-DA)
To familiarize the trainees with RA-simulator, each trainee will receive a general introduction to different RA techniques. After randomization, trainees allocated to the simulator group will perform several nerve blocks on the RA-simulator. An experienced staff anaesthesiologist will supervise all simulator sessions. After the first simulator session, each trainee will perform three subsequent simulator sessions. In the control group, trainees without simulator-based training will perform accordingly RAs under the supervision of a staff anaesthesiologist.

Task 6.4 RAAs Experts Assessment (Task Leader: UCC)
Experts in RA will evaluate the RAAs system with respect to its adaptation into clinical practice. Meaningful parameter concerning the evaluation by means of a cognitive walkthrough (see WP5T1) are (i) friendliness to users, (ii) easy and simple adjustment into the clinical setting, (iii) time sparing operation, and (iv) and possibly overall cost effectiveness. Improvement of day to day clinical praxis will be evaluated on patent related outcomes, such as safety of the operation of the RAAs, accuracy during block performance, volume and spread of the local anaesthetic, area of distribution and duration of the block. The expert's assessmentwill be done by an expert group build from one representative of each of the three medical centers (UKADA, Germany, KUL, Belgium and UCC, Ireland).

Task 6.5 RAAs Evaluation Design (Task Leader: KUL)
A precise study protocol will be set up and functions as an "operating manual" for evaluation of the prototypes. The format and content of the protocol will follow the medical professional code of conduct, the European

Union Good Clinical Practice Guidance issued by the ICH-GCP and the EN ISO 14155 that represents global accepted quality standards for conduction clinical trials with medical devices. Every protocol for evaluation of RASim and RAAs resp. will describe the background and the reasons for the trial, the scientific rationale, objectives, design, methodology, statistical considerations and organisations of the planned CTs. It also provides a common reference document to the trial administrators, the physician, nurses and clinic administrators for site responsibilities during the trial. All data to be collected will be either entered on a case report form (CRF) and are to be considered source data or will directly be entered into a suitable data base. Preparation of an appropriate CRF and its mapping into a database will be done within this task.

Task 6.6 RAAs Patients & Ethics (Task Leader: UKA-CTCA)
According to the regulatory and ethical authorities documents for the patient information and informed consent for participating of study subjects into the trials will be finalized. UKA-CTCA will be responsible for obtaining clinical trial authorization for the application of the RAAs as required by the Medical Device Acts of Germany, Belgium and Ireland (e.g. §20 of the German Medical Device Act). The study will be submitted to the responsible Competent Authorities and Ethics Committee for every participating study site in Germany (UKA-DA), Belgium (KUL), and Ireland (UCC).

Task 6.7 RAAs Evaluation Conduction (Task Leader: KUL)
After randomization patients are allocated to a control group (A) or to the RAA guided group (B). Patients of group A will receive regional anaesthesia without the assistant guided system by extensive experienced anaesthesiologists. In the other group same anaesthesiologists will perform regional anaesthesia by using the RAA system. The performance of regional anaesthesia will be measured by several parameters, including success rates, time to perform the nerve block etc. All residents will be supervised and evaluated by experienced senior anaesthesiologists. To perform this study, both qualitative and quantitative measurements will be developed and subsequently applied.

Person-Months per Participant

Participant number [10]	Participant short name [11]	Person-months per participant
1	UKA	33.00
4	UCC	18.00
9	KU Leuven	12.00
	Total	63.00

List of deliverables

Deliverable Number [61]	Deliverable Title	Lead beneficiary number	Estimated indicative person-months	Nature [62]	Dissemination level [63]	Delivery date [64]
D6.1	SOP for RASim-Guided Training of Physicians	1	21.00	R	PU	27
D6.2	SOP for RAAs-Guided Application of RA	9	21.00	R	PU	30
D6.3	Ethic and Regulatory Approvals	1	21.00	O	RE	30
		Total	63.00			

Description of deliverables

D6.1) SOP for RASim-Guided Training of Physicians: The evaluation of the RA simulator and RA Assistant will form the basis for the framework and development of an SOP RASim-Guided training tool for residents in the field of anaesthesia. This SOP will contain a detailed description and structured report following an RCT and several walkthroughs to meet the requirements of residents to safely learn and practise different RA techniques.

Each step of this work package will be examined and re-evaluated with respect to quality, content and timely data distribution to all participating partners. [month 27]

D6.2) SOP for RAAs-Guided Application of RA: This SOP will contain a detailed description and structured report following an RCT and several walkthroughs to meet the requirements of residents to safely learn and practise different RA techniques. Each step of this work package will be examined and re-evaluated with respect to quality, content and timely data distribution to all participating partners. [month 30]

D6.3) Ethic and Regulatory Approvals: Approvals of responsible Competent Authorities and Ethics Committee of every participating study sites in Germany (UKA-DA), Belgium (KUL) and Ireland (UCC) will be obtained for the use of the investigational devices in clinical trials. [month 30]

Schedule of relevant Milestones

Milestone number [59]	Milestone name	Lead beneficiary number	Delivery date from Annex I [60]	Comments
MS7	RASimAs prototypes deployed at the clinical trial sites	9	27	

WT3:
Work package description

Project Number [1]	610425	Project Acronym [2]	RASimAs

One form per Work Package

Work package number [53]	WP7	Type of activity [54]	RTD
Work package title	Regulatory Affairs and Quality Assurance		
Start month	1		
End month	36		
Lead beneficiary number [55]	1		

Objectives

The overall objective of this work package is to ensure compliance with all legal requirements in our research involving humans and focuses on the maximum patient's safety during the RASimAs evaluation (WP6). This includes particularly the production of Technical File (TF), Investigator's Brochure, Clinical Trial Protocol including Patient Information and Informed Consent Form and Electronic Data Capture System for a multi-center, multi-national clinical trial (CT) in Germany, Ireland and Belgium. The evaluation of the assistant system is planned to be a highly regulated Phase Ib/IIa clinical trial according to the European Medical Device Directive and will be designed to assess safety and proof-of-principle of the RASimAs assistant system prototype in patients scheduled for surgeries requiring RA. The partners involved in this work package are already experienced in the development of software (embedded or stand-alone) and have each implemented Quality Management Systems. The preparation of the TF will ensure compliance with the relevant directives, guidelines and normatives such as Medical Device Directive (MDD, 93/42/EEC, 2007/47/EG, the national acts on medical devices, DIN EN ISO 13485, DIN EN ISO 14971, DIN EN ISO 62366, DIN EN ISO 62304. Under the guidance of the consortium leader (UKA-IMI) the interfaces between all contributions of the partners to the prototypes (hard- and software) will be analyzed, evaluated and documented.

Description of work and role of partners

Task 7.1 Technical File Development (Task Leader: UKA-CTCA)
The performance of a CT in any one of the EU member states requires the preparation of an Investigator's Brochure (IB). The IB is an extraction of data relevant for the investigators with regard to the planned CT from the extensive Technical File (TF) in order to ensure the safe and intended use by investigators under standardized conditions in the CT. The Technical File preparation will begin early in the project and will be based on the results from WP 3, 4, and 5. The technical file holds all data on the essential requirements, safety and usability of the medical device. It will be continuously updated with all new and relevant information as it becomes available throughout the lifespan of the entire project.

Task 7.2 Electronic Data Capture (EDC) (Task Leader: UKA-IMI)
Electronic data capture (EDC) is a computer-based system designed for electronic collection of clinical data related to clinical trials. OpenClinica (https://openclinica.com/) will be installed and hosted at UKA-IMI to record all data captured in the RASim and RAAs evaluation. OpenClinica provides a web-based interface for data entry, plausibility checks and reporting tools. All data will be entered into electronic case report forms (eCRF) to collect all data from each participating site. The sponsor is responsible for designing a CRF that accurately represents the protocol of the clinical trial, as well as managing its production, monitoring the data collection and auditing the content of the filled-in CRFs. EDC increases data accuracy and optimizes the whole documentation process in these multi-centre trials.

Task 7.3 Investigator's Brochure (IB) Development (Task Leader: UKA-CTCA)
Principle Investigators of the CTs are Prof. Rossaint (UKA-DA, Germany), Prof. Shorten (UCC, Ireland)and Prof. Van de Velde (KU LEUVEN, Belgium) (see draft in Appendix 5.2). As official Sponsor's Representative in the sense of the European Medical Device Directive UKA-CTC-A will issue an Audit Plan and ensure overall Quality Management of the study. The Investigator's Brochure (IB) will be prepared according to a current and manifold used template provided by the UKA-CTC-A. The IB is based on the technical file and a

vital source of information for the investigators and everyone involved in the clinical trial, since the IB will include information as well as the instructions for use.

Task 7.4 Quality Assurance (QA) (Task Leader: UKA-CTCA)
The CTC-A will represent the sponsor of the study and will take over their responsibilities as specified in the respective national laws which have been issued in order to implement the requirements of the EU MDD. A QA plan will be prepared early in the project and before start of the clinical trial. QA methods like use of standardized operation procedures for planning, performance and evaluation of CT and regular onsite monitoring will be implemented.

Person-Months per Participant

Participant number [10]	Participant short name [11]	Person-months per participant
1	UKA	27.00
2	RWTH	2.00
5	URJC	4.00
6	FORTH	2.00
7	INRIA	2.00
8	UNIZA	2.00
10	SINTEF	3.00
11	SG	4.00
	Total	46.00

List of deliverables

Delive-rable Number [61]	Deliverable Title	Lead benefi-ciary number	Estimated indicative person-months	Nature [62]	Dissemi-nation level [63]	Delivery date [64]
D7.1	Quality Assurance Plan (QA-Plan)	1	4.00	R	CO	3
D7.2	Technical Files	1	5.00	R	CO	27
D7.3	Clinical Trial Protocol	1	5.00	R	PU	27
D7.4	Patient Informed Consent Form	1	4.00	R	PU	27
D7.5	eCRF & EDC System, incl. report	1	7.00	O	PU	24
D7.6	Investigator's Brochure (IB)	1	8.00	R	PU	24
D7.7	Annual Ethics Report 1	1	4.00	R	PU	12
D7.8	Annual Ethics Report 2	1	4.00	R	PU	24
D7.9	Annual Ethics Report 3	1	5.00	R	PU	36
		Total	46.00			

Description of deliverables

D7.1) Quality Assurance Plan (QA-Plan): The sponsor of a clinical study is obliged to develop and introduce quality control measures such as standardized operation procedures and regular site monitoring to ensure accurate processes. [month 3]

D7.2) Technical Files: An extensive Technical File (TF) of the medical devices will be developed according to the requirements of CE marking directives and the development of an Investigator`s Brochure for the clinical trials. [month 27]

D7.3) Clinical Trial Protocol: Precise Clinical Trial Protocols will be prepared for executing the clinical trials by the investigator. The Protocol will include all necessary information such as scientific rationale, potential risks and benefits, study objectives, outcome measures, study design, enrolment and withdrawal, inclusion and exclusion criteria, strategies for recruitment and retention, treatment procedures, study schedule, procedures and evaluations, assessment of safety, clinical monitoring, statistical consideration, source documents, quality control and assurance, ethics and data handling. [month 27]

D7.4) Patient Informed Consent Form: According to the recommendations of the ethical and regulatory authorities a document for patient information and informed consent for participating of study subjects into trials will be finished. [month 27]

D7.5) eCRF & EDC System, incl. report: Performing the clinical trials, all parameters will be captured in an electronic Case Report Form (eCRF). It is planned to implement the eCRFs within the open source system OpenClinica for Electronic Data Capture (EDC). The deliverable is in form of a web-address accessible with personalized login data via the Internet. Then web page will allow feeding the patient-specific clinical data into the corresponding report form, and automatically transfer the data into the database. [month 24]

D7.6) Investigator's Brochure (IB): An Investigator`s Brochure based on the Technical File of the medical device will be prepared. The IB summarizes all information and instructions of critical importance for the investigator for the performance of a clinical trial. [month 24]

D7.7) Annual Ethics Report 1: State and progress of the clinical trials will be reported to the leading Ethics Committee. The Ethics Report especially contains information about recruiting and drop-out of study subjects, adverse events and potential revaluation of the benefit-risk-assessment. [month 12]

D7.8) Annual Ethics Report 2: State and progress of the clinical trials will be reported to the leading Ethics Committee. The Ethics Report especially contains information about recruiting and drop-out of study subjects, adverse events and potential revaluation of the benefit-risk-assessment. [month 24]

D7.9) Annual Ethics Report 3: State and progress of the clinical trials will be reported to the leading Ethics Committee. The Ethics Report especially contains information about recruiting and drop-out of study subjects, adverse events and potential revaluation of the benefit-risk-assessment. [month 36]

Schedule of relevant Milestones

Milestone number [59]	Milestone name	Lead benefi-ciary number	Delivery date from Annex I [60]	Comments
MS8	Quality Assurance Plan (QA-Plan) released	1	9	
MS9	Electronic Data Capture (EDC) system and Investigator’s Brochure (IB) released	1	24	
MS10	Clinical Trial Protocol (CTP) and Patient Informed Consent Form (ICF) released	1	27	

WT3:
Work package description

Project Number [1]	610425	Project Acronym [2]	RASimAs

One form per Work Package

Work package number [53]	WP8	Type of activity [54]	RTD
Work package title	Dissemination & Exploitation		
Start month	1		
End month	36		
Lead beneficiary number [55]	1		

Objectives

The RASimAs Consortium will raise awareness of the objectives and disseminate the project's results to key target audiences in academia, industry, medical professionals, and patients. The Consortium is aware of the need to communicate results to the scientific community, technology companies, and to the general public. Active participating on (scientific) conferences and meetings provide further options receiving the opinions of other experts in this field. Members of the Consortium and any of their employees attending scientific meetings will make available any relevant information obtained at the meeting, thereby ensuring that other members of the project are informed about related research being carried out in the field in the EU or other parts of the world.

Description of work and role of partners

Task 8.1 Scientific Dissemination (Task Leader: UKA-DA)
This task focuses on the dissemination of project results through a variety of channels. The efforts will start at project kick off with mentions on the partner website and a dedicated press release. During the course of the project, dissemination of research to the broad scientific community will be achieved via publication of original papers in peer reviewed, international scientific journals, oral presentations and posters at conferences (such as the annual meeting of the European Society of Regional Anaesthesia and Pain Therapy, ESRA), workshops and seminars, as well as by written reports to the European Commission which will be made available on the project's web site. Once the prototypes have been evaluated, clinical reports will be created and published on the partner websites, as well as on relevant medical websites. In addition, the project will publish articles or white paper and make presentations at industry conferences etc (please refer to Sect. 3.2 for more details). These will not constitute separate project deliverables, but regular progress reports produced in WP1 Management will list articles published. Specifically, this task will generate

-Original papers in peer-reviewed international scientific journals as well as oral presentations and posters at conferences will be published continuously during the project runtime and whenever available.
-Workshops and conferences at the annual meeting of ESRA will be convened. Also, the RASimAs team intend to participate in the seminars organised by the Virtual Physiological Human (VPH) Network of Excellence. At the end of the RASimAs project, VPH 2016 for instance may be hosted in Aachen by the RASimAs Team.
-Website of the project (see task 8.2) that will provide news and papers to the public.

Task 8.2 Public Dissemination (Task Leader: UKA-IMI)
Informing the general public about the activities and results emerging from the Consortium will be a fundamental measure of its success. The consortium will take the necessary steps to inform third parties of its activities by arranging lectures and presentations to local interested groups (e.g. local and community anaesthesiologists) and by participating in European groups or initiatives where the particular expertise in the consortium may contribute to improving public awareness or making more informed policy decisions. The RASimAs website will contentiously inform about the project, related events, publications, and press releases. A public section will be made available to the general public and will contain information relevant to project objectives, structure, participating organizations, expected achievements, publications, etc. For the public section, all partners are encouraged to write short and informative articles that describe their work in lay terms and why their work is of interest, importance and benefit to society. The website contents will be updated on a regular basis. Furthermore, results will be divulged via Twitter. Towards the end of the project, the project leader will make a blog post depicting his personal experiences during the implementation of the project.

Task 8.3 Patenting & Trade Secret Protection (Tasks Leader: UKA-IMI)
If the Steering Committee determines that any results submitted by a partner deserve to be protected by a patent or kept as a trade secret, the technology will be presented to the Technology Transfer Office of the Institution, who in conjunction with the appropriate industrial partners' institution(s) will decide on patenting or trade secret protection. An Intellectual Property Right (IPR) manager will be appointed as a member of the Steering Committee assuming the responsibilities for directing activities related to IPR including:

-Creation and maintenance of a register of IPR belonging to the consortium members.
-Creation and maintenance of a register of IPR generated during the project including ownership, restrictions on access, and licensing agreements.
-Organization of IPR strategy seminars to make members of the consortium perceptive and receptive to potential IPR in their work.
-Set up of a process for the approval of project-related publications, potential IPR, moderating disputes arising between consortium partners on any of the above mentioned issues, reporting to and advising the project management.

Task 8.4 Commercial Exploitation (Leader: SG)
This task focuses on the exploitation of project results. The task will leverage the result of clinical trials. The data of these reports will be used to build a product launch plan. Based on this cost-benefit analysis, a plan will be produced, including the terms and conditions for turning the prototypes into commercial products.
This task will also promote the results of the project to targeted audiences of new organizations, by arranging meetings and customized presentations (for ex. other medical system providers interested in licensing the RaSimAs technology). The core strategy will be to use the extensive contact network amongst consortium members as a starting point to get in touch with new potential users of this new technology.

Person-Months per Participant

Participant number [10]	Participant short name [11]	Person-months per participant
1	UKA	18.00
2	RWTH	2.00
8	UNIZA	4.00
9	KU Leuven	6.00
10	SINTEF	2.00
11	SG	3.00
	Total	35.00

List of deliverables

Delive-rable Number [61]	Deliverable Title	Lead benefi-ciary number	Estimated indicative person-months	Nature [62]	Dissemi-nation level [63]	Delivery date [64]
D8.1	Project Website continuously updated, journalistic descriptions of the project, press releases, video and other media	1	5.00	O	PU	2
D8.2	Dissemination Plan	1	5.00	R	RE	6
D8.3	IPR Directory	1	6.00	R	CO	36
D8.4	Exploitation Plan 1	10	6.00	R	RE	12
D8.5	Exploitation Plan 2	10	6.00	R	RE	24

WT3:
Work package description

List of deliverables

Delive-rable Number [61]	Deliverable Title	Lead benefi-ciary number	Estimated indicative person-months	Nature [62]	Dissemi-nation level [63]	Delivery date [64]
D8.6	Press release about project results; film or photos about using project technology	1	1.00	O	PU	30
D8.7	Final Report on Dissemination and Exploitation	10	6.00	R	RE	36
		Total	35.00			

Description of deliverables

D8.1) Project Website continuously updated, journalistic descriptions of the project, press releases, video and other media: The RASimAs website will continuously inform about the project, related events, publications, and press releases. A public section will be made available to the general public and will contain information relevant to project objectives, structure, participating organizations, expected achievements, publications, etc. With the website a Twitter account account will be opened to inform the public with short update from the project. A press release at the start will be used to raise awareness of the new project. A journalistic description of the project will inform the public in a detailed way about the RASimAs ideas and plans. Furthermore, results will be divulged via Twitter. Towards the end of the project, the project leader will make a blog post depicting his personal experiences during the implementation of the project. [month 2]

D8.2) Dissemination Plan: The various dissemination activities will contain the publication of manuscripts, participation in national and international conferences and the creation of a website. After successful completion of each work package the results will be offered to the public in a timely fashion to put the scientific achievements of the project into the context of the scientific landscape. [month 6]

D8.3) IPR Directory: The IPR Directory will include a) a register of IPR belonging to the consortium members and b) a register of IPR which will be generated during the project including ownership, restriction on access and licensing agreements. [month 36]

D8.4) Exploitation Plan 1: Plan for turning prototypes into commercial products including potential customers, cost-benefit analysis and terms and conditions. [month 12]

D8.5) Exploitation Plan 2: Plan for turning prototypes into commercial products including potential customers, cost-benefit analysis and terms and conditions. [month 24]

D8.6) Press release about project results; film or photos about using project technology: A Press release about project results will be published near the end of the project. A Film or photos about using project technology will be made public to visualise the developments and their possible future use. [month 30]

D8.7) Final Report on Dissemination and Exploitation: Report on the results of the dissemination and exploitation activities of the RASimAs consortium partners. [month 36]

Schedule of relevant Milestones

Milestone number [59]	Milestone name	Lead benefi-ciary number	Delivery date from Annex I [60]	Comments
MS11	Project Website established	1	2	
MS12	Dissemination Plan released	1	6	
MS13	Exploitation Plan released	10	24	

WT4:
List of Milestones

Project Number [1]	610425	Project Acronym [2]	RASimAs

List and Schedule of Milestones

Milestone number [59]	Milestone name	WP number [53]	Lead beneficiary number	Delivery date from Annex I [60]	Comments
MS1	RASimAs integrated platform initial demonstration	WP2	6	14	
MS2	Final version of patient-specific library released	WP3	7	18	
MS3	Haptic rendering algorithms, simulator core, and ultrasound module developed	WP4	5	24	
MS4	Training courseware developed; RAA system specification released	WP4	5	27	
MS5	RASim function available on the portable prototypes	WP5	10	24	
MS6	RAAs function available on the portable prototypes	WP5	10	27	
MS7	RASimAs prototypes deployed at the clinical trial sites	WP6	9	27	
MS8	Quality Assurance Plan (QA-Plan) released	WP7	1	9	
MS9	Electronic Data Capture (EDC) system and Investigator's Brochure (IB) released	WP7	1	24	
MS10	Clinical Trial Protocol (CTP) and Patient Informed Consent Form (ICF) released	WP7	1	27	
MS11	Project Website established	WP8	1	2	
MS12	Dissemination Plan released	WP8	1	6	
MS13	Exploitation Plan released	WP8	10	24	

WT5:
Tentative schedule of Project Reviews

Project Number [1]	610425	Project Acronym [2]	RASimAs

Tentative schedule of Project Reviews

Review number [65]	Tentative timing	Planned venue of review	Comments, if any
RV 1	12	Aachen	
RV 2	24	Aachen	
RV 3	36	Aachen	

WT6:
Project Effort by Beneficiary and Work Package

Project Number [1]	610425	Project Acronym [2]	RASimAs

Indicative efforts (man-months) per Beneficiary per Work Package

Beneficiary number and short-name	WP 1	WP 2	WP 3	WP 4	WP 5	WP 6	WP 7	WP 8	Total per Beneficiary
1 - UKA	12.00	19.00	16.00	0.00	0.00	33.00	27.00	18.00	125.00
2 - RWTH	10.00	3.00	0.00	23.00	9.00	0.00	2.00	2.00	49.00
3 - Bangor	0.00	2.00	18.00	5.00	0.00	0.00	0.00	0.00	25.00
4 - UCC	0.00	3.00	0.00	0.00	0.00	18.00	0.00	0.00	21.00
5 - URJC	0.00	5.00	4.00	25.00	8.00	0.00	4.00	0.00	46.00
6 - FORTH	0.00	11.00	18.00	10.00	3.00	0.00	2.00	0.00	44.00
7 - INRIA	0.00	2.00	14.00	13.00	3.00	0.00	2.00	0.00	34.00
8 - UNIZA	0.00	6.00	0.00	6.00	4.00	0.00	2.00	4.00	22.00
9 - KU Leuven	0.00	0.00	2.00	0.00	0.00	12.00	0.00	6.00	20.00
10 - SINTEF	0.00	4.00	0.00	15.00	9.00	0.00	3.00	2.00	33.00
11 - SG	0.00	8.00	0.00	13.00	16.00	0.00	4.00	3.00	44.00
Total	22.00	63.00	72.00	110.00	52.00	63.00	46.00	35.00	463.00

WT7:
Project Effort by Activity type per Beneficiary

Project Number [1]	610425	Project Acronym [2]	RASimAs

Indicative efforts per Activity Type per Beneficiary

Activity type	Part. 1 UKA	Part. 2 RWTH	Part. 3 Bangor	Part. 4 UCC	Part. 5 URJC	Part. 6 FORTH	Part. 7 INRIA	Part. 8 UNIZA	Part. 9 KU Leuv	Part. 10 SINTEF	Part. 11 SG	Total
1. RTD/Innovation activities												
WP 2	19.00	3.00	2.00	3.00	5.00	11.00	2.00	6.00	0.00	4.00	8.00	63.00
WP 3	16.00	0.00	18.00	0.00	4.00	18.00	14.00	0.00	2.00	0.00	0.00	72.00
WP 4	0.00	23.00	5.00	0.00	25.00	10.00	13.00	6.00	0.00	15.00	13.00	110.00
WP 6	33.00	0.00	0.00	18.00	0.00	0.00	0.00	0.00	12.00	0.00	0.00	63.00
WP 7	27.00	2.00	0.00	0.00	4.00	2.00	2.00	2.00	0.00	3.00	4.00	46.00
WP 8	18.00	2.00	0.00	0.00	0.00	0.00	0.00	4.00	6.00	2.00	3.00	35.00
Total Research	113.00	30.00	25.00	21.00	38.00	41.00	31.00	18.00	20.00	24.00	28.00	389.00
2. Demonstration activities												
WP 5	0.00	9.00	0.00	0.00	8.00	3.00	3.00	4.00	0.00	9.00	16.00	52.00
Total Demo	0.00	9.00	0.00	0.00	8.00	3.00	3.00	4.00	0.00	9.00	16.00	52.00
3. Consortium Management activities												
WP 1	12.00	10.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	22.00
Total Management	12.00	10.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	22.00
4. Other activities												
Total other	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Total	125.00	49.00	25.00	21.00	46.00	44.00	34.00	22.00	20.00	33.00	44.00	463.00

WT8:
Project Effort and costs

Project Number [1]	610425	Project Acronym [2]	RASimAs

Project efforts and costs

Beneficiary number	Beneficiary short name	Estimated eligible costs (whole duration of the project)						Requested EU contribution (€)
		Effort (PM)	Personnel costs (€)	Subcontracting (€)	Other Direct costs (€)	Indirect costs OR lump sum, flat-rate or scale-of-unit (€)	Total costs	
1	UKA	125.00	659,944.00	57,200.00	57,100.00	430,226.00	1,204,470.00	929,312.00
2	RWTH	49.00	265,900.00	6,000.00	18,000.00	170,340.00	460,240.00	346,180.00
3	Bangor	25.00	132,596.00	0.00	7,000.00	83,757.00	223,353.00	167,514.00
4	UCC	21.00	105,000.00	0.00	7,000.00	67,200.00	179,200.00	134,400.00
5	URJC	46.00	174,225.00	0.00	10,000.00	110,534.00	294,759.00	206,851.00
6	FORTH	44.00	158,400.00	0.00	14,200.00	137,808.00	310,408.00	227,757.00
7	INRIA	34.00	160,633.00	0.00	7,000.00	141,784.00	309,417.00	225,766.00
8	UNIZA	22.00	42,700.00	0.00	22,000.00	38,820.00	103,520.00	74,600.00
9	KU Leuven	20.00	110,000.00	0.00	7,000.00	70,200.00	187,200.00	140,400.00
10	SINTEF	33.00	350,966.00	1,500.00	78,885.00	328,153.00	759,504.00	523,699.00
11	SG	44.00	314,600.00	0.00	11,200.00	195,480.00	521,280.00	345,200.00
Total		463.00	2,474,964.00	64,700.00	239,385.00	1,774,302.00	4,553,351.00	3,321,679.00

1. Project number

The project number has been assigned by the Commission as the unique identifier for your project. It cannot be changed. The project number **should appear on each page of the grant agreement preparation documents (part A and part B)** to prevent errors during its handling.

2. Project acronym

Use the project acronym as given in the submitted proposal. It cannot be changed unless agreed so during the negotiations. The same acronym **should appear on each page of the grant agreement preparation documents (part A and part B)** to prevent errors during its handling.

53. Work Package number

Work package number: WP1, WP2, WP3, ..., WPn

54. Type of activity

For all FP7 projects each work package must relate to one (and only one) of the following possible types of activity (only if applicable for the chosen funding scheme – must correspond to the GPF Form Ax.v):

• **RTD/INNO =** Research and technological development including scientific coordination - applicable for Collaborative Projects and Networks of Excellence

• **DEM =** Demonstration - applicable for collaborative projects and Research for the Benefit of Specific Groups

• **MGT =** Management of the consortium - applicable for all funding schemes

• **OTHER =** Other specific activities, applicable for all funding schemes

• **COORD =** Coordination activities – applicable only for CAs

• **SUPP =** Support activities – applicable only for SAs

55. Lead beneficiary number

Number of the beneficiary leading the work in this work package.

56. Person-months per work package

The total number of person-months allocated to each work package.

57. Start month

Relative start date for the work in the specific work packages, month 1 marking the start date of the project, and all other start dates being relative to this start date.

58. End month

Relative end date, month 1 marking the start date of the project, and all end dates being relative to this start date.

59. Milestone number

Milestone number:MS1, MS2, …, MSn

60. Delivery date for Milestone

Month in which the milestone will be achieved. Month 1 marking the start date of the project, and all delivery dates being relative to this start date.

61. Deliverable number

Deliverable numbers in order of delivery dates: D1 – Dn

62. Nature

Please indicate the nature of the deliverable using one of the following codes

R = Report, **P** = Prototype, **D** = Demonstrator, **O** = Other

63. Dissemination level

Please indicate the dissemination level using one of the following codes:

• **PU =** Public

• **PP =** Restricted to other programme participants (including the Commission Services)

• **RE =** Restricted to a group specified by the consortium (including the Commission Services)

• **CO =** Confidential, only for members of the consortium (including the Commission Services)

• **Restreint UE =** Classified with the classification level "Restreint UE" according to Commission Decision 2001/844 and amendments

• **Confidentiel UE =** Classified with the mention of the classification level "Confidentiel UE" according to Commission Decision 2001/844 and amendments

• **Secret UE =** Classified with the mention of the classification level "Secret UE" according to Commission Decision 2001/844 and amendments

64. Delivery date for Deliverable

Month in which the deliverables will be available. Month 1 marking the start date of the project, and all delivery dates being relative to this start date

65. Review number

Review number: RV1, RV2, ..., RVn

66. Tentative timing of reviews

Month after which the review will take place. Month 1 marking the start date of the project, and all delivery dates being relative to this start date.

67. Person-months per Deliverable

The total number of person-month allocated to each deliverable.

Annex I: Description of work, part B

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LIST OF ACRONYMS

AR	Augmented Reality
BDSG	German Federal Data Protection Act (Bundesdatenschutzgesetz)
BfArM	Bundesministerium für Arzneimittel und Medizinprodukte
BSI	Bundesamt für Sicherheit in der Informationstechnik
CCC	Center for Computing and Communication
CE	Conformité Européenne
CI	Coordinating Investigator
CNS	Central Nervous System
CPU	Central Processing Unit
CT	Computed Tomography
CTM	Clinical Trial Manager
CTP	Clinical Trial Protocol
CTO	Chief Technical Officer
DFG	Deutsche Forschungsgemeinschaft (German Research Foundation)
DICOM	Digital Imaging and Communications in Medicine
DOF	Degree of Freedom
DPO	Data Protection Officer
DRG	Diagnosis-Related Group
EAB	Ethics Advisory Board
EEA	European Economic Area
ESRA	European Society of Regional Anaesthesia & Pain Therapy
FAMHP	Federal Agency for Medicines and Health Products
FEM	Finite Element Model
GCP	Good Clinical Practice

GPU	Graphical Processing Unit
ICH	International Conference on Harmonization
ICF	Informed Consent Form
ICT	Information and Communications Technology
IMB	Irish Medicines Board
KPI	Key Performance Indicator
LAN	Local Area Network
LEM	Long Element Model
M	Milestone
MPG	German Medical Device Act
MRI	Magnetic Resonance Imaging
MRA	Magnetic Resonance Angiography
NRW	Northrhine Westfalia
NTT	Number To be Treated
OR	Operation Room
PACS	Picture Archiving and Communication System
PCMFS	Point Collocation-based Method of Finite Spheres
PNB	Peripheral Nerve Block
PNS	Peripheral Nervous System
RA	Regional Anaesthesia
T	Task
TMF	Institute of Technology, Methods and Infrastructure for Networked Medical Research
RWTH	Rheinisch-Westfaelische Technische Hochschule
SC	Steering Committee
SME	Small and Medium Enterprise
SOP	Standard Operating Procedure
SSH	Secure Shell
SSL	Secure Sockets Layer
VPH	Virtual Physiological Human
VR	Virtual Reality
WP	Work Package
WPL	Work Package Leader

1. CONCEPT AND OBJECTIVES, PROGRESS BEYOND STATE OF THE ART, S/T METHODOLOGY AND WORK PLAN

1.1. Concept and objectives

Regional anaesthesia (RA) has been used increasingly in replacement or addition of general anaesthesia during the past two decades due to its documented advantages of reduced postoperative pain, earlier mobility, shorter hospital stay, and significantly lower costs[1]. The British Journal of

[1] Gonano C, Kettner SC, Ernstbrunner M, Schebesta K, Chiari A, Marhofer P. Comparison of economical aspects of interscalene brachial plexus blockade and general anaesthesia for arthroscopic shoulder surgery. Br J Anaesth 2009; 103(3): 428-33

Anaesthesia has estimated costs savings of € 100.000 per year and operation theatre[2] by appropriately applied peripheral nerve blocks (PNB) in substitute of general anaesthesia.

> ***"Under appropriate conditions, greater than € 100.000 per year per operating theatre can be saved without compromising care with the use of ultrasound-guided regional blocks." [Br J Anaesthesia 2012; 104(5): 541]***

1.1.1. General concept

Generally, RA is performed using electrical nerve stimulation and/or ultrasound-guided techniques, without significantly differences in cost savings as compared to general anaesthesia[3]. However, a safe performance of RA requires good theoretical, practical, and non-cognitive skills to allow trainees to achieve confidence in performing RA and to keep complications to a minimum. Current training methods for RA include cadavers, video teaching, ultrasound guidance, and simple virtual patient modelling[4].

The advantage of using simulators in medicine is the creation of a realistic environment with standardized and reproducible scenarios without endangering patients. Despite the broad acceptance of virtual reality (VR) to educate trainees, the limited numbers of VR-based simulators for RA narrow their use for training purposes. Furthermore, current VR-based simulators for RA disregard individual patients' anatomy and also lack sufficiently realistic haptic feedback[5].

The first part of the project focuses on the Regional Anaesthesia Simulator (RASim) prototype. RASimAs proposes a patient-specific flexible training environment with VR by using multimodal representations of both visual and haptics with intuitive interactions to form a plausible simulation (Phase 1). This simulator will be applicable to all body regions of relevance and will support RA training using electrical nerve stimulation, ultrasound guidance, or a combination of both. Relying on several standard models of multiple variations of anatomy, the VR training system will be also applicable when lacking patient data. In contrast with current VR systems that provide only rudimentary haptic feedback, an advanced haptic framework will be provided as part of the prototype.

Universitätsklinikum Aachen and Rheinisch-Westfälische Technische Hochschule (RWTH) Aachen University have collaborated on an interactive VR-based simulator, University College Cork (UCC) has researched hapto-visual medical simulators. Universidad Rey Juan Carlos (URJC), Foundation for Research and Technology Hellas (FORTH), National Institute for Research in Computer Science and Control (INRIA), Zilinska Univerzita (UNIZA) are renowned experts in image processing algorithms and libraries. The consortium will leverage previous research from Bangor University (BANGOR) on haptic needles used for medical training simulators.

> ***A multidisciplinary team from academia, SME, and clinical partners is assembled into one Consortium that will add value and expertise to European research in the area of the Virtual Physiological Human (VPH).***

The second part of the project focuses on the development of a Regional Anaesthesia Assistant (RAAs) prototype. The RASimAs project proposes an innovative approach where the patient-specific models generated by the Regional Anaesthesia Simulator for training are used to develop the Regional Anaesthesia Assistant, in order to improve the actual performance of RA procedures (Phase 2). In this second part of the RASimAs project, we will develop a needle tracking system for

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[2] Marhofer P, Harrop-Griffiths W, Kettner SC, Kirchmair L. Fifteen years of ultrasound guidance in regional anaesthesia: part I. Br J Anaesthesia 2010; 104(5): 538-46

[3] Liu SS, Strodtbeck WM, Richman JM, Wu CL. A comparison of regional versus general anesthesia for ambulatory anesthesia: A meta-analysis of randomized controlled trials. Anesthesia & Analgesia 2005; 101(6): 1634-42

[4] Smith HM, Kopp SL, Jacob AK, Torsher LC, Hebl JR. Designing and implementing a comprehensive learner-centered regional anesthesia curriculum. Reg Anesth Pain Med 2009; 34: 88Y94

[5] Grottke O, Ntouba A, Ullrich S, Liao W, Fried E, Prescher A, Deserno TM, Kuhlen T, Rossaint R. Virtual reality-based simulator for training in regional anaesthesia. Br J Anaesth 2009; 103(4): 594-600

assisted RA. The underlying framework will consist of a number of patients datasets retrieved from magnetic resonance imaging (MRI) and computed tomography (CT) scans. Next to real-time ultrasound imaging the pre-recorded datasets will be displayed to guide the trainee while performing the RA. The combination of pre-calculated needle adjustments based on the datasets will allow the trainee to guide the needle within a restricted area to find the right position for the RA.

The framework resulting from Phase 1 and Phase 2 is referred to as Regional Anaesthesia Simulation and Assistance (RASimAs).

The third part of the project is dedicated to the comprehensive evaluation of the RASimAs prototype (Phase 3). Europe's leading medical centres for RA procedures, such as Universitätsklinikum Aachen (UKA) and Katholieke Universiteit Leuven (KU LEUVEN) have been included in the consortium to perform Expert Groups, Cognitive Walkthroughs, and Controlled Clinical Trials. The project also benefits from the support of the European Society of Regional Anaesthesia and Pain Therapy (ESRA) as its current president (Prof. Marc Van de Velde, Katholieke Universiteit Leuven) is a key member of the RASimAs Consortium.

In addition, the consortium benefits from the participation of a research-performing SME, SenseGraphics AB (SG) which has already successfully developed and marketed ICT products addressing the medical industry. The company will play a key role in understanding the market requirements for a (future) commercial system and planning the development of new products based on RASimAs technologies (post-project).

1.1.2. Objectives

The main objectives of the RASimAs consortium are:

- To develop an individualized VR-based simulator for RA as training tool for both electrical nerve stimulation and ultrasound-guided RA that is based on a portable and inexpensive technological platform;
- To improve the training (and make it realistic) by developing an advanced haptic feedback framework;
- To improve the clinical procedure by developing a real time needle tracking system for VR-assisted RA;
- To perform controlled user studies and clinical trials to assess the framework's impact on individuals and the European society;
- To directly disseminate the results for immediate product development and commercialization;
- To incorporate and document VR-based RA in the curriculum of anaesthesiology trainees;
- To impact European healthcare systems by reducing the costs and improving the clinical outcome of RA procedures.

1.1.3. Key innovation and patent search analysis

The key innovations of the project are the following:

- Use of patient-specific data (MRI/MRA scans, CT scans, ultrasound imaging) to improve the quality of the Virtual Physiological Human (VPH) model;
- Simulate output ultrasound images in complex scenarios (such as tissue deformation occurring during the procedure);
- Use advanced haptics, six degrees of freedom input/output and 3D stereoscopic rendering for realistic feedback of the training tool (Regional Anaesthesia Simulator);
- Merge relevant image processing libraries and algorithms for rendering and image fusion to support the segmentation of various soft tissues and to facilitate the creation of patient-specific data;
- Develop needle tracking approaches for the guidance tool (Regional Anaesthesia Assistant);
- Provide algorithms to change the pose of VPH models.

The consortium has conducted a thorough patent search in the course of the preparation of this application, in order to identify prior art in the field of medical VR-based simulators and haptic technologies (Tab. 1).

So far, no patents have been filed that meet the scope and objectives of RASimAs.

Patent Number	VR-based Simulators
WO 2012106706	Hybrid physical-virtual reality simulation for clinical training capable of providing feedback to a physical anatomic model.
US 20120251987 A1	System and method for virtual reality simulation of local dental anesthesiological techniques and skills training
US 6,773,263	Medical simulator
US 7,249,952	Methods and apparatus for simulating dental procedures and for training dental students
US 7,812,815	Compact haptic and augmented virtual reality system
US 7,261,566	System and method for training medical professionals to perform a nerve block procedure
US 7,665,995	Medical training simulator including contact-less sensors
US 8,162,668	Medical training simulator including contact-less sensors
US 6,113,395	Selectable instruments with homing devices for haptic virtual reality medical simulation
US 7,202,851	Haptic interface for palpation simulation
US 7,307,619	Haptic interface for palpation simulation
EP 1766596	Medical simulation system and method
EP 1733369	Vascular-access simulation system with skin-interaction features
EP 2497077	Haptic needle as part of medical training simulator (BANGOR)

Table 1: *Results of patent search. Patents filed by Consortium members are highlighted in orange.*

1.1.4. Measurable objectives and key performance indicators (KPIs)

This section focuses on the measurement methods and the expected progress during the course of the project. The RASimAs project addresses all three objectives of the call:

- *Objective 1*: Significant reduction of costs through the use of VPH technologies. RASimAs will increase the replacement of GA by RA and improve the success rate of RA procedures, thus decreasing costs by an estimated 100,000 Euros per year and operating theatre[6].
- *Objective 2*: Strengthened evidence of the clinical benefits in using computer-based models. RASimAs will demonstrate the clinical benefits of the technology by conducting controlled clinical trials with patient-specific models.
- *Objective 3*: Acceleration of the deployment of VPH technologies in clinical environments and increased acceptance and use of predictive models by healthcare professionals. RASimAs will enrich the VPH models with patient-specific data, in order to improve clinician performance even in RA procedures where significant inter-subject differences exist.

[6] Marhofer P, Harrop-Griffiths W, Kettner SC, Kirchmair L. Fifteen years of ultrasound guidance in regional anaesthesia: part I. Br J Anaesthesia 2010; 104(5): 538-46

RASimAs aims at (i) cost reduction by use of VPH technologies, (ii) proving clinical benefits in using computer-based models, and (iii) increasing acceptance and use of predictive models by healthcare professionals.

Table 2 lists the major objectives and related key performance indicators (KPIs) that have been defined to objectively measure the project performance. Please note that if the number of patients or trainees at UKA-DA, UCC, and KU LEUVEN is insufficient, other medical centres will be re-cruited.

Objectives			Key Performance Indicator and Measurement Method	Month			Work Packages
1	2	3		12	24	36	
X	X		Reduced number of failed blocks	N/A	< 5%	< 2.5%	WP5, WP6
X			More cost-effective training programs. Proficiency achieved in 4 weeks	N/A	6 weeks	4 weeks	WP6
	X		Lower occurrences of misdistribution of local anaesthesia	N/A	< 5%	< 2.5%	WP5, WP6
	X		Lower occurrences of intramuscular location of the needle tip before injection	N/A	< 8%	< 4%	WP5, WP6
	X		Lower errors in correlating the sidedness of the patient with the sidedness of the ultrasound image	N/A	< 3%	< 1.5%	WP5, WP6
	X		Lower errors of needle-insertion site and angle with respect to the probe preventing accurate needle visualization	N/A	< 4%	< 2%	WP5, WP6
		X	Number of peer-reviewed scientific publications	6	12	18	WP8
	X		Physicians trained on patient-specific data	N/A	5	65	WP7
	X	X	Patients treated with RASimAs	N/A	N/A	40	WP7

Table 2: *Key performance indicators (KPI) in relation to the three major objectives of the RASimAs Project.*

1.2. Progress beyond the state-of-the-art

Regional anaesthesia (RA) has been used increasingly during the past two decades. The advantages of RA include a reduction in morbidity and mortality, superior postoperative analgesia, and enhanced cost-effectiveness. These benefits are accompanied by a low rate of serious complications as compared to general anaesthesia[7]. Besides RA can reduce postoperative opioid and antiemetic consumption, shorten recovery-room stays, and expedite hospital discharge, all culminating in greater patient satisfaction. Finally, RA allows for rapid postoperative recovery of cognitive function[8] and has an important role in preventive analgesia[9].

[7] Liu CC, Strodtbeck WM, Richman JM, Wu CL. A comparison of regional versus general anesthesia for ambulatory anesthesia: a meta-analysis of randomized controlled trials. Anesthesia & Analgesia 2005; 101(6): 1634-42

[8] Steinmetz J, Funder KS, Dahl BT, Rasmussen LS. Depth of anaesthesia and post-operative cognitive dysfunction. Acta Anaesthesiologica Scandinavica 2010; 54(2): 162–68

[9] Aguirre J, Del Moral A, Cobo I, Borgeat A, Blumenthal S. The role of continuous peripheral nerve blocks. Anesthesiology Research & Practice 2012; Article ID 560879, 20 pages, doi:10.1155/2012/560879

1.2.1. Regional anaesthesia

CURRENT TECHNOLOGIES

Usually, RA is performed using electrical nerve stimulation and/or ultrasound-guided techniques. The performance of RA using electrical nerve stimulation requires the localisation of nerves (i.e. nerve stimulation and paresthesiae induction) based on anatomical assumptions on surface landmarks. This approach may be difficult regarding remarkable variation in human anatomy. By providing an objective estimate of needle-to-nerve distance, nerve stimulation enables practitioners to deposit local anaesthetic. The technique capitalizes on physiology that allows electrical current passing from the needle tip to depolarize a mixed nerve without causing a painful sensory response.

The utility of ultrasound-guided RA as an alternative to electrical nerve stimulation has increased in popularity over the past 5 years. The use of ultrasound imaging for nerve localization is an innovative application of an old technology that addresses some of the shortcomings of the traditional electrical nerve stimulation techniques. The single most important advantage of ultrasound for nerve blocks is the ability to confirm local anaesthetic spread around the target nerve. Besides imaging the needle and nerve, ultrasound clearly reveals the surrounding hazardous structures, including blood vessels, pleura, and viscera. However, based on the current evidence form several studies it is not clear whether ultrasound-guided regional anaesthesia represents the new standard for RA in terms of efficacy and safety. Thus, both electrical nerve stimulation and ultrasound-guided RA are currently applied in anaesthesia.

The successful performance of RA requires good theoretical, practical, and non-cognitive skills to allow trainees to achieve confidence in performing RA and to minimize complications. Trainees in the field of anaesthesiology are taught manual techniques using an ‘apprenticeship’ approach, in which patients are necessarily exposed to inexperienced practitioners and in which trainers undergo little or no formal tuition in education at theoretical or practical levels. In general, trainees acquire some relevant theoretical knowledge of the anatomy, physiology and pharmacology. Subsequently, when the opportunity arises in the clinical setting, they are routinely taught by demonstration or through direct supervision.

In Europe, the nature of postgraduate medical training is changing greatly with less teaching and learning hours available. This is partly due to the European Working Time Directive, the increase in transnational mobility of doctors (trainees and independent practitioners), altered patient expectations and new forms of governance of training and practice. One of the implications of these changes are that young doctors will acquire less ‘hands-on’ training during everyday work, in particular in psychomotor skills. This paradigm shift in medical education, towards ‘competence-based training’, where trainee doctors will have achieved a level of competency before they can perform on real patients, require new tools, educational theories, teaching techniques and curriculum. To allow trainees practical training, currently several training methods for RA including cadavers, video teaching, ultrasound guidance, and simple virtual patient modelling are used.

RASIMAS INNOVATIONS

Medical simulators can provide a safe, effective, and realistic learning experience. Simulators enable a level of competency to be attained before these skills are put into practice in a clinical environment. As with keyhole surgery 15-20 years ago, virtual reality represents a major development in healthcare for which inadequate expertise exists worldwide. Therefore, virtual medical training systems have been developed and used in different fields and medical disciplines.

Recently, research and development of virtual reality and augmented reality to assist or guide surgeons during the procedure has increased (Fig. 1). Augmented Reality (AR) systems describe a class of systems that use real-time computing to overlay virtual information on the real world. AR environments are promising tools in several medical training and simulation applications but they have rarely been applied to needle insertion simulation and guidance where soft tissue deformation (related to palpation and needle insertion) is very complex to simulate and display.

Advances in haptic interfaces make it possible to provide real-time kinesthetic feedback with up to six degrees of freedom (DOF) as part of medical simulators (Fig. 2). Various force feedback devices can be used with different levels, such as the PHANTOM Omni Haptic Device (Sensable Corp.) with x, y and z force feedback or the Bimanual Surgical Manipulator from Immersion, Corp., which simulates the force feedback on a simulated surgical grasping device, or computer mouse with force feedback in the x-y plane.

RASimAs will use augmented reality and visio-haptics and combine general VPH models with patient-specific data available from diagnostics to assist the anaesthesiologists during the procedure.

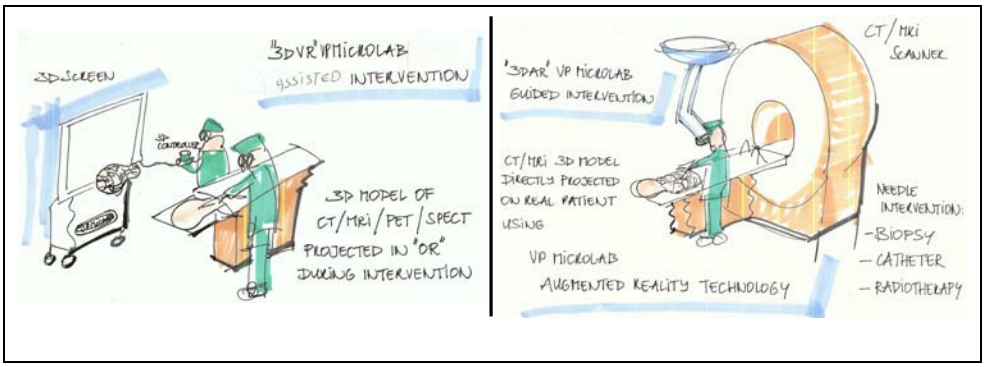

Figure 1: *General concepts of assisted (left) vs. guided (right) interventions.*
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RASimAs will use 3D stereoscopic displays and advanced soft tissue deformation models to provide an ultra-realistic experience to clinicians. RASimAs will simulate anatomical landmarks such as bone and pulse that are covered by skin tissue, with true haptic rendering and 6 DOF force feedback, in order to enable manipulation of the skin surface and subsurface structures by dragging tissue with virtual fingers.

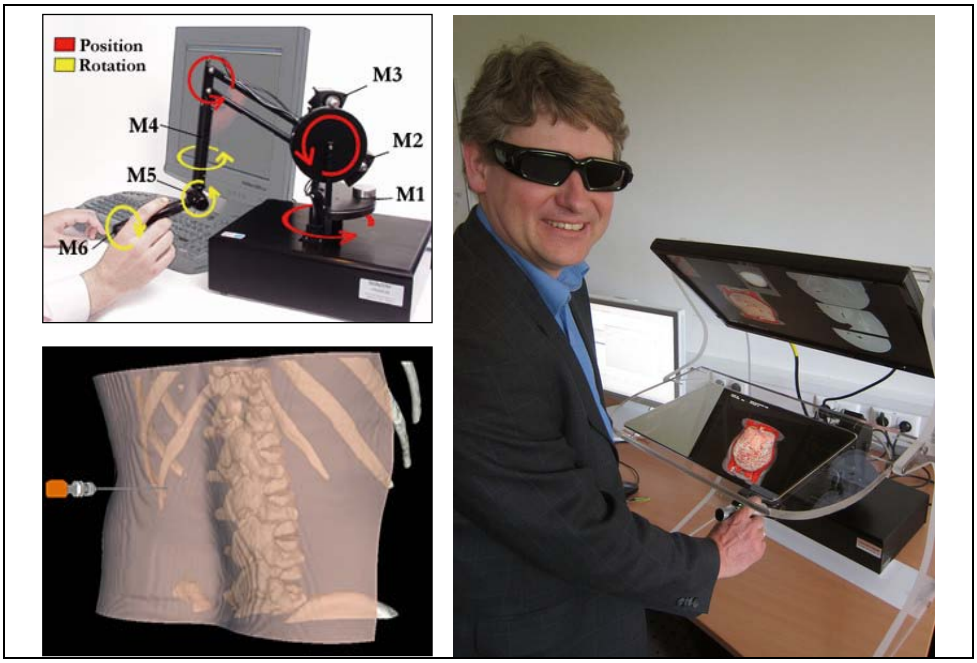

Figure 2: *For VR-based training of lumbar punctuation, the immersive VR workstation (right) is equipped with shutter glasses and haptic feedback device with six degrees of freedom (6DOF).*

1.2.2. Simulation of regional anaesthesia

CURRENT TECHNOLOGIES

The advantage of using VR-based simulators in medicine is the creation of a realistic environment with standardized and reproducible scenarios. The development of new simulators and the recognition of their utility for training and continuing medical education have led to widespread use in medicine. Numerous simulators specialize on needle procedures for different areas of applications, such as acupuncture, lumbar puncture, and intravenous procedures.

Spinal anaesthesia and epidural blocks are two of the most frequently applied RA procedures. For this reason – and presumably since these procedures do not involve electric stimulation, as opposed to standard RA – there are already a number of simulators for these specific applications.

However, our prior art search has only identified two simulators for peripheral RA available or under development. One VR-based RA simulator was developed by Energid Technologies in the context of a research contract for the United States Army[10] but did not result in a commercial product. This simulator used a commercially available 3D virtual patient model dataset (Zygote[11]). Electric nerve stimulation was simulated with a geometric distance-based approach and tissue deformation was approximated with a mesh-free point-based approach.

The second system is a commercial simulator named SAILOR[12], which is distributed as a supplement to a multimedia atlas for nerve blocks. Although the approach comprises different procedures, they are limited to a single patient model and allow for mouse interaction only, without tissue deformation. Existing regional anaesthesia simulators such as SAILOR currently use “pseudo-haptic” interfaces relying on haptic “illusions”: the combination of the manipulated object’s decel-

[10] Lim YJ, Le T, Valdivia P, Tardella N. Simulation-based military regional anesthesia training system. US Army Telemedicine and Advanced Technology Research Center (TATRC), Medical Research and Materiel Command (MRMC), Fort Detrick, MD. Contract W81XWH-06-C-0052. Dec 2008.

[11] Zygote Media Group. 3D models and 3D animations of the male and female anatomy. 2009. http://www.3dscience.com

[12] Bibin L, Lécuyer A, Burkhardtz JM, Delbos A, Bonnet M. SAILOR: a 3-D medical simulator of loco-regional anaesthesia based on desktop virtual reality and pseudo-haptic feedback. Proc ACM Symp Virtual Reality Software and Technology, 2008.

eration and the increase in force exerted on the interface to make the object move gives the user an impression of resistance and friction, despite the fact he/she is not using a haptic interface.

In a previous pilot study[13], we tested the acceptability of a VPH model to perform RA. All participants showed a high degree of acceptance of VR-based simulators. However, they stressed the importance of incorporating other nerve blocks, supporting ultrasound visualization, and using true haptic feedback.

RASIMAS INNOVATIONS

RASimAs provides significant improvement over the only commercial RA simulator currently available (SAILOR).

- *Incorporating all peripheral nerve blocks*: RASimAs will not be limited to the simulation of femoral nerve blocks. RASimAs will develop plausible representations of anatomical structures and physics-based parameters for the soft tissue simulation, visualisation and haptic rendering of at least two major major PNB targets: femoral nerve block and sciatic nerve block.
- *Simulating ultrasound image guided nerve block*: RASimAs will provide virtual ultrasound images, using an interactive clipping plane algorithm to create dynamic cross sections of anatomy structures used for acoustics-based real-time ray-casting to synthesize an ultrasound scan plane. The simulated ultrasound image will be rendered graphically on the display based on the probe position and angle.
- *Adding true visio-haptic feedback*: RASimAs will run in a virtual environment combining stereoscopic rendering (for 3D perception) for complete immersion and six degrees of freedom (6DOF) input/output for needle navigation and ultrasound probe interaction.

RASimAs will focus on incorporating other nerve blocks, supporting ultrasound visualization, providing true haptic feedback, and support training on patient-specific data in the VR-based RA simulator.

1.2.3. General vs. patient-specific models

CURRENT TECHNOLOGIES

Existing simulators (for example SAILOR) are based on generic commercial VPH models such as Zygote or Poser with some additional internal anatomy landmarks. However, the anatomical relations of which to the target nerves show considerable variability (Fig. 3).

For example, such variability becomes readily apparent to clinicians who regularly block the femoral nerve under ultrasound guidance. At the level of the groin skin crease the femoral artery may or may not have given off its major branch, the profunda femoris artery: the posterior division of the femoral nerve can lie posterior or lateral to the femoral artery and occasionally will be seen between the femoral and profunda femoris arteries. Furthermore, the lateral circumflex femoral artery, which usually arises from the profunda femoris but sometimes the femoral artery, can occasionally be seen just distal to the groin skin crease passing between the divisions of the femoral nerve. Such variability can pose serious challenges to even trained practitioners.

RASIMAS INNOVATIONS

The project will greatly enhance the state of the art by fitting automatically relevant patient data into VPH template models to generate patient-specific training modules, instead of relying on generic models. Clinicians can use these before the patient undergoes the intervention to be optimally prepared for the RA procedure. The training component especially addresses learners but also experienced anaesthesiologists having a complicated patient or using a new set up.

[13] Grottke O, Ntouba A, Ullrich S, Liao W, Fried E, Prescher A, Deserno TM, Kuhlen T, Rossaint R. Virtual reality-based simulator for training in regional anaesthesia. Br J Anaesth 2009; 103(4): 594-600

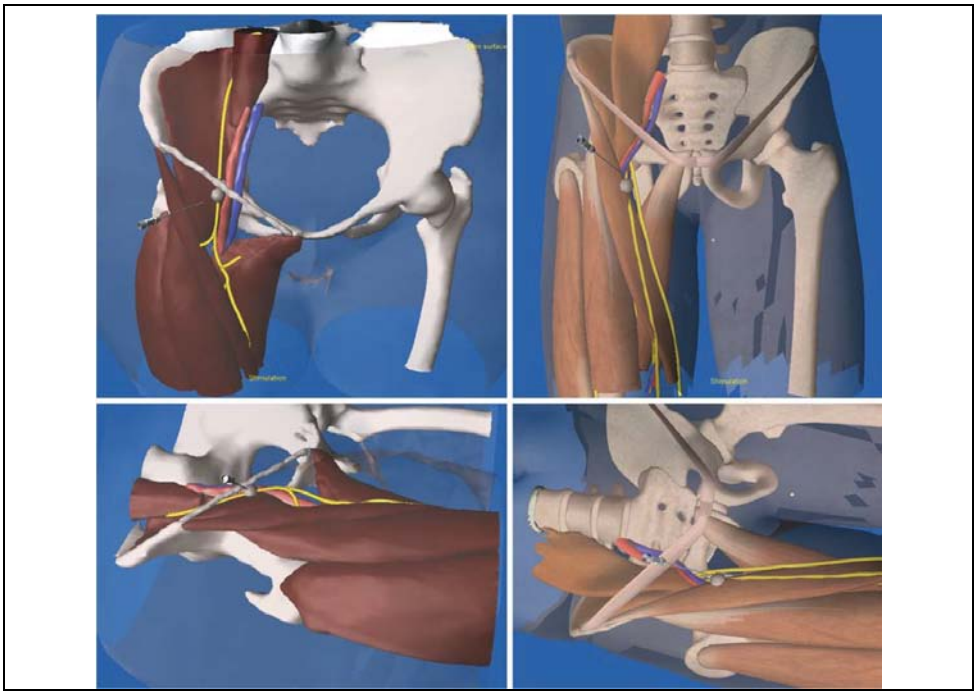

Figure 3: *Screenshots of two different data-sets that have been used in a previous pilot user study. The left column shows a manual segmented dataset and the right column shows the commercial Zygote dataset. The anatomy has been reduced to the essential components for the femoralis block procedure.*

For any RA, the nerves are of particularly interest. This is problematic because nerves can only be visualised by MRI if they are thick and situated superficially. The central nervous system (CNS) is easily detectable because of the higher relative amount of fat. The peripheral nervous system (PNS) is more difficult because of the connective tissue surrounding each axon (endoneurium), bundle (perineurium) and the whole nerve (epineurium). The main nerves are frequently surrounded by fat, which supports our concepts of automated segmentation. Special coils built for each body region can improve image quality, but the areas where the nerves enter the torso (axilla, hip) are problematic. Here, it is critical to be able to use MRI equipment with a field strength of 3 or even 9 Tesla.

Being located close to the RASimAs consortium core, research centers in Maastricht (The Netherlands) and Aachen/Jülich (Germany) operate two of the five MRI machines in the world with a field strength of 9 Tesla.

These high-power machines will be used to create a variety of general models that can also be enriched with CT or ultrasound imaging. VR-guided RA training is using skin, individual muscle, bone, cartilage, blood vessel, fat, and nerve (Fig. 4). However, connective tissue is relevant as well because it is giving resistance and must be also considered for designing a realistic training module.

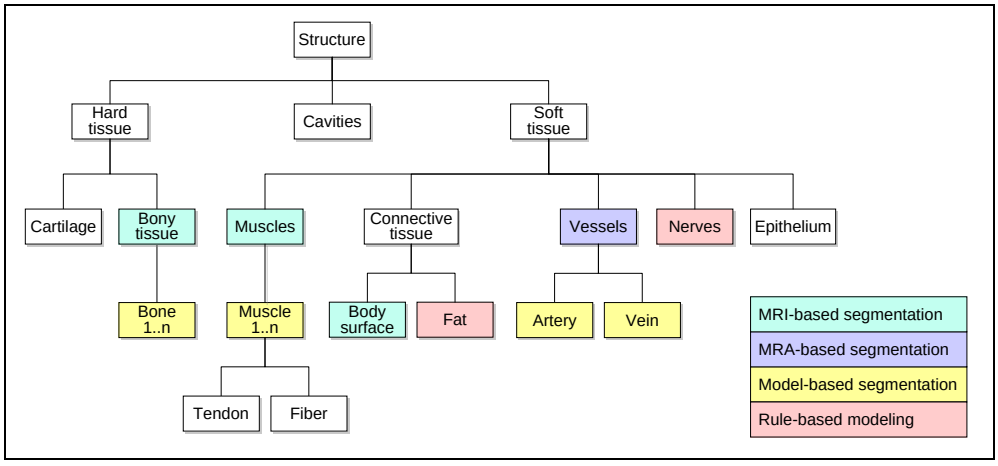

Figure 4: *Anatomical ontology with structures that are subdivided into tissue types and cavities to describe the components of the human body. Exemplarily, the coloured boxes represent structures that are relevant for the simulation of the inguinal region.*

Once the patient-specific data has been obtained, it is transferred into the RASimAs framework and registered. Data can come from morphologic data already collected during the diagnostic phase or non-invasive MRI/MRA data acquired during the RA procedure.

The resulting patient-specific model is generated to be used by the trainee with haptic feedback and augmented visualization in the virtual environment (cf. Fig. 1). During the assisted procedure, the model is linked in real time to the patient's ultrasound data acquired by the physician during the RA procedure.

RASimAs value-add is that it can make additional use of patient-specific data obtained during the diagnostic or therapeutic phase without additional costs, resulting in a more accurate VPH models.

1.2.4. Image processing libraries and algorithms

CURRENT TECHNOLOGIES

Gathering additional information out of existing data requires sophisticated image processing, analysis, and image data management. On the one hand, general models are composed from virtual human data and commercial dataset's such as Zygote, and on the other hand, subject-specific data is generated from patient-specific imaging. Although there is no commercial technology yet available allowing fusing generic and patient-specific data, model-based intervention planning and model-guided intervention technologies have been successfully applied in recent research[14].

Therefore, up to now, medical simulators have generally been characterized by their reliance on a generic anatomical model, typically obtained at the cost of extensive user interaction, and by biomechanical computations based on mass-spring networks[15].

There is a need to develop algorithms at the interface between image computing and computational modelling that enable transformation of state-of-the-art imagery of specific subjects into model parameters. Although initial steps have been made in this direction[14], there are still challenges associated with parameter estimation in large-scale non-linear and sometimes discrete models from imaging data. In addition to challenges associated to complex inverse problems, some of the difficulties stem from the need to establish appropriate relationship between the model parameters and the parameters actually measurable through imaging.

[14] Deserno TM, Handels H, Meinzer HP, Tolxdorff T. Image analysis and modeling in medical image computing: recent developments and advances. Methods Inf Med 2012; 51(5): 395-7.

[15] Audette MA, Fuchs A, Astley O, Koseki Y, Chinzei K. Towards patient-specific anatomical model generation for finite element-based surgical simulation. In: Proceedings of the 2003 international conference on surgery simulation and soft tissue modelling (IS4TM'03); p. 340-52

RASIMAS INNOVATIONS

The general idea is to substitute lacks in subject-specific information by that adopted from the general models in order to build VPH models (Fig. 5).

RASimAs will create specific ontologies enabling conceptual mapping between imaging modalities and model parameters so that it will be possible to fully streamline the process of model building and its personalisation.

This requires a consistent management of data. In the clinical environment of picture archiving and communication systems (PACS), the Digital Imaging and Communications in Medicine (DICOM) standards provides methods and means to transfer and exchange subject-specific image data ensuring data privacy and security issues. All data for the RASimAs project will be pseudonymised, i.e. an obfuscated identifier is used for data addressing and locating, which is generated from the patient's name, date of birth, and other identifying metadata.

Furthermore, image processing libraries will be composed for the RASimAs project to support segmentation of different types of soft tissue (cf. Fig. 4) from 3D data and multi-dimensional (2D to

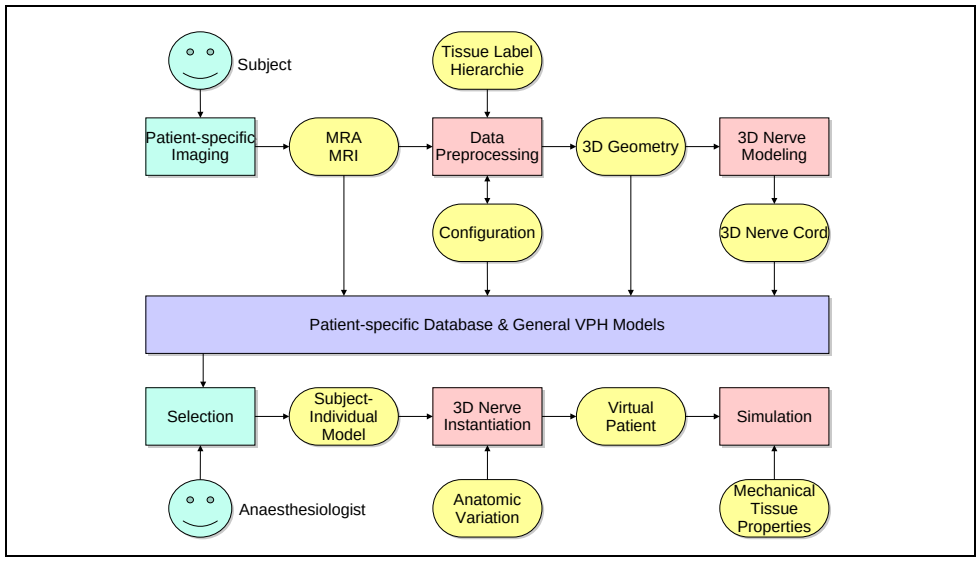

Figure 5: *The data flow describes all the steps from a real subject to the RA training and guidance. The patient-specific subject database with the VPH models forms the core component of RASimAs.*

3D, 3D to 2D) registration techniques that allow multi-modal (CT, MRI, ultrasound) co-registration of multi-individual (subject-specific, general) images. Virtual ultrasound will be generated from CT and MRI data, assuming a certain acoustic model and seek tissue differences along virtual ultrasound rays that are passing through the tissue. Since visualization and haptics are the most relevant elements of human-machine interfaces, algorithms for rendering and image fusion will be selected and integrated.

The RASimAs Consortium includes leading experts in medical image processing, management and visualization: algorithms need rather selection, integration and optimization than development, since the Consortium is referring to a considerably history of related research and experience.

1.2.5. Soft tissue deformation models

CURRENT TECHNOLOGIES

A number of models can be used to simulate soft tissue deformation[16]: for example mass-spring-damper systems, finite element methods (FEMs), long element models (LEMs) and point collocation-based method of finite spheres (PCMFS).

Because RA procedures involve needle-tissue interaction, realistic modelling and simulation of soft tissue deformation is the most important requirement for a RA simulator. Linear elasticity-based FEMs have been the most prevalent technique for simulating invasive operations.

Modelling and simulation of invasive tissue deformation in a FEM framework is significantly more challenging than non-invasive procedure modelling primarily due to two factors. First, it is difficult to measure the fracture toughness of non-homogeneous soft tissues to accurately model the rupture process. Second, invasive procedure simulation involves breaking and re-meshing of nodes, which is computationally expensive for reliable simulation. Research in needle insertion has examined the following topics: modelling and simulation of needle-tissue interaction forces, tissue deformation, and deflection of the needle during insertion and path-planning of needle trajectories based on tissue deformation.

RASIMAS INNOVATIONS

While mass-spring approaches are very popular and often found in other commercial simulators, they are not physics-based (Fig. 6). One of the novelties and advances of RASimAS is the combination of physics-based co-rotational and non-linear finite element method (FEM) approaches with haptic rendering, which is very seldom found in related work. This allows for the usage of real world-measured continuum mechanics parameters, resembling accurate tissue properties. Due to the computational burden of using FEMs for modelling invasive procedures coupled with the difficulty in characterizing the nonlinear behaviour of real tissues during rupture, very few studies so far have implemented non-linear and co-rotational FEMs. However, GPU-accelerated solutions with parallel processing capabilities, bigger memory and faster read-write speeds are now available in commercial hardware platforms. In addition, RASimAS includes leading experts in real time-capable FEM implementations and will use SOFA[17], an open source framework with an active community allowing several standard FEM implementations.

RASimAs will use non-linear FEMs and co-rotational FEMs such as the co-rotational with polar method and the co-rotational with QR decomposition method.

In order to develop a RA simulator that incorporates realistic soft tissue deformation models along with haptic feedback, RASimAs will address the following challenges:

- Formulating a methodology to incorporate this experimental data in a continuum mechanics

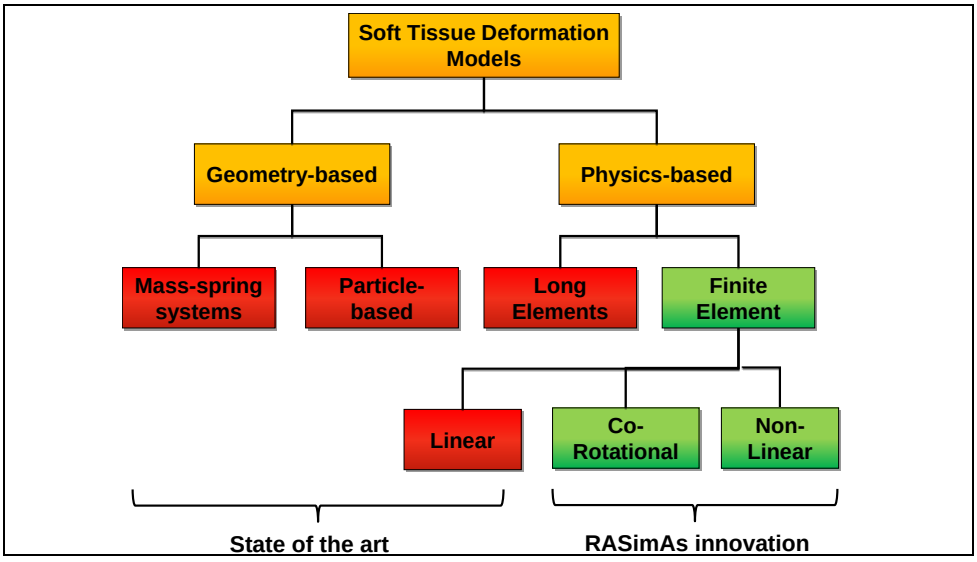

Figure 6: *Summary of soft tissue deformation models. The models selected for the RASimAs project are highlighted in green.*

framework to simulate realistic deformations of organs;

- Making simplifications to the computational model such that the simulation runs in real time but does not compromise the effective realism of the tissue response.

1.2.6. Innovation Summary

Table 3 summarized the innovations resulting from RASimAs.

RASimAs will be the first medical simulator and assistant that can combine 3D stereoscopic visualization, 6DOF input with haptic feedback, ultrasound or electric nerve guidance together with hyper-realistic models based on patient-specific data and advanced soft tissue deformation simulation.

Existing Solution	Selected RASimAs Innovations
RA assistance systems are based on ultrasound and electric nerve simulations, which require significant training.	RASimAs will use an advanced VR engine to provide training (before the procedure) and an advanced AR engine for guidance (during the procedure), leveraging shared data sets and supplementing each other appropriately. It will be possible to use the system in conjunction with ultrasound or electric nerve stimulation.
RA simulators have only rudimentary visualization technologies (2D) and input/output mechanisms (computer mouse, 3DOF).	RASimAs' VR engine will use stereoscopic rendering (for 3D perception) to enhance immersion. In addition, the simulator will provide an intuitive six degrees of freedom (DOF) input with haptic feedback for needle and US probe navigation.
VPH models used in RA are based on commercial (generic) models.	RASimAS will be able to fuse patient-specific data (from MRI, MRA or US imaging) into the VPH model used by the simulator and assistant system, using advanced image processing libraries and algorithms.
Soft tissue deformation models based on linear FE methods (short computation time but not suitable for large deformations).	RASimAs will leverage improvements in commercial hardware platforms (GPU, parallel processing) to implement non-linear FE methods (more resource intensive but also more accurate) to simulate soft tissue deformation related to needle insertion and provide true haptic feedback.

Table 3: Summary of RASimAs innovations.

1.3. S/T Methodology and associated work plan

1.3.1. Overall strategy and general description

The entire work plan clearly is structured into eight work packages (WP) that are composed of three parts: (i) the simulator system (Fig. 7, red), (ii) the assistant system (Fig. 6, yellow), and (iii) a comprehensive evaluation by means of controlled clinical trials (Fig. 6, green). These parts are framed with work packages and tasks on management and overall quality assurance. Dissemination of project results as well as patient-specific data acquisition is performed during the entire working phase, too.

WP2 to WP4 provide the technological basis and the model data to be used for simulation as well as assistance (WP5). The evaluation phase (WP6) is composed of RASim and RAAs evaluation. WP1 (Project Management), WP7 (Overall Quality Assurance), and WP8 (Dissemination and Exploitation) frame the core parts entirely. For instance, the technical files, which are needed to conduct the clinical study in Part 3 using the software and systems developed in Parts 1 and 2, are recorded and updated during the entire project.

Figure 7 emphasizes another advantage of our overall strategy: the two lines for simulation and assistant systems are independent, which makes the project robust to technological obstacles that may occur during the working phase. In other words, if development or evaluation of either the RASim or RAAs component may fail, the other still can be implemented successfully.

The project structure of RASimAs ensures that development or evaluation of either the RASim or RAAs component may fail, the other still can be completes successfully.

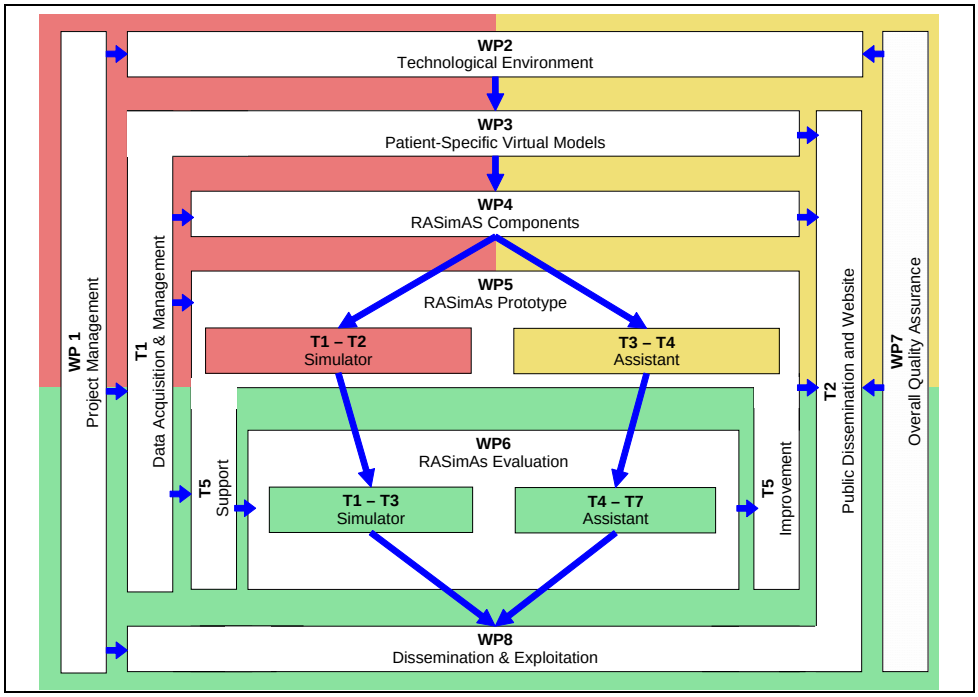

Figure 7: *The composition of work packages is indicated in three parts, (i) simulator system, red; (ii) assistant system, yellow; and (iii) comprehensive evaluation, green.*

Risk Management

This project implementation plan, produced at the start of the project, is subject to revision in the course of the project, in accordance with the procedures for project re-planning outlined in the Project Management section. Scientific work is accompanied by continuous quality assurance and risk analysis (Fig. 8). By means of internal reviews, quantitative indicators are obtained to initiate – when needed – project recovery plans.

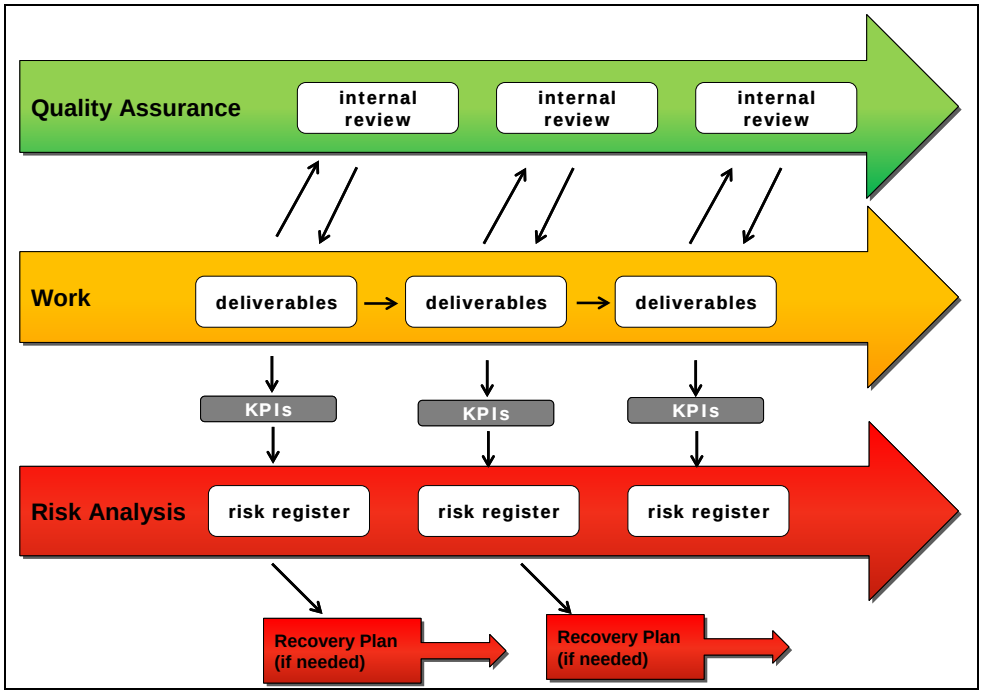

Figure 8: *Risk management. The scientific work is accompanied by continuous quality assurance and risk analysis.*

One of the main reasons that project adjustments may be necessary is as a result of regular risk assessment in the project. The initial list of risks presented in Table 4 is a start to this process. More detailed assessment of risks will be carried out regularly, based on practical experiences.

Scientific Risk	Impact	Probability	Remedial Actions
Low update rate of simulation algorithms.	Medium	Medium	Optimize algorithms, reduce complexity of data sets, interpolate between update steps and use separate computational threads to keep visual and haptic rendering at sufficiently high rates.
Failing of automatic segmentation algorithms.	High	Medium	Experiment with different segmentation strategies. Create more manually segmented and expert-reviewed entries of VPHs for a model atlas.
To large complexity and noisiness of initial data for machine learning algorithms.	Medium	Medium	Develop stable algorithms by reducing and preliminary transforming the initial data.
Not enough communication among the groups in charge of mechanical modelling, haptic feedback algorithms, and tool- tissue interaction modelling.	High	Low	Define clear goals, roles, and responsibilities for all partners in the groups involved in these tasks. Schedule periodic on-line and/or personal meetings for reviewing and planning. Include mechanisms for ensuring an adequate interaction among partners.

The chosen haptic devices are insufficient for training of the procedure with respect to fidelity, displayable forces, or work space	Medium	Medium	Experiment with different haptic devices. Adapt simulation algorithms to compensate eventual deficiencies.
A single PC platform might being unable to run accurate physiologic models as well as haptic and other devices, all in real time.	High	Medium	Exploit the graphical processing unit (GPU) to offset the central processing unit (CPU) load.
Face validity of simulator fails	High	Low	Base simulator core on detailed task analysis.
Clinical Risk	**Impact**	**Probability**	**Remedial Actions**
The clinical impact study should encompass safety and efficacy, but safety is prone to Type II error in small scale clinical trials (false negative if an error was made, but there was no consequence on safety).	High	Medium	Include "result / outcome" measures as well as "process" measures[18] in clinical evaluations.
Lack of insight into the training needs of Generation Y and Z health professionals.	Medium	Medium	Flag potential for all training tools to be portable, mobile and sources of achievable / searchable datasets.
Economical Risk	**Impact**	**Probability**	**Remedial Actions**
RA is performed in a complex dynamic environment. Even if the clinical efficacy of RASimAs is proven, its cost effectiveness may be difficult to quantify precisely.	High	Medium	Develop a robust economic methodology as part of the exploitation plan.

Table 4: Risks and risk mitigation.

1.3.2. Timing of work packages and their components

The Gantt Chart (Fig. 9) clearly indicated four critical milestones which the project management will observe and control, and at which will be decided whether adjustments of the scientific work conducted are necessary – depending on the results obtained so far.

[18] For example the success of a PNB should not be sufficient to determine the safety and efficiency of the procedure, but other process-related measures should be carried, such as distribution of local anaesthesia, possible intramuscular location of the needle tip before injection, correlation between the sidedness of the patient with the sidedness of the ultra-sound image, possible errors of needle-insertion site and angle with respect to the probe preventing accurate needle visualization (see chapter 1.1.5 KPIs for more detail).

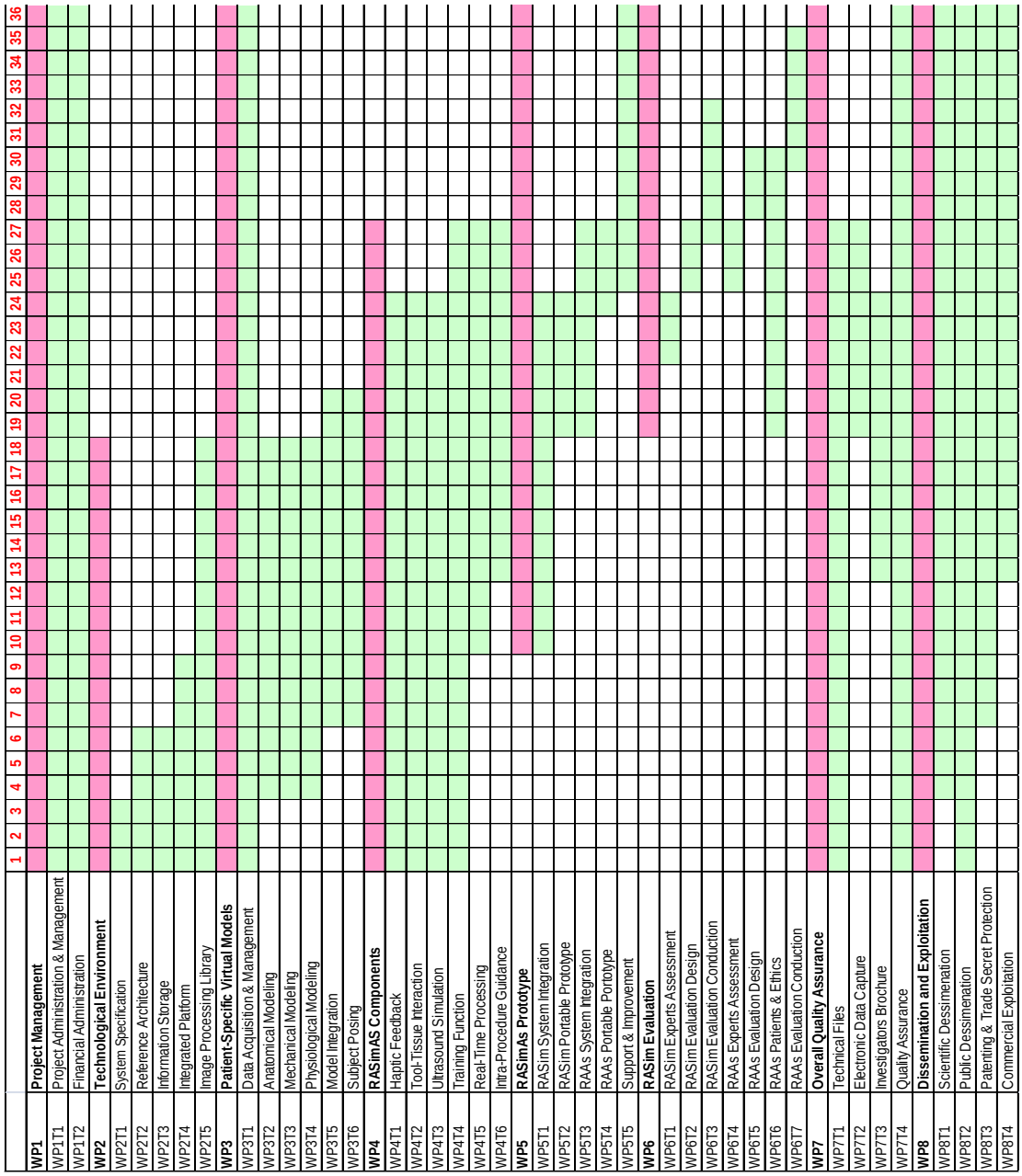

Figure 9: *Gantt Chart indicating the 4 critical milestones defined to control the project.*

WP / T	Descriptions	Type	Number	1a	1b	1c	2a	2b	3	4	5	6	7	8	9	10	11	Total
			Leader	UKA IMI	UKA DA	UKA CTCA	RWTH VR	RWTH EUPM	BANGOR	UCC	URJC	FORTH	INRIA	UNIZA	KU LEUVEN	SINTEF	SG	PM
			Total PM	80	17	28	37	12	25	21	46	44	34	22	20	33	44	463
WP1	**Project Management**	**MGT**	**UKA-IMI**	**12**	**0**	**0**	**0**	**10**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**22**
WP1T1	Project Administration & Management		UKA-IMI	12				1										13
WP1T2	Financial Administration		UKA-EUPM	0				9										9
WP2	**Technological Environment**	**RTD**	**FORTH**	**19**	**0**	**0**	**3**	**0**	**2**	**3**	**5**	**11**	**2**	**6**	**0**	**4**	**8**	**63**
WP2T1	System Specification		UCC	2			1		2	3	1	1		1		1	2	14
WP2T2	Reference Architecture		FORTH	3							1	3		2		1	2	12
WP2T3	Information Storage		FORTH	3							1			2		0,5		6,5
WP2T4	Integrated Platform		FORTH	3							1	3		1		0,5	2	10,5
WP2T5	Image Processing Library		UKA-IMI	8			2				1	4	2			1	2	20
WP3	**Patient-Specific Virtual Models**	**RTD**	**INRIA**	**16**	**0**	**0**	**0**	**0**	**18**	**0**	**4**	**18**	**14**	**0**	**2**	**0**	**0**	**72**
WP3T1	Data Acquisition & Management		UKA-IMI	12									3					15
WP3T2	Anatomical Modeling		UKA-IMI									5	6		2			13
WP3T3	Mechanical Modeling		INRIA						4			5	5					14
WP3T4	Physiological Modeling		BANGOR						4			5						9
WP3T5	Model Integration		FORTH	4					4			3						11
WP3T6	Subject Posing		URJC						6		4							10
WP4	**RASimAs Components**	**RTD**	**URJC**	**0**	**0**	**0**	**23**	**0**	**5**	**0**	**25**	**10**	**13**	**6**	**0**	**15**	**13**	**110**
WP4T1	Haptic Feedback		URJC				4				9		4,5				5	22,5
WP4T2	Tool-Tissue Interaction		INRIA				4				5		3				3	15
WP4T3	Ultrasound Simulation		RWTH-VR				11				5		5,5			1	4	26,5
WP4T4	Training Function		URJC				4		3		6						1	14
WP4T5	Real-Time Processing		SINTEF									5		4		8		17
WP4T6	Intra-Procedure Guidance		SINTEF						2			5		2		6		15
WP5	**RASimAS Prototype**	**DEMO**	**SINTEF**	**0**	**0**	**0**	**9**	**0**	**0**	**0**	**8**	**3**	**3**	**4**	**0**	**9**	**16**	**52**
WP5T1	RASim System Integration		SG				5				5			4			10	24
WP5T2	RASim Portable Prototype		SG				4				3						6	13
WP5T3	RAAs System Integration		SINTEF										3			4		7
WP5T4	RAAs Portable Portotype		SINTEF									3				4		7
WP5T5	Support & Improvement		SINTEF													1		1
WP6	**RASimAs Evaluation**	**RTD**	**KU LEUVEN**	**8**	**12**	**13**	**0**	**0**	**0**	**18**	**0**	**0**	**0**	**0**	**12**	**0**	**0**	**63**
WP6T1	RASim Experts Assessment		UCC	2	2					4					2			10
WP6T2	RASim Evaluation Design		UKA-DA	2	3	2				1					1			9
WP5T3	RASim Evaluation Conduction		UKA-DA		3	1				3					3			10
WP6T4	RAAs Experts Assessment		UCC	2						4					2			8
WP6T5	RAAs Evaluation Design		KU-LEUVEN	2		2				1					3			8
WP6T6	RAAs Patients & Ethics		UKA-CTCA		1	8				1					1			11
WP6T7	RAAs Evaluation Conduction		KU-LEUVEN		3	0				4								7
WP7	**Overall Quality Assurance**	**RTD**	**UKA-CTCA**	**10**	**2**	**15**	**2**	**0**	**0**	**0**	**4**	**2**	**2**	**2**	**0**	**3**	**4**	**46**
WP7T1	Technical Files		UKA-CTCA	2		4	2				2	2	2	2		1	2	19
WP7T2	Electronic Data Capture		UKA-IMI	5		3												8
WP7T3	Investigators Brochure		UKA-CTCA		2	5												7
WP7T4	Quality Assurance		UKA-CTCA	3		3					2					2	2	12
WP8	**Dissemination and Exploitation**	**OTHE**	**UKA-IMI**	**15**	**3**	**0**	**0**	**2**	**0**	**0**	**0**	**0**	**0**	**4**	**6**	**2**	**3**	**35**
WP8T1	Scientific Dissemination		UKA-DA	4										2	3			9
WP8T2	Public Dessimenation		UKA-IMI	4	3									2	3	2		14
WP8T3	Patenting & Trade Secret Protection		UKA-IMI	3				2										5
WP8T4	Commercial Exploitation		SG	4													3	7

Figure 10: Detailed effort in person month per work package and task.

2. IMPLEMENTATION

2.1. Management structure and procedures

The management structure has been designed to ensure effectiveness, decisiveness, flexibility and excellence of work of all RASimAs partners (Fig. 10). It is based on the liaison of the Coordinator with the European Commission (EC). An independent Advisory Board (AB) will be created to support the Coordinator (Fig. 10).

A lean management structure is designed to ensure the efficient and effective implementation of this multidisciplinary project as well as the accomplishment of all tasks and objectives within time and budget.

2.1.1. Project management bodies

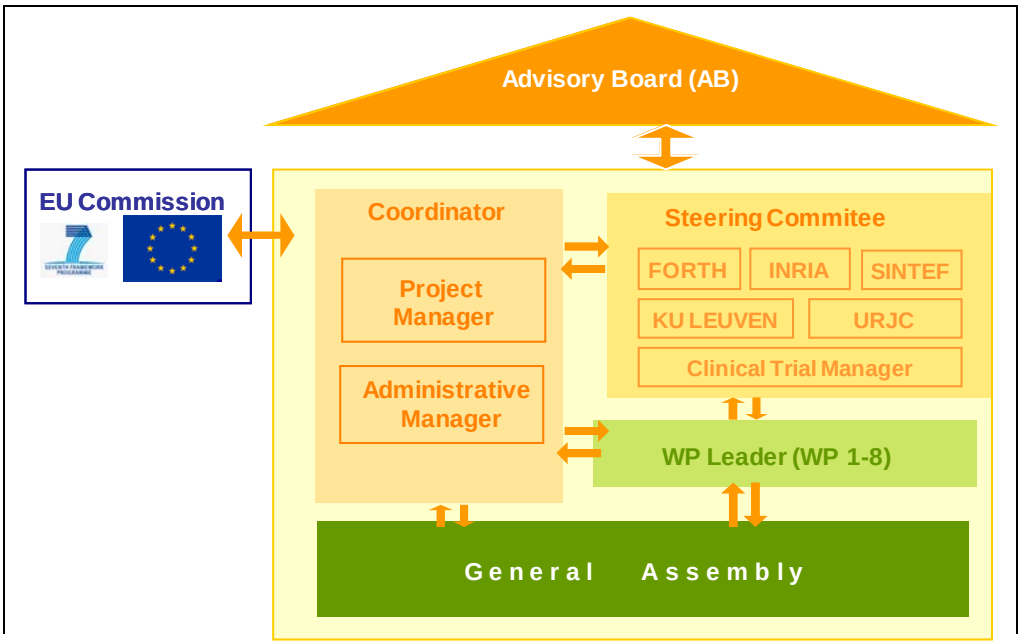

***Figure 11:** RASimAs Lean Management Structure.*

GENERAL ASSEMBLY

The General Assembly (GA) is the decision-making body of the consortium, consisting of one representative from each project partner, chaired by Project Manager. The GA will meet annually. The GA will principally guide the strategic decisions of the project, in particular:

- Decisions of major and strategic relevance.
- Management of knowledge.
- Management of intellectual property rights.
- Technical direction of the project.

The GA will monitor the overall project implementation and therefore compare scheduled project goals and actual project progress to ensure optimal project implementation. This will involve the following tasks:

- Optimize the overall quality of the deliverables and project results.
- Decide on appropriate adjustments, if necessary - this may involve the formation of task groups focusing on specific bottlenecks.
- Approve formally the deliverables and of each milestone accomplished.
- Approve formally the project results prior to dissemination and exploitation;
- Review and evaluate project results.
- Oversee and protect project results and IPR prior to being available to the public.

- Decide on patenting and licenses procedures within the project.
- Make decisions regarding possible modifications of Annex 1 for approval by the Commission.
- Decision on the entry of a new partner into the consortium or the withdrawal of a partner

WORK PACKAGE LEADER

The Work Package Leader (WPL) is one person from the partner leading the WP. Being connected directly to coordinator his principle responsibilities are:

- Accomplish the scientific work and research;
- Monitor and control the scheduled work plan considering deliverables and milestones;
- Report to the Steering Committee (SC) the results and progress of research;
- Report to the Coordinator in case any difficulty or delay arises related to the WP;
- Inform immediately the Coordinator of difficulties within the scientific research.

STEERING COMMITTEE

The Steering Committee (SC) is considered as task force for immediate adjustment between the work package leaders and the coordinator. It is chaired by the Project Manager and consists of one representative of each work package leading partner (FORTH, INRIA, KU LEUVEN, URJC, SINTEF), and a Clinical Trial Manager (CTM). It will oversee the scientific research and collaborative work of the project.The principle responsibilities are:

- Scientific and technical coordination and continuity among work packages.
- Discuss the technical and research aspects and progress;
- Discuss and approve the implementation plan for the next project period;
- Consider appropriate adjustments;
- Report regularly to the GA on the scientific project activities and progress.
- Optimize use of knowledge generated within the scientific community and the public.

COORDINATOR

The Coordinator (UKA) is the sole point of contact, interfacing with the European Commission, assuring that all rights and obligations of the partners are in compliance with the provisions of the EC and is responsible for the overall management of RASimAs as well as the implementation and continuity of the scientific work. The Coordinator is responsible for the overall project management of RASimAs.

Because the small, flexible and manageable work units throughout the Consortium, the scientists are relieved form a significant portion of the administrative burden.

UKA is ideally positioned to be the Coordinator as it has already been involved in a large number (~20 projects) of FP7 projects, either as coordinator or contributor. The Coordinator is responsible for the distribution of the EC Contribution, ensuring the accomplishment of all project tasks and deliverables and for the timely reporting of the results to the EC.

Principle responsibilities are:

- Establish efficient and effective administrative procedures;
- Provide guidelines and templates for administrative and financial matters;
- Ensure the timely distribution of the EC Contribution to the partners;
- Monitor the EC contribution according to the pre-defined tasks and deliverables;
- Collect relevant data results of all partners for a timely distribution to the EC;
- Prepare and organize meetings and provide minutes.

2.1.2. Project coordination and management

The Coordinator is built from the Project Manager and the Administrative Manager.

PROJECT MANAGER

The Project Manager of RASimAs will be Prof. Dr. Thomas Deserno (UKA-IMI), who has extensive experience in coordinating interdisciplinary project teams with medical and technical partners. In more than 20 years, he played key roles in scientific projects funded by

- European Union, 7th Framework Programme, Marie Curie Actions IRSES
- European Foundation for the Study of Diabetis (EFSD)
- Ambient Assisted Living (AAL Joint Programme)
- German Federal Ministry of Education and Science (BMBF)
- German Research Foundation (DFG)
- German Federation of Industrial Research Associations (AiF)
- Deutsche Bundesstiftung Umwelt (DBU, one of Europe's largest foundations)

The Project Manager is responsible for the distribution of the EC Contribution, ensuring the accomplishment of all project tasks and deliverables and for the timely reporting of the results to the EC.

The Project Manager will be supported by a support team whose duties will include (i) following up progress reports, deliverables etc. are produced according to plan; alert the relevant managerial bodies to any discrepancies which arise; (ii) advising project participants on the details of administrative and other data required in reports; (iii) taking care of all practical arrangements in connection with arrangements for meetings etc; and (iv) maintaining an electronic infrastructure for ease of communication within the Consortium, and for controlled, shared access to project documents.

ADMINISTRATIVE MANAGER

The Project Manager is assisted by the Administrative Manager in day-to-day management of administrative and financial issues. Sebastian Dornieden (RWTH-EUPM) is acting as the Administrative Manager of RASimAs. So far, RWTH-EUPM has signed 140 and 157 projects in FP5 and FP6, respectively. Currently, RWTH-EUPM signed more than 130 Grant Agreements in FP7 with around 60 Mio € EC Contribution.

The Administrative Manager monitors and verifies the accounting of the EC Contribution according to the scheduled work plan with its deliverables and milestones, verifying the expenditures by half-time of the reporting periods. In order to ensure a timely reporting of all partners, administrative documents, cost statements and audit certificates will be collected prior to the reporting periods. All documents, necessary for the liaison with the EC, will be forwarded from the partners to the Coordinator for final approval and submission to the EC.

CLINICAL TRIAL MANAGER

The Clinical Trial Manager (CTM) will be an intermediary between the Work Package Leaders (WPL) and the Coordinator, responsible for the monitoring of scientific work with respect to the clinical trial. It is envisaged that UKA-CTCA is appointed as CTM and will guide the Consortium according to the respective provisions and regulations for clinical trials in Europe. Due to the strict timetable, it is necessary to control and monitor the research progress and implement available results to the tasks of the clinical trial.

Dr. Alexandra Greindl will act as CTM. She has been involved in more than 30 clinical trials of out which 5 trials are European multi-centre trials. As certified Quality Management Authorized Representative, she is experienced in optimisation of workflows and the establishment of standard procedures to generate accurate, consistent, complete and reliable data within clinical trials.

RASimAs provides a clear strategy, an organized management structure and professional researchers with prior EC project management experience.

2.1.3. Advisory Board AB

An independent Advisory Board (AB) will be established from leading experts in the field, composed of academia, industry, and European hospitals. The General Assembly will make recommendations concerning experts to join the AB and agree on its members. The idea of the Advisory Board is to interconnect the RASimAs Group with latest results from research and development, ongoing project in related fields, and other related initiatives of the European Commission, in particular ongoing projects and networks of excellence. The Advisory Board shall convene on invitation of the Coordinator or the General Assembly.

2.1.4. Quality assurance

The project will employ the following main mechanisms for quality assurance in the project:

- A project quality handbook, derived from experience in earlier projects, customized for this project and updated as required, including practical guidelines on use of web-based file sharing and work support tool, procedures for publications, procedures for deliverable reviews.
- Feedback from Commission reviews. Project management will foster an attitude where these reviews are treated as part of the project's QA, rather than as an adversarial assessment.
- An early-warning system based on project monitoring tools (project virtual room and issue tracking system) enabling the detection of deviations from the work plan. RASimAs will use the web-based open source software Collabtive (http://collabtive.o-dyn.de/) for project tracking and the open source TRAC (http://trac.edgewall.org/) system for issue-tracking

2.1.5. Decision-making mechanisms

This section describes the mechanisms for reaching decisions, in a Consortium with multiple partners, each with their own goals. The general principle will be to try to achieve decisions by informal means and consensus, using formal procedures such as voting only when essential. Nevertheless: all decisions which can have an impact on project progress (whether reached formally or not) will be documented, for visibility within the Consortium.

Precise details of the remit of the various management bodies and of voting procedures are carefully defined in the *Consortium Agreement*. The most important principles are outlined in Table 8.

2.1.6. Conflict resolution

Identification of any conflicts which arise in the project is the responsibility of all project participants. Any signs of disagreement between project participants should be notified to the work-package leader or project manager (as appropriate), who should then instigate the conflict resolution procedure, escalating to higher levels only if necessary:

1. The manager should separately contact all parties either in person or by telephone, to identify the different viewpoints (it is important not to use email: that medium very often leads to a rapid escalation of disagreements). Based on a clarification of viewpoints, the manager should try to propose a solution. If one is achieved, it should be recorded in a short report; if not, no documents should be produced, and the problem escalated.

Level	Decision Mechanism	Escalate If
Work package	Verbal consensus only, meetings regular and as needed	No consensus is reached
Steering committee	Verbal consensus, vote if necessary, simple majority, meetings every 12 weeks	One partner insists

Table 5: Principles of decision making mechanism.

2. If Level 1 fails, the matter should be taken up by the Steering Committee (at a special meeting, if need be). At this level, all work should be in writing. If conflicts relate to matters which would normally be assessed as part of the annual reviews by the Commission, the views of the Commission should be sought.
3. If Level 2 fails, the General assembly shall decide (at a special meeting, if need be) about necessary intervention by the Commission and/or legal action as last escalations possible.

2.1.7. Project adjustment and change management

In an ambitious and dynamic project of this kind, changes in requirement changes are to be expected and will generate changes to the project plans. Handling changes in project plans will be therefore be regarded as a normal part of project management, to be carried out without undue formalities.

Project progress will be continuously monitored, and where discrepancies between plans and progress are observed (or predicted), corrective actions will be initiated. In particular, the Steering Committee will carry out risk assessment at their regular meetings. This involves identifying project risks, assessing their probability, and determining the nature of the consequences should the risk be incurred. If the risk level is judged to be high, changes in project planning may be necessary. A set of project risks has already been identified (see Section 1.3.1 *Risk Management*). It will serve as the basis for risk assessment at the first meeting of the Steering Committee, and will be continuously updated thereafter.

Decisions on any necessary adjustment or re-planning of detailed tasks at the *Work Package Level* will be made by the work package leader, in consultation with all partners involved in the work package. Results should be reported to the project manager. *Project Level* changes will be the responsibility of the Steering Committee (except in the case of *major* changes, see below). In addition to any reviews arising from regular risk assessment, the detailed project plan will be reviewed at least once per year, and revised if necessary.

Certain types of adjustments may require the approval of the Commission, according to the terms of the contract. It will be the responsibility of the Project Manager to contact the Commission regarding such matters.

Project re-planning that results in changes deemed to be *major* must be handled by the General Assembly, using voting procedures. Changes will be deemed to be major if any one partner protests about a proposed change, or automatically if the change involves:

- Modifications to the *Consortium Agreement* or to the management structures and principles.
- Problems with the performance of any partner, or partner request to leave the Consortium.
- Re-allocation of budget between work packages and/or partners.

Implementation of major changes may necessitate a change in the overall project plan, detailed project plans or the work breakdown structure of the project. As explained above, the management structure of the project essentially follows the work breakdown structure of the project. The management structure can therefore adapt to changes in the work breakdown structure.

2.2. Beneficiaries

Participant No.	**1A**
Short Name	**UKA-IMI**
WP Participation	**WP1**, WP2, WP3, WP6, WP7, **WP8**
Organization Name	Universitaetsklinikum Aachen
Country	Germany
Organization Type	University / Hospital
Webpage	http://www.ukaachen.de/content/folder/1018014

Description of Legal Entity

The Uniklinik RWTH Aachen (UKA) is a modern centre for high performance medicine which offers the highest level of treatment, i.e. 32 departments and 25 institutes cover the entire spectrum of modern medicine. Approximately 1,400 beds are available for inpatient medical care. Annually about 45,000 inpatients and 200,000 outpatients benefit from the highest standards of medical treatment. UKA is a place for interdisciplinary research of scientists, physicians and engineers, with 67 professors and about 1,200 scientific assistants. The division ***"Medical Image Processing", Department of Medical Informatics***, is headed by Prof. Dr. Thomas M. Deserno. In general, the research aims at developing architectures and processing methodologies of intelligent medical systems. Equipped with diverse sensors such as x-ray, video endoscopy, magnetic resonance, or ultrasound, such systems must convert their perception meaningfully into certain actions or results according to the actual context. Segmentation, analysis and quantitative evaluation of medical images as well as their adequate representation form the basis of these systems, whereby flexibility and robustness are substantial requirements.

Main Task Attributed in the Project

Prof. Deserno is the Coordinator of RASimAs and leads WP1 (Management), WP8 (Dissemination) and ensures the scientific expertise of the integration of image processing work flows and support networking and integration within the Consortium.

Relevant Project Experiences

Prof. Deserno coordinated the IRMA project on Image Retrieval in Medical Applications, funded by the German Research Foundation (DFG) in 2001, aiming at the development and implementation of high-level methods for content-based image retrieval (CBIR) with prototypical application to medico-diagnostic tasks. In addition to common global features, extensive knowledge has been gathered in multi-scale partitioning and modelling of medical images. The project comprises a multi-layer software architecture that maps all operations in the CBIR chain. The software platform features database-linked data storage and allows quick and easy integration of additional image processing algorithms. The architecture supports scalable distributed processing on heterogeneous networks. It has been applied successfully to other domains of image and video processing, such as automatic analyses of sewer condition. The RASimAs project will profit from this infrastructure.

Key Personnel

Prof. Dr.rer.nat. Dipl.-Ing. Thomas M. Deserno (né Lehmann) received the Diploma degree in electrical engineering (School of Engineering), the PhD degree in computer science (School of Science), and the habilitation in medical informatics (School of Medicine) from the RWTH Aachen University in 1992, 1998 and 2004, respectively. He has published more than 100 papers and several textbooks on medical image processing and medical informatics and serves on the International Editorial Boards of Dentomaxillofacial Radiology, Methods of Information in Medicine, and World Journal of Radiology. He is Co-Editor of the International Journal of Healthcare Information Systems and Informatics (http://irma-project.org/deserno).

Participant No.	**1B**
Short Name	**UKA-DA**
WP Participation	WP6, WP7, WP8
Organization Name	Universitaetsklinikum Aachen
Country	Germany
Organization Type	University / Hospital
Webpage	http://www.ukaachen.de/content/folder/1016090

Description of Legal Entity

Professor Dr. Rolf Rossaint is the Head of the ***Department of Anaesthesiology*** since 1997. Currently the clinic employs 80 physicians. Main areas of research encompass the development and application virtual based projects (e.g. telemedicine and regional anaesthesia), the exploration of the mechanisms of acute lung injury, sepsis, xenon anaesthesia and coagulation management in trauma patients.

Main Task Attributed in the Project

The Department of Anaesthesiology will have significant participation of the assessment and development of the developed RASimAs prototypes.

Relevant Project Experiences

Together with the Department of Medical Informatics and the Department of Virtual Reality, Prof. Rolf Rossaint initiated a project for regional anaesthesia in 2006, funded by the DFG. The aim of this project was to develop a Virtual reality (VR)-based simulator to offer trainees a safe environment to learn and practice different regional anaesthesia techniques. Based on a substantial clinical knowledge about regional anaesthesia Rolf Rossaint guided this project in conjunction with Priv.-Doz. Dr. Oliver Grottke. Both founded the basis for the translation of clinical medicine in virtual environments. The performance of several phase-II and phase-III studies facilitated the realization of pilot projects to evaluate the RASIM simulator for daily clinical practice. .

Key Personnel

Prof. Dr. med. Rolf Rossaint is Head of the Department of Anaesthesiology at the Uniklinik RWTH Aachen and Vice-Rector for Research at RWTH Aachen, Germany. Dr. Rossaint studied medicine at the University of Düsseldorf, Germany, and is board-certified in anaesthesiology. Prior to his present appointment, he was Associate Professor in the Clinics for Anaesthesiology and Surgical Intensive Care at the Humboldt University of Berlin, Germany. Prof. Rossaint was the recipient of the E.-K. Frey Prize (1993), the Pulmedica Prize (1996), the Annual Scientific Award (1996) from the European Academy of Anaesthesiology and the Poster Award of 25th International Symposium on Intensive Care and Emergency Medicine 2005. Since 2010 he is a member of the National Academy of Science (Leopoldina). He has (co)-authored over 400 articles in peer-reviewed journals.

Priv.-Doz. Dr. med. Oliver Grottke is working at the Department of Anaesthesiology at the Uniklinik RWTH Aachen and will be one of the principle investigators of this project. After medical studies at the University of Hannover and abroad, he received his PhD degree from the university of Maastricht. His main areas of research encompass experimental haemostasis and virtual reality based medicine.

Participant No.	**1C**
Short Name	**UKA-CTC-A**
WP Participation	WP6, **WP7**
Organization Name	Universitaetsklinikum Aachen
Country	Germany
Organization Type	University / Hospital
Webpage	http://www.medizin.rwth-aachen.de/cms/Medizin/Die_Fakultaet/Einrichtungen/~coen/Klinisches_Studienzentrum_Aachen

Description of Legal Entity

The ***Clinical Trial Center Aachen (CTC-A)*** is an institution of the Medical Faculty of RWTH Aachen University, located at University Hospital Aachen. The CTC-A equals the institutions which have been set up for the support of researchers at many universities, mostly known as KKS or ZKS. It is the Clinical Trial Centre's purpose to methodically and scientifically support the project management of clinical research projects at RWTH Aachen University, especially those intensively regulated (Medical Act / Medical Device Act).

Main Task Attributed in the Project

The Coordinator will benefit from the CTCA staff`s extensive expertise in protocol writing, submission to various international ethics committees and other appropriate authorities, filing with local authorities, project and data management of multicenter clinical trials. The CTCA represents the Rector of RWTH Aachen University as sponsor (as defined in §3 German Medical Device Act). It will guarantee appropriate processes and work flows for initiation, conduction and completing of clinical trials that are fully in the scope of every legal and ethical requirement.

Relevant Project Experiences

CTC-A staff has extensive expertise in protocol writing, medical statistics, submission of application to various international ethics committees and competent authorities, filing with local authorities, project and data management of multi-centre clinical trials, medical writing according to European Guidelines (E3/E6). Furthermore the CTC-A is very experienced in multi-professional overall project management including initiation of improved processes and adequate reporting within a consortium. The RWTH Aachen University has decided to split the legally defined responsibilities of the sponsor-investigator into roles of the sponsor and roles of the investigator as defined in § 4 German Medical Act. The CTC-A is sponsor for a total of 107 different Clinical Trials, since 2004. A Quality Management System (QMS) for Clinical Trials is maintained and regularly implements Quality Assurance and Quality Control measures alongside the development and design as well as performance and reporting of clinical trials. The quality management system of the Clinical Trial Centre complies with all relevant guidelines and also comprises a data protection system according to the Act to Strengthen the Security of Federal Information Technology (BSI-Act-BSIG). For the quality management system ISO 9001:2008 certification is planned to be achieved in 2013. The quality management system consists of the quality management handbook and the quality assurance handbook, comprising standard operating procedures, working instructions, forms, templates and checklists for all relevant tasks in accordance with the Helsinki Declaration, ICH-GCP, and German regulations.

Key Personnel

Dr. rer.nat. Dipl.-Biol. Alexandra Greindl received the Diploma degree focusing on molecular biology and genetics and PhD degree in Biology/Natural Science from the RWTH Aachen University, Germany. She has more than 10 years experience as research scientist in fundamental and applied research and project coordination of numerous preclinical projects in industrial and academic environments. Since October 2011, she is assigned as certified quality management representative and coordinator of clinical research.

Participant No.	**2A**
Short Name	**RWTH-VR**
WP Participation	WP2, WP4, WP5, WP7, WP8
Organization Name	Rheinisch-Westfaelische Technische Hochschule Aachen
Country	Germany
Organization Type	University
Webpage	http://www.rz.rwth-aachen.de

Description of Legal Entity

RWTH Aachen University, established in 1870, is divided into 9 faculties. Approximately 35,831 students are enrolled in 126 courses of study. The number of foreign students (5,000) substantiates the university's international orientation. Every year, about 5.000 graduates and doctoral graduates leave the university. Approximately 480 professors as well as 4492 academic and 2346 non-academic colleagues work at RWTH Aachen University. The university budget amounts to 748 million Euros of which about 314 million Euros are third-party expenditures. Moreover, special fields of research, 20 graduate colleges, among them 9 founded by the German Research Foundation, 16 affiliated institutes with strong industrial alignment illustrate the university's considerable research potential. ***The Virtual Reality (VR) Group*** at RWTH Aachen University is researching new visualization and VR methods and develops this technology forward towards applicability in scientific applications. As a part of the University's Centre for Computing & Communication, the group is particularly exploiting high performance compute resources, with the goal to develop comprehensive visualization frameworks that allow for an intuitive, explorative analysis of complex technical, physical and natural phenomena.

Main Task Attributed in the Project

The VR group will contribute to the development of physically-based modelling and haptic interactions for simulation and assistance for regional anaesthesia.

Relevant Project Experiences

The VR Group participated in the DFG-funded Regional Anaesthesia Project initiated in 2006 in cooperation with the Department of Medical Informatics and the Department of Anaesthesiology of the University Hospital Aachen. During the project, a virtual reality-based simulator prototype was built with the goal to create a safe training environment to learn regional anaesthesia techniques. Specialized haptic rendering algorithms for the purpose of palpation and needle interaction were developed, combined with FEM-based soft tissue simulation and integrated into parallel software architecture for interactive simulation. The system was deployed on a mobile as well as on a stationary immersive system and evaluated by subject matter experts. Results were published in peer reviewed journals as well as conferences and had been honored with a best paper award on the IEEE VR conference. Besides the Regional Anaesthesia Project, the VR Group is involved in another interdisciplinary DFG-funded research project focusing on the development of a VR-based training simulator for a maxillofacial surgical procedure.

Key Personnel

Prof. Dr. Torsten Kuhlen studied Computer Science at RWTH Aachen University, where he received his diploma and PhD in 1992 and 1998, respectively. He is founder of the VR Group, Center for Computing and Communication, RWTH University. Since 2008 he is full professor in the Department of Computer Science. He is co-author of about 150 peer-reviewed publications and has been serving as program chair, program committee member, and reviewer for various renowned international conferences on Virtual Reality, Computer Graphics and Visualization.

Participant No.	**2B**
Short Name	**RWTH-EUPM**
WP Participation	WP1, WP8
Organization Name	Rheinisch-Westfaelische Technische Hochschule Aachen
Country	Germany
Organization Type	University
Webpage	http://www.rwth-aachen.de

Description of Legal Entity

The number of foreign students (14 %) confirms the University's international reputation. RWTH Aachen University, with 465 professorships, is strongly oriented toward the current needs of industry, commerce, and the professions and has a significant portfolio of innovations, patents, and licenses. The individual institutes collaborate very effectively across departments and faculties in interdisciplinary groups and forums. As an effect the university is German-wide ranked first in raising third-party funds from businesses, industry as well as from national and EU programs. The future strategy of RWTH to become an integrated, interdisciplinary technical university is supported by funds from the national Excellence Initiative and several strategic partnerships, e.g. IDEA League and the JARA Jülich Aachen Research Alliance. Interdisciplinary research especially in the field of engineering and medicine is consolidated within the excellence initiative and visible on the new research campus, between RWTH and UKA, with the first established Cluster "Biomedical Engineering".

Main Task Attributed in the Project

For RASimAs the ***EU Project Management Office***, established at the Division for Research Funding of RWTH Aachen University, is responsible for the professional project management in financial and administrative matters and will support the Coordinator in all administrative and financial issues.

Relevant Project Experiences

Relevant Project Experience. The EU Project Management Office of RWTH Aachen University (RWTH-EUPM) provides consultancy services for researchers and assists RWTH and UKA Institutes through the entire project lifecycle. With nearly 120 signed FP7 Grant Agreements in "Cooperation", 15% are coordinated, the EU Project Management Office has extensive experience with the contractual, financial and administrative procedures of EU projects.

Key Personnel

Sebastian Dornieden has worked in several public bodies and gained considerable expertise in consulting and managing projects in the field of innovation and research funded by the European Union (e.g. projects in the EIT Climate KIC) and national institutions. During the project runtime addition personnel (N.N.) of the EU Project Management Office might assume responsibility for the project or its specific tasks.

Participant No.	3	
Short Name	**Bangor**	
WP Participation	WP2, WP3, WP4	
Organization Name	Visualization and Medical Graphics, Bangor University	
Country	United Kingdom	
Organization Type	University	
Webpage	http://www.vmg.cs.bangor.ac.uk/	

Description of Legal Entity

Bangor University was founded in 1884 and is dedicated to academic excellence. We have over 10,000 students, 23 academic Schools grouped in to 6 Colleges and over 650 teaching staff. The Visualization and Medical Graphics Research group within the University's School of Computer Science will participate in the project. This is the largest research group within the School and research interests include medical visualization, virtual environments, information visualization and visual analytics, use of haptics interfaces, segmentation, artificial life, high dynamic range imaging, and augmented reality.

Main Task Attributed in the Project

Bangor will contribute to the development of virtual- reality based modelling and haptic interactions for training and assistance of regional anaesthesia.

Relevant Project Experiences

The Visualization & Medical Graphics (VMG) group is the largest research group within the School of Computer Science at Bangor University. Our research interests include medical visualization, virtual environments, information visualization and visual analytics, use of haptics interfaces, segmentation, artificial life, high dynamic range imaging, and augmented reality.

Key Personnel

Professor Nigel W. John established research activities at Bangor in visualization and medical graphics in 2003, and leads a dynamic and growing group of researchers active in this field. He is a Director of the Wales Research Institute of Visual Computing (RIVIC), and the NISCHR funded Advanced Medical Imaging and Visualization Unit. In 2006 he was awarded the 12th annual Satava Award to acknowledge accomplishments in the field of computer graphics and medical visualization. In 2009 he was elected as a Fellow of the Eurographics Association. He is also a member of the Editorial Board and Associate Editor of the journal Computer Graphics Forum. His primary research interests are in the application of computer graphics, haptics, and virtual environments to medical applications.

Dr. Franck P. Vidal will be Bangor's principle investigator on this project. His main research interests are in modelling and simulating complex and computationally intensive phenomena in medical physics (e.g. photon transport in radiology and radiotherapy), medical imaging (including tomographic reconstruction and volume segmentation) and medical graphics. In particular, he is investigating the use of advance visualisation methods, programming massively parallel processors, artificial evolution and haptics.

Dr. Serban R. Pop is a named researcher to be funded on the RaSimAs project. He was formerly a Research Fellow at the School of Mathematical Sciences, Centre for Mathematical Medicine, University of Nottingham where his main research topic was angiogenesis in wound healing, blood rheology and microcirculation of blood. At Bangor his research focus is on problems related to the virtual physiological human, starting with the modelling of blood flow in a diseased vascular system.

Participant No.	**4**
Short Name	**UCC**
WP Participation	WP2, WP6
Organization Name	Department of Anaesthesia, University College Cork
Country	Ireland
Organization Type	University / Hospital
Webpage	http://www.ucc.ie/en/

Description of Legal Entity

UCC was established in 1845. University College, Cork is one of four constituent universities of the federal National University of Ireland, and was awarded the Irish University of the year for 2003 and 2005. UCC's affiliate hospital, Cork University Hospital (CUH) is the largest university teaching hospital in Ireland with over 1000 inpatient beds and is the only Level 1 Trauma centre in the country. CUH has 25,500 inpatient admissions, 27,000 day cases, and 58,000 emergency cases (A&E) annually, making it one of the busiest hospitals in the country.

Main Task Attributed in the Project

UCC will significantly participate in the design, assessment and evaluation of the RASimAs prototypes.

Relevant Project Experiences

The Department of Anaesthesia and Intensive Care Medicine at CUH has a staff of 26 specialist anaesthesiologists and 28 resident anaesthesiologists in training delivering an anaesthesia case load in excess of 25,000 cases per annum. Five of the specialist anaesthesiology staff have shared academic roles with UCC and contribute to under- and post-graduate teaching and clinical research. UCC was partner in the Haystack project, a joint venture developing a system to support continuing professional development for doctors. The project built on research in the area of visuo-haptics, supporting training and assessment of competence by specifically developing a medical training simulator for ultrasound guided regional anaesthesia.

Key Personnel

Prof. George Shorten, MD, PhD was formerly Assistant Professor of Anaesthesiology at Harvard Medical School and appointed as the first Professor of Anaesthesia and Intensive Care Medicine at the Cork University Hospital, Ireland in 1997. He is reviewer and consultant for the U.S. Department of Health "Clinical Practice Guidelines on Acute Pain Management: Operative or Medical Procedures and Trauma". George Shorten is Author of approximately 150 articles for peer review journals and has been serving as reviewer and editor of different considerable journals and publications respectively. He is founder and National Director of MSc Aanaesthesia NUI/RCSI 2002-5.

Dr. Brian O`Donnell is consultant anaesthetist and clinical senior lecturer at the Cork University Hospital, Ireland since 2009. He has special interest in ultrasound guided Regional Anaesthesia, Medical Education and Clinical Research. He was significantly involved in the Haystack Project, funded by the Irish National Digital Research Center (NDRC).

Participant No.	**5**
Short Name	**URJC**
WP Participation	WP2, WP3, **WP4**, WP5, WP7
Organization Name	Modelling and Virtual Reality Group, Universidad Rey Juan Carlos
Country	Spain
Organization Type	University
Webpage	http://www.urjc.es/version_ingles

Description of Legal Entity

The URJC is the youngest public university in Madrid, operating since September 1997. It has reached a relevant teaching and research infrastructure. With respect to the academic areas most closely related to this proposal, the URJC offers degrees on Computer Science/Informatics, Computer Engineering, Software Engineering and Telecommunication Engineering. Also, it offers a number of Masters, such as the Master on Computer Graphics, Games and Virtual Reality, taught since 1996. PhD programs in Computer Science, Graphics and Imaging have been offered since 1998.

Main Task Attributed in the Project

URJC will contribute highly relevant works on the topics of contact mechanics, dynamic deformation modeling, haptic rendering, robotic manipulator design, visuo-haptic mixed reality, and medical applications of visuo-haptic simulation (with strong collaborations both with industry and hospitals on arthroscopy training). GMRV enjoys several facilities to be used in the project, such as a 4-wall CAVE immersive display, more than 10 haptic devices, or a Flock-of-Birds magnetic tracking system.

Relevant Project Experiences

The GMRV group designed and developed previously an arthroscopy simulator first distributed by GMV (INSIGHT ARTHRO VR) and nowadays sold by Simbionix (ARTHRO MENTOR). Members of the URJC group have published numerous relevant papers on simulation and haptic rendering at top conferences and journals, and have also organized workshops and tutorials on haptic rendering at virtual reality, robotics, and computer graphics conferences. E.g., they are the recipients of the Best Student Paper Award at the last IEEE World Haptics Conference. Profs. Pastor and Otaduy also lead national projects on visualization, simulation and haptic technology, and Prof. Otaduy leads the 2011 ERC Starting Grant ‘Animetrics’ on modelling of complex mechanical phenomena.

Key Personnel

Prof. Luis Pastor received is Engineer Degree from the UPM (Madrid, Spain), his MSEE from Drexel U. (Philadelphia) and his PhD in the UPM. His research interests include visualization, virtual reality and parallel processing, having published around 70 book chapters and refereed journal and conference papers.

Prof. Miguel A. Otaduy is an Associate Professor of Computer Science at URJC since 2008. He obtained a PhD from the University of North Carolina at Chapel Hill in 2004. From 2005 to 2008, he was a research associate at the Computer Graphics Lab of ETH Zürich. He has published over 60 papers in the areas of computer graphics, haptics, virtual reality, computer animation, or robotics. At the age of 35, he has an h-index of 20. He is program chair for several conferences (ACM Symposia and SIGGRAPH, Eurographics Symposia, IEEE World Haptics Conference 2013).

Dr. Marcos García Lorenzo obtained a Computer Science Degree and PhD at UPM (Madrid, Spain) in 2002 and 2007, respectively. In his PhD, he worked on simulation of elastic objects in interactive applications. In2008, he was a research fellow at the GV2 group in TCD (Dublin, Ireland). Since 2011, he is Associate Professor of Computer Science at URJC.

Participant No.	**6**
Short Name	**FORTH**
WP Participation	**WP2**, WP3, WP4, WP5, WP7
Organization Name	Foundation for Research and Technology, Hellas
Country	Greece
Organization Type	Research Institute
Webpage	http://www.ics.forth.gr/

Description of Legal Entity

The Foundation for Research and Technology – Hellas (FORTH) is one of the largest research centres of Greece with well - organised facilities and a highly qualified staff. The research and technological focus of the foundation is centred on selected areas of great scientific, social, and economic interest. The Institute of Computer Science (ICS), since its establishment in 1983, is a pioneering contributor towards the deployment and adoption of Information Society Technologies in Greece and plays a leading role in worldwide efforts towards the development of an Information Society accessible and acceptable by all citizens.

Main Task Attributed in the Project

ICS with the Computational Medicine Laboratory (CML) will be involved and contribute to the current project. FORTH will lead the development of technological environment necessary to build up reference architecture, information storage and an integrated platform.

Relevant Project Experiences

FORTH will contribute its extensive experience in modelling of medical image structures for virtual reality-based inter-subject-specific imaging within the EC initiative Virtual Physiological Human (VPH). The FORTH group is currently Coordinator of 2 EC FP7 projects on cancer modelling (ContraCancrum http://www.contracancrum.eu and TUMOR http://www.tumor-project.eu), and is actively involved in providing open access image analysis/modelling tools in the clinical setting for the promotion of predictive oncology within the wider Virtual Physiological Human (VPH) EC initiative.

Key Personnel

Dr. Kostas Marias holds a Principal Researcher position in the Institute of Computer Science (ICS-Forth). During 2001-2003, he worked as a researcher at the university of Oxford. He completed his PhD in the field of Medical Image Analysis/ Medical Physics in 2001 (UCL London, Royal Free Hospital) working in the Medical Vision Lab, University of Oxford. He also holds an MSc degree from Imperial College of Science, Technology and Medicine in Physical Science and Engineering in Medicine and an electrical Engineering diploma from the national the National Technical University of Athens (N.T.U.A). Recently, he has coordinates 2 EC FP7 projects. His research interests are in the areas of medical image analysis, cancer imaging and molecular and gene expression imaging, and he has published more than 80 papers in international journals and conference proceedings in the above fields.

Participant No.	**7**
Short Name	**INRIA**
WP Participation	WP2, **WP3**, WP4, WP5, WP7
Organization Name	SHARCA Team, Inria Lille – Nord Europe Research Center
Country	France
Organization Type	Research Institute
Webpage	http://www.inria.fr

Description of Legal Entity

INRA, the French Institute for research in computer science and control, is the only French public institute entirely dedicated to research in information and communication science and technology (ICST). Throughout its eight research centres, INRIA has a workforce of 4,300 (3,400 of whom are scientists from INRIA and its partner organizations) such as CNRS (the French National Centre for Scientific Research), Universities and leading engineering schools). They work in about 200 research teams. Many INRIA researchers are also professors who supervise around 1,200 doctoral students and their theses contributes to INRIA's research projects. INRIA has an annual budget of 250 million Euro, 25% of which comes from its own research contracts and development products. In its 2008-2012 Strategic Plan, INRIA has defined different scientific priorities in (i) Modelling: simulation and optimisation of complex dynamic systems; (ii) Programming: security and reliability of computing systems; (iii) Communication: information, and ubiquitous computing, (iv) Interaction with real and virtual worlds, and (v) Computational engineering, sciences, and medicine. As its strategy closely combines scientific excellence with technology transfer, it develops collaborations with the economic world through strategic industrial partners and about 100 companies have stemmed from INRIA since 1984. Concerning the FP7, INRIA is involved in about 180 selected proposals including 95 in the ICT theme of the Cooperation Programme and 25 ERC grants.

Main Task Attributed in the Project

INRIA will lead WP3 with its longstanding experience and expertise to develop patient specific models regarding to physiological, mechanical and nerve model aspects as well.

Relevant Project Experiences

Relevant Project Experience. SHACRA Team (Simulation in Healthcare using Computer Research Advances) focuses on Computational Medicine and Neurosciences domain. The purpose of SHACRA is to address the key scientific problems of the multidisciplinary field of computer-based medical simulation. Research works are conducted in several key areas, such as anatomical modelling, biomechanical modelling, parallel and GPU computing, physiological modelling, and interaction models. Using a common software framework (SOFA, a multi-model framework for interactive physical simulation) as well as key clinical collaborations, our research will lead to more advanced simulations, ultimately aimed at per-operative guidance. Our cumulated scientific production in the domain of computer-assisted medicine amounts to an average of 25 peer-reviewed articles in international journals, 45 peer-reviewed articles in international conferences, and 6 Ph.D. defended every year. SHACRA European Projects: PASSPORT (Patient Specific Simulation and PreOperative Realistic Training for Liver Surgery).

Key Personnel

Dr. Stephane Cotin decided after his PhD to take a position at Mitsubishi Electric Research Laboratory in Cambridge, after which he joined Harvard Medical School in Boston USA to continue his research on surgical simulation. He is today internationally renowned worldwide for his work on real-time simulation for surgical procedures.

Participant No.	**8**
Short Name	**UNIZA**
WP Participation	WP2, WP4, WP5, WP7, WP8
Organization Name	Department of Informatics, University of Zilina
Country	Slovakia
Organization Type	University
Webpage	http://www.fri.uniza.sk/en

Description of Legal Entity

The University of Žilina was established in 1953. The University of Žilina is the only university located in the northwest region of the Slovak Republic. In terms of professional profile, the University is unique in Slovakia as it has a long tradition of providing education in the fields of communications. The University is an educational institution with a broad profile in many areas of technology, management and natural science. Permanently developed activity at ZU for more than 15 years is Biomedical Engineering realized in cooperation with the medical universities in Slovakia. Main topics in this area can be found in design of medical equipment and software. The University has established contacts with many universities abroad. Professors and research workers at the University participate in international educational and research projects, including the EU projects TEMPUS, COPERNICUS, COST, LLP/ERASMUS, Leonardo da Vinci, than CEEPUS, National Scholarship Programme, and DAAD. The academic staffs are actively involved in cooperation within the EU´s 6th and 7th Framework programmes.

Main Task Attributed in the Project

UNIZA will provide its expertise for the development of an appropriate technical environment (WP 1) for creation of the image processing library (WP 2).

Relevant Project Experiences

The Faculty of Management Sciences and Informatics of the University of Žilina has priority in training in interdisciplinary courses and focuses on education on biomedical informatics. The Faculty is strongly involved in many practical collaborative industry and research projects on national and international level with medical applications. (for example, EU projects “Centre translational medicine” and “Create a new diagnostic algorithm for selected cancers”). The “Int. Workshop on Biomedical Informatics” is a traditional event held at the Faculty.

Key Personnel

Dr. Elena Zaitseva graduated from Belarusian State University of Informatics & Radioelectronics (Minsk, Belarus) with Master degree and PhD in Computer Science in 1989 and 1994, respectively. She worked as Associated Professor at different Belarusian Universities till 2004. Since 2004 she is at the Department of Informatics of the University of Žilina (Slovakia). She was a principal investigator of eight research projects, results of which were new algorithms and methods for analysis of multi-valued data. She was an investigator in more than 30 research projects, results of which were: the creation of dynamic systems modelling and decision support systems, optic recognition systems of handwriting font with support for artificial intelligence. These projects were supported by grants of the European Regional Development Fund, NATO Collaborative Linkage Grant, Ministry of Education and Slovak Academy of Sciences, Belarusian Republic Fund of Fundamental Researches, Belarusian Computerization Fund and others. She has worked in the program committees of more 20 international conferences. She is a member of the Technical Committee and Chair of the Working Group “Information Technology and Telecommunications” of European Safety and Reliability Association and of Advisory Board of the Journal of Reliability and Statistical Studies (JRSS) and Editorial Board of the Journal Computer Science and Engineering (Scientific & Academic Publishing).

Participant No.	**9**
Short Name	**KU LEUVEN**
WP Participation	WP3, **WP6**, WP8
Organization Name	Department of Anaesthesiology, Catholic University of Leuven
Country	Belgium
Organization Type	University / Hospital
Webpage	http://www.kuleuven.be/english/

Description of Legal Entity

The Catholic University of Leuven was founded in 1425. It is a research-intensive, internationally oriented university that carries out both fundamental and applied research. It is strongly inter- and multidisciplinary in focus and strives for international excellence. From a basis of social responsibility and scientific expertise, KU Leuven provides high-quality, comprehensive health care, including specialized tertiary care, in its University Hospitals. In doing so it strives toward optimum accessibility and respect for all patients. Within the Catholic University of Leuven, the University Hospitals constitute an autonomous organization. They include different teaching hospitals, providing diversified and specialized medical care at top level to both ambulant and hospitalized patients. High quality patient care and a leading role in many disciplines place the University Hospitals of Leuven among the top level of outstanding European centres for advanced medicine. The permanent medical staff of the University Hospitals mainly consists of academicians from the Faculty of Medicine of the Catholic University Leuven.

Main Task Attributed in the Project

KU LEUVEN as medical partner within the consortium will specifically provide its medical exercise to assess, validate and evaluate the RASimAs prototypes with view to its usage as training and assistance tool respectively.

Relevant Project Experiences

The Department of Anaesthesiology was founded in 1948 as part of the Department of Surgery and became independent in 1951. To ensure that we can conduct and complete studies in an appropriate and efficient way in accordance with protocol and regulatory guidelines, an adequate clinical research team is available within the Department of Anaesthesiology. The team is responsible for an expeditious and safe patient turnover in complex multi-disciplinary and multi–centre trials. The team has the skills to manage the organisational, administrative and practical aspects of clinical research projects. A full time study nurse and part time administrator are responsible for safe and effective processing of studies.

Key Personnel

Prof. Dr. Marc Van de Velde MD, PhD obtained his medical degree at the Catholic University of Louvain in Belgium in 1991, where he completed his residency in Anaesthesiology and received his PhD degree in 1996 and 2000, respectively. Since November 2010, he is Head of the Department of Anaesthesiology at the Catholic University Leuven and Full Professor at the Leuven University Hospitals. He has given over 210 invited lectures at the international and national level, has published 50 articles in peer reviewed journals and has co-authored 4 book chapters. He is co-editor of several books on anaesthesia and critical care. He was member of the Committee of the Obstetric Anaesthetists Association from 2003 – 2009 and is currently president of the European Society of Regional Anaesthesia and Pain Therapy (ESRA). He is also Chair of the Scientific Subcommittee on Obstetric Anaesthesia of the European Society of Anaesthesiology (ESA). His primary clinical interest focuses on obstetric anaesthesia and anaesthesia for children and adults with congenital heart disease undergoing non cardiac surgery. Most of his current research focuses on obstetric anaesthesia.

Participant No.	**10**
Short Name	**SINTEF**
WP Participation	WP2, WP3, WP4, **WP5**, WP7, WP8
Organization Name	Department of Medical Technology, Stiftelsen SINTEF
Country	Norway
Organization Type	Research Institute
Webpage	http://www.sintef.no; http://www.usigt.no

Description of Legal Entity

SINTEF is a multidisciplinary R&D institute with 2200 employees, structured into six business areas and the largest independent research organization in Scandinavia. SINTEF creates value through knowledge generation, research and innovation, and develop technological solutions that are brought into practical use. The Department of Medical Technology has more than 15 years of extensive experience in navigation technology, processing and visualisation of medical data (MR, CT), ultrasound, and simulation and training in minimally invasive therapy related to R&D at the National Centre for Ultrasound and Image-Guided Therapy in Trondheim. In close collaboration with Trondheim University Hospital (St. Olavs Hospital) and the Norwegian University of Science and Technology (NTNU), the interdisciplinary research team has performed technological and clinical research, which has been internationally awarded. The team is internationally leading in ultrasound-based navigation and image-guided therapy.

Main Task Attributed in the Project

SINTEF is mainly involved in the following tasks: 4.5 (Real-Time Model Processing) and 4.6 (Intra-Procedure Guidance Development). SINTEF is also responsible for the assistant prototype. In general, ultrasound (including simulation), guidance, medical image (GPU) computing, e.g. registration and interventional navigation system development are key competence areas for SINTEF Medical Technology.

Relevant Project Experiences

SINTEF is one of three partners in the National Competence Centre for Ultrasound and Image-Guided Therapy, a close collaboration (and co-loacted on the hospital campus) between clinicians and engineers. It is part of the several leading projects, such as:

- Operating Room of the Future at St. Olavs Hospital together with several industry partners (such as Siemens, Olympus, Covidien);

- MI-Lab, a centre for research-based innovation in medical imaging that aims to facilitate cost efficient healthcare and improve patient outcome through innovations in medical imaging;

- FUSIMO (Patient specific modeling and simulation of focused ultrasound in moving organs), EU funded

- IIIOS (Integrated Interventional Imaging Operating System), EU funded

- 3MiCRON (Three modality contrast imaging using multi-functionalized micro-balloons), EU funded.

Key Personnel

Dr. Frank Lindseth is a Senior Research Scientist and Project Manager for software development in surgical navigation and visualization. He has been with SINTEF since 1996, receiving his PhD in ultrasound-guided minimally invasive surgery in 2002 and finished a PostDoc study related to the navigation system of the future**. Dr. Thomas Langø** is Senior Research Scientist and Project Manager for large national and EU projects with particularly expertise in ultrasound-guided laparoscopic therapy, navigated bronchoscopy and clinical tool guidance. Dr Langø is member of iSMIT (Int. Society for Medical Innovation and Technology) steering committee, ISCAS (International Society for Computer Aided Surgery) board member, and Technology Committee of EAES (European Association for Endoscopic Surgery). **MSc Christian Askeland** is Senior Software Engineer and head of hardware and software integration for a clinical navigation platform.

Participant No.	**11**
Short Name	**SG**
WP Participation	WP2, WP4, WP5, WP7, WP8
Organization Name	SenseGraphics AB
Country	Sweden
Organization Type	SME
Webpage	www.sensegraphics.com

Description of Legal Entity

SenseGraphics was founded in year 2004, devoted to the science of multi-modal interaction and real 3D stereo visualisation, with the vision to facilitate and support application development of haptic (touch, force feedback), and co-located hapto-visual, applications. SenseGraphics' flagship product H3DAPI sets the standard for multimodal research, medical and industrial application development in real 3D graphics as available under both Open Source (GNU GPL) and commercial license. SenseGraphics' latest invention, HAPI haptic engine, is used for adding haptic interactions to graphical or other scientific applications, which makes it easier for these applications to be haptic-enabled with minimal rewriting of the existing code.

Main Task Attributed in the Project

SenseGraphics will be an important partner in WP4 and will contribute scientific and operational expertise in the integration of virtual patient- specific models into the RA Simulator.

Relevant Project Experiences

Relevant Project Experience. Through the open source community, www.H3D.org, SenseGraphics has been able to quickly spread its software and gain broad, world-wide user support for H3DAPI. The community offers today Wikis, tutorials and free support based forums to more than 3700 users. SenseGraphics' current customers include renowned haptic research centres from all over the world, which develop various applications including training simulators for medical surgeons and dentists, for stroke rehabilitation, as well as molecular docking and other industrial simulators (Uppsala University, The Royal Institute of Technology, Sweden, Rehabilitation Institute of Chicago, US, Imperial College of London, UK). Several customers have already started building commercial applications on top of H3DAPI (Swemac in Sweden, MOOG/ACTA in the Netherlands, Medaphor in UK and Bioskill in Germany). Besides an effective software development platform, SenseGraphics provides a series of workbenches customized to create the perfect environment for haptic interaction.

Key Personnel

Key Personnel. Daniel Evestedt is one of the co-founders and the CTO of SenseGraphics. Daniel has an M.Sc. from Uppsala University and has over 10 years of experience researching and developing haptic systems. Since 2007 he is a member of the Web3D consortium and part of the Medical working group.

Sebastian Ullrich is a researcher and developer for medical simulation at SenseGraphics. He received his M.S. (2005) and Ph.D. (2011) degrees in computer science from RWTH Aachen University. From 2007 to 2008 he worked as a visiting researcher at the National Institute of Informatics in Tokyo, Japan. His research interests are primarily virtual reality, medical simulation with a special focus on soft-body physics simulation and haptic rendering. Since 2008 he is a member of the Web3D consortium and part of the Medical working group. For his Ph.D. thesis he worked on bimanual haptic interaction with regional anaesthesia as a case study.

2.3. Consortium as a whole

RASimAs gathers a group of high profile experts from the ICT and medical field of various European countries such as Sweden and The Netherlands for VR hardware; Germany and Belgium for anaesthesiology; Spain and United Kingdom for haptics algorithm; and Greece, Ireland, France, and Slovakia for image processing libraries. It is important to note that many of the Consortium partners have previously cooperated in RTD and other projects (Tab. 9).

Partner		UKA-IMI	UKA-DA	UKA-CTCA	RWTH-VR	RWTH-EUPM	BANGOR	UCC	URJC	FORTH	INRIA	UNIZA	KU LEUVEN	SG	Project
No.	Short Name														
1A	UKA-IMI		X		X										Rasim, www.rasim.info
1A	UKA-IMI			X											Database, www.ctca.de
1B	UKA-DA							X					X		ESRA, www.esraeurope.org
1C	UKA-CTC-A	X													Project management clinical trials
2A	RWTH-VR								X						EU Grant, Human Brian Project (FET Flagship)
2B	RWTH-EUPM			X											Several EU FP7 Projects
3	BANGOR				X									X	MedX3D, http://www.h3dapi.org/modules/mediawiki/index.php/MedX3D
4	UCC													X	Haystack www.ndrc.ie/haystack
5	URJC										X				PhD Student Exchange
6	FORTH								X						Wearhap (FP7 ICT)
7	INRIA													X	(not public yet)
8	UNIZA		X												EU FP7 Project Proposals
11	SG							X							MedCap www.medcap.eu
11	SG						X								CRalVE www.craive.org.uk

Table 6: *Previous cooperation of RASimAs partners.*

2.3.1. Expertise and capabilities of the Consortium

Table 10 summarizes the capabilities, expertise and infrastructure that each partner will contribute to accomplish their major goal for which they are responsible; however it is understood that there will be a great deal of cross-interaction and cross-pollination that will combine all participants into a single unit dedicated to develop a VR-based and patient specific training and assistant guide for the performance of regional anaesthesia.

Partner		Roles								Capabilities and Expertise							
No.	Short Name	WP1	WP2	WP3	WP4	WP5	WP6	WP7	WP8	Coordination & Management	Technical environment	Patient-specific VPH models	VR-based prototypes	Evaluation	Regional Anaesthesia	Human trials	Exploitation
1A	UKA-IMI	**L**	X	X			X	X	X	X	X	X	X	X	X	X	X
1B	UKA-DA						X	X	X		X			X	X	X	X
1C	UKA-CTC-A						X	**L**		X						X	
2A	RWTH-VR		X		X	X		X			X	X	X	X			X
2B	RWTH-EUPM	X							X	X							
3	BANGOR		X	X	X						X	X	X				X
4	UCC		X				X				X	X	X				
5	URJC		X	X	**L**	X		X			X	X	X	X			X
6	FORTH		**L**	X	X	X		X			X	X	X				
7	INRIA		X	**L**	X	X		X			X	X	X				
8	UNIZA		X		X	X		X	X		X		X				X
9	KU LEUVEN			X			**L**		X			X		X	X	X	
10	SINTEF		X		X	**L**		X	X		X		X	X			
11	SG		X		X	X		X	X		X	X	X	X			X

Table 7: Leaders and partners of RASimAs WPs and their specific capabilities and responsibilities (L = leader, X = contributor).

2.3.2. Resources and infrastructure of the Consortium

In addition to the specific competencies and responsibilities that are contributed by leaders and partners of the RASimAs work packages, Table 11 shows the specific resources and infrastructures of the RASimAs Consortium.

Partner		Resources and Infrastructures											
No.	Short Name	Patients & Image Data Acquisition	Prototyping	Image Processing Algorithms & Libraries	Knowledge Management	Atlas Data & Models	Haptic Algorithms	VR Hardware, Components, Systems	User Studies	Quality Management	Regulatory Affairs	Tissue Interaction	Evaluation Methods	Image Management & Interfaces
1A	UKA-IMI			X	X								X	X
1B	UKA-DA	X							X				X	
1C	UKA-CTC-A									X	X		X	
2A	RWTH-VR				X		X	X				X		
2B	RWTH-EUPM									X				
3	BANGOR			X				X						
4	UCC				X									
5	URJC			X	X			X						
6	FORTH				X									X
7	INRIA			X										
8	UNIZA			X									X	
9	KU LEUVEN	X							X					
10	SINTEF		X	X				X						X
11	SG		X				X	X						

Table 8: Resources and infrastructure of RASimAs Consortium.

Subcontracting

The Consortium will contribute to the scientific work and research with their capabilities and resources detailed above, but some parts of the project need to be subcontracted (Tab. 12).

Within the RTD activities, the Coordinator has reserved 29,000 € for scientific events and conferences, the Partner 1C-UKA-CTCA has reserved 23,200 € for accountancy fees for the national ethical authorities due to ethical aspects of the clinical trial. The project management (Partner 2 (RWTH-EUPM) has reserved 6,000 € for organizing project meetings. Subcontracting costs within the management activities are only claimed for external auditing, following the 375,000 € rule in FP7 for subcontracts (Tab. 12).

<table>
<tr><th colspan="2">Partner</th><th>Budget</th><th>Justification</th></tr>
<tr><th>No.</th><th>Name</th><th></th><th></th></tr>
<tr><td>1</td><td>UKA</td><td>10,000 €</td><td>Costs for scientific events and conferences: Individual subcontractors are not determined yet. Subcontracting will be used for the professional organisation of scientific events and conferences of the consortium. This comprises e.g. calls for papers, venue issues, technical aspects, catering and participant management.</td></tr>
<tr><td>1</td><td>UKA</td><td>20,000 €</td><td>External experts for scientific tasks: Individual subcontractors are not determined yet. Subcontracting shall be used to invite international experts to scientific talks on conferences of the consortium. The money shall be used to account for (travel) expenses of the experts.</td></tr>
<tr><td>1</td><td>UKA</td><td>23,200 €</td><td>Accountancy fees for national ethic authorities: Subcontracting costs are defined from the fees of the respective Ethics Committees (EC) and Competent Authorities (CA) from Germany, Belgium and Ireland for the two planned multi-center trials according to the following table:
<table>
<tr><td>Multicenter Trials
(Germany / Belgium / Ireland)</td><td>Clinical Trial 1
(regulated by the Code of Professional Conduct)</td><td>Clinical Trial 2
(regulated by the Medical Device Act)</td></tr>
<tr><td>Ethics Committees (EC)</td><td>Lead EC 1200,-- €
Participating ECs 2x 1000,-- €</td><td>Lead EC 2300,-- €
Participating ECs 2x 1200,-- €</td></tr>
<tr><td>Competent Authorities (CA)</td><td>Not applicable</td><td>3 Sites x 5100,-- €</td></tr>
<tr><td>Total</td><td>3200,-- €</td><td>20000,00 €</td></tr>
</table></td></tr>
<tr><td>2</td><td>RWTH</td><td>6,000 €</td><td>Costs for project meetings: Subcontracting shall be used to organise the regular project meetings (steering committee, general assembly, advisory board) in terms of venue and catering.</td></tr>
<tr><td colspan="2">Total RTD</td><td>59,200 €</td><td></td></tr>
<tr><td>1</td><td>UKA</td><td>4,000 €</td><td>External auditing: Subcontracting shall be used for an independent external auditor. Individual subcontractors are not determined yet.</td></tr>
<tr><td>10</td><td>SINTEF</td><td>1,500 €</td><td>External auditing: Subcontracting shall be used for an independent external auditor. Individual subcontractors are not determined yet.</td></tr>
<tr><td colspan="2">Total MGT</td><td>5,500 €</td><td></td></tr>
</table>

Table 9: Subcontracting costs in RTD and management

The Subcontracting will be done following national legislation regulations, and will be in compliance with article II.7.2 of the EC Grant agreement.

2.4. Resources to be committed

The RASimAs project combines scientific excellence of academia, university hospitals, research institutes, clinical trial centers and a research-intense SME from 9 different European countries. The requested EC Contribution is well-balanced between universities (24%), university hospitals (36%), research institutes (30%) and SME (10%) (Fig. 13).

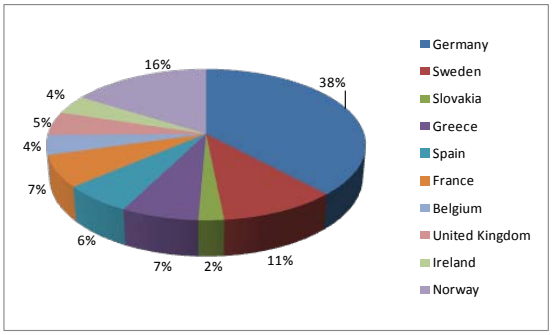

Figure 12: Allocation of budget according to the type of institution

The requested EC Contribution is well-balanced between the different partners of the RASimAs Consortium in Europe. All partners contribute with a high impact of person months and have defined their work as well as the other direct costs in a highly reflected and economical way.

The Consortium is convinced that the resources defined for RASimAs are necessary for the accomplishment and success of the project. All positions have been defined in a reasonable manner with a total budget of 4,553,351 € and a requested EC contribution of 3,321,679 €.

Partner		RTD	DEMO	MGT	Total	EC Contribution
1A	UKA-IMI	643,760 €	0 €	103,840 €	747.600 €	**586,660 €**
1B	UKA-DA	191,680 €	0 €	0 €	191,680 €	**143,760 €**
1C	UKA-CTC-A	265,190 €	0 €	0 €	265,190 €	**198,892 €**
2A	RWTH-VR	257,600 €	79,200 €	0 €	336,800 €	**232,800 €**
2B	RWTH-EUPM	40,240 €	0 €	83,200 €	123,440 €	**113,380 €**
3	BANGOR	223,353 €	0 €	0 €	223,353 €	**167,515 €**
4	UCC	179,200 €	0 €	0 €	179,200 €	**134,400 €**
5	URJC	237,889 €	56,870 €	0 €	294,759 €	**206,851 €**
6	FORTH	290,212 €	20,196 €	0 €	310,408 €	**227,757 €**
7	INRIA	284,233 €	25,184 €	0 €	309,417 €	**225,766 €**
8	UNIZA	91,360 €	12,160 €	0 €	103,520 €	**74,600 €**
9	KU LEUVEN	187,200 €	0 €	0 €	187,200 €	**140,400 €**
10	SINTEF	572,790 €	185,214 €	1,500 €	759,504 €	**523,699 €**
11	SG	338,240 €	183.040 €	0 €	521,280 €	**345,200 €**
Total costs		**3,802,947 €**	**561.864 € €**	**188,540 €**	**4,553,351 €**	
Requested EC Contribution.		**2,852,211 €**	**280,932 €**	**188,540 €**		**3,321,679 €**

Only the Project Manager and Administrative Manager are requesting personnel costs for the management of the Consortium.

The highest amount of the budget (2,034,328 €) is assigned to the personnel costs, due to the high involvement of highly qualified personnel concerning the development of RASimAs as well as conducting the clinical trial.

Type of Costs	RTD	DEMO	MGT	Total
Personnel	2,034,328 €	326,236 €	114,400 €	2,474,964 €
Subcontracting	59,200 €	0 €	5,500 €	64,700 €
Other direct costs	239,385 €	0 €	0 €	239,385 €
Indirect costs	1,470,035 €	235,629 €	68,640 €	1,774,304 €
Total costs	**3,802,948 €**	**561,865 €**	**188,540 €**	**4,553,353 €**
Requested EC Contribution	**2,852,211 €**	**280,932 €**	**188,540 €**	**3,321,679 €**

Table 11: Allocation of total budget and EC contribution.

The total of RTD other costs is 239,385 €, including costs for technical equipment needed for the development of the RASimAs technology and for technical equipment needed for the production of the RASimAS prototypes and travel costs for all partners.

Partner		Budget	Justification
No.	Short Name		
8	UNIZA	15,000 €	Software, PC and x3850X5 server
10	SINTEF	8,059 €	Rack
10	SINTEF	10,165 €	High-end workstation and graphics card
10	SINTEF	10,165 €	3D display
10	SINTEF	16,667 €	Tracking-technology / manipulator
10	SINTEF	7,624 €	Haptics
10	SINTEF	3,812 €	Ultrasound equipment (dummy probe, videograbbing card etc.)
11	SG	4,200 €	Haptic hardware and device
Total RTD		**75,692 €**	

Table 12: Detailed description of equipment costs in RTD

The requested EC Contribution is well-balanced between the different partners of the RASimAs Consortium in Europe. All partners contribute with a high impact of person months and have defined their work as well as the other direct costs in a highly reflected and economical way.

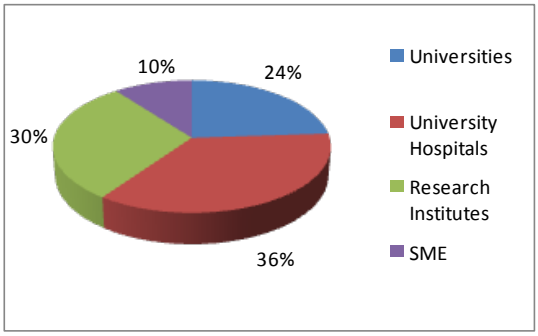

Figure 13: *Allocation of budget according to the European country.*

3. IMPACT

3.1. Strategic impact

In many cases, general anaesthesia (GA) is still favoured over regional anaesthesia (RA) even when RA should theoretically be the method of choice. In fact, the replacement of GA by RA procedures is slow, despite its documented benefits for patients: lower cardiovascular stress and other complications, reduced postoperative pain, earlier mobility, shorter hospital stay, and ultimately

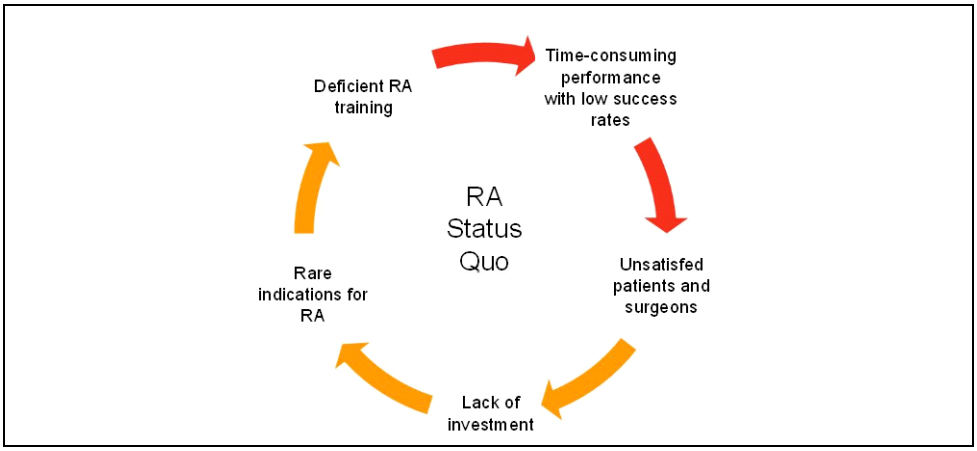

Figure 14: *Status quo of RA procedures.*

The slow adoption of RA instead of GA in operation theatres is due to the lack of physician training, as poorly trained physicians perform RA procedures with a moderate success rate (between 90 and 95% depending on procedure), leading to patient and surgeon dissatisfaction. This in turn leads hospitals to delay investments in RA equipment, thus reducing the possibilities for physicians to improve their training (Fig. 15).

Therefore, the key challenge to tackle in order to increase the market adoption of RA procedures is indeed the training of physicians.

> ***RASimAs is expected to bring significant clinical, economic and scientific impacts in line with the expected impacts listed in the call. In particular the results of RASimAs will enable to stimulate the replacement of general anaesthesia by regional anaesthesia in many cases, leading to improved patient care, reduced complications and lower costs.***

The call focuses on three categories of impact (clinical, economic, and scientific), all of which are addressed by the RASimAs consortium.

- *Clinical Impact*: strengthened evidence of the clinical benefits in using computer-based models. RASimAs will demonstrate the clinical benefits of the technology by conducting controlled clinical trials with patient-specific models.
- *Scientific Impact*: acceleration of the deployment of VPH technologies in clinical environments and increased acceptance and use of predictive models by healthcare professionals. RASimAs will enrich the VPH models with subject-specific data, in order to improve clinician performance even in RA procedures where significant inter-subject differences exist.
- *Economic Impact*: significant reduction of costs through the use of VPH technologies. RASimAs will increase the replacement of GA by RA and improve the success rate of RA procedures, thus decreasing costs by an estimated 100,000 Euros by year and operating theatre.

The following chapters will address more in details each of these impacts and the steps required to reach them as well as the Consortium's contributions to standards and European dimension.

3.1.1. Clinical Impacts

The RASimAS project will result in the development of medical equipment for training and guidance of anaesthetists in RA procedures. The RASimAS project will integrate patient-specific data into clinical anaesthesia practice, enabling the widespread safe and effective performance of peripheral nerve blocks (PNB).

RASimAs will accelerate the deployment of VPH technologies in clinical environments and increase confidence in decision support systems based on predictive models.

Successful RA procedures require high cognitive and procedural skills that can only be obtained during 1) training and 2) repeated practice.

The RASimAs simulator provides support to the training phase (1) in order to improve the practitioner's skills before the practice phase occurs. This allows even novice anaesthetists to start clinical RA procedures with sufficient skills, as their engagement with real patients occur at a higher point in the learning curve, making the procedures safer and more comfortable for the patient.

The RASimAs assistant provides support to the clinical phase (2) by integrating predictive anatomic models in order to improve the success rate of RA procedures. It is known that human anatomy differs significantly from person to person, and even between right and left side of the same person. Therefore, a patient-specific VPH model created from data acquired during the diagnostic phase can significantly improve the confidence of the practitioner in conducting RA procedures.

RASimAs will deliver strengthened evidence of the clinical benefits in using computer-based models.

The RASimAS project will objectively evaluate the simulation and guidance technology. A multicentre randomised controlled trial will validate the impact of RASimAS in improving RA training and demonstrate the translation of procedural skills acquired in the virtual reality (VR) environment to the operating theatre (OT) environment (VR to OT skills transfer).

RASimAs will provide a stronger evidence of the clinical impacts of "disease" (clinical outcome) prediction.

Peripheral Nerve Block may result in inadvertent injury to the nerve and surrounding anatomical structures. Improved training of anaesthetists using the VPH models combined with guidance tool will help the performance of successful PNB using appropriate quantities of active drug and prevent inadvertent injury to nerves and surrounding structures.

3.1.2. Scientific Impacts

The concept of predictive models of human anatomy and physiology/pathophysiology is intuitive in clinical medicine. Recently, anatomical knowledge relevant to peripheral nerve block has increased significantly with the advent of ultrasonography.

RASimAs will increase acceptance and use of predictive models by healthcare professionals.

RASimAs introduces the novel concept of live augmentation of RA imaging by combining VPH models with patient-specific data collected during the RA procedure. The RASimAs assistant can augment the ultrasound image collected during the RA procedure to automatically identify anatomical landmarks (nerves, blood vessels) based on the VPH model entered into the system. A system that allowes true patient specific data to be gathered and processed by an automated ultrasound volume segmentation process will be a significant scientific advance allowing preprocedural rehearsal with actual patient data.

RASimAs will deliver a very first Regional Anaesthesia Assistant System (RAAs) combined with true real-time patient-specific data.

The consortium intends to maximize the scientific impact of the RASimAs project by developing scientific presentations and articles on the topic of VR-based simulators and assistants for RA pro-

cedures and presenting them via the European Society of Regional Anesthesia and Pain Therapy (ESRA), led by its president Prof. Marc van de Velde (KU LEUVEN).

RASimAs' scientific impact will be supported by the European Society of Regional Anesthesia and Pain Therapy, a leading organization of 2600 members in Europe.

The next ESRA conference will take place in Glasgow in September 2013 and will be used as a launchpad for the RASimAS project scientific dissemination. The consortium will communicate the project scientific progress in the Regional Anesthesia & Pain Medicine (RAPM) Journal and the ESRA newsletters.

3.1.3. Economic Impacts

The use of VPH technologies will enable anaesthetists to confidently identify desired PNB end-points, perform successful PNB and avoid unintended injury to target nerves and surrounding structures. This will increase the success rate of PNB in clinical practice, stimulating the use of RA procedures in replacement of GA procedures.

RASimAs will significantly reduce costs by using patient-specific VPH technologies applicable for training purposes, individual prediction of anatomical and physiological structures and treatment outcomes.

Besides medical advantages, implementation of RA processes into medical treatment paths will optimize the workflow in combination with significant cost savings. In particular, there are considerable cost savings when RA procedures are used instead of GA procedures: recently in 2010, the British Journal of Anaesthesia has estimated costs savings of € 100.000 per year and operation theatre[19].

In a study conducted in 2005, the effective savings by substituting conventional with regional anaesthesia have been calculated for the portfolio of diagnosis-related groups (DRG) offered by University Hospital Dresden, Germany[20]. According to the most relevant procedures, the saving estimates due to RA (Tab. 18) are based on reducing effective time of anaesthesia. Process times have been measured based on the electronic protocols of the procedure. The number to be treated (NTT) determines the average number of patients that undergo the respective procedure to circumvent one adverse event such as additional respiration, intensive care, or death. Hence, NTT emphasizes the risk reduction due to RA and its impact in healthcare quality provided by the RA procedures.

3.1.4. Contribution to standards

The RASimAs project will make use of several open source frameworks, and therefore, contribute to these communities:

- Simulation Open Framework Architecture (SOFA) for soft tissue simulation;
- Medical Imaging Interaction Toolkit (MITK) for image processing/segmentation;

[19] Marhofer P, Harrop-Griffiths W, Kettner SC, Kirchmair L. Fifteen years of ultrasound guidance in regional anaesthesia: part I. Br J Anaesthesia 2010; 104(5): 538-46

[20] Heller AR, Bauer KR, Eberlein-Gonska, Albrecht DM, Koch T. Regionalanästhesie als Wettbewerbsvorteil im Kranlkenhaus. Strategische Umfeldanalyse. Anaesthesist 2009; 58: 459-68 [in German]

Procedure	DRG Code	Time (min)	Costs (Euro)	Number to be treated	Savings (Euro/case)	Savings (Euro/year)
Colon resection	G18A	250	521.00	4	432.00	33,227.00
Gastrectomies	G19Z	330	651.00	8	427.00	1,707.00
Lung resections	E05A	215	460.00	5	1,022.00	11,243.00
Postrectomies	M01A	240	502.00	20	2,187.00	236,179.00
Nephrectomies	L13Z	238	493.00	12	1,465.00	95,312.00
Knee prosthetics	I44Z	170	372.00	34	1,681.00	467,359.00
Wertheim procedures	N027Z	300	614.00	n/a	936.00	9,360.00
Sum						**854,288.00**

Table 13: Effective cost savings from substituting conventional with regional anaesthesia.

  - Open source C++ library Visualization Toolkit VTK for visualization;
  - The Insight Segmentation and Registration Toolkit (ITK);
- H3D API for visio-haptic systems;
  - Bullet Physics Library for collision detection;
  - CHAI 3D for haptic device support and haptic rendering.

Furthermore, the Web3D Consortium has established a Medical Working Group (MWG), which is developing an open interoperable standard for the representation of human anatomy based on input from a wide variety of imaging modalities. If a patient has undergone multiple types of scans (CAT, MRI, PET) these may all be viewed and registered giving the physician and patient a clearer view of the underlying issues. Researchers can take the exported data from many different types of equipment and fuse them into a coherent 3D data set that can be used both for patient education, diagnostics and surgical training.

> ***Several members of the proposal's consortium (SG, Bangor) are already actively involved in the Web3D Consortium's Medical Working Group (MWG), chaired by Prof. Nigel John (Bangor).***

The focus of the working group is to specify and implement MedX3D – an extension to the open and royalty-free X3D ISO standard to support advanced medical visualization functionality and medical data exchange (Fig. 16). MedX3D is tightly focused on medical applications that can benefit from real time 3D visualization.

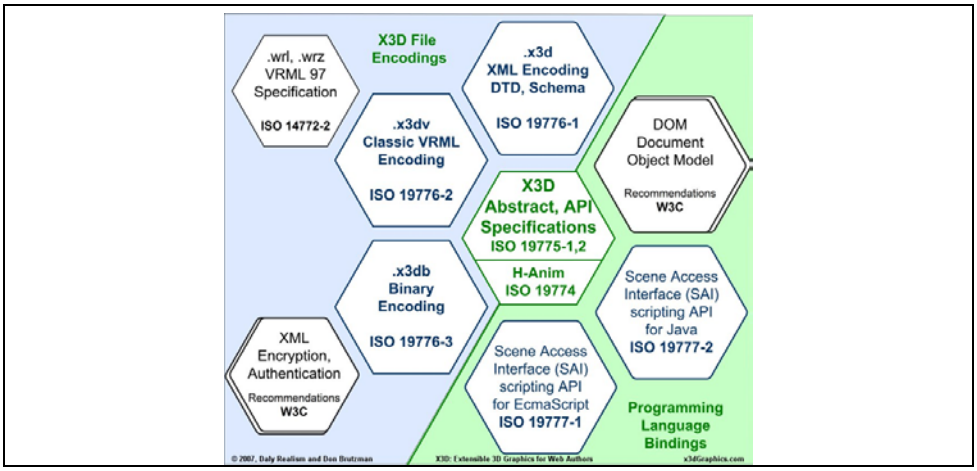

Figure 14: *X3D and MedX3D are connecting file encoding standards with programming language bindings and the related standards.*

The RASimAs project results will therefore specifically contribute to the MedX3D standard: medical applications that can benefit from real time 3D visualization; 3D image rendering for planning and guiding medical procedures; image fusion-the association of specific 2D images from multimodal (CT, MRI, Ultrasound) scans with one another or with existing 3D images of a given patient.

Web3D-MWG is also participating in the DICOM Working Group 11 for the purpose of defining a presentation standard for reproducible medical imaging, in particular for n-dimensional data from X3D. Future work will be focused on creating standards for soft-body physics and haptic rendering, which are much needed for medical simulators. These standards (and their forthcoming extensions) will benefit from the RASimAs project and are perfectly aligned with the overall goals of VPH initiative.

3.1.5. European dimension and impact on EU policies

The technical work of the project involves a wide range of challenging tasks, and finding partners with the appropriate complementary skills and background was a difficult task. The consortium believes that it would not have been possible to do so within any single country.

In particular, the interdisciplinary approach of RASimAs (medical informatics, anaesthesiology, image processing libraries, haptic algorithms, VR hardware and interfaces) requires a unique combination of skills that can only be provided by the best scientists of various European countries such as Sweden and Norway for VR hardware; Germany and Belgium for anaesthesiology; Spain and United Kingdom for haptics algorithm; and Greece, Ireland, France, and Slovakia for image processing libraries.

Partners of the RASimAs consortium (such as KU LEUVEN, UCC and UKA-DA) are strongly involved in the European Society of Anaesthesiology and Pain Therapy (ESRA) and hold active discussions about actual and target status of anaesthesia. Prof Marc van de Velde (KU LEUVEN) is the President of the ESRA.

Several partners of the RASimAs consortium (SG, Bangor) are members of the Web3d Medical Working Group (cf. Section 3.1.4), which is an interdisciplinary and international effort. The different backgrounds of the members range from medical subject matter experts, over computer scientists from academia to engineers and experts from industry. Thus potential users and future providers are involved as well as experts to work on technical solutions.

3.1.6. Concertation activities with other ICT funded projects

The RASimAs consortium has identified other FP7 funded VPH projects (just completed or ongoing) and other activities that could offer opportunities for cross-fertilization and contribution form the project team, for example:

- RICORDO (Researching Interoperability using Core Reference Datasets and Ontologies for the Virtual Physiological Human): FP7 STREP (2010-2012), focusing on the creation of a communal annotation strategy that supports the interoperability of VPHDMs across different biological scales (vertical integration).
- VPH-SHARE (Virtual Physiological Human: Sharing for Healthcare – A Research Environment): FP7 IP (2011-2015), focusing on (i) exposing and share data and knowledge, (ii) jointly developing multi-scale models for the composition of new VPH workflows, (iii) facilitating collaborations within the VPH community.
- The RASimAs team intend to participate in the seminars organised by the Virtual Physiological Human (VPH) Network of Excellence. At the end of the RASimAs project, VPH 2016 for instance, may be hosted in Aachen by the RASimAs team.
- Mandate on Health Interoperability (M/403)

In addition to specific bilateral cooperation with other projects, the project team will be present at concertation events for the area of the project organised by the European Commission. Moreover, the Advisory Board will be an additional source and a door opener for further clustering activities with international projects.

3.2. Plan for the use and dissemination of foreground

3.2.1. Dissemination strategy

As regional anaesthesia offers a lot of benefits outweighing general anaesthesia in many cases, the project aims to bring evidence by delivering novel tools for application of regional anaesthesia and to raise a new awareness of health professionals for the added value of this method.

For this, important institutions, like the European Commission as well as national healthcare organisations have to be involved in the dissemination strategy. The project results shall also call the attention of patients as well as health professionals for novel patient management concerning application of peripheral nerve blocks. Beyond that the project results shall initiate a vital discussion and initiate further research within the European scientific community. For this purpose, the dissemination strategy plays an important role in achieving the impacts of the project. In order to reach these ambitious aims, the dissemination strategy has to follow a holistic approach. The project addresses different target groups; hence dissemination measures are designed according to the information requirements of each of these groups (Fig. 17).

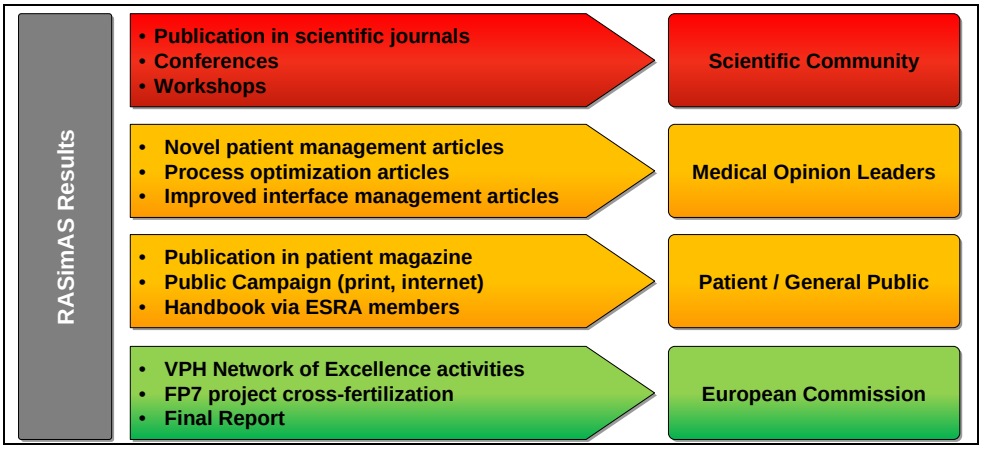

Figure 16: *Levels of RASimAs dissemination.*

The work will be published in international journals with high impact factor and will be presented at national meetings, e.g. in Germany, at the German Society of Anaesthesiology and Intensive Care. There are similar international meetings where work will be presented as posters and put forward for oral presentations. These include the international annual congress at the European Society of Regional Anaesthesia and Pain Therapy (ESRA). Dissemination and exploitation of the RASimAs project results is an essential endeavour of the participants. A single work package (WP8) has been designed for the dissemination and exploitation of the project's results to ensure that all participants will be aware, contribute and share results and other knowledge gained from the project with as wide an audience as possible and in a timely manner.

The first deliverable of WP8 is a dissemination plan of scientific results as they become available during the duration of the project; the plan is designed to guarantee a systematic and consistent approach to result dissemination. The plan will support the Steering Committee to foster dialogue and scientific review of results to insure that all information that will be made public rests on sound scientific thought, pertinent and constructive to bridge the gap between science and public. Dissemination of project results on a European level will be easily reached, due to the integration of the partners in European research, having already established dialogue with the scientific community.

3.2.2. Dissemination activities

The dissemination plan will encompass approaches to ensure timely propagation of results to the scientific community as well as to the interested public. Findings and results of RASimAs will first be examined and evaluated by members of the consortium. Once approved by the consortium they will be made available to the scientific community and the public. Attention will be paid to ensure

that appropriate findings will be communicated to anaesthetists as well as experts of other areas using regional anaesthesia. The dissemination plan includes:

- Procedures for the systematic examination of results to determine appropriateness of publication and/or protection for intellectual properties;
- A strategic approach to ensure awareness of results by the scientific community and the public;
- Structured collection of feedback from scientists, stakeholders and patients.

Measures for dissemination activities will be documented in the plan. The Commission will be kept informed of the dissemination activities in due time (Press Releases, website launch, articles, etc.) to enable a proper relay of these activities within Europa, the eHealth newsletter, Health Tech Wire platform, etc. The following processes have been agreed upon by the consortium:

VISUAL IDENTITY OF THE RASIMAS TEAM

The consortium has designed a logo, used for the proposal submission. The project management will provide templates of the logo, which together with the EC emblem will be used in all presentations to enhance the project's visibility.

WEBSITE

A project website will be designed to inform participating partners of the objectives and tasks of each work package (the domain www.rasimas.eu has been reserved by the consortium); to inform each participant of all results in a timely manner and to be able to have the participants comment and review the results; to communicate among the participants and other scientists in a co-coordinated and integrated fashion. The project management will ensure that the website will be updated regularly and that all meetings' minutes are uploaded in a timely manner. It is planned to link the RASimAs website to other relevant websites, so that The RASimAs website will not be a stand-alone "business card" website but will serve as a source of information for interested scientists, companies and patients. The website will be partitioned to have a secure area accessible only to members of the RASimAs consortium and an area accessible to the public. Results with appropriate explanations will be published in the public area of the website and participants of RASimAs will be encouraged to write short, non-scientific summaries of the objectives, the diseases, the science and results.

NEWSLETTER

The website will offer a registration for the bi-annual RASimAs newsletter, which will publish relevant information about the collaborative work of the consortium, objectives and tasks as well as information on events and publications.

PRESS RELEASES

The SC will use existing public relations venues of the partners to create awareness of the collaborative work of the consortium by press releases. Press releases will also serve as a medium to inform the public about new research findings of RASimAs.

EVENTS

Events will be used as a platform to present the work of the RASimAs consortium and project results; therefore the annual conference of the European Society of Regional Anaesthesia and Pain Therapy (ESRA) is intended to generate visibility for the scientific community. The work of the consortium will be presented to the public during events organised by the partner's institutions.

PUBLICATIONS AND SCIENTIFIC CONFERENCES

Dissemination of research results to the scientific community will be achieved via:

- *Journal articles*: European Journal of Anesthesiology, British Journal of Anesthesia, Anesthesiology Research and Practice, Best Practice & Research Clinical Anaesthesiology, Regional Anesthesia and Pain Medicine; International Journal of Computer-Assisted Radiology and Surgery.

- *Poster and conferences*: ESRA workshops, International Anesthesia Research Society (IARS) annual meeting, World Congress of Regional Anesthesia and Pain Therapy, SPIE Medical Imaging, SIIM Annual Meeting, Medical Image Computing and Computer-Assisted Inventions (MICCAI).
- *EC collaboration activities*: VPH NoE, VPH conferences, CORDIS newswire.

In all cases, the financial support of the European Commission will be acknowledged in the appropriate section of the communication. Members of the Consortium will also be encouraged to participate in regional conferences and scientific meetings. This will not only be a means by which to disseminate the progress of the project but also to receive the opinions of other experts in the field. Members of the consortium and any of their employees attending scientific meetings will make available any relevant information obtained at the meeting, thereby ensuring the other members of the project are informed about related research carried out in the field in the EU or other parts of the world. Members of the consortium will be encouraged to present whenever possible seminars to discuss objectives and results to inform student and faculty of RASimAs.

3.2.3. Exploitation of project results

MARKET POTENTIAL

Although the medical simulation industry is relatively small (a recent survey found that the global market is approximately 500M Euros a year), it is growing extremely fast. Haptic feedback in medical devices has opened the door to better simulation, accelerating the growth of the market. The RASimAs consortium believes it can capture a significant market share based on the need for RA training tools. SG already sells medical simulator components and is in a prime position to commercialize the productized versions of RASimAs, at the end of the project. The patient-specific libraries developed by the academic partners will also be licensed to other VPH model suppliers or simulator manufacturers, in order to increase the dissemination of the results.

INDIVIDUAL DISSEMINATION AND EXPLOITATION PLANS

Each partner has foreseen the following individual exploitation plan for the RASimAs project. The core aspects of these plans are listed in Table 17.

Partner	Short Term	Long Term
UKA	UKA will publish 5 peer reviewed articles during the 3 year project and prepare conference presentations at SPIE Medical Imaging and the SIIM Annual Meetings will be	UKA will establish a course based on the project results aiming at training 40 clinicians by year.
RWTH	RWTH-VR will publish 5 peer reviewed articles on acknowledged national and international conferences and journals.	RWTH-VR will publish 5 peer reviewed articles on acknowledged national and international conferences and journals.
BANGOR	BANGOR will produce at least one scientific paper that will be disseminated in biomedical engineering journals, such as IEEE TBME, and the annual MMVR conference.	RASimAs will further develop BANGOR's portfolio of medical training simulators (complementary to its ultrasound guided needle puncture simulator for interventional radiology). We will be able to exploit new technology through the Advanced Medical Imaging and Visualization Unit, which is funded by the Wales Government to work directly in deploying visual computing solutions within hospitals.
UCC	UCC will contribute substantively to the academic writing, editorial oversight and publication of all output manuscripts relating	UCC will incorporate the RASimAS into the existing postgraduate PNB training programme at Cork University Hospital, integrate

	to technology validation studies and studies of educational and clinical outcomes. UCC will take the lead in publishing 4 academic articles.	the RASimAS into the simulation programme at UCC (ASSET Centre), and incorporate the RASimAS into the design of the new MSc in Regional Anaesthesia at UCC.
URJC	URJC will publish 3 peer-reviewed articles in specialized journals and will present project results in international conference proceedings with anonymous evaluation and contrasted quality indexes. URJC will develop a PhD thesis on the project topic.	URJC in cooperation with partners will develop a new framework for development of medical simulators. Patents if appropriated.
FORTH	FORTH will publish at least 3 articles in the first two years, and produce two graduate and one PhD scholarships on the topic of the project.	FORTH will collaborate with the University Hospital of Heraklion for exploiting RASimAs ICT tools in the clinical setting and training numerous professionals in RASimAs modelling technologies
INRIA	INRIA will publish 5 articles in peer reviewed conferences or journals on the results obtained during the course of the project.	INRIA will integrate direct and derived results of the project into the Open Source SOFA framework, and will make it available to the simulation community.
UNIZA	UNIZA will publish 5 peer reviewed articles. UNIZA will represent project findings by ESRA newsletters and organize special section of the “Digital Technology” conference organized in cooperation with ESRA.	Developed methods and algorithms will be included in course “Knowledge discovery in Databases” for students of the second level (about 45 students by year).
KU LEUVEN	KU LEUVEN will incorporate project findings in communications conducted during the annual ESRA conference. At ESRA conference, KU LEUVEN will demonstrate the portable prototype system.	KU LEUVEN will leverage the ESRA network to recruit a community of early adopters for the RASimAs system among ESRA members
SINTEF	SINTEF will develop the technology for ultrasound-assisted RA. Based on the results obtained during the course of the project SINTEF will publish at least two peer reviewed articles / proceedings and present the RASimAs platform in media and at relevant conferences (e.g. SMIT). RASimAs deliveries, competence and clinical assessments will in general be exploited for further scientific work related to less invasive image-guided interventions and increased emphasis on publication in this field of R&D.	SINTEF will collaborate with the University hospital in Trondheim, Norway, to integrate the RASimAs platform into clinical training (simulator) and practice (assistant). SINTEF will also work to adapt the RASimAs technology to other applications and increase the use of VPH models in clinical practice, especially to guiding interventions augmented by ultrasound. The overall goal is to further develop and deploy computer assisted interventional technology that increases patient safety, improves skills of the clinical teams, and efficiency of clinical specialists and innovates health care and companies world-wide. The validation of skills training is a particular strategic area for SINTEF, and the development and deployment of the training and learning part of the RASimAs project will be exploited in strong collaboration with the clinical partners to make this a valuable future tool for improving patient outcome.
SG	SG will develop one new patent derived	SG will prepare and launch a new simulator

	from the project research. Furthermore, interface specifications and expert knowledge gained from the project will be added to the X3D ISO standard.	product based on the project research together with the external partner Medaphor, whom is also on the advisory board of this project.

Table 14: Exploitation plans and potential.

3.2.4. IPR management

The management of intellectual property (IP) will be implemented as task in WP 8 (WP8T3) within the management of dissemination and exploitation. The according management structures have been detailed in Section 2 of the proposal.

Measures for the exploitation of the RASimAs results comprise the reporting by the participants of results that may merit IP status, the collection and evaluation by the Steering Committee led by UKA and the pursuit of patents protection by the appropriate partner, university and/or industrial partner. The following measures for the exploitation of results worth of IP protection will be implemented:

- Systematic reporting and collection of all results that merit exploitation;
- Evaluation of market acceptance and market value;
- Preparation and application for patents and licensing of technology where appropriate.

All aspects relating to IP rights and the management of knowledge and IP rights will be negotiated in the Consortium Agreement. These will include existing knowledge (background) from partners, necessary for a proper execution of the tasks and objectives as well as newly generated knowledge. The Steering Committee will ensure that issues related to IP rights are properly assessed in accordance with fundamental ethical rules and principles recognised at EU level. General conditions for the use of knowledge are:

- Valuable information (foreground) should be protected;
- Information (foreground) resulting from the project is owned by the participant generating it;
- Information (foreground) generated jointly, will be jointly owned, unless the participants concerned agree to a different solution.

At the stage of producing the proposal, the consortium has already considered what kind of strategy should be followed concerning IPR issues for the main results of the project, and reached preliminary agreement on this. The basic principle on which we are agreed is that research and development results must be available to a large audience to facilitate wide adoption of project results, while in the meantime having options in place for rewarding those that invested.

The consortium agreement is summarised in Table 18.

Type of Result	Scientific Publication	Consortium Partners	Third Parties Outside the Consortium
Training courseware	Allowed	Public	
RASim and RAA prototype specifications	Allowed	Use rights Patents	Available at the discretion of the respective owners, but with a pricing level appropriate for mass-market adoption.
RASim and RAA proprietary software components (haptic rendering algorithms, simulator core and ultrasound module).	Allowed	Use rights Patents	Available at the discretion of the respective owners, but with a pricing level appropriate for mass-market adoption.

Patient-specific libraries	Allowed	Use rights	Anonymously available with written consent of the subject.
Clinical trial results	Allowed	Public	

Table 15: IPR management of project results.

4. ETHICAL ISSUES

4.1. Introduction

The work in RASimAs focuses on pre-clinical validation and small scale clinical trials demonstrating and providing clinical evidence of the benefits of the use of computer-based models in training and treatment, respectively. The RASimAs Consortium will address scrupulously all ethical, legal, social, and safety issues raised by its research and medical activities. RASimAs adheres to legislation and approval of regulatory authority prior to any activity.

It should be emphasized that the research efforts conducted by the RASimAs Consortium will accommodate relevant Community legislation and recommendations by competent authorities (e.g., the European Group on Ethics in Science and New Technologies), while respecting the principles of the Helsinki Declaration. The framework that will be established for the RASimAs activities will use the highest standards of Good Clinical Practice (GCP) and ethics that are applied in Europe. The Consortium is aware and will follow the guidelines of the International, European and National (i.e., Germany, Belgium, Ireland) legislations in all the various aspects of the research as detailed below.

The participants will comply in every step of their research with generally accepted principles, rules of good scientific practices, and the following normative standards and guidelines:

The "Charter of Fundamental Rights" of the European Union (2000/C 364/01)
EU Directive 93/42/EWG (Medical Device Directive- MDD)
Directive 95/46/EC (Protection of individual Data)
Declaration of Helsinki (Seoul, 2008)
Nuremberg Code (1947)
International Conference on Harmonization – Good Clinical Practice (ICH-GCP)

All participants confirm that the proposed research does not involve any of the issues or research activities that are

- Aiming at human cloning for reproductive purposes;
- Intended to modify the genetic heritage of human beings which could make such changes heritable;
- Intended to create human embryos solely for the purpose of research or for the purpose of stem cell procurement, including by means of somatic cell nuclear transfer;
- Involving the use of human embryos or embryonic stem cells with the exception of banked or isolated human embryonic stem cells in culture.

4.2. Project ethics management

The project includes several levels of management of ethical issues which may arise during the project lifetime.

4.2.1. First level: coordination and project management

The Coordinator, assisted by the project manager, in close collaboration with the UKA-CTCA (Partner 1C) will ensure that all activities of each partner in the RASimAs Consortium are in full

agreement with the national and international regulations. All the participants will comply with the Charter of Fundamental Rights of the EU and following EU / international legislation and texts. For each relevant task, the Coordinator will provide to the Commission copies of the necessary authorisations obtained from the relevant bodies. Furthermore, the UKA-CTCA and the WP6 team will control that each partner conducting the clinical trial is trained to all ethical issues and challenges posed by the project and has the same basic knowledge on the ethical and safety issues raised by the project.

4.2.2. Second level: the Advisory Board (AB)

Concerning the clinical trials for evaluation of RASim and RAAs the Advisory Board (AB) of RASimAs will consist of both active participants and external experts, beyond the Consortium, related to the three responsible independent ethics committees (Germany, Belgium, Ireland) and will be established before the start of the project. The partners of the EAB within the Consortium consists of the Coordinator, representatives of the medical partners, as well as the sponsor's representative (UKA-CTCA) having the legal responsibility for an ethically and legally sound proceeding. The UKA-CTCA has strong interest in ethical issues and will be responsible for smooth lines of communication between the Consortium, the independent ethics committees and relevant regulatory authorities to meet all necessary requirements for fulfilling and maintaining highest ethical standards. The EAB will meet simultaneously with the Steering Committee or upon request. The Coordinator will provide an annual report on its activities to the Commission.

The EAB will take into account the multidisciplinary nature of ethical issues (e.g. data protection) arising during the implementation of the project. The EAB will form an integral part of the management of the project. The EAB will contribute to establishing and applying data protection rules and ensuring subjects` protection during design of interventional trials.

Responsibilities on ethical issues are clearly assigned within the RASimAs Consortium.

In particular, the EAB will supervise that all the ethics committee approvals and informed consent documents will be sent to the European Commission by the Coordinator, and that proper insurance/indemnity arrangements are made, both prior to the commencement of the relevant part of the study. It will draft advice in relation to the recruitment strategy and review the drafts of the informed consent forms to make sure that they properly address: (i) all relevant study related aspects and procedures, (ii) usage of data and data protection, (iii) information about withdrawal of consent, (iv) study related benefits and risks, (v) options for request of removal of their coded data from the study,(vi) information about patient insurance and (vii) contact informations

During the RASimAs kick off meeting, an introduction to the programme's ethical, legal and safety related issues will be given by the team coordinating the clinical trial (UKA-IMI, UKA-CTCA), supported by the AB (e.g. patient informed consent form, use of clinical data, etc.), with the aim to provide participants the relevant information pertinent to the RASimAs research proposal. Following this workshop, specific ethical rules within the Consortium will be implemented and controlled by the AB via their integrated communication activities and the RASimAs Intranet.

Trans-disciplinary collaboration between all stakeholders, including the local ethical authorities will ensure that due account is taken of the ethical and societal concerns, our obligations towards future generations and international organisations. Via their integrated communication activities, RASimAs researchers will allow for mutual education and dialogue. They will also ensure that the RASimAs network have the means to continuously assess the societal relevance and adequacy of the analysis and evaluation of network activities.

4.3. Legal aspects

Clinical trials are regulated both by national and international legal and ethical rules. International clinical trials are regulated by the guidelines established by the Nuremberg Code (1947) and the revised Declaration of Helsinki (2008, Seoul). In addition, each country has respective legal and ethical requirements that must be acknowledged. The two clinical trials involving adult subjects

able to give informed consent, will be conducted by Partner 1B (UKA-DA, Germany), Partner 4 (UCC, Ireland) and Partner 9 (KU LEUVEN, Belgium).

4.3.1. EU legislation

The Commission shall never be considered as a sponsor for clinical trials in the sense of Directive 93/42/EWG of the European Parliament on the approximation of the laws, regulations and administrative provisions of the Member States relating to the implementation of good clinical practice in the conduct of clinical trials on medicinal devices.

Research studies in countries participating in RASimAs are regulated by both national and international legal and ethical rules. Concerning international statutes, the Nuremberg Code (1947), the Revised Declaration of Helsinki (1975), and the convention for the protection of human rights and dignity of human being with regard to the application of biology and medicine called the "Convention on Human Rights and Biomedicine" (Council of Europe, 1997) are the main international guidelines for medical research. In other aspects, in each country, national legal and ethical requirements will be fulfilled.

The framework that will be established for the RASimAs activities will use the highest standards in Good Clinical Practices and Ethics that are applied in Europe.

4.3.2. National regulations

National Medical Device Acts are a transformation of EU directives into national law. The aim is to regulate safety, appropriateness and capacity of the medical devices as well as to secure the well-being and the required protection of patients, users, and third persons.

Manufacturers have to provide comprehensive documentation of clinical data which are both current and scientific provable to reach a technical level receiving the Conformité Européenne (CE)-certification is a matter of form. Conduction of clinical trials underlies strict legal guidelines. The sponsor of a clinical trial will bear the full responsibility. ICH-GCP and the normative EN ISO 14155 provides global quality standards and some aspects of these standards are reflected also in the national laws.

4.4. Research on humans

The RASimAs project will develop and provide a new prototype supporting regional anaesthesia (RA) by training tools of a simulator (RASim) and by guidance of performance of RA on patients by an assistant system (RAAs). Respectively clinical trials are the final step in assessment and evaluation of the proof-of-principle and will be conducted under well-defined and controlled laboratory conditions. To increase data quality by eliminating confounders both experiments for evaluation of RASim and of RAAs will be conducted with randomized directed subjects. Both clinical trials will be object of WP7 of the RASimAs project.

4.4.1. Ethical and regulatory aspects

Table 19 lists the ethics committees and competent authorities that are involved in the RASimAs evaluation studies. Approvals by the relevant competent authorities and ethics bodies will be obtained prior to the commencement of the trials. Copies of approval will be submitted to the European Commission before commencing research activities.

4.4.2. Research involving trainee anaesthesiologists & patients

Clinical trials (WP7) will be performed in adult subjects able to give informed consent. The RASimAs Consortium provides three study sites in Germany, Belgium, and Ireland, which are participating and equally recruiting trainee anaesthesiologists as volunteers as well as patients. In particular, there are two tasks of evaluation planned:

- *Evaluation of RASim*: Application of a training simulator system for physicians will be evaluated by involving first year anaesthetists. The doctors in training give their informed consent to be

Partner	Ethics Committee (EC)	Competent Authority (CA)
UKA (Germany)	Ethik-Kommission des Universitätsklinikums der RWTH Aachen Chairman: Prof. Dr. med. G. Schmalzing Pauwelsstr. 30 52074 Aachen, Germany Fon: +49 241 8089963 Fax: +49 241 8082012	BfArM Bundesministerium für Arzneimittel und Medizinprodukte
KU LEUVEN (Belgium)	Commissie Medische Ethiek/Klinisch Onderzoek Chairman: Prof. Dr. W. Van den Bogaert Herestraat 49 3000 Leuven, Belgium Fon: +32 16 348600 Fax: +32 16 348601	FAMHP Federal Agency for Medicines and Health Products
UCC (Ireland)	Ethics Committee of the Cork Teaching Hospitals Research Chairman: Dr. Michael Hyland Lancaster Hall, 6 Little Hanover Street Cork, Ireland Fon: +353 21 4903500 Fax: +353 21 4903506	IMB Irish Medicines Board

Table 16: Relevant Ethics Committees and Competent Authorities.

randomized in treatment or in control group and to be observed and recorded during training sessions in regional anaesthesia.

- *Evaluation of RAAs*: The evaluation of the regional anaesthesia assistant system will be done within the clinical environment with patients scheduled for elective surgery and giving informed consent voluntary to be randomized and directed to the treatment group (Assistant guided RA) or to the control group receiving RA based on the physician's experience. No patients will be included who have to undergo an emergency procedure.

For evaluation of RASim, 60 first year anaesthetists will be included to investigate effectiveness and efficacy of previous simulator-based training before performing regional anaesthesia on patients under supervision of an extensive experienced senior anaesthetist. Study subjects will be matched to the control group (no simulator-based training) or to the treatment group (with simulator-based training) by randomization after given informed consent.

The evaluation of RAAs needs its usage within the clinical environment in fact. For this purpose 40 patients scheduled for elective surgery and suited for regional anaesthesia will be asked to participate within this study. After obtaining informed consent of every patient they will be randomized to the control group (RA performed conventionally) or to the treatment group (RA performed under augmented reality-based guidance).

Clinical trials will be done by experienced anaesthetists adhering to legislation including patients able to give informed consent.

In conclusion, the sponsor believes this study to be carefully designed and expects no additional study-related risks due to participating into this study, because the regional anaesthesia is performed due to therapeutic reasons. No additional diagnostic or treatment procedure related to the study will be performed. If medical images generated during routine diagnosis procedures are available for single patients, they will be applicated to the RAA system and used for guidance. RAA-guided support in patients where medical images are not available will be performed by using

a generated patient-specific model. In ealier stages of the project a library existing of a collection of fully anonymized MRI and CT images from clinical and research will be developed to assemble different patient-specific models. Patients will be treated by senior anaesthetists who are extensively experienced in the performance of RA. Although there might lack any direct specific or spontaneous benefit for the individual patient, the evaluation of the RA assistant will improve performance and management of RA in common and gain trust in usage of patient-specific VPH models. We expect to improve the quote of success of RA and evade general anaesthesia in many cases.

4.4.3. Incidental findings

Incidental findings that are discovered unintentionally and are unrelated to the current medical condition and treatment being performed will be documented and communicated to the study subject. The study doctor is responsible to inform the subject and to initiate appropriate measures by directing the subject to a relevant site for further diagnostic and treatment procedures.

4.4.4. Insurance

The clinical trial protocols will be submitted to the appropriate institutional ethics committees and appropriate national and local authorities of the Partners. The clinical trial protocols will be explained in detail verbally to the patient and detailed in the patient information sheet and informed consent form according to the standard operating procedures (SOPs) of the Clinical Trial Centre Aachen (UKA-CTCA, Partner 1C) and national requirements.

Insurance and indemnification arrangements will be in place according to the European Medical Device Directive (and the local medical device acts, respectively) prior to the commencement of the clinical trials providing for the adequate protection of the patients enrolled in the clinical trials.

The sponsor RWTH Aachen University will contract an appropriate insurance with HDI Gerling, taking into account the respective requirements of each country site and will provide written evidence of such insurance prior to the commencement of the study (see Appendix, 5.4 Insurance protection for clinical trial). Insurance terms and conditions will be available on the part of Investigator and will be handed over to the patient in his respective mother language.

4.4.5. Informed consent and methodology

All study subjects are adults able to give their informed consent. They will be asked to participate in the RASimAs project in the planned trials by providing data sets concerning the application of RASimAs prototypes and are entitled to choose whether or not to take part. Their decision is voluntary and they should be competent to understand what is involved. Information will be given in both oral and written form, in the native language, by the treating physician with regards to the nature, scope and possible consequences of the study. Informed consent forms and information sheets will be presented to the EC prior to the commencement of the research.

All study subjects are adults able to give their informed consent in a voluntary decision.

Prior to participating in a study, all subjects have to give their informed consent. The subject will have enough time, at least 24 hours to decide whether to participate or not. If the subject will not participate or the subject withdraws consent no disadvantages will result.

The information about the elective procedure in general and the information about the clinical investigation will be done separately and by two different physicians. Informed consent forms will be submitted to the Steering Committee via the Coordinator and modified if necessary. This process is monitored and controlled by Advisory Board. The consent form will be harmonized with those of the other relevant beneficiaries. As a final step, this consent will be obtained according to the participant's local ethical regulations, but information provided to the study subject can be completed to fulfil RASimAs' own ethical requirements, if necessary. The consent form will be provided to the

clinics and will be kept locally, in the study subject's personal file. The study consent form will briefly identify the nature of the investigation.

The study subject may always change his / her opinion in the course of the study. Details on the possibility of study participants to request removal of their coded data from the study will be included in the informed consent information form. The ethical principle of respect for persons requires that subjects be given the opportunity to choose what shall and shall not happen to them. Valid informed consent requires:

- The disclosure of relevant information to prospective subjects about the research;
- Their comprehension of the information;
- Their voluntary agreement, free of coercion and undue influence, to research participation.

The process of informed decision-making by research subjects generally includes discussion of the research study with the Coordinating Investigator (CI) of the clinical trial (see Appendix 5.2), and others as appropriate, and signing the written informed consent document. Depending on the nature, type and duration of the research, ongoing discussion with and education of subjects about the study may continue long after the informed consent document is signed.

The informed consent methodology is based on disclosure, comprehension, and voluntary agreement.

Generally, after the Investigator has explained the research study to the subject, the subject's informed consent is documented by signing the "Information letter to the patient" and the written consent document, which Ethical Committee must have previously reviewed and approved. The subject is given a copy of the signed document and the signed consent documents are retained according to the policies of the institution where the research is conducted.

The research investigators are responsible for ensuring that informed consent shall be understandable to the subject and obtained in writing from the subject in circumstances that are not coercive and that offer the subject sufficient opportunity to decide whether she/he should participate. The consent document should not contain language that implies or suggests that the subject gives up any legal rights or releases research investigators from liability for negligence. For that, the research investigators must provide the following information to each subject in writing:

- A statement that the study involves research;
- An explanation of the purpose of the research and the expected duration of the subject's participation;
- A description of the procedures to be followed and identification of any procedures that are experimental;
- A description of any foreseeable risks or discomforts to the subject, an estimate of their likelihood, and a description of what steps will be taken to prevent or minimize them;
- A description of any benefits to the subject or to others that may reasonably be expected from the research. Monetary compensation is not a benefit. If compensation is to be provided to research subjects or healthy volunteers, the amount should be stated in the consent document;
- A disclosure of any appropriate alternative procedures or courses of treatment that might be advantageous to the subject;
- A statement describing to what extent records will be kept confidential, including a description of who may have access to research records;
- An explanation and description of any compensation and any medical treatments that are available if research subjects are injured; where further information may be obtained, and whom to contact in the event of a research-related injury and about research subject's rights (including the Clinical Centre's Patient Representative and telephone number);
- A statement that participation is voluntary and that refusal to participate or discontinuing participation at any time will involve no penalty or loss of benefits to which the subject is otherwise entitled;

- A statement that the particular treatment or procedure may involve risks if the subject is or may become pregnant;
- A description of circumstances in which the subject's participation may be terminated by the investigator without the subject's consent;
- A statement that there are no costs to the subject that may result from participation in the research;
- A description what will happen if the subject decides to withdraw from the research and how withdrawal will be handled;
- A statement that the investigator will notify subjects of any significant new findings developed during the course of the study that may affect them and influence their willingness to continue participation;
- A statement of the approximate number of subjects involved in the study and that there will be neither remuneration nor financial compensation provided to subjects;
- A statement that none of the investigators has potential financial or other conflicts of interest in the conduct of the study.

> ***The well-being and the security as well as the protection of privacy will be guaranteed at any time of the project. Only extensive experienced investigators will lead and conduct the clinical trials.***

The investigators will terminate conduction of the clinical projects at once for the single study subject or if needed for the whole trial if deviations of the trial protocols do not match the legal and ethical requirements any more. Therefore the clinical trial protocols will serve as operating manuals that meet every legal and ethical requirement for conducting clinical trials.

4.5. Research on human data collections

Data is collected and processed according to the European Data Protection and clinical trial Directives (95/46/EC and 93/42/EWG) and will be managed by the Department of Medical Informatics (UKA-IMI, Partner 1A), Universitätsklinikum Aachen, Germany.

The proceeding and concept of data collection within the project concerning the individual privacy will be approved by the responsible local ethics committees.

In RASimAs, all data is collected and processed according to the European Data Protection Directive (95/46/EC) on the Protection of Individuals with Regard to the Processing of Personal Data and on the Free Movement of such Data and the European Clinical Trials Directive (2001/20/EC) on Good Clinical Practice in the Conduct of Clinical Trials on Medicinal Products for Human Use.

Within the EU, Germany is one of the countries enforcing the highest standards in personal data protection. Accordingly, the German Federal Data Protection Act (Bundesdatenschutzgesetz, BDSG) of 20 December 1990 (BGBl. I 1990 S.2954) amendments of 14 September 1994 (BGBl. I S. 2325) will be respected. Furthermore, the RASimAs data management will be conformant to the German Federal Office for Information Security (BSI) Act to Strengthen the Security of Federal Information Technology (BSI-Act-BSIG) of 14 August 2009.

> ***Extreme care will be taken to protect all patient information in all discussions, public presentations and publications. Data will be protected at the investigator level as well at the Consortium level and regularly scheduled back-up of all data will be mandatory.***

The data management of RASimAs provides a framework of data protection and security measures designed to guarantee that all data is safe from unforeseen, unintended, unwanted or malevolent use. This ensures the right of any individual expecting that personal information will be processed securely and will not be disseminated in any form without their written consent.

4.5.1. Responsibility and management structure

For both, RASim and RAAs evaluation studies, the data management and eCRF hosting will be performed by the Coordinator, Department of Medical Informatics (UKA-IMI, Partner 1A). The responsible Chief Technical Officer (CTO) is the Project Manager of RASimAs, Prof. Dr.rer.nat. Dipl.-Ing. Thomas M. Deserno, engineer and computer scientists with research focus on image processing and image data management, interfacing and communication. Accordingly, the relevant data protection authority for RASimAs is represented by Mr. Ulrich Lepper (Northrhine-Westfalia), who is supported by Mr. Joachim Josef Willems, Data Protection Officer (DPO) at the RWTH Aachen University Medical Centre. Both will be informed in detail on all data issues with RASimAs.

UKA-IMI operates a server farm composed of several virtual servers running on shared hardware systems operated with Linux. The hardware is based around industry standard and highly redundant components. Access is controlled through multiple firewalls as well as by the use of Secure Shell (SSH) and Secure Sockets Layer (SSL) to identify persons accessing the system and to encrypt all data transmissions to and from the storage systems.

Based on this server farm, UKA-IMI provides virtual server systems for clinical trials, tele-medical applications and medical databases for several departments of the University Hospital Aachen, such as the Department of Anaesthesiology (UKA-DA, Partner 1B). Furthermore, UKA-IMI is operating the central databases at the Clinical Trial Centre Aachen (UKA-CTCA, Partner 1C). Currently, the ISO 27001 certification for medical data hosting is under preparation.

On a regular schedule, UKA-IMI offers specific training on data protection and privacy issues for personnel at RWTH Aachen Medical Centre involved in clinical trials. This training includes the general concepts and requirements as well as specific issues arising from the UKA-IMI data management. This training will be made mandatory for scientists and study personal of RASimAs.

4.5.2. Data protection and physical safety

Physically, the UKA-IMI computers are stored in irremovable racks that are hosted in a special air-conditioned server room. Access to this room is granted by special keys only, which are exclusively provided to the system administrators and to the Security and Fire Departments of Aachen University Hospital. The server farm is connected to an emergency power supply guaranteeing a controlled regular shut down of the systems in case of any disconnection to the electrical power.

Using encrypted data transfer (AES 128-Bit encoding), all server backups are performed in cooperation with the Centre for Computing and Communication (CCC) of RWTH Aachen University, which is hosting the backup hardware in different protected locations. Based on the IBM Tivoli® Storage Manager, master as well as incremental backups are scheduled regularly allowing instant server reconfiguration and database reconstruction on a daily bases. Since a virtual server can be installed easily on any suitable hardware, the highest system availability is obtained for RASimAs even in worst-case scenarios.

PHYSICAL SAFETY RULES

The following physical safety rules apply to all RASimAs research:

- *Beneficiary area*: Anytime, the access to the office is limited by keyed lock. The office is protected by a general electronic security system at the main entrances of the building that will detect door opening, intrusions, and smoke.
- *Protection of servers*: Access to the computer's room, including database server, is controlled by keyed lock. Only system team staff is allowed entrance to this room and consequently to access system terminals. Each entry must be logged with name, time and date.
- *Backup*: Each server is backed up daily on a secondary backup server, hosted at CCC in different locations. Third-level backups at CCC are kept in a fire-resistant safe.
- *Archiving*: Study data files, treatment allocation files (if any), and specific programs are saved on 3 separated media (DAT or paper and CDROM) in common format (ASCII or CSV), and are under the control of the principal investigator and are located in a separated building.

- *Standard operating procedure (SOP)*: Backup, safety actions and disaster recovery plan are described in written documents that have been certified by the DPO.

DATA INTEGRITY

OpenClinica is the world's leading open source clinical trials software for electronic data capture and clinical data management. It provides browser-embedded user interfaces to an SQL-based database engine. According to the design of the trials (WP7 of RASimAs), a specific database will be developed using OpenClinica. Electronic case report forms (eCRF) will be provided for all relevant data, and consistency and plausibility checks will be performed automatically and instantly on data entry.

DATA SECURITY AND PRIVACY

The RASimAs study database will be made available via the Internet. Access to the database is controlled by individual user accounts on different access levels (e.g., data entry, monitor, principle investigator). All accounts will be defined by unique user names and individual passwords, which are built according to the general recommendations of BSI. All data hosted in the database is pseudonym, which means that the individual delivering the data entries cannot be identified without additional information. This information is stored exclusively at the study centres in Germany and Austria.

> ***To handle patient-specific image data, UKA-IMI also provides electronic pseudonymisation services, where the database with identifying data is strictly separated from that hosting the medical data, and temporary keys are exchanged during a session allowing privileged users to assess and update the pseudonymised data.***

Such serviced are established following the generic concept developed by the German Institute of Technology, Methods, and Infrastructure for Networked Medical Research (TMF), Berlin.

Disclosure of information from the study to third parties will be limited to those persons undertaking legitimate peer review of the scientific and ethical aspects of the study. High priority will be assigned to participant confidentiality and welfare.

DATA LIFETIME

The RASimAs Research Subject information and Consent Form specifies the time points of data collection. From the last patient out or premature termination date, the German MPG requires data archiving for at least 10 years (§12 Abs. 2, MPG & §3 Abs. 2, 3, 4 MPKPV). Generated by the study management software that is operated for the sponsor of the study (the Rector of RWTH Aachen University, represented by UKA-CTCA, Partner 1C), an alert will be generated automatically after 10 years.

Complete data destruction includes databases hosted on IMI server and CCC backup systems as well as the subject identification locks, which will be destroyed at the study centres. Electronic data erosion will be performed by overwriting the storage media with random sequences. This process will be initiated by the CTO and surveyed by the DPO.

Data usage, however, will be restricted to six month after last patient out. All statistical analysis and publication of result will be done within this time. All access privileges to the database will be retained withdrawn as early as possible, depending to the access levels, but latest after six month of last patient out.

SOFTWARE SECURITY

The following software security rules apply to all RASimAs research:

- *Authentication*: Each user has its own username and individual password, composed of at least six characters including regular and capital letters, and digits or symbols. When the password is chosen by the user, re-use of a previously used password is forbidden.
- *Connection modalities*: Privileged account (root, admin or system for example) connections are forbidden outside of computer room. Remote access to these accounts is forbidden. Connec-

tions are logged and after each connection user ID and date of previous connection is recorded. For all users, automatic disconnection occurs after inactivity of five to twenty minutes depending on application and/or system.

- *Data confidentiality*: Data transfers are encrypted (SSL). Each system intervention is logged in a registry (with date, and technician name).
- *Internet*: Beneficiaries' local area network (LAN) is protected from internet by a wired firewall.

SUMMARY ON DATA PROTECTION ISSUES

In summary, all described efforts are done in order to ensure that data processing within the RASimAs project is compliant with the European Data Protection Directive (95/46/EC). In particular, all data is:

- *Fairly and lawfully processed*: The patients included in RASimAs are informed that their data is being collected, who is holding the information, who is controlling the data, what the data will be used for, how long the data will be kept, and whom the information may be disclosed to.
- *Processed for limited purposes*: All data is used only for the purposes for which it was collected.
- *Adequate, relevant and not excessive*: The amount of data collected, processed and archived is strictly limited to support but not exceed the well defined purposes.
- *Accurate and up-to-date*: This principle ensures that accurate data is being held, as hold inaccurate information may not hold any purpose.
- *Not kept longer than necessary*: As described before, all data collected in RASimAs will be kept only for the time for which it is necessary supporting the study.
- *Processed in accordance with the data subject's rights*: Data management in RASimAs ensures the rights of all subjects included in the study to access the data collected, to prevent its processing (including direct marketing), to object to decisions made by automatic processing, to claim for compensation, to invoke rectification, blocking, erasure and destruction, and the right to ask the Commissioner to assess whether the act has been contravened.
- *Secure*: Appropriate procedures have been installed and appropriate measures will be taken to ensure that unauthorised or unlawful access, accidental loss, or destruction of personal data does not occur.
- *Not transferred to countries without adequate protection*: In RASimAs personal data is not transferred to countries outside the European Economic Area (EEA), and all precautions have been installed to en-sure data privacy and avoid unintentionally transfer to those countries.

4.5.3. Ethical issues table

Table 20 summarises the ethical issues related to the RASimAs project.

Ethical Issue	YES	Page
Informed Consent		
Does the proposal involve children?		
Does the proposal involve patients?	X	Sect. 4.4.2 Page 85
Does the proposal involve persons not able to give consent?		
Does the proposal involve adult healthy volunteers?		
Biological Research		
Does the proposal involve human genetic material?		
Does the proposal involve human biological samples?		

Does the proposal involve human biological data collection?		
Does the proposal involve human embryos?		
Does the proposal involve human foetal tissue or cells?		
Does the proposal involve human embryonic stem cells?		
Privacy		
Does the proposal involve processing of genetic information or personal data (e.g. health, sexual lifestyle, ethnicity, political opinion, religious or philosophical conviction)?		
Does the proposal involve tracking the location or observation of people without their knowledge?		
Research on Animals		
Does the proposal involve research on animals?		
Are those animals transgenic small laboratory animals?		
Are those animals transgenic farm animals?		
Are those animals cloned farm animals?		
Are those animals non-human primates?		
Research Involving Third Countries		
Is any part of the research carried out in countries outside of the European Union and FP7 Associated states?		
Dual Use		
Does the research have direct military application?		
Does the research have the potential for terrorist abuse?		
ICT Implants		
Does the proposal involve clinical trials of ICT implants?		
(IF NONE) I CONFIRM THAT NONE OF THE ABOVE ISSUES APPLY TO MY PROROSAL		

Table 17: Ethical issues.

5. APPENDIX

5.1. Reference projects & publications

This appendix provides information showing that the partners are active in technical and commercial work related to the topics of RASimAs. The selected articles and reference projects are listed here by consortium members and are not exhaustive.

5.1.1. Rasim

In cooperation of UKA-DA, UKA-IMI, and RWTH-VR, a virtual patient architecture in conjunction with an intuitive VR-based RA training environment has been developed.

www.rasim.info

The modular architecture allows processing individual subject-data and creating a virtual patient database. This database is used as input for the simulator application that features multimodal representations (both visual and rudimentary haptic) and a plausible simulation. From this research, the following points matters:

- A flexible data structure has been developed, which encapsulates functional anatomy, physiological data, and geometry extracted from medical imaging data. Due to the modular setup of the data structure and the separation from the simulation algorithms, patient-specific datasets from the database can be used. The entries in the database can be extended with new regions so that other procedures can be implemented. Commercial datasets such as Zygote provide accurate models with high resolution and details. Therefore, they are very useful as references as well as for prototyping. However, such datasets do not consider anatomical variations.
- A three-dimensional (3D) nerve modelling technique has been developed to construct virtual nerves from control points. Conventional desktop input devices (i.e., mouse and keyboard) as well as a 6-degree of freedom (DOF) input devices can be used for intuitive spatial positioning. Automatic computation of tangents (Catmull–Rom method) was combined with manual definition (Hermite method) for selected points. As a result, a hierarchical tree data structure based on splines is obtained. Nerves which innervate muscles end at the adjacent muscle with a myoceptor. This is a physical entity that translates the electric impulse to muscle stimuli. The associated tangents are used as parameters for standard interpolation techniques.
- In addition, specialized algorithms have been developed for the haptic tool-tissue interaction supporting simultaneous palpation and needle puncturing in simulated RA. Haptic simulation has been coupled to a soft-tissue simulation based on the co-rotational finite element method. The tool-tissue simulation covers deformations. Here, besides linear elastic simulation techniques, more accurate methods for simulation of non-linear tissue behaviour have been applied. In addition, approaches to simulate inhomogeneous tissues have been developed, which are suitable to simulate stacked material layers. Spring-based, Euler beam-based, and finite element-based methods for needle bending have been taken into account.

5.1.2. Haystack

Haystack is an international project combining expertise from clinical, academic and commercial partners to develop a system to support continuing professional development for doctors.

www.ucc.ie/en/telforhealth/research/haystack

The project was built on research in the area of visio-haptics, and supports training and assessment of competence by specifically developing a medical training simulator for ultrasound-guided RA. Haystack has designed, developed, and validated a hapto-visual simulator for the axillary brachial plexus block. The project has been collaboration between the National Digital Research Centre Ltd., Republic of Ireland, UCC, and MD.

Haystack has applied a Participatory Design model. This places the users (i.e. clinicians) in the centre of the development process and actively directs the developers in their process of creating

new technology. Task and error analysis of ultrasound-guided axillary brachial plexus blocks was utilized to direct the design of a VR-based medical training and assessment environment. Importantly, the device is capable of providing detailed objective feedback of performance to a learner. Through precise formative feedback, a learner can adapt future attempts as part of a deliberate practice model. The learner can also experience a large variety of anatomical and other clinical variation without awaiting “chance” clinical encounters. Thus, Haystacks aims to provide a safe, effective, and realistic learning experience.

The training and assessment environment has been designed to:

- Identify clinically relevant metrics and errors;
- Provide useful feedback based on actual performance and errors;
- Individualize training by adapting to a trainee's previous performance and errors.

Furthermore, the Haystack group has already addressed integrating VR-based learning methods into formal, curriculum-based training, with the associated benefits of decreasing the incidence of clinical errors and consequently improving patient safety.

5.1.3. Publications

In this section, we list the 5 most important previous publications by each of the partners with respect to their particular research and/or development topic within the RASimAs Consortium.

UKA

Harmsen M, Fischer B, Schramm H, Seidl T, Deserno TM. Support vector machine classification based on correlation prototypes applied to bone age assessment. IEEE Trans Inf Technol Biomed 2012; in press

Deserno TM, Welter P, Horsch A, Toward a repository for standardized medical image and signal case data annotated with ground truth, J Digit Imaging 2012; 25(2): 213-26.

Kirstein S, Müller K, Walecki-Mingers M, Deserno TM, Robust adaptive flow line detection in sewer pipes, Autom Constr 2012; 21(1): 24-31.

Fischer B, Welter P, Günther RW, Deserno TM, Web-based bone age assessment by content-based image retrieval for case-based reasoning Int J Comput Assist Radiol Surg 2012; 7(3): 389-99.

Welter P, Riesmeier J, Fischer B, Grouls C, Kuhl C, Deserno TM, Bridging the integration gap from imaging to information systems A uniform data concept for content-based image retrieval in computer-aided diagnosis, J Am Med Inform Assoc 2011; 18(4): 506-510.

RWTH

Heesen M, Klöhr S, Rossaint R, Walters M, Straube S, van de Velde M. Insertion of an intrathecal catheter following accidental dural puncture: a meta-analysis. Int J Obstet Anesth 2012; in press.

Stoppe C, Werker T, Rossaint R, Dollo F, Lue H, Wonisch W, Menon A, Goetzenich A, Bruells CS, Coburn M, Kopp R, Bucala R, Bernhagen J, Rex S. What Is the significance of perioperative release of macrophage migration inhibitory factor in cardiac surgery. Antioxid Redox Signal 2013; in press

Grottke O, Braunschweig T, Spronk HM, Esch S, Rieg AD, van Oerle R, ten Cate H, Fitzner C, Tolba R, Rossaint R. Increasing concentrations of prothrombin complex concentrate induce disseminated intravascular coagulation in a pig model of coagulopathy with blunt liver injury. Blood 2011;118(7):1943-51.

Grottke O, Ntouba A, Ullrich S, Liao W, Fried E, Prescher A, Deserno TM, Kuhlen T, Rossaint R. Virtual reality-based simulator for training in regional anaesthesia. Br J Anaesth 2009;103(4):594-600.

Ullrich S, Frommen T, Rossaint R, Kuhlen T. Virtual reality-based regional anaesthesia simulator for axillary nerve blocks. Stud Health Technol Inform 2009;142:392-4.

BANGOR

Vidal FP, Villard PF Lutton E. Tuning of patient specific deformable models using an adaptive evolutionary optimization strategy. IEEE Tran Biomed Eng 2012; in press

Ap Cenydd L, John NW, Bloj M, Walter A, Phillips NI. Visualizing the surface of a living human brain. IEEE Computer Graph Appl 2012;32(2):55-65.

Coles TR, John NW, Gould DA, Caldwell DG. Integrating haptics with augmented reality in a femoral palpation and needle insertion training simulation. IEEE Trans Haptics 2011;4(3): 199-209.

Coles TR, Meglan D, John NW. The role of haptics in medical training simulators: A survey of the state of the art". IEEE Trans Haptics 2011;4(1): 51-66.

Vidal FP, John NW, Healey AE, Gould DA. Simulation of ultrasound guided needle puncture using patient specific data with 3D textures and volume haptics. Computer Animat Virtual World 2008; 19(2):111-27.

UCC

O'Sullivan O, Aboulafia A, Iohom G, O'Donnell BD, Shorten GD. Proactive error analysis of ultrasound-guided axillary brachial plexus block performance. Reg Anesth Pain Med 2011;36(5):502-7.

Chittoodan S, Breen D, O'Donnell BD, Iohom G., Long versus short axis ultrasound guided approach for internal jugular vein cannulation: a prospective randomised controlled trial. Med Ultrason 2011;13(1):21-5 .

O'Donnell B, Riordan J, Ahmad I, Iohom G., Brief reports: a clinical evaluation of block characteristics using one milliliter 2% lidocaine in ultrasound-guided axillary brachial plexus block. Anesth Analg 2010;111(3):808-10.

O'Donnell BD, Ryan H, O'Sullivan O, Iohom G. Ultrasound-guided axillary brachial plexus block with 20 milliliters local anesthetic mixture versus general anesthesia for upper limb trauma surgery: an observer-blinded, prospective, randomized, controlled trial, Anesth Analg 2009;109(1):279-83.

O'Donnell BD, Iohom G., An estimation of the minimum effective anesthetic volume of 2% lidocaine in ultrasound-guided axillary brachial plexus block. Anesthesiology 2009;111(1):25-9.

URJC

Tang M, Manocha D, Otaduy MA, Tong R. Continuous penalty forces. ACM Trans Graph 2012; 31(4):107

Zurdo JS, Brito JP, Otaduy MA. Animating wrinkles by example on non-skinned cloth. IEEE Trans Vis Computer Graph 2012;9(1):149-58.

Corenthy L, Martin JS, Otaduy MA, García M. Volume haptic rendering with dynamically extracted isosurface. Proc Haptics Symp 2012; in press.

Cosco FI, Garre C, Bruno F, Muzzupappa M, Otaduy MA. Visuo-haptic mixed reality with unobstructed tool-hand integration. IEEE Trans Vis Computer Graph 2012; in press

García M, Otaduy MA, O'Sullivanofia C. Perceptually validated global/local deformations. J Vis Comput Anim 2010;21(3-4): 245-54.

FORTH

Sakkalis V, Manikis G, Papanikolaou N, Karatzanis I, Marias K. A software prototype for the assessment of tumor treatment response using diffusion and perfusion MR imaging. Proc EMBC 2012.

Marias K, Dionysiou DD, Sakkalis V, Graf N, Bohle R, Coveney PV, Wan S, Folarin A, Büchler P, Reyes M, Clapworthy G, Liu E, Sabczynski J, Bily T, Roniotis A, Tsiknakis MN. Clinically-driven design of multiscale cancer models: the contra cancrum project paradigm. J. R. Soc Interface Focus 2011;1:450-61.

Roniotis A, Manikis G, Sakkalis V, Zervakis ME, Karatzanis I, Marias K. High grade glioma diffusive modeling using statistical tissue information and diffusion tensors extracted from atlases. IEEE Trans Inform Tech Biomed. 2011;16(2):255-63.

Manikis G, Sakkalis V, Zabulis X, Karamaounas N, Triantafyllou A, Douma S, Zamboulis C, Marias K. An image analysis framework for the early assessment of hypertensive retinopathy signs. Proc Int Conf e-Health Bioeng, Iasi, Romania, 24-26 Nov 2011.

Farmaki C, Marias K, Sakkalis V, Graf N. Spatially adaptive active contours: a semi-automatic tumor segmentation framework. Int J Comput Ass Radiol Surg 2010;5(4):369-84.

INRIA

Panel P, Bajka M, El Ghoneimi A, Chis C, Le Tohic A, Cotin S. Hysteroscopic placement of tubal sterilization implants: virtual simulator training. Surg Endosc 2012;26(7):1986-96.

Peterlik I, Duriez C, Cotin S. Constraint-based haptic rendering using deformable virtual mechanisms. IEEE Trans Haptics 2012;4(3):175-87.

Courtecuisse H, Jung H, Allard J, Duriez C, Lee DY, Cotin S. GPU-based real-time soft tissue Deformation with cutting and haptic feedback. Progr Biophys Molecul Biol 2010;103(2-3):159-68.

Peterlik I, Duriez C, Cotin S. Asynchronous haptic simulation of contacting deformable objects with variable stiffness. Proc IEEE Int Conf Intell Robot Syst (IROS) 2011; p. 2608-13.

Bilger A, Dequidt J, Duriez C, Cotin S. Biomechanical simulation of electrode migration for deep brain stimulation. Lect Notes Computer Sci 2012;6891:339-46.

UNIZA

Zaitseva E. Importance measures in reliability analysis of healthcare system. Adv Intell Soft Comput 2012; 98:119-133.

Zaitseva E, Levashenko V. Multi-state system analysis based on multiple-valued decision diagram. J Reliabil Stat Stud 2012;5:107-18.

Levashenko V, Zaitseva E. Fuzzy decision trees in medical decision making support system, Proc FedCSIS 2012; in press

Rusin M, Zaitseva E. Hierarchical heterogeneous ant colony optimization, Proc FedCSIS 2012; in press.

Levashenko V, Zaitseva E, Puuronen S, Fuzzy classified based on fuzzy decision tree. Proc IEEE EUROCON 2007; p.823-7.

KU LEUVEN

Allegaert K, Kulo A, Verbesselt R, Hopchet L, Deprest J, de Hoon J, Devlieger R, Van de Velde M. The pharmacokinetics of a high intravenous dose of paracetamol after caesarean delivery: the effect of gestational age. Eur J Anaesthesiol 2012; in press.

Heesen M, Klohr S, Hofmann T, Roissant R, Devroe S, Straube S, Van de Velde M. Maternal and foetal effects of remifentanil for general anaesthesia in parturients undergoing caesarean section: a systematic review and meta-analysis. Acta Anaesthesiol Scand 2012; in press.

Walters MA, Van de Velde M, Wilms G. Acute intrathecal haematoma following neuraxial anaesthesia: diagnostic delay after apparently normal radiological imaging. Int J Obstetric Anesth 2012;21:181-4.

Van de Velde M. Emergency Caesarean delivery: is supplementary maternal oxygen necessary? Brit J Anaesth 2009;102:1-2.

Van de Velde M, Berends N, Kumar A, Devroe S, Devlieger R, Vandermeersch N, De Buck F. Effects of epidural clonidine and neostigmine following intrathecal labour analgesia: a randomised, double-blind, placebo controlled trial. Intl J Obstetric Anesthesia 2009;18:207-14.

SINTEF

Lindseth F, Langø T, Selbekk T, Hansen R, Reinertsen I, Askeland C, Solheim O, Unsgård G, Mårvik R, Nagelhus Hernes TA. Ultrasound-based guidance and therapy., In: Gunarathne GPP (Ed.) Advancements and Breakthroughs in Ultrasound Imaging, InTech 2013; ISBN: 978-953-51-1159-7, DOI: 10.5772/55884.

Langø T, Vijayan S, Rethy A et al. Navigated laparoscopic ultrasound in abdominal soft tissue surgery - Technological overview and perspectives. Int J Comput Assist Radiol Surg 2012; 7(4): 585-99.

Langø T, Tangen GA, Mårvik R et al. Navigation in laparoscopy – Prototype research platform for improved image-guided surgery. Minim Invasive Ther Allied Technol, 2008; 17(1): 17-33.

Unsgård G, Solheim O, Lindseth F, Selbekk T. Intraoperative imaging with 3D ultrasound in neurosurgery. Acta Neurochirurgica 2011; 109(Suppl.): 181-6.

Reinertsen I, Jakola AS, Friderichsen P, Lindseth F, Solheim O, Selbekk T, Unsgård G.
A new system for 3D ultrasound-guided placement of cerebral ventricle catheters.
Int J Comput Assist Radiol Surg 2012; 7(1): 151-7. DOI: 10.1007/s11548-011-0622-0.

Gjerald SU, Brekken R, Hergum T, D'hooge J.
Real-time ultrasound simulation using the GPU.
IEEE Trans Ultrason Ferroelectr Freq Control. 2012; May; 59(5): 885-92.

SG

Polys NF, Ullrich S, Evestedt D, Wood AD, Aratow M. A fresh look at immersive volume rendering: challenges and capabilities Proc IEEE WIVI 2013; accepted.

Ullrich S, Kuhlen T, Polys NF, Evestedt D, Aratow M, John NW. Quantizing the void: extending Web3D for space-filling haptic meshes. Stud Health Technol Inform 2011;163:670-6.

5.2. Clinical trial protocols

5.2.1. Study Protocol – The RASimAs Project: (RASim) System

5.2.2. Study Protocol – The RASimAs Project: (RAAs) System

5.3. Informed consent form

5.3.1. Research Subject Information – The RASimAs Project: (RASim) System

5.3.2. Research Subject Information – The RASimAs Project: (RAAs) System

5.4. Insurance protection for clinical trial

-STUDY PROTOCOL-

-The RASimAs Project -

Evaluation of the Regional Anaesthesia Simulator (RASim) System

Version 02, Date 2013-06-23

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STUDY TITLE	**Evaluation of the Regional Anaesthesia Simulator (RASim) System**
SHORT NAME	**RASim**
CTC-A STUDY-NO	**12-165a**
STUDY DURATION	**Total duration:** 6 month
STUDY DESIGN	Open, multi-site, international, prospective, controlled, randomized cohort trial
LEGAL ASPECTS	Declaration of Helsinki ICH-GCP Data Protection Acts

INTRODUCTION

Regional anaesthesia (RA) has been used increasingly during the past two decades due to the perceived advantages of reduced postoperative pain, earlier mobility, shorter hospital stay, and significantly lower costs. Generally, RA is performed using electrical nerve stimulation and/or ultrasound-guided techniques. However, a safe performance of RA requires good theoretical, practical, and non-cognitive skills to allow trainees to achieve confidence in performing RA and to keep complications to a minimum. Current training methods for RA include cadavers, video teaching, ultrasound guidance, and simple virtual patient modelling. The advantage of using simulators in medicine is the creation of a realistic environment with standardized and reproducible scenarios without endangering patients. Despite the broad acceptance of virtual reality (VR) to educate trainees, the limited numbers of VR-based simulators for RA narrow their use for training purposes. Furthermore, current VR-based simulators for RA disregard individual patients' anatomy and also lack sufficiently realistic haptic feedback. Synergistically fusing results obtained from recent research in Europe, we propose a patient-specific flexible training environment with VR by using multimodal representations of both visual and haptics with intuitive interactions to from a plausible simulation. This simulator will be applicable to all body regions of relevance and will support RA training using electrical nerve stimulation, ultrasound guidance, or a combination of both. Relying on several general as well as patient specific Virtual Physiological Human (VPH) models of multiple variations of anatomy, the VR training system will be also applicable when lacking patient data. Realistic haptic feedback will be provided.

In Europe, the nature of postgraduate medical training is changing greatly with less teaching and learning hours available. This is partly due to the European Working Time Directive, the increase in transnational mobility of doctors (trainees and independent practitioners), altered patient expectations and new forms of governance of training and practice. One of the implications of these changes are that young doctors will acquire less 'hands-on' training during everyday work, in particular in psychomotor skills. This paradigm shift in medical education, towards 'competence-based training', where trainee doctors will have achieved a level of competency before they can perform on real patients, require new tools, educational theories, teaching techniques and curriculum. To allow trainees practical

training, currently several training methods for RA including cadavers, video teaching, ultrasound guidance, and simple virtual patient modelling are used.

Spinal anaesthesia and epidural blocks are two of the most frequently applied RA procedures. For this reason – and presumably since these procedures do not involve electric stimulation, as opposed to standard RA – there exist quite a number of simulators for these specific applications. At present only two simulators for peripheral RA are available or under development. One VR-based RA simulator is under development for the United States Army. This simulator uses a commercially available 3D virtual patient model dataset as basis. Muscle contractions and limb movements are induced by a very basic geometry-based nerve stimulation that is not described in detail. The second system is a commercialized simulator named SAILOR, which is distributed as a supplement to a multimedia atlas for nerve blocks. Although the approach comprises different procedures, they are limited to a single patient model and allow for mouse interaction only. SAILOR, however, does not support VR hardware that might have been used for intuitive input, haptic feedback, or stereoscopic rendering.

To overcome the constraints of these simulators, we have developed in an interdisciplinary approach a VR-based simulator on the basis of different patients' anatomies using MRI and magnetic resonance angiography (MRA) datasets of the inguinal region. The system is running in a virtual environment and utilizes stereoscopic rendering (for 3D perception) to enhance immersion. In addition, the simulator provides an intuitive six degrees of freedom (DOF) input for needle navigation. By simulating the electric impulse stimulation, both femoral and sciatic nerve blocks can be carried out. Furthermore, we aim at using our patient-specific models that have been generated for training in order to additionally improve the actual performance of RA procedures.

AIM OF STUDY

The aim of the study is the evaluation of the RASim system concerning self-directed learning and training including detection of errors and weak points, and the study of the learning curve. Results of this study will provide useful feedback based on actual performance and errors and will lead to improved and individualized training by adapting to a trainee`s previous performance and errors.

END POINTS/ PARAMETERS

The performance of regional anaesthesia after simulator-based training will be measured by several metric and ordinal scaled parameters including:

- Success rate to perform RA
- Time to identify and locate relevant anatomical structures
- Right positioning of the needle
- Time to perform a specific nerve block
- Time of onset of nerve block
- Acceptance of trainees of the VR-based simulator

STUDY POPULATION

20 first year anaesthetics trainees per study site (n = total of 60 trainees) will be included to

the study. After randomization, trainees will be allocated to the simulator group receiving simulation-based training or to the control group without simulation-based training.	
INCLUSION CRITERIA	• First year anaesthetics trainees • Male and female subjects above the age of 18 • Signed written informed consent prior to study participation
EXCLUSION CRITERIA	No exclusion criteria are defined.
RANDOMISATION	Subjects will be assigned to a specified "treatment" group or to a control group according to a random list, which will be generated in the study centre before the beginning of the study.

TREATMENT

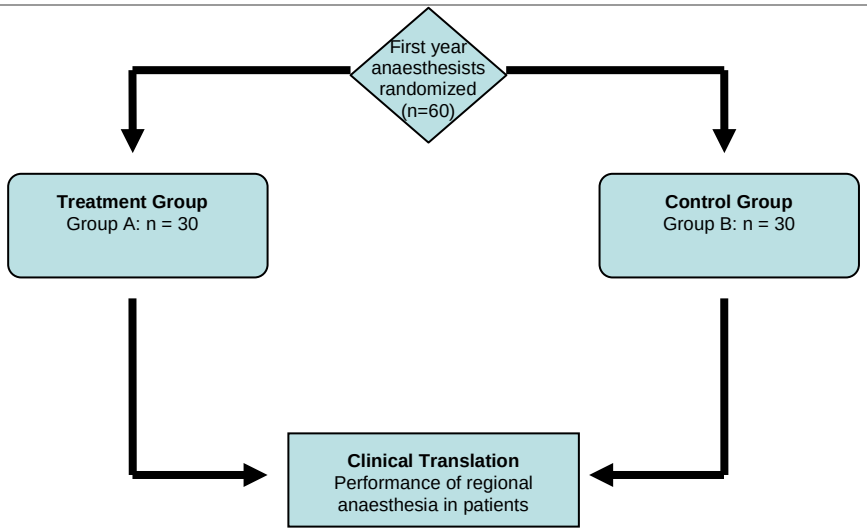
The treatment represents the performance of different several nerve blocks on the RA-simulator during 4 subsequent simulator sessions supervised by an experienced staff anaesthesiologist. To get familiar, each trainee randomized to the treatment group, will attend to individual simulation training.

Group A: Treatment group (n=30)

Group B: Control group without training sessions (n=30)

After completion of the treatment phase every study subject of each group will perform several nerve blocks in patients scheduled for elective surgery. For the upper extremity several approaches to the brachial plexus, including interscalene brachial plexus block, axillary block and infraclavicular block. For lower extremity RA the femoral nerve block, lumbar plexus block (posterior) and and popliteal fossa block will be performed.

All residents will be supervised and evaluated by blinded anaesthesiologists.



STUDY TERMINATION	The study can be prematurely terminated if one of the following aspects is applicable: • Non-adherence to the study protocol, the declaration of Helsinki, ICH-GCP and/or applicable regulatory requirements • Withdrawal of informed consent
DATA ENTRY	All data to be collected will be either entered on a case report form (CRF) and are to be considered source data or will directly be entered into a suitable data base.
DATA QUALITY	Standardization procedures will be implemented to ensure accurate, consistent, complete and reliable data, including methods to ensure standardization among the sites (e.g., training, newsletters, investigator meetings, monitoring, centralized evaluations, and validation methods). The monitors will be trained during a monitoring kick-off meeting. To prepare the investigators and to standardize performance a training will be held during an investigators' meeting before study start. This study will be monitored regularly by a qualified monitor from the Clinical Trial Center-Aachen (CTC-A) according to GCP guidelines and the respective SOPs of the CTC-A.
ETHICAL/ LEGAL ASPECTS	This study will be performed in accordance with the principles of good clinical practice based on the revised Declaration of Helsinki that guarantees high quality standards concerning the conduction of studies

	with clinical application. The project manager will contact every relevant Ethics Committee for requesting the Ethics Committee`s opinion. Subject inclusion will not be started until ethical approval is given. Changes in the protocol will not be made without favourable opinion of the Ethics Committee. The protocol and the Informed Consent Form with all information sheets will be presented to the EC as well before recruitment of study subjects will be started.

DATA PROTECTION

It is ensured that subject related data are not handed out to third parties.

All subjects will be identified by a unique randomization number. Each investigator holds a subject identification list according to the SOPs of the leading study site which will allow the identification of the subjects by holding information about the subject's personal data and randomization number. This list will be safely filed by the investigator in the investigator's file and a room/locker with limited access.

The subject's informed consent, which bears subject's printed name and signature will accordingly filed separately in the investigators file.

Access to non-coded data will be allowed solely to check validity and to guarantee a high qualitative study performance, and such access will be limited strictly to authorized individuals (e.g. monitors of the Clinical Trial Center-Aachen, Germany responsible for the quality management within this project to ensure quality criteria of objectivity, validity and reliability) who have been bound to confidentiality. If the results of the study are published, the subject's identity will remain confidential. Only anonymized data will be used for transfer to third parties and publication respectively.

The subject will be informed of procedures to protect subject privacy. Although recorded data will be passed on in a coded version only to authorized individuals, re-identification by the investigator will be possible by the study number assigned to the subject.

STATISTICS	Statistical analysis will be performed at the coordinating site in Aachen, Germany. Recorded datasets will be analysed descriptively by using location and dispersion parameters and different statistical correlation and conditional distributions.
PUBLICATION	A final study report will be written for this study, regardless of the outcome. The report will be compiled with the support of the principal investigator and submitted to the European Commission and the Ethics Committees that approved the study. This final report is to be available 6 months after receipt of the results of the statistical analysis. The study results will be published in an appropriate

	international journal and presented at international congresses.
INSURANCE	No insurance for study participants has been contracted. The study is not performed under the Drug Laws or under laws regulating medicinal products of the participating countries; therefore, no obligation for subject insurance is applicable. All physicians involved in the study will be insured for liability by their employers.
FINANCING	The study is part of the RASimAs project and financially supported by the *7th EU-Framework Programme.*

STATEMENT OF COMPLIANCE

Investigational Site(s)

I have thoroughly read and reviewed the study protocol. Having understood the requirements and conditions of the study protocol, I agree to perform the study according to the study protocol, the case report form, the Declaration of Helsinki and regulatory authority requirements (Data Protection Act).

I also agree to:

- Sign this study protocol before the study formally starts.
- Wait until I have received approval from the appropriate Ethics Committee before enrolling any subject in this study.
- Obtain informed consent for all subjects prior to any study-related action performed.
- Permit study-related monitoring and audits by the CTC-A as coordinating study center responsible for overall quality assurance
- Provide direct access to all study-related records, source documents, and subject files for the monitor, auditor or Ethics Committee upon request.

Furthermore, I understand that:

- the content of the study protocol is confidential and proprietary to the RASimAs Consortium
- any deviation from the study protocol may lead to the loss of high data quality needed for successful conduction and targeting of the study and its tasks.

With my signature below, I also acknowledge receipt of the study protocol.

SPONSOR`S REPRESENTATIVE

Verena Deserno Clinical Trial Center (CTC-A) University Hospital Aachen Germany	Aachen, Germany _____

COORDINATING INVESTIGATOR

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INVESTIGATOR

Prof. Dr. Marc van de Velde Department of Anaesthesia-Catholic University of Leuven Belgium	Leuven, Belgium _____

INVESTIGATOR

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-STUDY PROTOCOL-

-The RASimAs Project -

Evaluation of the Regional Anaesthesia Assistant (RAAs) System

Version 02, 2013-06-23

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ETHICS COMMITTEES

ETHICS COMMITTEE

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Ethics Committee of the Catholic University Leuven
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STUDY TITLE	**Evaluation of the Regional Anaesthesia Assistant System (RAAs)**
SHORT NAME	**RAAs**
CTC-A STUDY-NO	**12-165b**
STUDY DURATION	**Total duration:** 4 month **Duration for single patient:** 1 day
STUDY DESIGN	Open, multi-site, international, prospective, controlled, randomized interventional trial
LEGAL ASPECTS	➢ Declaration of Helsinki ➢ Medical Device Directives (MDD): • 93/42/EEC • 2007/47/EG ➢ National Acts on Medical Devices ➢ Relevant European Normatives • DIN EN ISO 13485 • DIN EN ISO 14971 • DIN EN ISO 62366 • DIN EN ISO 62304

INTRODUCTION

Regional anaesthesia (RA) is an anaesthesia method affecting a large part of the body, such as a limb or the lower half of the body. It is a technique used for surgical operations or for post operative pain relief. Regional anaesthetic techniques can be divided into central and peripheral techniques. The central techniques include the so called neuraxial blockade (epidural anaesthesia, spinal anaesthesia). The peripheral techniques can be further divided into plexus blocks such as brachial plexus blocks, and single nerve blocks. Regional anaesthesia may be performed as a single shot or with a continuous catheter through which medication is given over a prolonged period, e.g. continuous peripheral nerve block.

RA differs from Local Anaesthesia in which only a small part of the body, such as tooth or skin area are affected. On the other hand it differs from General Anaesthesia (GA) in which a medical coma is induced. Unlike general anaesthesia, with RA patients may remain awake during the procedure, resulting in reduced side-effects and enabling the surgeon to converse with the patient during the procedure if required. However, many patients prefer to receive sedation either during the block, the procedure, or both. Furthermore all side effects related to general anaesthesia, and which can be severe, are avoided. A safe performance of RA requires good theoretical, practical, and non-cognitive skills to allow trainees to achieve confidence in performing RA and to keep complications to a minimum. The RASimAs Group proposes an innovative approach where the patient-specific models

generated by the Regional Anaesthesia Simulator for training (Phase 1 of the RASimAs project) are used to develop the Regional Anaesthesia Assistant, in order to improve the actual performance of RA procedures (Phase 2). In this second part of the RASimAs project, we will develop a needle tracking system for assisted RA. The underlying framework will consist of a number of patient datasets retrieved from magnetic resonance imaging (MRI) and computed tomography (CT) scans. If medical images generated during routine diagnosis procedures are available for single patients, they will be applicated to the RAA system and used for guidance. RAA-guided support in patients where medical images are not available will be performed by using a generated patient-specific model. In ealier stages of the project a library existing of a collection of fully anonymized MRI and CT images from clinical and research will be developed to assemble different patient-specific models. Next to real-time ultrasound imaging the pre-recorded datasets will be displayed to guide the trainee while performing the RA. The required registration of pre-achieved and real-time achieved data is supported by Virtual Physiological Human (VPH) models.

The combination of pre-calculated needle adjustments based on the datasets will allow the trainee to guide the needle within a restricted area to find the right position for the RA.

AIM OF STUDY

The study will give evidence for the functionality of the usage of RAAs in the clinical application. Clinical application of the assistant system is needed as most important step for assessment of the proof-of-principle.

ENDPOINTS

Several parameters will be detected to evaluate and assess the performance of RA with or without guidance of the physicians by RAAs:

- Time to identify and locate relevant anatomical structures
- Time to perform a specific nerve block
- Success rates to perform RA (number of attempts)
- Time of onset of nerve block

STUDY POPULATION

Recruitment phase is stopped after inclusion of 40 patients providing fully analysable datasets (successfully performed regional anaesthesia). Female and male patients will be included equally. The collective consists of patients who are presented to the department of anaesthesia for regional anaesthesia due to elective surgery.

INCLUSION CRITERIA	• Patients scheduled for elective surgery and requiring regional anaesthesia • American Society of Anaesthesiologists (ASA) classification I-III • Male and female patients aged 18 years or above • Written informed consent prior to study participation
EXCLUSION CRITERIA	• Patients undergoing emergency procedures • Patients with contraindications to regional anaesthesia •

	• Allergy against local anaesthetics • History of bleeding tendency (e.g. von-Willebrand-disease, thrombocytopenia) or anticoagulant therapy • American Society of Anaesthesiologists (ASA) classification greater than III • Diseases of the CNS • Alcohol or drug abuse • Expected non-compliance • Patients unwilling or unable to give informed consent, patients with limited ability to comply with instructions for this study and limited contractual capability • Patients who are committed to an institution and/or penitentiary by judicial or official order. • Employees and other dependents of the investigator
NUMBER OF PATIENTS	Patients will be recruited equally by the three participating study sites until 40 individual evaluably datasets are reached in total.
RANDOMIZATION	Patients will be assigned to a specified “investigational group” or to a “control group” according to a random list, which will be generated in the study center before the beginning of the study.

DEVICES

The regional anaesthesia assistant system (RAAs) is developed as a portable prototype. 3D display devices are provided to the physicians, where additional information is displayed during the procedure. In particular, the ultrasound image that is acquired by the physician is mapped onto the 3D model of the subject to support a better orientation and localization of structures during the RA procedure. The assistant system is additional, that means the information that would be available to the physician during the intervention without the RAAs system will be available also, without any alteration.

INFORMED CONSENT

The patients screened for this study will voluntarily confirm their willingness to participate in the trial, after having been informed by a physician in writing and verbally of all aspects of the trial that are relevant to the subject's decision to participate. The study doctor will explain that non-participating and withdrawal of consent will not lead to any disadvantages for further treatment. The information about the elective procedure in general and the information about the clinical investigation will be done separately and by two different physicians. The study subjects will have at least 24 hours or longer to decide wether to participate or not. The study doctor and the study team respectively will be available to answer any questions.

They will be informed about requirements concerning data protection and have to agree to the direct access to their individual data. Subjects will be informed that they are free to withdraw from the study at any time at their own discretion without necessarily giving

reasons.

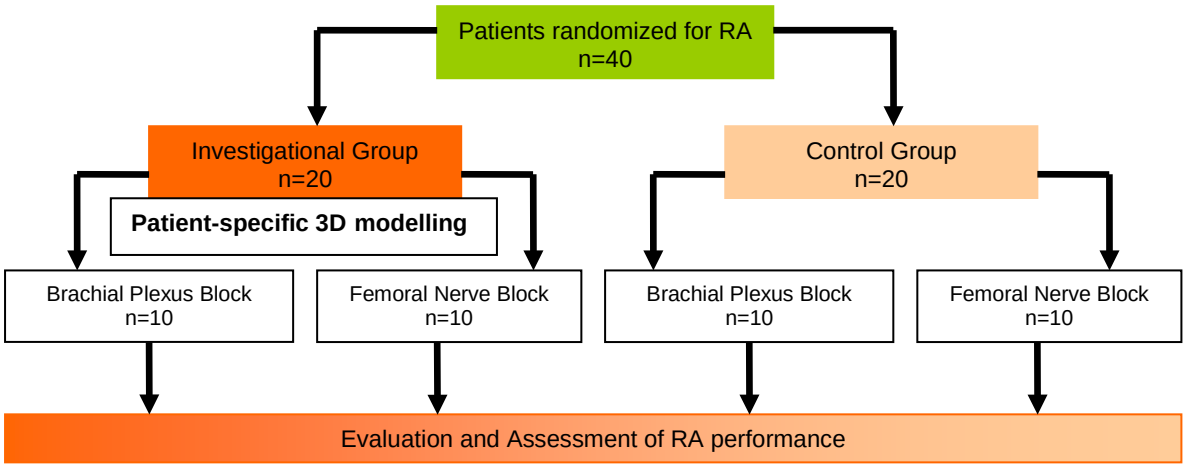
STUDY SCHEDULE

After signed written consent is obtained patients will be randomized to an investigational group or to the control group:

Investigational Group (n=20) → RA is performed by assistance of the Regional Anaesthesia Assistant system

Control Group (n=20) → RA performed soley due to the physicians experience and without additional information of a patient-specific 3D model generated by the RAAs

In each group two different nerve blocks will be assessed with an equal share. For the upper extremity the brachial plexus block and for the lower extremity the femoral nerve block will be performed.



STUDY TERMINATION	The study can be prematurely terminated if one of the following aspects is applicable: • Non-adherence to the study protocol, the declaration of Helsinki and/or applicable regulatory requirements • Missing compliance, patient does not follow instructions by the study team • Withdrawal of informed consent • Safety and well-being of the patients is not ensured any longer • Subject's enrolment is unsatisfactory • The risks and benefits of continuing the study have been reassessed, and the risk outweigh any potential benefits • The incidence of AEs constitutes a potential health

	hazard to the subjects
INCIDENTAL FINDINGS Incidental findings that are discovered unintentionally and are unrelated to the current medical condition and treatment being performed will be documented and communicated to the study subject. The study doctor is responsible to inform the subject and to initiate appropriate measures by directing the subject to a relevant site for further diagnostic and treatment procedures.	
BENEFIT-RISK-ASSESSMENT In conclusion, the sponsor believes this study to be carefully designed and expects ***no study related risks*** due to participating into this study. Regional anaesthesia will be performed within the ordinary health care and information about potential risks of conduction of regional anaesthesia will be done separately by a different physician. Therefor there will be no additional risks from undergoing the procedure within this trial. Only the RAA-guided support to perform RA will fall under the scope of investigation of this trial. Patients will not undergo any additional imaging procedure (MRI, CT) or treatments. Patients will be treated by senior anaesthesists who are extensively experienced in the performance of regional anaesthesia. Potential risks related to regional anaesthesia in common will be explained to the patients during the routine standard procedures that are applicable in the hospital. Maybe, there will be no benefit for the single patient but evaluation of the regional anaesthesia assistant will improve performance and management of regional anaesthesia in common. We expect to improve the quote of success of RA and evade general anaesthesia in many cases.	
DATA ENTRY	All data to be collected will be either entered on a case report form (CRF) and are to be considered source data or will directly be entered into a suitable data base. Automatic print outs as well as patient records and electronic patients are considered source data. The investigator will keep the subject's files and original data as long as possible and according to the local methods and facilities. The investigator should maintain the trial documents as specified in the ICH-GCP-Guideline. The investigator/institution should take measures to prevent accidental or premature destruction of these documents. Study documents may not be destroyed by study site personnel prior to the retention period specified above without the prior written consent of the sponsor. The principal investigator must inform the sponsor in due time if the principal investigator leaves the institution during the retention period. This rule also applies when the institution closes within the retention period.
DATA QUALITY	Standardization procedures will be implemented to ensure accurate, consistent, complete and reliable data, including methods to ensure standardization among sites (e.g., training, newsletters, investigator meetings, monitoring, centralized evaluations, and validation methods). Quality criteria as objectivity,

	validity and reliability will be applicable at any time of data collection. It is the responsibility of the study sponsor to ensure that proper monitoring of this investigation is conducted. Appropriately trained personnel appointed by the Clinical Trial Center Aachen (CTC-A) will conduct monitoring activities, as needed. The monitors will be trained during a monitoring kick-off meeting. To prepare the investigators and to standardize performance a training will be held during an investigators' meeting before study start. This study will be monitored regularly by a qualified monitor from the CTC-A according to GCP guidelines and the respective SOPs of the CTC-A.
ADVERSE EVENTS	Adverse Events and Serious Adverse Events will be documented, assessed and reported according to the SOPs of the CTC-A.
ETHICAL/ LEGAL ASPECTS	The study is conducted according to the ethical principles that have its seeds in the Declaration of Helsinki. The quality management system (QMS) of the CTC-A implements all requirements needed for planning, conduction and completion of ICH-GCP conformable clinical studies. The QMS applies to all relevant ethical and legal aspects. Approvals will be obtained from all relevant Competent Authorities and responsible Ethics Committees for each site prior to the commencement of this study and submitted to the European Commission (EC). The protocol and the Informed Consent Form with all information sheets will be presented to the EC as well before recruitment of study subjects will be started.
PATIENT IDENTIFICATION	A patient identification code list that identifies the patient by number, name and date of birth is kept and maintained at the study site. Only the study team has access to the identification code list. Copying is not allowed at any time.

DATA PROTECTION

It is ensured that subject related data are not handed out to third parties.

All subjects will be identified by a unique randomization number. Each investigator holds a subject identification list according to the Sponsors SOP which will allow the identification of the subjects by holding information about the subject's personal data and randomization number. This list will be safely filed by the investigator in the investigator's file and a room/locker with limited access.

The subject's informed consent, which bears subject's printed name and signature will accordingly filed separately in the investigators file.

Access to non-coded data will be allowed solely to check validity and to guarantee a high qualitative study performance, and such access will be limited strictly to authorized individuals (e.g. monitors of the Clinical Trial Center-Aachen, Germany responsible for the

quality management and coordination of this study) who have been bound to confidentiality. If the results of the study are published, the subject's identity will remain confidential. Only anonymised data will be used for transfer to third parties and publication respectively. The subject will be informed of procedures to protect subject privacy. Although recorded data will be passed on in a coded version only to authorized individuals, re-identification by the investigator will be possible by the study number assigned to the subject.	
STATISTICS	Statistical analysis will be performed at the coordinating site in Aachen, Germany.
PUBLICATION	The study results will be published in an appropriate journal. The Ethics Committees will be informed about the study results.
INSURANCE	For the planned clinical trial in patients undergoing RA, the study will be performed under the regulations of the European Medical Device Directive (and the local medical device acts, respectively). An appropriate insurance will be contracted by the sponsor RWTH Aachen University with HDI Gerling, taking into account the respective requirements of each countries site. In the case of fault-based incidences the patients are insured by the general liability insurance of each. participating study sites.
FINANCING	The study is part of the RASimAs project and financially supported by the *7th EU-Framework Programme.*

STATEMENT OF COMPLIANCE

Investigational Site(s)

I have thoroughly read and reviewed the clinical study protocol. Having understood the requirements and conditions of the clinical study protocol, I agree to perform the clinical study according to the clinical study protocol, the case report form, European Medical Device Directives (MDD: 93/42/EEC and 2007/47/EG), German Medical Device Act (MPG), European Normatives (DIN EN ISO 13485; 14971; 62366), the Declaration of Helsinki and the international guideline for Good Clinical Practice (ICH-GCP).

I also agree to:

- Sign this clinical study protocol before the study formally starts.
- Wait until I have received approval from the appropriate Ethics Committees before enrolling any subject in this study.
- Obtain informed consent for all subjects prior to any study-related action performed.
- Start the study only after all legal requirements in my country have been fulfilled and approved.
- Permit study-related monitoring and audits by the CTC-A as the sponsor`s representative.
- Provide direct access to all study-related records, source documents, and subject files for the monitor, auditor, IEC/IRB, or regulatory authority upon request.
- Report to the sponsor, within 24 hours, any adverse event (AE) that is serious, whether considered treatment related or not

Furthermore, I understand that:

- changes to the clinical study protocol must be made in the form of an amendment that has the prior written approval of the appropriate Ethics Committee
- the content of the clinical study protocol is confidential and proprietary to the RASimAs Consortium
- any deviation from the clinical study protocol may lead to early termination of the study site.

With my signature below, I also acknowledge receipt of the study protocol.

SPONSOR`S REPRESENTATIVE

Verena Deserno Clinical Trial Center (CTC-A) University Hospital Aachen Germany	Aachen, Germany _____

COORDINATING INVESTIGATOR

Prof. Dr. med. Rolf Rossaint Department of Anaesthesia- University Hospital Aachen Pauwelsstr. 30 52074 Aachen Germany	Aachen, Germany _____

INVESTIGATOR

Prof. Dr. Marc van de Velde Department of Anaesthesia-Catholic University of Leuven Belgium	Leuven, Belgium _____

INVESTIGATOR

Dr. Brian o`Donnell Department of Anaesthesia-University College Cork Ireland	Cork, Ireland _____

Research Subject Information and Informed Consent Form

-The RASimAs Project -

Evaluation of the Regional Anaesthesia Simulator (RASim) System

Version 02, 2013-06-23

Study Short Name: RASim

Sponsor Study No.: 12-165a

Study Sponsor: RWTH Aachen University for the Medical Faculty,
represented by the Clinical Trial Center Aachen (CTC-A),
Pauwelsstraße 30, 52074 Aachen, Germany
T:+492418080092
F:+49241803380092
E-Mail: vdeserno@ukaachen.de

Coordinating Investigator: Univ.-Prof. Dr. med. Rolf Rossaint
Department of Anaesthesiology,
RWTH Aachen University Hospital
Pauwelsstraße 30, 52074 Aachen, Germany,
T:+492418088179
F:+49241882406
E-Mail: anaesthesiologie@ukaachen.de

Dear Ladies and Gentlemen,

This form describes a type of research study concerning new methods of occupational training of regional anaesthesia. The study is voluntary and it is your option to take part. This form explains the study. The last page asks you to make a decision to participate or not.

Some of the information is required by law. The study will be performed equally at three European study sites (Germany, Belgium and Ireland). 60 first year anaesthetics will be included in this study

This form has been reviewed by the responsible local ethics (as an independent committee that reviews the ethical aspects of research studies to help protect the rights and welfare of study participants):

Germany:
Ethics Committee of the University Hospital RWTH Aachen
Chairman: Prof. Dr. med. G. Schmalzing
Pauwelsstr. 30
52074 Aachen, Germany
Fon: +49 241 80 89963
Fax: +49 241 80 82012

Belgium:
Ethics Committee of the Catholic University Leuven
Commissie Medische Ethiek/Klinisch Onderzoek
Chairman: Prof. Dr. W. Van den Bogaert
Herestraat 49
3000 Leuven, Belgium
Fon: +3216348600
Fax: +3216348601

Ireland:
Ethics Committee of the Cork Teaching Hospitals Research
Chairman: Dr. Michael Hyland
Lancaster Hall,
6 Little Hanover Street,
Cork, Ireland
Fon: +353 21 4903500
Fax: +353 21 4903506

Subject Initials_____

1 WHAT IS "CONSENT"

It is voluntary and represents your choice to participate in a study. If you decide to participate, you must initial each page of this form and sign and date the last section of the form. Your signature confirms you understand and wish to participate in the study.

It is important to make your decision after the following:

1. Study staff personnel have explained the study to you (including objectives of the study, data to be collected, protection of privacy)
2. You must understand the purpose of the study and the risks
3. You are willing to complete all visits and procedures for the duration of the study.

Take as much time as you need to decide. Study staff will be available for all concerns or questions.

You may decide to stop your participation at any time throughout the study, even if you have signed this form.

There are no disadvantages for you if you decide not to take part or to stop participation after signed informed consent.

2 BACKGROUND

Regional anaesthesia (RA) has been used increasingly during the past two decades. The advantages of RA include:

- Reduction in morbidity and mortality
- Earlier mobility
- Superior postoperative analgesia
- Shorter hospital stay
- Enhanced cost-effectiveness

The performance of RA necessitates blocking the peripheral nerves by local injection of anaesthetic. Clinically this is achieved by the insertion of the injection needle close to the peripheral nerve, which is visualized with ultrasound and/or the proximity of the needle to the nerve is assessed with an electric nerve stimulator. This technique requires good theoretical, practical, and non-cognitive skills to allow trainees to achieve confidence in performing regional anaesthesia and to keep complications to a minimum. Current training methods for RA include cadavers, video-teaching and simple virtual patient modeling. These techniques have their limited capabilities and do not consider individual anatomy. An individualized virtual-reality-based simulator for RA as a training tool for both visualization by ultrasound and electrical nerve stimulation is developed as portable and inexpensive technological platform within the **RASimAs** Project funded by the the *7th EU-Framework Programme.* The simulator will enrich realistic training with haptic feedback to the trainees. The advantage of using simulators in medicine is the creation of a realistic environment with standardized and

Subject Initials_____

reproducible scenarios without endangering patients. Despite the broad acceptance of virtual reality (VR) to educate trainees, the limited numbers of VR-based simulators for RA narrow their use for training purposes. Furthermore, current VR-based simulators for RA disregard individual patients anatomy and also lack sufficiently realistic haptic feedback. One aim of the RASimAs project is the development of a specific flexible training environment with VR by using multimodal representations of both visual and haptics with intuitive interactions to form a plausible simulation. This simulator will be applicable to all body regions of relevance and will support RA training using electrical nerve stimulation, ultrasound guidance or a combination of both. Relying on several standard models of multiple variations of anatomy, the VR training system will be also applicable when lacking patient data. Realistic haptic feedback will be provided.

3 THE PURPOSE OF THIS STUDY

The purpose of this study is to evaluate the effectiveness of the VR-simulator developed during the RASimAs project as a new training tool for performing different regional anaesthesia (RA) techniques.

It is important to see how trainees in regional anaesthesia will respond to this training treatment by monitoring the quality of performed regional anaesthesia in patients after training sessions.

4 OBJECTIVES

Primary objective of the study is to evaluate the success rate to perform RA. Indicators for success will be:

- Time to identify and locate relevant anatomical structures
- Right positioning of the needle
- Time to perform a specific nerve block
- Time of onset of nerve block

Secondary objective is to evaluate the acceptance of the trainees of the VR-simulator.

5 STUDY "TREATMENT" AND SCHEDULE

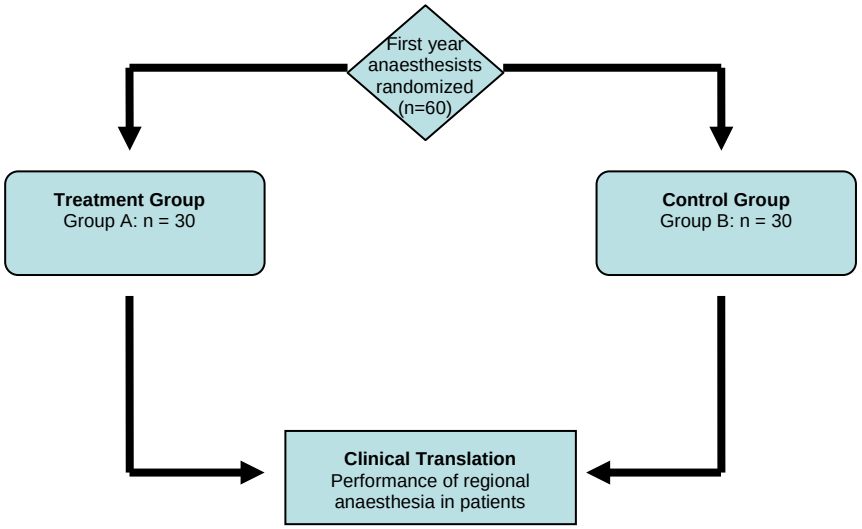
The treatment represents the performance of different several nerve blocks on the RA-simulator during 4 subsequent simulator sessions supervised by an experienced staff anaesthesiologist. To get familiar, each trainee randomized to the treatment group, will attend to individual simulation training.

Group A: Treatment group (n=30)

Group B: Control group without training sessions (n=30)

Subject Initials_____

After completion of the treatment phase every study subject of each group will perform several nerve blocks in patients scheduled for elective surgery. For the upper extremity nerve blocks will be performed to the brachial plexus, including interscalene brachial plexus block, axillary block and infraclavicular block. The femoral nerve block will be performed for the lower extremity. All residents will be supervised and evaluated by blinded anaesthesiologists.



6 WHAT AM I EXPECTED TO DO IN THE STUDY?

Total duration of the study is 6 months at three study sites located in Germany, Belgium and Ireland. Every study participant randomized to the treatment group will take part in four different training sessions that are supervised by an experienced staff anaesthesiologist. After training sessions completed the trainees will perform regional anaesthesia at different body regions in patients. This will be done under supervision and evaluation of experienced and blinded senior anaesthesists. Duration for the single study participant will be four weeks.

7 STUDY RESULTS

The results of the study will be evaluated by statisticians at the coordinating site (Aachen, Germany). All data will be reviewed and used for future developments. The study results will be published in an appropriate international journal and presented at international congresses.

Subject Initials_____

8 TERMINATION OF THE STUDY

Your participation in the research study is voluntary. If you decide not to participate in the study, you will not be penalized or lose any benefits to which you are entitled. You may choose to stop your participation at any time as well, without giving a reason. Your decision will not affect the future medical education you receive.

If you decide to withdraw from the study, it is important to contact the study staff and inform them of your decision. All personal data collected previously will be deleted.

9 BENEFITS

Learning of regional anaesthetic techniques by using electric nerve stimulation as well as using ultrasound-guided nerve blocks require extensive experience obtainable by training and instruction by an expert for regional anaesthesia. In this study, you have the possibility for extensive training and involvement to perform several nerve blocks in patients under supervision of specialized anaesthesists independent of which group you are allocated to.

10 EXPENSES

There will be no cost to you to participate in the study.

11 INSURANCE

No insurance for study participants has been contracted. The study is not performed under the Drug Laws or under laws regulating medicinal products of the participating countries; therefore, no obligation for subject insurance is applicable. All physicians involved in the study are insured for liability by their employers.

12 QUALITY ASSURANCE

The study will be performed in accordance with the Declaration of Helsinki and in Good Clinical Practice (GCP) Guidelines. Standardization procedures will be implemented to ensure accurate, consistent, complete and reliable data. Therefore this study will be conducted accordingly to the quality management system of the Clinical Trial Center-Aachen (CTC-A), University Hospital Aachen, Germany as coordinating study site.

The quality management system of the CTC-A implements all requirements for planning, conduction, evaluation and termination of clinical trials according to all relevant ethical and legal claims. Data will be also monitored by the CTC-A.

Subject Initials_____

13 CONFIDENTIALITY

You will be identified only by a specific study identification number. The information contained in the study records will be kept as confidential as possible within the law. The results of the study may be published or presented for scientific purposes, but your identity will not be revealed. Your personal information will be kept in a secure file.

Your study information will be used in two ways.

1. Study Management – Information collected will be checked at the clinic to make sure the study is being run correctly and completed properly.
2. Study Findings – Information about you will be combined with information about other people in the study. This study information will be used to learn about the regional anaesthesia simulator. All information will be coded to maintain confidentiality.

When you sign this consent form, you are agreeing to have your personal information used as described in this consent form.

Do not sign this consent form unless you have had a chance to ask questions and have received satisfactory answers to all of your questions.

If you agree to participate in this study, you will receive a copy of the signed and dated consent form for your records.

Subject Initials_____

By signing below, I show that:

1. I have read this form and understand the study
2. I have discussed the study, asked questions and I'm satisfied with the answers
3. I have had time to make my decision
4. I agree to take part in the study
5. I have been given names of study staff who I can call
6. I agree that the study staff and others may have access to my personal information, as described in this consent form
7. I have received a copy of the informed consent form

YES □ **NO** □

Printed Name of Study Participant:

_____

Subject Signature: Date:

_____ _____

DDMMMYYYY

Printed Name of Person Conducting Informed Consent Discussion:

_____

Subject Initials_____

Statement of Investigator

(Investigator must sign the consent form on the same date as the subject)

I acknowledge my responsibility for the care and well-being of the above subject, to respect the rights and wishes of the subject and to conduct the study according to applicable Good Clinical Practice Guidelines and regulations.

Printed Name of Investigator:

_____

Investigator Signature: Date:

_____ _____

DDMMMYYYY

Subject Initials_____

Research Subject Information and Informed Consent Form

- The RASimAs Project -

Evaluation of the Regional Anaesthesia Assistant (RAAs) System

Version 02, Date 2013-06-23

Study Short Name: RAAs

Sponsor Study No.: 12-165b

Study Sponsor: RWTH Aachen University for the Medical Faculty,
represented by the Clinical Trial Center Aachen (CTC-A),
Pauwelsstraße 30, 52074 Aachen, Germany
T: +492418037238
F: +49241803380092
E-Mail: vdeserno@ukaachen.de

Coordinating Investigator: Univ.-Prof. Dr. med. Rolf Rossaint
Department of Anaesthesiology, RWTH Aachen University Hospital
Pauwelsstraße 30, 52074 Aachen, Germany,
T:+4924180 88179
F:+4924180 82406
E-Mail: rrossaint@ukaachen.de

Dear Patient,

This form describes a clinical trial, a type of research study that will be conducted at three different study sites in three European Countries (Germany, Belgium and Ireland).

Your study doctor will explain the study to you. The study is voluntary and it is your option to take part. This form explains the study. The last page asks you to make a decision to participate or not. Law requires some of the information.

This form has been reviewed by the responsible local ethics (as an independent committee that reviews the ethical aspects of research studies to help protect the rights and welfare of study participants):

Germany:
Ethics Committee of the University Hospital RWTH Aachen
Chairman: Prof. Dr. med. G. Schmalzing
Pauwelsstr. 30
52074 Aachen, Germany
Fon: +49 241 80 89963
Fax: +49 241 80 82012

Belgium:
Ethics Committee of the Catholic University Leuven
Commissie Medische Ethiek/Klinisch Onderzoek
Chairman: Prof. Dr. W. Van den Bogaert
Herestraat 49
3000 Leuven, Belgium
Fon: +32 16 34 86 00
Fax: +32 16 34 86 01

Ireland:
Ethics Committee of the Cork Teaching Hospitals Research
Chairman: Dr. Michael Hyland
Lancaster Hall,
6 Little Hanover Street,
Cork, Ireland
Fon: +353 21 4903500
Fax: +353 21 4903506

Subject Initials_____

1 WHAT IS "CONSENT"

It is voluntary and represents your choice to participate in a clinical study. A study doctor will inform you about the study and your participation separately from the information about the procedure of regional anaesthesia as necessary therapeutical procedure. That will be done by a different doctor. If you decide to participate, you must initial each page of this form and sign and date the last section of the form. Your signature confirms you understand and wish to participate in the study. It is important to make your decision after the following:

1. Study staff personnel have explained the study to you
2. You must understand the purpose of the study and the risks and
3. You are willing to complete all visits and procedures for the duration of the study.

You should take this form home with you to discuss with family, friends, a medical professional or any other person you feel comfortable with to help you make your decision. You will have at least 24 hours and as much time as you need respectively to decide wether to participate in this clinical investigation or not. The study staff will be available for all concerns or questions.

You may decide to stop your participation at any time throughout the study, even if you have signed this form. The study doctor may withdraw you from the study if it is in your best interest. There will be no disadvantages arising for you if you don`t want to participate or if you withdraw your consent.

2 STUDY BACKGROUND

2.1 WHAT IS REGIONAL ANAESTHESIA?

Regional anaesthesia is a technique to sedate large part of the body without loosing consciousness. It is different from the local anaesthesia that affects only small parts of the body such as tooth for example. In many cases general anaesthesia could be avoided and regional anaesthesia is the method of choice. The conduction of regional anaesthesia entails a lot of advantages compared to general anaesthesia.

<u>Outstanding benefits for the patients are:</u>

- Longer pain suppression, that can be maintained over several days which is important in patients who have to be treated postoperatively with physiotherapy
- Less cardiovascular stress
- Shortened length of hospital stay
- no loss of consciousness
- no necessity of ventilation
- no risk of aspiration
- less risk of postoperative sickness and minimized probability for adverse drug reactions or allergies

Subject Initials_____

For the successful performance of regional anaesthesia the physician has to position the needle for injection of the narcotic drug very close to the nerve to block feeling of pain of a body region. The physician can be supported by ultrasound techniques to localize the course of nerves and to position the needle correctly. But besides this technical support a strong knowledge of anatomical structures and strong experience is still needed for the performance of regional anaesthesia.

3 WHO CAN PARTICIPATE INTO THIS STUDY?

Every patient that is foreseen to receive a regional anaesthesia within the regular medical care and fulfilling the inclusion and exclusion criteria is allowed to participate into this study.

3.1 INCLUSION CRITERIA

- Patients scheduled for elective surgery and regional aneasthesia
- Male and female patients aged 18 years or above
- Written informed consent prior to study participation

3.2 EXCLUSION CRITERIA

- Patients undergoing anticoagulant therapy
- Hypersensitivity against local anaesthetics
- Diseases of the CNS
- Alcohol or drug abuse
- Expected non compliance
- Patients unwilling or unable to give informed consent, patients with limited ability to comply with instructions for this study
- Patients who are committed to an institution and/ or penitentiary by judical or official order
- Employees and other dependents of the investigator

4 WHO SHOULD I CALL IF I HAVE ANY CONCERNS OR QUESTIONS?

4.1 STUDY PRINCIPLE INVESTIGATOR

You may speak with the study doctor or study staff about concerns or questions you have. Prof. <*place to enter Name of Investigator*> number is <*place to enter number*>.

4.2 CONTACT POINT FOR PEOPLE INVOLVED IN CLINICAL TRIALS

Please contact the Competent authority, who is not affiliated with the study or the study team, if you:

Subject Initials_____

1. Have questions about your role and rights as a research study participant
2. Wish to obtain more information about general clinical research
3. Have concerns, complaints or general questions about the research study
4. Wish to provide input and feedback about the research study.

The address of the contact point at the Competent Authority for people involved in a clinical trial, their legal representative or one of their authorised representatives is as follows:

<Place to enter respective national CA>

5 THE PURPOSE OF THIS STUDY

You are being invited to participate in this study sponsored by RWTH Aachen University for the Medical Faculty located in Aachen, Germany because you will receive a regional anaesthesia. This study is part of an EU- funded project entitled “RASimAs” that aims to improve training and performance of regional anaesthesia by computer- based simulation and guiding systems. To improve and enhance the performance of regional anaesthesia computer- based training simulators and assistant systems are developed. In this systems medical images of specific tissue structures of the individual patient will be saved and can be combined with ultrasound pictures of the same body region to estimate the best point to place the needle for injection. The purpose of this study is to test the effectiveness of the developed computer- based assistant system.

It is planned to include a total number of 40 patients in this study.

6 STUDY TREATMENT

The procedure of the regional anaesthesia itself is not the objective of this study. If you choose to participate into this study you will be directed either to the investigational group or to the control group by random choice.

6.1 CONTROL GROUP

Patients directed to the control group will receive regional anaesthesia where the physician without support of the Regional Anaesthesia Assistant System performs the positioning of the needle to inject the anesthetic drug.

6.2 INVESTIGATIONAL GROUP

Patients directed to the investigational group will receive regional anaesthesia where the positioning of the needle to inject the narcotic drug is performed by the physician under guidance of the Regional Anaesthesia Assistant System (RAAs). No procedures for diagnosis or treatment will be undertaken within this study.

Subject Initials_____

7 OBJECTIVES

This study is conducted to show if the performance of regional anaesthesia will be improved by using RAAs. Therefore the investigators will examine measure the time that is necessary to identify the optimal position point of the needle, the time to perform a specific nerve block and the time of onset of nerve block.

8 BENEFIT & RISK EVALUATION

There is no direct guaranteed benefit if you decide to participate in this study. The information collected during this study will help for further improvement of regional anaesthesia as a still established anaesthesia technique.

The regional anaesthesia will be undertaken for therapeutical reasons. Study participating therefore does not cause any risks in addition. Information about potential risks related to regional anaesthesia will be done separately within the clinical routine processes by a different physician. Patients will be treated by senior anaesthesists who are extensively experienced in the performance of regional anaesthesia.

9 DO I HAVE TO STAY IN THE STUDY?

Your participation in the research study is voluntary. If you decide not to participate in the study, you will not be penalized or lose any benefits to which you are entitled. You may choose to stop your participation at any time as well, without giving a reason. Your decision will not affect the future medical care you receive.

If you decide to withdraw from the study, it is important to contact the study staff and inform them of your decision.

We may ask you to leave the study if:

1. You do not follow instructions for treatment and follow up visits
2. A new health problem during the study
3. The study doctor thinks it is in your best interest to stop
4. You do not consent to changes made to the study plan.

The Sponsor (RWTH Aachen University for the Medical Faculty), regulatory authority or the study doctor may choose to stop the study at any time. If this occurs, we will give you the reason at that time.

Subject Initials_____

10 WHAT HAPPENS IF I LEAVE THE STUDY?

If you decide to leave the study no more information will be collected for the study. However, all personal data collected previously will be deleted.

We will not perform any genetic analysis, which possibly could lead to misuse of personal genetic information. In general, it is possible that genetic information could be used to deny access to employment or insurance or lead to discrimination. Since we do not perform any genetic testing, no special precautions to keep your genetic information confidential are needed.

11 WILL I RECEIVE PAYMENT FOR PARTICIPATING IN THE STUDY?

Payment for participating in the study is not foreseen.

12 WILL THERE BE ANY EXPENSES FOR ME TO PARTICIPATE IN THE STUDY?

All procedures will be at no cost to you, the public health plan or your private medical insurance (if applicable).

13 SUBJECT INSURANCE

If you suffer any injury as a direct result of you participating, necessary medical treatment will be available at no charge to you. By signing this consent form you are not waiving your legal rights or releasing the study doctor or sponsor form their legal and professional responsibilities.

A special patient insurance according to the European Medical Device Directive has been contracted with Gerling Konzern Industrie Versicherungs-AG, Am Schönenkamp 45, 40599 Düsseldorf T:+49 211 7482-5404, F:+49 211 7482-465. The insurance number is XXXX. The maximum amount of coverage per study subject for this study is 500.000 €.

<Or adjust to the applicable study site in Belgium or Ireland>

The insurance will cover the time period that the patient participates in the trial. During the study the patients involved are obliged to comply with the following rules: a) to come for regular visits at the date advised, b) to comply with the orders of the investigator, c) to report immediately to the investigator any changes in any medication, d) to contact the investigator in case of health problems.

14 QUALITY ASSURANCE

The study will be performed in accordance with the Declaration of Helsinki and Good Clinical Practice (GCP) Guidelines. All information collected must be standardized terminology and

Subject Initials_____

processes of the collection of accurate, consistent and reliable data. This study will be performed according to valid standard operating procedures of the clinics and sponsor. Data will be monitored by IMI, Institute of medical informatics, RWTH Aachen University, Germany.

15 CONFIDENTIALITY

Your medical records pertaining to participation in this study will be available for review by RWTH Aachen (Sponsor of the study) and the IMI, Institute of medical informatics, RWTH Aachen University, Germany and governmental agencies that are involved in the evaluation of new medical devices. However, you will be identified only by a specific study identification number. The information contained in the study records will be kept as confidential as possible within the law. The results of the study may be published or presented for scientific purposes, but your identity will not be revealed. Your personal information will be kept in a secure file and kept for 25 years as per regulatory guidelines.

Your study information will be used in two ways.

1. **Study Management** – Information collected will be checked at the clinic to make sure the study is being run correctly and completed properly. People who work for the sponsor and others (ethics boards or government officials that approve new drugs and devices, such as <choose BfArM or FHAMP or IMB> may check how the study is being conducted. All information will be kept confidential.
2. **Study Findings** – Medical information about you will be combined with information about other people in the study . This study information will be used to learn about the study medical device/procedure. All information will be coded to maintain confidentiality.

When you sign this consent form, you are agreeing to have your personal and medical information used as described in this consent form.

Do not sign this consent form unless you have had a chance to ask questions and have received satisfactory answers to all of your questions.

If you agree to participate in this study, you will receive a copy of the signed and dated consent form for your records.

Subject Initials_____

By signing below, I show that:

1. I have read this form and understand the study
2. I have discussed the study, asked questions and I'm satisfied with the answers
3. I have had time to make my decision
4. I agree to take part in the study
5. I have been given names of study staff who I can call
6. I agree that the sponsor, study staff and others may have access to my medical and personal information, as described in this consent for
7. I agree that the study doctor or study staff may tell my doctor or other medical professionals that I am taking part in this study.
8. I have received a copy of the informed consent form as well as a copy of the insurance policy and conditions

YES □ **NO** □

Printed Name of Study Participant:

_____

Subject Signature: Date:

_____ _____

DDMMMYYYY

Printed Name of Person Conducting Informed Consent Discussion:

_____

Subject Initials_____

Statement of Investigator

(Investigator must sign the consent form on the same date as the subject)

I acknowledge my responsibility for the care and well-being of the above subject, to respect the rights and wishes of the subject and to conduct the study according to applicable Good Clinical Practice guidelines and regulations.

Printed Name of Investigator:

_____

Investigator Signature: Date:

_____ _____

DDMMMYYYY

Subject Initials_____

per E-Mail an: seschwarz@ukaachen.de

ECCLESIA mildenberger HOSPITAL GmbH · Klingenbergstr. 4 · 32758 Detmold

Universitätsklinikum Aachen
Anstalt d. öffentlichen Rechts
Herrn Sebastian Schwarz
Pauwelsstr. 30
52074 Aachen

Markus Niggemeier
EMH
Telefon: 05231 603-6391
Telefax: 05231 603-606391
E-Mail: mniggemeier@em-hospital.de

Detmold, 20.06.2013

Insurance protection for clinical trials
Insurant: Universitätsklinikum Aachen, Pauwelsstr. 30, 52074 Aachen, Germany
Reference number: 2330 33 0901

Dear Mr. Schwarz,

Reference is made to the today's phone call.

Subject to a risk check by the insurer, it is possible to arrange insurance cover for clinical trials, which are conducted in the countries Germany, Ireland and Belgium.

If you need further information, please do not hesitate to contact us.

Mit freundlichen Grüßen

ECCLESIA mildenberger HOSPITAL GmbH

i.V. i.A.

ECCLESIA mildenberger HOSPITAL GmbH
Geschäftsführer:
Ingo Gurcke, Franz-Michael Petry, Manfred Klocke
Amtsgericht Lemgo, HRB 6123
Hausanschrift: Klingenbergstraße 4, 32758 Detmold

Ein Unternehmen der ECCLESIA Gruppe

Commerzbank AG
Kto.-Nr. 282 345 700
BLZ 480 800 20
USt-Id-Nr. DE 124601328
Versicherungsvermittlerregister-Nr. D-T9IZ-O1LZM-41