THESIS ON INFORMATICS AND SYSTEM ENGINEERING C97

Phantom organs and their applications in robotic surgery and radiology training

Asko Ristolainen

TALLINN UNIVERSITY OF TECHNOLOGY
Faculty of Information Technology
Centre for Biorobotics

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Supervisor: Prof. Maarja Kruusmaa
Centre for Biorobotics
Faculty of Information Technology
Tallinn University of Technology
Tallinn, Estonia

Opponents: Dr. Adam Stokes
Scottish Microelectronics Centre
School of Engineering
The University of Edinburgh
Edinburgh, United Kingdom

Dr. Georgios Mylonas
Faculty of Medicine
Department of Surgery & Cancer
Imperial College London
London, United Kingdom

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Declaration:
Hereby I declare that this doctoral thesis, my original investigation and achievement, submitted for the doctoral degree at Tallinn University of Technology has not been submitted for any academic degree.

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Fantoomorganid ning nende rakendused robotkirurgias ning radioloogide õppetöös

Asko Ristolainen

Contents

List of Publications

This thesis is written based on the following articles:

- A Hunt, A., Ristolainen, A., Ross, P., Opik, R., Krumme, A., Kruusmaa, M. (2013). Low cost anatomically realistic renal biopsy phantoms for interventional radiology trainees. European journal of radiology, 82(4), 594-600.
- B Ristolainen, A., Colucci, G., Kruusmaa, M. (2013). A Phantom Pig Abdomen as an Alternative for Testing Robotic Surgical Systems: Our Experience. Alternatives to laboratory animals: ATLA, 41(5), 359-367.
- C Ristolainen, A., Ross, P., Gavšin, J., Semjonov, E., Kruusmaa, M. (2014). Economically affordable anatomical kidney phantom with calyxes for puncture and drainage training in interventional urology and radiology. Acta radiologica short reports, 3(5).

Other Related Work

The following is list of articles that are published in the same field and are directly related to the thesis but not included as appendices.

1. Opik, R., Hunt, A., Ristolainen, A., Aubin, P. M., Kruusmaa, M. (2012, June). Development of high fidelity liver and kidney phantom organs for use with robotic surgical systems. In Biomedical Robotics and Biomechatronics (BioRob), 2012 4th IEEE RAS & EMBS International Conference on (pp. 425-430). IEEE.
2. Maris, B., Dall'Alba, D., Fiorini, P., Ristolainen, A., Li, L., Gavshin, Y., Barsi, A., Adhikarla, V.K. (2013). A phantom study for the validation of a surgical navigation system based on real-time segmentation and registration methods. International Journal of Computer Assisted Radiology and Surgery (IJCARS), 8: 1/S1: 381-382
3. Dodi, R., Ferraguti, F., Ristolainen, A., Secchi, C., Sanna, A. (2014). Planning and Simulation of Percutaneous Cryoablation. AASRI Procedia, 6, 118-122.
4. R. Muradore, P. Fiorini, G. Akgun, D. E. Barkana, M. Bonfe, F. Boriero, A. Caprara, G. De Rossi, R. Dodi, O. J. Elle, F. Ferraguti, L. Gasperotti, R. Gassert, K. Mathiassen, D. Handini, O. Lambercy, L. Li, M. Kruusmaa, A. O. Manurung, G. Meruzzi, H. Q. P. Nguyen, N. Preda, G. Riolfo, A. Ristolainen, A. Sanna, C. Secchi, M. Torsello, and A. E. Yantac, "Development of a Cognitive Robotic System for Simple Surgical Tasks," *Int. J. Adv. Robot. Syst.*, 2015.
5. Patent application "A patient specific anatomical kidney phantom", PCT application number PCT/EP2014/054448, filed 24.04.2013

Author's Contribution to the Publications

The author has contributed to the previously listed articles as follows:

A Developed the reconstruction method of phantom organs from computed tomography scans. Prepared the kidney phantoms for radiology training.

B Developed the pig phantom. Prepared the organ models from computed tomography data. Manufactured the pig abdominal casing. Prepared the organ molds and casted the organs. Validated of the organs against tissue samples from abattoir and prepared the experiments for testing minimally invasive surgical platforms. Wrote the paper.

C Developed and fabricated the kidney phantoms with calyces. Prepared the examination of residents. Scanned the cadaver organs and analyzed the accuracy of the reconstruction method of the kidney phantoms. Wrote the paper.

Introduction

This thesis focuses on the development of anatomically correct organ replicas, or in other words phantoms, that are used to test new technologies in robotic surgery and to train radiology residents in performing various needle procedures under ultrasound and fluoroscopy guidance. In this work we describe a method for reproducing anatomically correct organ phantoms where we mimic the physical properties of the soft tissues with affordable materials and exploit computer tomography scans to reconstruct the shape of the real organs. We use the reconstruction method to develop phantoms for two robotic surgery projects where the phantoms were used to test new safety and procedural techniques. To widen the applications of the phantoms we turned to radiologists. We developed phantoms that are used in training and in qualitative evaluation of interventional radiology residents. The cooperation with radiologists led to commercialization of the phantoms.

Motivation

The demands on cutting down medical costs, improving patient safety, reducing hospital stay etc. have caused a paradigm change in replacing conventional treatment and examination methods with minimally invasive ones. This change challenges the medical community to adapt new technologies and methods while keeping and improving healthcare quality and patients' wellbeing. For example radiologists need to maintain and acquire new skills hand in hand with the improvement of imaging technologies and new treatment methods. Similarly many surgical procedures have been replaced with laparoscopic counterparts after laparoscopy was introduced by Dr. Semm [1]. Lately many laparoscopic procedures have been improved with visual magnification, stabilization, simulation possibilities and reduced number of incisions in a form of laparoscopic robotic surgery.

Robotic surgery has been around for 25 [2] years and the number of procedures that have being replaced with robotic counterparts is increasing. New robotic technologies and methods need to go through rigorous evaluation as the surgical robotic platforms are just as reliable as their designers. One way to test new technologies of robotic surgery without using cadavers or animals as test subjects is to use phantoms. Phantoms provide a good testing basis for the early experiments where repeated test are needed. In this work phantoms were initially designed, fabricated and tested in projects SAFROS, Patient Safety in Robotic Surgery, European Union 7th Framework (FP7) project and I-SUR, Intelligent Surgical Robotic (FP7) project). The motivation for producing phantoms in SAFROS project came from the aim of reducing the number of animal experiments in the final phase of the project. In order to have a similar environment to experiments with pigs, a pig abdominal phantom was designed and fabricated. The artificial organs of the pig phantom had to mimic the real tissue properties (ultrasound, computed tomography and mechanical properties) and at the same time had to be relatively cheap for repeated tests. Similarly phantoms were needed in the I-SUR project to test automated surgery procedures (e.g. automated guidance of cryoablation needle into kidney tumor under ultrasound guidance, automated suturing of a wound). The project began with the development of technologies for automated needle guidance into the kidney, so a partial human abdominal phantom with replaceable kidneys was designed and fabricated.

In order to widen the application area of phantoms also after the robotic surgery projects had ended, the phantoms were demonstrated in a hospital where they immediately received good feedback and were used as training platforms for radiology residents. Phantom organs have been found useful in acquiring skills, keeping the level of competence and raising the confidence of trainees and professional radiologists. So the second motivation of the thesis came from designing affordable anatomically correct training devices for radiology and other trainees in an economic situation where demands of cutting down costs in medicine are high.

Contribution of the Thesis

The contributions of this thesis are as follows:

- Development of affordable method for producing organ replicas (so called phantoms) based on computed tomography scans and their reconstruction accuracy evaluation method
- Implementation of phantoms in testing robotic surgery systems
- Developing methods for improving the training of radiology residents by using anatomically correct organ phantoms
- Introducing phantoms in the radiologists' every-day practice
- Developing methods for mass production of phantoms

Outline of the Thesis

The thesis is divided into 3 parts. The first chapter gives an overview of phantoms, describes the phantom material calibration, organ reconstruction method and its accuracy. The second chapter brings out two examples of phantoms that were developed to evaluate novel robotic surgery equipment, methods and concepts in two European projects. The third chapter describes the phantoms use in radiologists' work and training which led to commercialization of the phantoms.

1 Phantoms

This chapter gives a short overview of the history and current state of the art of medical phantoms. The phantom development is described starting from the calibration of tissue mimicking materials and finishing with phantom organ reconstruction accuracy evaluation.

1.1 History and overview

Artificial organs or so called phantoms have found their way into various fields of medicine. Through the history phantoms have been applied for different reasons. According to their application they can be categorized as follows:

- imaging phantoms for calibrating and evaluation of different medical imaging devices,
- training phantoms for testing and training interventional techniques,
- custom made phantoms for research purposes.

Imaging phantoms have been used in medical physics and health physics since X-ray imaging was discovered by Roentgen in 1895 [3], [4]. It was soon realized however, that high radiation dosages are harmful to the patients. So the first phantoms were developed by physicists to validate the limitations of their x-ray systems and to make dosimetry measurements. About 50 years later a new imaging technique was discovered – the energy of ultrasound (**US**) was used for medical reasons by dr. George Ludwig at the Naval Medical Research Institute, Bethesda, Maryland in the late 1940s [5]. In 1949 dr. John Wild first used ultrasound to assess the thickness of bowel tissue [6]. Since 1960s various modes of ultrasound have been developed and tissue phantoms have been used for characterization and calibration of ultrasound imaging systems [7]. Early phantoms were designed for the calibration and testing purposes of diagnostic ultrasound machines where accurate imitation of the ultrasonic characteristics of human tissue was paramount [8]. Phantoms with similar purposes have been developed for magnet resonance imaging (**MRI**) and for positron emission tomography (**PET**). Nowadays there are many companies that provide calibration phantoms for US (*Kyoto Kagaku, Computerized Imaging Reference Systems Inc. (CIRS), Gammex Inc., ATS Laboratories Inc.*), computed tomography (**CT**) (*The Phantom Laboratory, CIRS, Gammex Inc., Fluke Biomedical*), PET (*Biodex Medical Systems Inc., CIRS, Capintec Inc.*) and MRI (*The Phantom Laboratory, Fluke Biomedical, High Precision Devices Inc., CIRS*) systems.

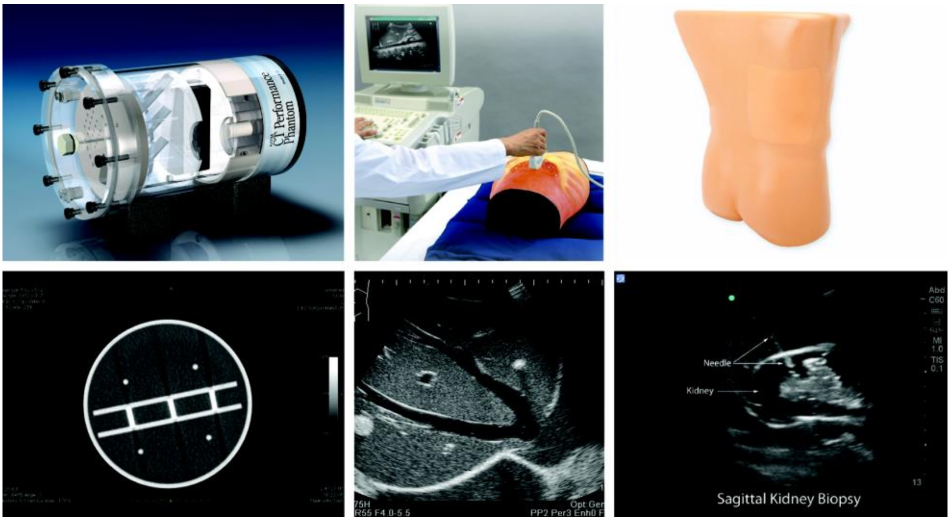

Figure 1.1 Examples of Imaging phantoms with sample images below (Left: CIRS's model 610 - phantom for evaluating CT machines performance, images acquired from [9]*; Middle: Kyoto Kagaku's ABDFAN phantom - ultrasound examination training model, images acquired from* [10]*; Right: Blue Phantom's Renal Biopsy Ultrasound Training Model – phantom for training ultrasound guided percutaneous kidney biopsy procedures, images acquired from* [11]*) A permission to reprint the images was acquired from the companies representatives.*

Imaging devices' improvement has broadened the spectra of analytical techniques and has introduced new minimally invasive treatment techniques [12]–[14]. Thus in addition to the training required to comprehend medical images, understanding how the treatment or analysis is performed (i.e. biopsies, drainages, conducting the scans, hand-eye coordination in using ultrasound probe etc.) needs additional training nowadays. Tissue mimicking phantoms that allow practicing different diagnostic and treatment techniques hand-in-hand with medical imaging devices have been developed to serve this purpose. There are number of ultrasound phantoms that have been developed for training examinations, biopsies (renal, abdominal, breast thyroid, prostate, and lumbar puncture), vascular access, fetal examinations, anesthetics etc. Some overviews of ultrasound training phantoms on the market can be seen in [15]–[17]. Similarly training phantoms have been developed for CT, MRI and PET imaging. Applications of phantoms in medical training are discussed further in the following paragraphs.

Training phantoms have also been used in other medical fields that do not include imaging techniques. In surgery simulation they have been used for centuries in the form of cadavers, animal models and recently, materials mimicking tissue or an organ [18]. One of the earliest works marking the era of modern medical trainers was a mannequin for training in mouth to mouth ventilation created in the early 1960s by Asmund Laerdal – the *Resusci-Anne*. The idea was introduced to Laerdal by Bjorn Lind and other prominent Norwegian anesthesiologists following Dr. Peter Safar's revelations about the superiority of mouth to mouth resuscitation. The mannequin allowed training the ABC of cardiopulmonary resuscitation (A standing for airway, B for breathing, and C for circulation) [19]. Over the past 50 years the variety of trainers made out of tissue mimicking materials has grown vastly. Nowadays there are number of various part task trainers [20] (that represent only a part of the real thing and will often comprise a limb or a body part or structure) available on the market that allow the physicians to gain first hand on experience and confidence without posing any risk to the patients. Task trainers are limited in their applicability but are portable, reusable and cheaper than animals, cadavers, mannequins or virtual reality simulators [21]. History and overview about trainers used in surgery and teaching technical skills is presented in [18], [20], [22], [23]. An overview about the available part task trainers can be found on the producers' homepages (e.g. Laerdal Skills [24], Simulab [25], SynDaver etc.).

In addition to phantoms, medical training has recently moved from physical trainers to virtual reality (VR) simulations. This advancement has been possible thanks to advances in medical imaging and with the ever improving computational power of computers. Advancements in medical imaging have allowed reconstructing patient specific training scenarios and growth in computational power of computers allows emulating more sophisticated and more realistic tissue interactions. A leg simulator was one of the first virtual reality simulations developed by Scott Delph [18][26] and Joseph Rosen from Stanford University in 1987. Around that time, the first virtual reality simulator was developed for general surgery by Lanier and Satava [18][27]. Since then there have been numerous VR simulators that have been developed to train and assess the skills of medical staff [18], [22], [23], [28], [29]. There are also other advancements in technology that have improved medical training, for example augmented reality, tool tracking systems etc. that could be further explored but do not fit in the scope of this thesis.

Custom-made phantoms are developed to fulfill the needs of scientific experiments that are not possible with phantoms found on the market. SAFROS and I-SUR projects required phantoms with US and CT imaging properties and also with elasticity close to real tissue. In the SAFROS project, a pig abdominal phantom was required to test robotic surgery of enucleation of benign pancreatic tumor as the final experiments of the project were supposed to be conducted on pigs. In the I-SUR project phantom consisting of a kidney with tumors and anatomically relevant surrounding space was required to develop an automated kidney tumor treatment procedure with cryoablation technique (performing cycles of freeze and defreeze to kill biological tissue). The market provides phantoms that partially satisfy the project's requirements, some of them are described (not exhaustive list) in Table 1. The last column of the table lists the disadvantages of the currently existing products for their usage in SAFROS and I-SUR projects.

Table 1 Commercially available phantoms on the market for percutaneous kidney access and abdominal surgery simulation

	Producer	Phantom, description	Imaging modality	Price[a]	Problems
I-SUR - kidney phantoms	Blue Phantom	Renal Biopsy Ultrasound Training Model, meant for training clinicians in the psycho-motor skills associated with ultrasound guided kidney biopsy procedures	US	$3,999	Too expensive to provide all to the partners with this model, cryoablation simulating possibility not clear
	Blue Phantom	Replacement kidneys for renal biopsy ultrasound training model, represents cortex, medulla; major and minor calyx	US	$399	Not usable without the Blue Phantom's Renal Biopsy Ultrasound Training Model
	Mediskills	Perc Trainer - PT, can be used for US procedures e.g. identification of stones, localization of the kidney, guided needle biopsy etc.	US, fluoroscopy	~£2500	No surrounding organs, no ribs
	Limbs & Things	Ultrasound Percutaneous Nephrostomy Trainer, for the acquisition of the skills for percutaneous nephrostomy under ultrasound guidance.	US	$869	No available pathologies, no surrounding tissues
	CIRS	Kidney Training Phantom, possible to practice various ultrasound guided interventional procedures i.e. cryosurgery, biopsies	US	$382	Missing surrounding tissue and no pathologies
SAFROS - abdominal phantom	CIRS	Multi-Modality Interventional 3-D Abdominal Phantom. The phantom contains simulated lungs, liver, hepatic vessels, ribs, vertebra, kidneys, abdominal aorta etc.	US, CT, MRI	$2,363	No access with laparoscopic tools to perform intraoperative experiments
	Kyoto Kagaku Co.	Abdominal Intraoperative & Laparoscopic Ultrasound Phantom "IOUSFAN" for simulating abdominal open intraoperative and laparoscopic ultrasound	US	$5,600	Organs with reduced size, not possible to replace single organ, too expensive
	Kyoto Kagaku Co.	ABDFAN Ultrasound Examination Training Model with ECHO-ZOU Internal Organ Anatomical Model. Training ultrasound scanning and learning anatomy under ultrasound.	US	$11,000	Not possible to cut and work intraoperatively

[a] Price received from manufacturer or resellers home pages

The phantoms on the market are either too expensive or there are drawbacks in the available anatomy, the anatomy is simplified or the phantom represents only one organ without surrounding tissues, the phantoms do not have required specific pathologies and the phantoms can be used for limited number of test cycles. In order to meet the requirements of SAFROS and I-SUR projects, the phantoms needed to be developed in-house.

1.2 Phantom development

One of the key points of phantom development is finding a suitable tissue mimicking material to create artificial organs. The following sections give an overview about the material development, tissue mimicking material calibration, shape reconstruction and validation. Reconstruction of human kidney was taken as a basis for validating the reconstruction quality as kidneys are relatively small compared to other abdominal organs and are with a simple shape.

1.2.1 Tissue mimicking materials

The choice of material used in the phantom organ is dependent on its application. In this work[1] phantoms were developed to mimic soft tissue ultrasonic (attenuation, US propagation speed), elasticity (Young's modulus and viscoelasticity of material) and computed tomography (radio density) properties. There is a variety of materials available for mimicking human soft tissue that can be classified as hydrogels, organogels and flexible elastomer materials. A thorough overview of tissue mimicking materials can be found in [7][30].

Gelatin gels were chosen to create artificial organs as the production methods are well described in the literature [31], [32] and the ultrasound and mechanical properties of gelatin gels can be easily controlled, the elasticity range and non-linearity can be widened by combining gelatin with oil [33]. Elasticity of the gelatin gels can be varied from 2.5 kPa to 500 kPa [32], US propagation speed of 1550-1650 m/s and US broadband attenuations 0.2-1.5 dB/(cm MHz) has been reported [26]. The drawbacks of using gelatin gels are that they are sensitive to bacteria (can be overcome with using additives, e.g. thimersol, p-methyl acid, etc.) and that the mechanical properties have a long settling time (up to 100 days from manufacturing) [32].

The gel consists of food gelatin and water composing the backbone of the material; formaldehyde that rises the gel's melting temperature and makes the gel stiffer by inducing cross-linking; alcohol to increase the sound propagation speed of the gel; graphite flakes or glass beads to increase the ultrasound attenuation and backscatter; and various substances that prevent bacterial invasion. The

[1] Phantom development described in this work is based on articles of Hunt et al [44] and Opik et al [107].

material preparation is well described in [31], [32]. During the preparation process the heating temperatures are kept low and durations short to prevent protein denaturation. Based on the literature and from experience, the gel manufacturing process had following steps:

- Gelatin and graphite flakes were added to water and allowed to hydrate for 10 min.
- The hydrated mixture was placed in a hot water bath (60–70 °C) and stirred constantly until the mixture cleared and its temperature rose to 32…40 °C.
- The mixture was placed in vacuum chamber for 10 min (approx. 10 kPa) to degas the solution. The solution cleared and bubbles surfaced.
- Formaldehyde was added while slowly stirring the solution.

The gel was then casted into mold, rotated until it cured to prevent the graphite from settling and placed in a refrigerator for further hardening and storage (5 °C).

1.2.2 Material calibration

The gelatin gels were calibrated against human kidney properties (US propagation speed, broadband US attenuation, Young's modulus and radiodensity) obtained from the literature. General US characteristics of soft tissue can be found from ICRU (International Commission on Radiation Units & Measurements) and AIUM (American Institute of Ultrasound Medicine) reports that specify the US propagation speed of 1540 ± 15 m/s and US broadband attenuation of 0.3 – 0.7 dB/(cm MHz) [27] [28]. The US propagation speed of human kidneys has been reported to vary from 1540 m/s to 1570 m/s [29] which overlap the respective figures of pigs, dogs and horses [30]. US broadband attenuation of 0.533 to 0.8 dB/(cm MHz) with mean of 0.73 dB/(cm MHz) measured in the interval of 1.5 to 3.5 MHz [30]. Elasticity of soft tissue is known to act very non-linearly and the Young's modulus depends on the amount of applied strain. In [31] shear wave elastography was used to measure the elasticity of human kidneys with validation done by performing biopsy on the patients. For healthy kidneys the elasticity of cortex and medulla were reported 0.7 ± 2.1 kPa and 5.1 ± 2.5 kPa respectively while for the same figures for unhealthy kidneys where 32.7 ± 2.4 kPa and 23.1 ± 5.6 kPa. From the results it was concluded that stiffness of human kidneys varies from 5 to 50 kPa. The radiodensity of the human kidney varies between 30 HU (Hounsfield units) and 50 HU [32] and is stoichiometrically calculated to be 43 HU [33].

Gel samples with varying concentrations of graphite, gelatin and formaldehyde solution were casted into cylindrical molds (46 mm diameter). US properties were measured in pulse-echo configuration (setup shown in Figure 1.2) using an US pulser/receiver (DPR300 from JSR Ultrasonics) and a 5 MHz transducer (SAUTERGmbH). Samples with different heights (12 mm and 17 mm) were prepared to measure US broadband attenuation by comparing the samples attenuation (in water) and subtracting the attenuation of water. US propagation speed was found from time-of-flight experiments. Young's modulus was measured in compression experiments on a custom-built DMA (Dynamic Mechanical Analysis) machine [41]. Radiodensity measurements were made using a multidetector CT scanner (Brilliance 64, Philips Healthcare) with larger samples (250 mL).

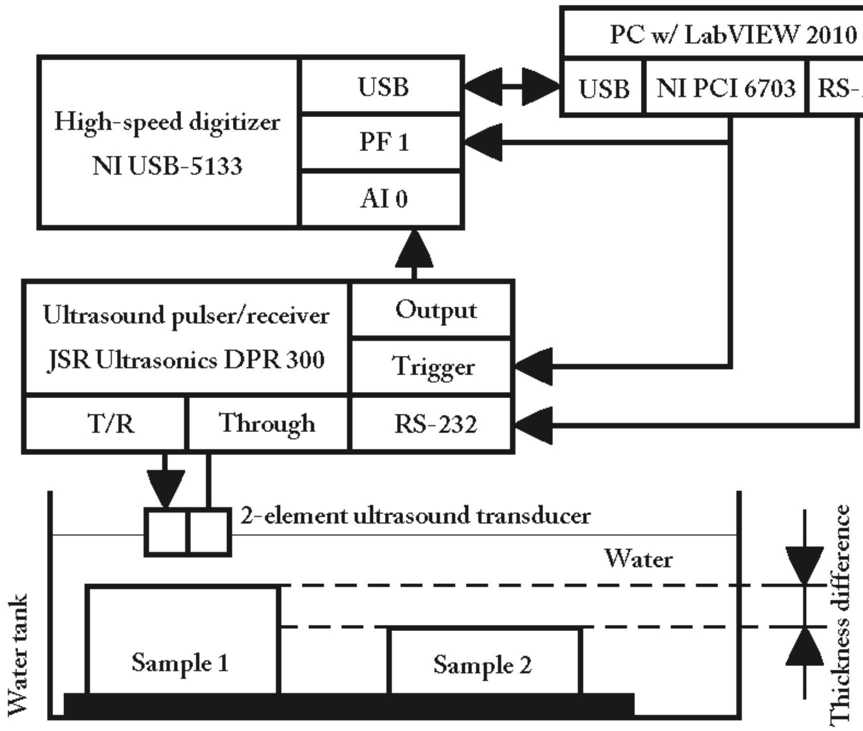

Figure 1.2 US attenuation measuring setup (image adapted from [42]*)*

Results of the Young's modulus measurements show that only formaldehyde and gelatin concentrations have a linear effect on the stiffness of the gels (graphite concentrations also made the material stiffer but had insignificant effect at the low concentrations that were used to cast phantoms (up to 1 wt.%)). In Figure 1.3 the gelatin gels' Young's modulus is plotted against gelatin and formaldehyde concentrations.

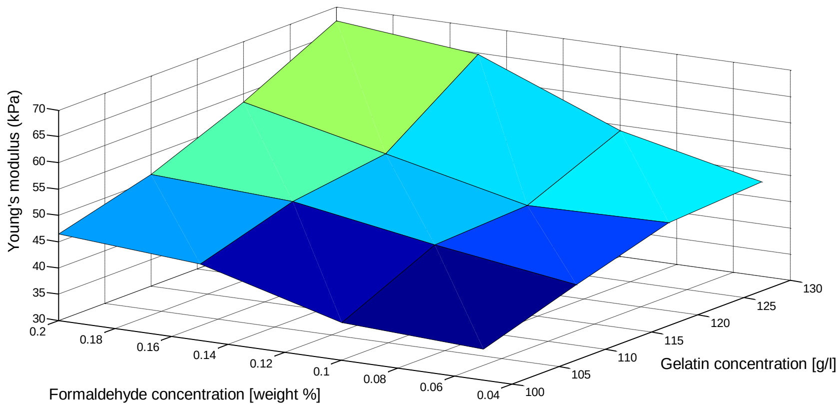

Figure 1.3 Young's modulus dependency on formaldehyde and gelatin concentrations

The calibration of US properties revealed that formaldehyde has insignificant effect on the US broadband attenuation. Gelatin concentration (from 100 g/l to 140 g/l with 10 g/l increments) also a small effect on attenuation and is plotted in Figure 1.4. Graphite flakes increases the attenuation of the gelatin gels and is plotted along with respect to gelatin concentration in Figure 1.5. In all the experiments US propagation speed was measured along with the attenuation and the average speed was 1495 m/s with 32 m/s standard deviation. No significant dependence on formaldehyde, gelatin or graphite concentrations were found at the measured compositions.

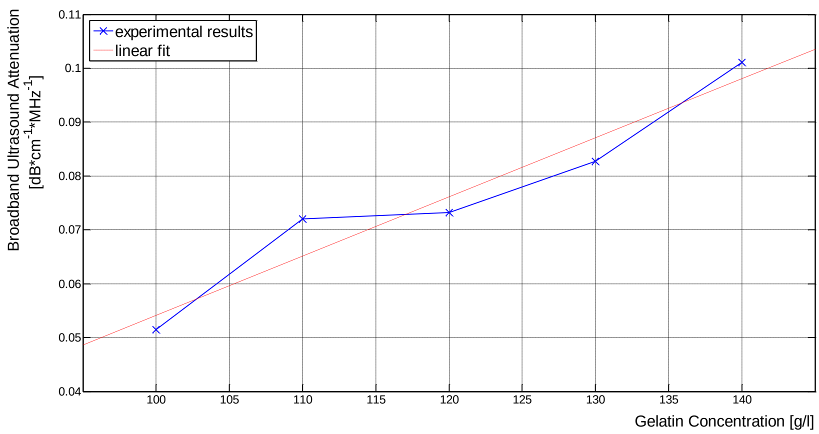

Figure 1.4 Gelatin effect on broadband US attenuation

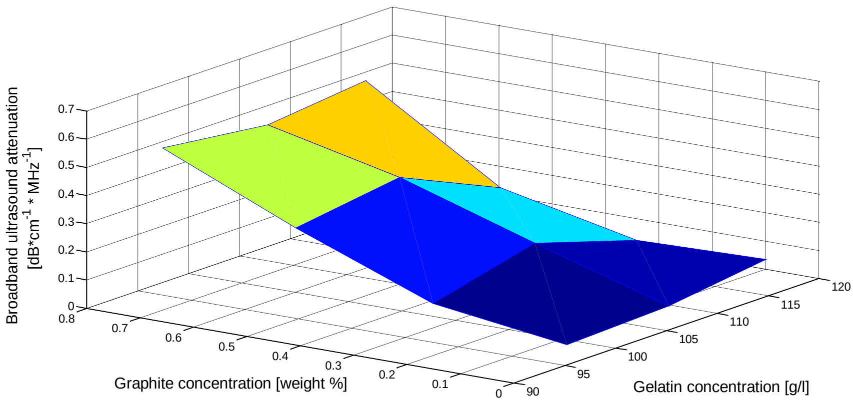

Figure 1.5 Broadband US attenuation in respect to gelatin and graphite concentrations

The main influencer of radiodensity of the gelatin gels in the experiments was the gelatin concentration. The concentration of formaldehyde had undistinguishable effects on the radiodensity and the increased graphite concentration only increased the standard deviation of radiodensity. The Hounsfield figures with respect to graphite concentration are plotted in Figure 1.6.

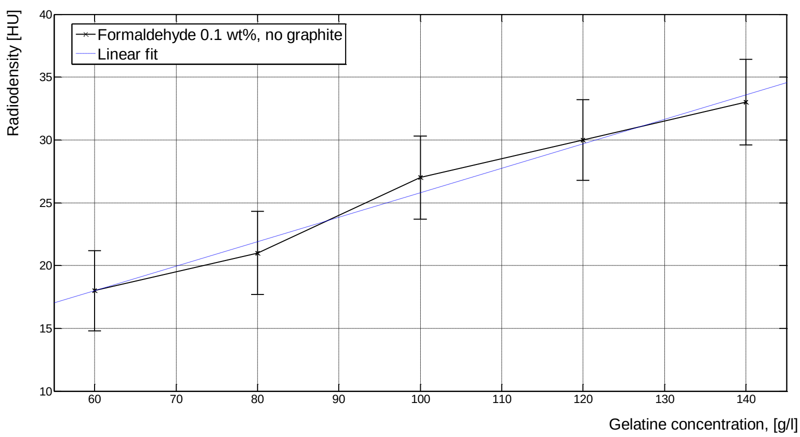

Figure 1.6 Gelatins mixture's radiodensity dependency on gelatin's concentration

From the material calibration experiments it was concluded that it is possible to replicate human kidneys in the range of elasticity of a pathological tissue (gelatin gels with Young's modulus below 10 kPa that would represent healthy tissue are very fragile). The realistic human kidney US broadband attenuation is achievable at 1 wt.% concentration of graphite and the US propagation speed matches the actual speed in a kidney with less than 5% error. The Hounsfield values of gelatin gels closely match the properties of kidneys. The gelatin gels properties are well tunable separately as they depend only on the concentrations of one or two ingredients.

1.2.3 Reconstruction of organs

The anatomically correct shape of the phantom organ is as important as its tissue mimicking properties. The possibility to reconstruct the artificial organs mimicking the patient specific anatomy is addressed in this section. Patient specific phantoms have a perspective to improve preoperative planning of procedures and also improve training quality.

Anonymized computed tomography scans[2] of patients were taken as a basis of the reconstruction. The reconstruction process is divided into following steps:

- The anonymized computed tomography scans were imported into 3D Slicer (3D Slicer is a community platform created for the purpose of subject specific image analysis and visualization [34]). The organs of interest were segmented manually or automatically using Simple Region Growing Segmentation algorithm;
- The segmentation results were validated by radiologists. All changes were made manually to the segmentation according to the radiologist recommendations.
- The segmented slices of the CT scan were fused together to form a three dimensional model of the segmented organ. A software package called *Model Maker* in 3D Slicer was used to create the models. The models were saved in *.stl (STereoLithography) format.
- The saved stereolithography models were imported into Geomagic Studio® (that is the complete toolbox for transforming 3D scanned data into highly accurate surface, polygon and native CAD models [35]) and the STL models were repaired and converted into CAD format
- Later SOLIDWORKS® 3D CAD software was used to design molds for casting the organs. The mold parts were saved in *.stl format and the parts of the mold were manufactured using a 3D printer
- The molds' inner surfaces were covered with a thin silicon layer to avoid leakages from the mold and to give a smooth finishing to the organs surfaces.
- Finally tissue mimicking material was casted into the mold.

The pipeline of the kidney organ reconstruction is visually explained in the Figure below.

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[2] An approval from Tallinn Medical Research Ethics Committee was granted before the work with patients CT scans and postmortem organs (decision number 2527)

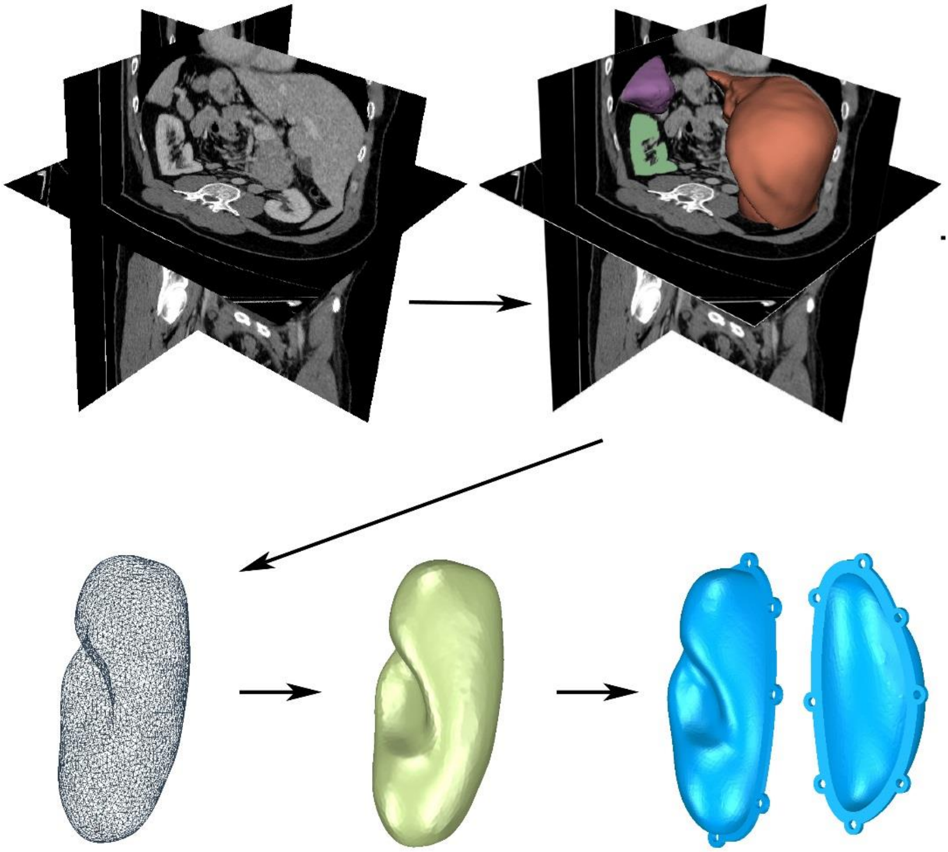

Figure 1.7 Organ reconstruction from CT scan (From left to right: (1) CT scan is opened in 3D Slicer software; (2) organs are segmented and models created; (3) models are saved as mesh in STereoLithography format; (4) organs are converted in native CAD format; (5) CAD software is used to create two or more-sided mold around the organ)

1.2.4 Validation of organ reconstruction

To ensure that the reconstruction of the organs is done accurately a validation procedure was introduced[3]. The evaluation was carried out on patients whose postmortem kidneys were scanned (by using DAVID-Laserscanner software with a Logitech C920 webcam and an Optoma ML300 LED video-projector) and compared the results with reconstructed models from CT data. Inclusion criteria were set for the patients: (1) the time between the autopsy and recording of the CT scan had to be 14 days or less; (2) only kidneys without acute pathology,

[3] The evaluation is described here is based on the article of Ristolainen et al [46]

without solid tumors and cysts less than 3cm were included. An approval from Tallinn Medical Research Ethics Committee was granted before the work with patients CT scans and postmortem organs (decision number 2527). The patient kidneys were scanned in The Center of Pathology at the East-Tallinn Central Hospital. The removal and preparation of cadaver kidneys was performed by Dr. Semjonov.

The computer models of kidneys were built using the following procedure:

- Patient kidneys were removed from the abdomen and excess fat around the kidney was removed;
- The ureter, renal vein, and the renal artery were cut off close to the renal pelvis;
- Each kidney was hung with a rotating hook to a portable frame and scanned 12 times from different angles to maximize the covered surface;
- The obtained scans were semi-automatically merged together into a single mesh. The mesh defined the surface of the kidney model.

The volumes of the physical kidneys and kidneys segmented from CT scans were compared. As it is hard to come by patients whose CT scan was taken short before the time of death and whose kidneys are without pathologies only 8 kidneys from 4 patients (2 patients were unsuitable) were enlisted in to evaluation analysis. The average volumetric difference of the scanned post mortem kidney models and models reconstructed from the CT data was less than 5% (4.7 ± 3.25 %). An example of the compared models are visualized in Figure 1.8 (on the right the kidney seems shorter as it was flat on the table when the image was taken).

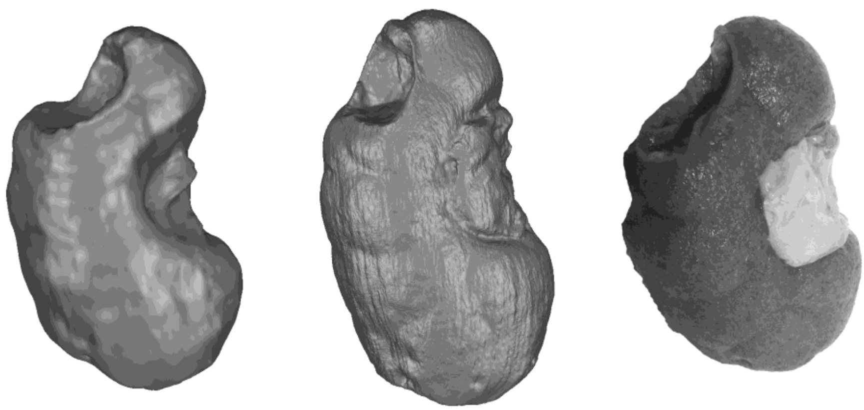

Figure 1.8 Comparing kidney models (Left - reconstructed kidney model form CT scan; Centre - post-mortem kidney can; Right - image of the scanned kidney)

1.3 Conclusion

In this chapter we described the calibration of gelatin mixtures to reproduce anatomically correct organ phantoms. The calibration of the gelatin mixtures showed that the material is suitable for mimicking the kidney organs mechanically and that gelatin's imaging properties fall in the same range as its anatomical counterparts.

Kidney was taken as basis of the reconstruction as they are small in size and with simple shapes. An anonymized computed tomography scan was used to reconstruct the kidney model and to create 3D printed mold around the kidney model. The casted kidney organs were validated volumetrically by comparing the post-mortem patient kidney scans with kidney models reconstructed from CT scans (difference was below 5%).

The organ reconstruction's high accuracy and the tissue mimicking material's low price set a firm ground for producing affordable phantoms for scientific and medical education purposes.

2 Robotic surgery and phantoms

This chapter gives a short overview of robotic surgery, describes the reconstruction methods and the calibrated gelatin gel's usage in development of phantoms in two robotic surgery projects SAFROS and I-SUR.

2.1 Introduction

The concept of robots as autonomous mechanical tools assisting humans started to find its practical realization more widely in the beginning of 20th century. Nowadays preprogrammed robots are used in heavy industry (for example car manufacturing assembly line) and are influencing our everyday life more and more. If robots are good at working with premeasured components on the assembly line then it would be appealing to use robots also in surgery with accurate imaging technologies allowing preoperative planning and intraoperative surveillance [45].

When laparoscopic surgery (by Prof Semm from Kiel, Germany [1]) was first introduced in the late 1970s, the method started to spread in Europe and later in USA after the benefits for patients (e.g. reduced hospital say, reduced pain, shorter recovery time etc.) became evident. The complications of the of laparoscopic surgery (e.g. poor ergonomics, 2D vision, limited articulation and the "fulcrum effect") also surfaced and instigated robotic surgery developers to improve the control of laparoscopic tools [45]. The improvements include filtered tremor of the surgeon hands in controlling the robotic tools movements, 3D vision over the workspace, magnification of tools movements etc. The first robotic system that was developed to aid surgeon in the operating theatre was called the Automated Endoscopic System for Optimal Positioning (AESOP) developed by Computer Motion (Santa Barbara, Ca, USA) that functioned as a camera holder (initially controlled manually and later by voice [46]) received the Food And Drug Administration (FDA) approval in 1993. Computer Motion developed the system further into entire minimally invasive surgical platform based on three AESOP arms, one holding the camera and two manipulating tools. The clinical work started in 1998 and resulted with an FDA approval in 2001 [45]. Computer Motion was acquired by Intuitive Surgical, Inc. in 2003 after what AESOP and ZEUS were discontinued. After that da Vinci Surgical System (by Intuitive Surgical, Inc.) remained the only system to the market with a FDA approval (received in 2001) allowed to perform general laparoscopic surgery. To compete with da Vinci and improve existing procedures, European Commission in cooperation with SOFAR S.p.A [47] initiated a project to develop tele-operated multi-arm surgical system Alf-X which received CE mark in 2011 [48].

Robotics has also been applied in other fields of surgery such as orthopedics, neurosurgery and urology. In 1985 first robotic surgery was performed on human with Unimat PUMA 200 robot to take biopsy samples from tumors in brain [49]. Six years later in 1991 a robot was used for the first time autonomously to remove tissue form patient's prostate. The system was called PROBOT developed in London Imperial College [50]. In 1992 robotics entered the field of orthopedic surgery, when total hip replacement was performed with a robot system named ROBODOC [51] cutting the cavity for the hip implant. Another orthopedic surgery (total knee arthroplasty) was automated by allowing the robot to perform the cutting of the tibia and femur with a system called Acrobot [52]. Similar systems was developed MAKO Surgical Corp. for minimally invasive knee resurfacing and ultraprecise hip arthroplasty. MAKO Surgical provides surgical implants with pre-mentioned systems for knee resurfacing (Robotic Arm Interactive Orthopedic System – RIO) and hip replacement (newer version of RIO (MAKOplasty® Total Hip Arthroplast) [45]. In the field of interventional radiology a robot called Cyberknife was developed to precisely target lesions with small bursts of radiation dosages to minimize the radiation exposure of healthy tissue [53]. One of the latest medical robotic systems, the Flex System (Medrobotics Corp., Raynham, MA, USA) [54], that received a green light (received CE mark in March 2014 [55]) for operating was in the field of transoral surgery to treat squamous cell cancer in the neck region.

In order to allow the robotic systems for clinical use they have to receive FDA approval in the USA or EC mark from European Commission. This means that robotic systems have to perform clinical tests to demonstrate their suitability and safety for the specific procedures they are aimed for. Before the actual clinical demonstrations take place the systems usually have gone through a long development phase that includes a number of experiments in realistic environments, either on cadavers, live animals or on artificial organ or body-part counterparts built from tissue mimicking materials. The evaluation tests of robotic surgery need to be repeatable to show that the surgery is safe and that the platform itself is reliable. As robotic surgery might be potentially harmful to patients when something happens to the system or with the surgeon while operating, the safety criteria needs to be embedded in the design phase and testing needs to start as early as possible to minimize the number of design flaws.

Testing on cadavers is expensive [56] and the availability of cadavers is limited [57][58]. In the sense of reality cadavers offer an excellent representation of anatomy but they lack realistic tactile feedback of living tissue, there is no bleeding during the experiments [59][60] and the number of work cycles is limited [56]. Animal models on the other hand provide realistic bleeding and also mimic the anatomy to certain extent (for example pigs). With animal models there are various problems starting from the ethical problems that come with killing healthy animals, cost of keeping the animal alive during experiments, difficulty of acquiring the permit for animal experiments, non-existing pathologies and finishing with the fact that all of the experiments vary to some degree. The legislation on animal experimentations vary between countries. In Europe, United Kingdom has the strongest legislation on animal testing [61][62] (the clearance applicants need to require 3 licenses) while for example law on animal experimentation in Japan is following the conceptual idea of self-regulation and the wellbeing of the animal is controlled by the scientist [63].

An alternative for animal and cadaver experiments are organ or body counterparts i.e. phantoms that can be applied for experiments in the early phase of the development when the robotic system is still unreliable for animal or human trials. Phantoms have many pros such as repeatability of experiments in short time frame, organs with specific pathologies for testing, low price (depending on the anatomical fidelity), tunable tissue properties, possibility to produce patient specific organ replicas, no ethical problems etc.

In the following sections examples of two different phantoms are described, were developed by the author. The first example is a pig abdominal phantom that was developed to reduce the number of animal experiments in the field of minimally invasive robotic surgery (MIRS) in FP7 project SAFROS. The pig abdominal phantom was used to demonstrate pancreatic tumor enucleation with MIRO surgical platform [64] and with surgical platform assembled using two KUKA Lightweight robots. The second phantom represented a section of a human abdomen and was developed in FP7 project I-SUR to demonstrate automated kidney tumor cryoablation under ultrasound guidance. The developments of the phantoms and the benefits of using them are described in the following sections.

2.2 Patient Safety in Robotics Surgery - The SAFROS project

The SAFROS project was a European Union’s Seventh Framework Program research project (FP7-ICT-2009.5.2) which goal was to address the development of technologies for patient safety in robotic surgery. Its aims were to define patient safety metrics for surgical procedures; to develop methods that abide by safety requirements; and to demonstrate that a properly controlled robotic surgery carried out in accordance to SAFROS safety criteria can improve the level of patient safety currently achievable by traditional surgery.

To demonstrate the safety criteria artificial phantoms with imaging properties were designed for the project as controlled models to assess quality and performance of medical image processing algorithms and surgical interventions. The phantoms allowed the project partners to minimize the extent of animal experimentation during validation of technologies for patient safety by substituting animal organs or body parts with realistic anatomically correct phantoms. The phantoms allowed to develop and test various technologies repeatedly in the same conditions and also to have control over the anatomical variance that is not possible with animal models.

2.2.1 Animal experiments and the 3R principle

The number of new devices developed in medicine and veterinary science continues to increase every year. According to the Derwent World Patents Index® (DWPI SM), there was an increase of 26% in the number of device patents in the medical field between 2012 and 2013 [65]. The use of animals during the development and validation phase of new devices is still the established practice.

Russell and Burch published The Principles of Humane Experimental Technique in 1959 [66], which established the basis of the well-known 3Rs principles of Refinement, Reduction and Replacement. The idea behind this concept was to give scientists a specific framework when designing and conducting experiments, in order to enhance the well-being of the animals involved (refinement), to improve the quality of the data while using fewer animals (reduction), and to consider alternatives to animals for conducting the experiments (replacement). The European Community embraced these principles for the first time in Directive 86/609/EEC [61], and they were recently integrated and addressed in more detail in Directive 2010/63/EU [67]. Now, the 3Rs principles constitute a prerequisite for good standards of practice in animal experimentation within the European Union.

Despite this new culture concerning the use of animals, the Sixth Report on the Statistics on the Number of Animals used for Experimental and other Scientific Purposes in the Member States of the European Union [61] showed that the total number of animals used for research and training purposes has only dropped from 12.1 million in 2005 to 12 million in 2008. If we take into account the different number of countries included (25 Member States in 2005 versus 27 Member States in 2008), the overall effect is somewhat disappointing. The decrease in the use of some species has been compensated by a sharp increase in the use of mammals, especially large ones. This trend has been confirmed by the analysis of the use of animals for education and training, and for the research and development of products and devices for medicine, dentistry and veterinary science (excluding toxicology and other safety evaluation).

One way of reducing the numbers of animals used for training and for the development of surgical tools (which nowadays also includes robotic surgery systems) is to use animal organs received from abattoirs. Recently, Laird et al. [68] used the abdominal organs of calves, placed inside a standard laparoscopic abdominal trainer, to practice and demonstrate laparoscopic nephrectomy. Waseda et al. [69] developed a box trainer that mimicked the human body with gas insufflation, and was filled with animal organs retrieved from an abattoir for various laparoscopic operations.

The problem with animal organs is that they can only be used for a limited amount of time. The unreliability of the equipment during the development phase is a major issue, as tests are often interrupted by equipment failures or malfunctions that affect the ability to readily carry out repeated tests in rapid sequence. The potential for significant variations in anatomical size and in structural relationships in the organs of the animals does not satisfy the need for a standard model. In addition, animal models' lack of pathological conditions [28] (availability of tumors and cysts) and causing pain to the animals to mimic such conditions is unethical.

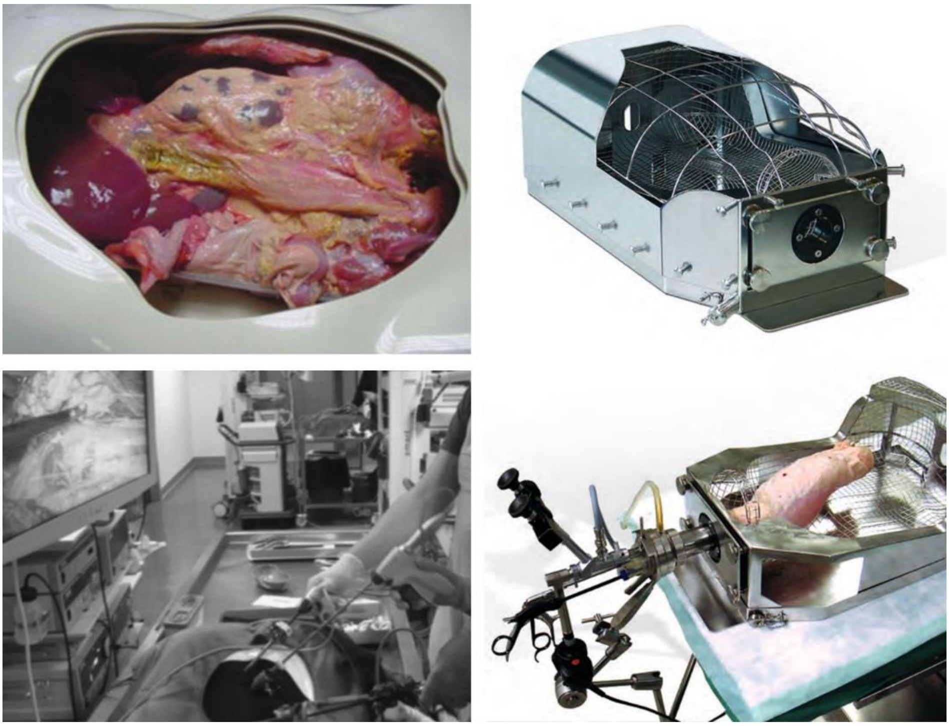

Figure 2.1 Box trainers with animal organs (images acquired from [68], [70]) Permission to use images (right side) of the MIC trainer was acquired from Richard Wolf GmbH and images on the right were reprinted with permission from JOURNAL OF ENDOUROLOGY 28/8, 2011, pp. 1377-1383, published by Mary Ann Liebert, Inc., New Rochelle, NY

In order to have control over the anatomical variance and reduce the number of animals in experiments in the SAFROS project according to the 3Rs principle an affordable and efficient pig abdominal phantom was developed. The following section gives an overview of the development of the high definition pig abdominal phantom. The phantom pig abdomen was created to test different devices and to analyze the overall surgical workflow of pancreatic tumor enucleation in minimally invasive robotic surgery (MIRS).

2.2.2 Pig abdominal phantom

Development

A simulation box was fabricated to mimic the structure of the intraoperative abdominal cavity of a pig during minimally-invasive surgery; it also included parameters for the simulation of an expanded volume within the cavity due to CO2 insufflation (pneumoperitoneum). The geometry of the simulation box and organs were reconstructed from a CT scan of a young pig (CT scans were retrieved from Memorial Sloan Kettering, NYC, USA, research group led by Professor Yuman Fong) using the same reconstruction method described in section 1.2.3. The CT scans were obtained from another institution from previous a study, where pigs had been used previously for a surgical procedure, to minimize the use of animals. The shape of the abdomen was altered using CAD software, to simulate the induction of the pneumoperitoneum. The box was fabricated from polystyrene foam sheets (Styrofoam 250 SL-A-N-40) and covered with glass fiber that was glued onto the smoothed outer layer, as well as onto the inner surfaces of the simulation box.

The abdominal artificial organs (liver, stomach, spleen, kidneys and pancreas) were cast into 3D printed molds made out of pigmented silicone (Dragon Skin® 10 Medium). The intestines and blood vessels (abdominal aorta, portal vein and vena cava) were built from textiles that were fashioned into tubes and covered with a thin layer of silicone (Dragon Skin® 10 Fast). The intestines were filled with sawdust, to give a realistic appearance and realistic CT properties. The overall cost of the phantom pig abdomen (materials and molds) was approximately 400€. The pancreas of the phantom pig abdomen is replaceable, and costs from 10€ to 15€ (when cast out of silicone rubber or gelatin mixture, respectively). The developed phantoms in various design stages and manufacturing stages are visualized in Figure 2.2. More overview of the pig abdominal phantom can found in [71].

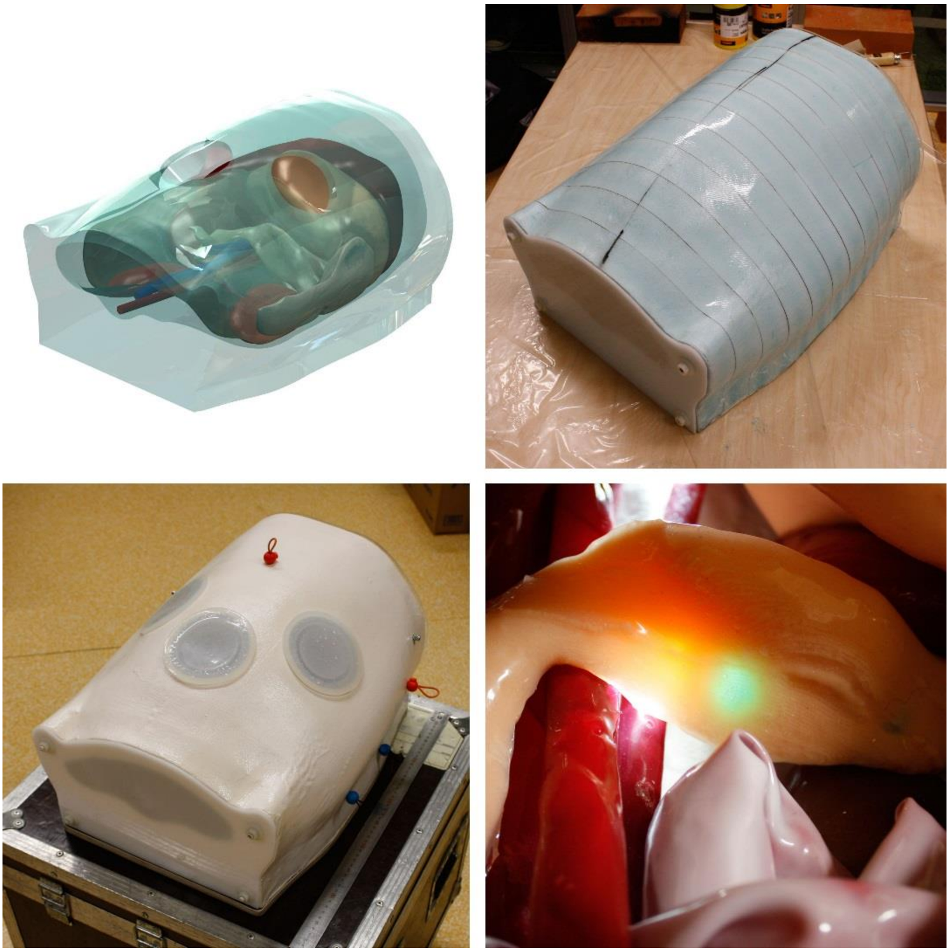

Figure 2.2 Pig abdominal phantom (from upper left to lower right: model of the abdomen reconstructed from CT; Styrofoam model of the abdomen covered with glass fiber, painted and assembled abdomen; view to the silicon pancreas through the middle port)

Usage in experiments and evaluation

The pig abdominal phantom was prepared for two tests, in both of which pancreatic tumor enucleation was used as the surgical procedure. The first test was conducted with a MIRO surgical platform [64]. The goal of the first test was to use the platform to demonstrate and validate the pancreatic surgery scenario by using a robotic surgery system (see Figure 2.3). The second test was conducted to demonstrate an intraoperative scenario of pancreatic surgery, with a surgical system assembled by using two KUKA Lightweight robots [72] and identification of the tumor with ultrasound guidance, during surgery, on the pancreas phantoms cast from gelatin (see Figure 2.4).

Figure 2.3Pig abdominal phantom tests at the German Aerospace Center

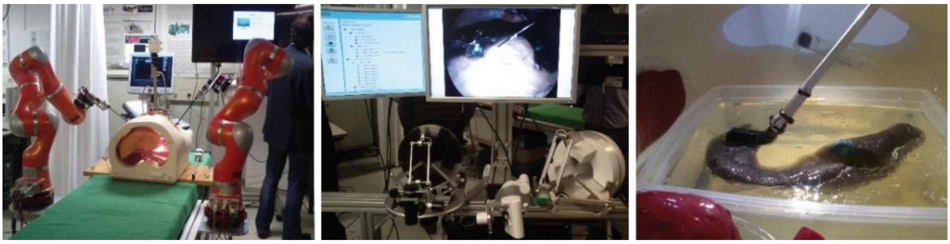

Figure 2.4 Pig abdominal phantom used to test intraoperative pancreatic surgery

The reconstruction quality of the pig abdominal phantom was evaluated in two ways: in comparison with the CT reconstruction, and after examination by a general surgeon who worked with the SAFROS project as a medical consultant (Dr. G. Colucci, from Worthing Hospital, UK) with previous experience in laparoscopy with pigs. The CT reconstruction quality was evaluated by one radiologists (Dr. Peeter Ross from East-Tallinn Central Hospital) and one veterinarian (Dr. Kalmer Kalmus from Estonian University of Life Sciences).

The CT reconstruction was evaluated visually by the radiologists and veterinarian and changes based on their comments were manually made in the segmented layers of the CT scan. The reconstructed organ models were later checked by a surgeon and the pancreas model was compared with pancreases received from abattoirs (see Figure 2.5).

Figure 2.5 Dissection of the pancreas, pancreases received from butcher and casted silicon pancreas with tumors on the right

Following are the surgeon's comments on the phantom evaluation:

> "The manufactured phantoms offered a good replica of the anatomical features of the abdominal cavity of the pig. The position and spatial relationships of the organs were consistent with the CT reconstruction. The rigid abdominal wall offered robust protection for the internal structure during the simulations, while the silicone pads covering the insertion points reproduced the stiffness of the trocar–skin interface. Since the organs were loosely attached to the posterior abdominal wall, their reactions to retraction were smooth and natural. The organs, specifically the pancreas, showed comparable tactile feedback in the silicone form, and realistic ultrasound properties in the gelatin form, similar to the real tissue. The Wirsung duct and the cystic lesions were clearly identifiable, allowing for the simulation of an intraoperative ultrasound-guided enucleation, with pre-operative localization of the cysts and duct."

In addition, several surgeons in Worthing Hospital were asked to compare the tactile feedback of the silicone model to that of real pancreatic parenchyma, whose feedback indicated a satisfactory comparison between the silicone model and living tissue.

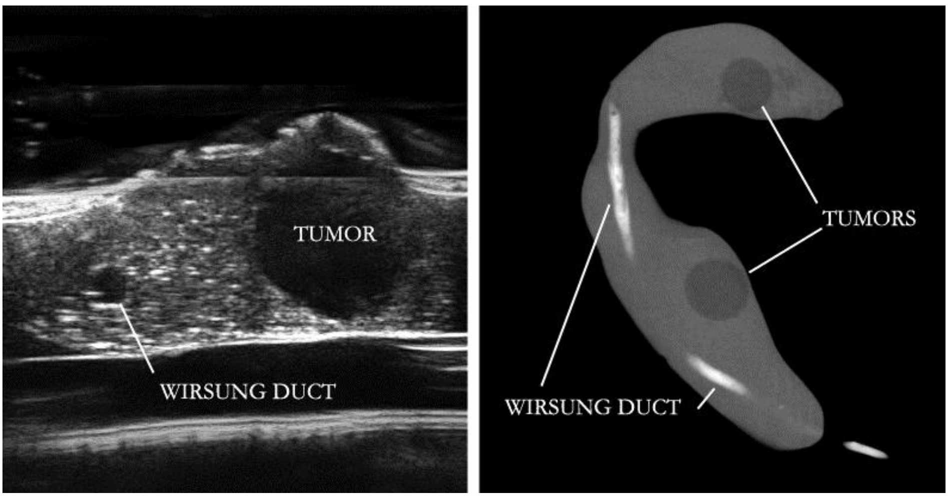

Figure 2.6 Segment from US scan (left) and CT scan (right) of the pancreas casted for intraoperative tests.

Alternative usage of the pig abdominal phantom

Beyond this project, the model can be used for other purposes. For example, phantoms have a role in training for both laparoscopic and robotic surgery. Even if there is an increasing use of virtual reality and simulators in robotic and laparoscopic surgery in general, we are far from having reliable simulators for complex operations. As further developments are made, high-definition phantoms will help to close this gap. For example, increased reality could be achieved through the fabrication of all internal organs with realistic ultrasound and CT properties.

The pig abdominal phantom has been also used outside of the SAFROS project in the field of MIRS [73].

2.3 Intelligent SUrgical Robotics – The I-SUR project

I-SUR project was a 7th Framework project focusing on development of general methods for cognitive surgical robots capable of performing autonomously simple surgical task (cutting, suturing and puncturing) by combining sensing, dexterity and cognitive capabilities.

In order to develop new automated surgical methods and validate the cognitive robots' capabilities and their safety, a patient model was needed in the project. Puncturing as the most challenging surgical task from the above-mentioned three surgical tasks faced the most complicated awareness problems (the poor visibility of ultrasound and the difficult detection/segmentation of anatomical features) and therefore required also a phantom with high dexterity. The challenge of developing a puncturing phantom was that it had to meet the requirements of different technologies: the phantom needed to be multi-layered to allow puncture force detection to develop situation awareness of the robot; ultrasound properties to allow organ's and its parts' localization and registration; CT properties to allow creation of preoperative models; an anatomically correct phantom to mimic real life scenarios; parts of the phantom needed to be interchangeable. Affordable price of the puncturing phantom was the main motivator for the phantom development in I-SUR project. Phantoms available on the market that satisfy the requirements of the puncturing tasks are too expensive and do not include all of the required features. Moreover, phantoms were needed by different partners throughout the project to work in a standardized anatomical environment before integrating different technologies into one robotic surgery platform. The following chapter describes how the anatomically correct features of the phantom were achieved and where the puncturing phantoms were used during the experiments.

2.3.1 Percutaneous abdominal ultrasound puncturing phantom

An anonymized male human CT scan was received from East-Tallinn Central hospital and used to reconstruct the volume of ¼ of the abdomen (right-hand posterior side of the abdomen) (an approval from Tallinn Medical Research Ethics Committee was granted before the work with patients CT scans (decision number 2527)). Besides the right kidney, the reconstruction covered also a section of liver, the ascending stretch of colon, ribs shadowing the liver, a simplified layer of skin and fat representing the right-hand posterior side of the abdomen. The reconstruction of the models followed the same method described in section 1.2.3. In addition to the reconstructed organs a watertight box surrounding the organs, fixators for the organs, molds for casting the organs and placement of the markers were designed in SOLIDWORKS® software.

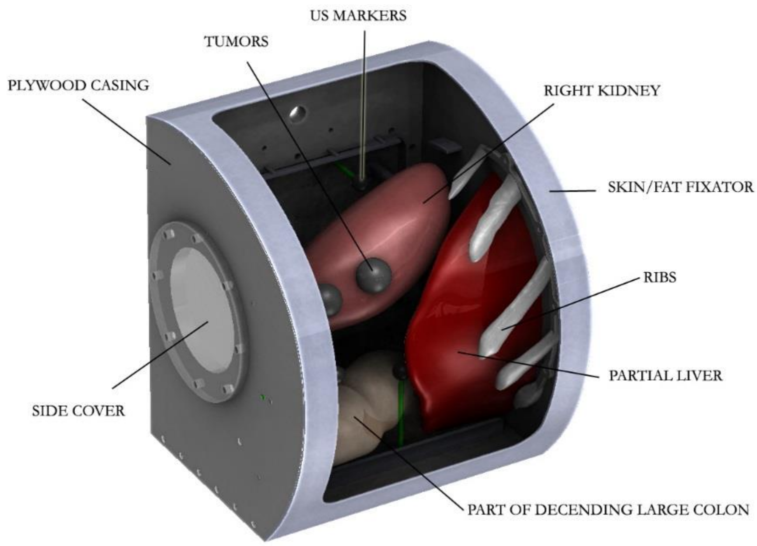

Figure 2.7 Kidney box phantom model and inner view

Two 20mm tumors were added to the lower pole on the posterior face on the kidney model. The fixators were designed to keep the liver, kidney and fat layer in place in the box. The organ molds, ribs and the fixators for liver, kidney and fat layer were 3D printed. The liver, kidney and fat layer were casted using gelatin mixtures with ultrasound-attenuating consistency (described in section 1.2.2); tumors of the kidney were casted from clear gelatin mixture and were later fixed on the surface of the casted kidney by melting the gelatin between two bodies.

The box surrounding the organs was prepared from parts milled out form plywood and assembled using plastic bolts. For the descending colon a simple cylindrical piece of fabric was used and attached to the phantom walls. The liver was fixed on the wall after casting of the box with bolts. The kidney was placed on two plastic rods on the box cover to keep it in the middle of the box. The fat layer was fixed on top of plastic supports, then covered with colored silicone (Dragon Skin series silicone) to represent human skin and finally fixed from outside with a plastic strip. To calibrate the intra-operative US images with the preoperative CT scan, four markers (made of 10 mm rubber spheres fixed on 3 mm plastic tubes) were placed inside the kidney box phantom behind the organs (so that they didn't shadow the organs) and as far away from each other as possible (for increasing the calibration accuracy). Positioning of the markers can be seen in Figure 2.7.

The surrounding space around the kidney, liver and colon was filled with water or clear gelatin mixture which allows the US-based inspection of inner structures of the phantom. A CT scan of the kidney box phantom was acquired using a multi-detector CT scanner (Brilliance 64, Philips Healthcare) at the East-Tallinn Central Hospital. The CT scan and the CAD models were used as the preoperative models of the abdomen during the planning of the surgical procedure.

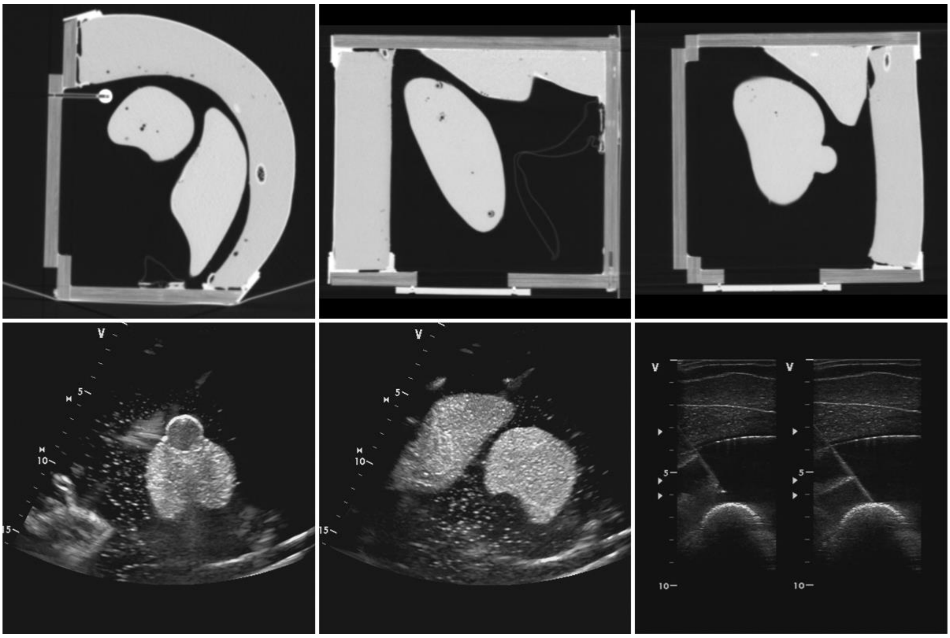

Figure 2.8 Kidney box phantom CT scan (upper row) and US images (lower row: left - visibility of the kidney and tumor with 4C probe; middle - visible kidney and liver with 4C probe; right - needle visibility near the tumor with 10L probe)

2.3.2 Applications of the puncturing phantom

Throughout the ISUR project the phantom helped to test various technologies and allowed the project partners to work on a standardized anatomical model (see Figure 2.7 and Figure 2.8). The following list demonstrates applications where the phantoms were used:

- The phantom model and CT data was used to calculate the best possible cryoablation needle insertion trajectories into the kidney tumor which target points were calculated according to the growth of ice-balls around the tip of the needle [74].

- In order to detect the organs, their borders and needle localization by ultrasound, the phantom was used in development and tuning of US-segmentation algorithms [75], [76].
- Testing the robots control and coordination framework for the automation of surgical tasks [77].
- Reasoning – detection of puncture and penetration events thanks to different stiffness's of the phantom materials
- Needle tracking and guidance accuracy evaluations [78].

The low price (the overall price of materials was approximately 50€ not including the labor) of the phantom made it possible to make the phantoms available to all project partners. More thorough overview of the puncturing task automation can be found in [78].

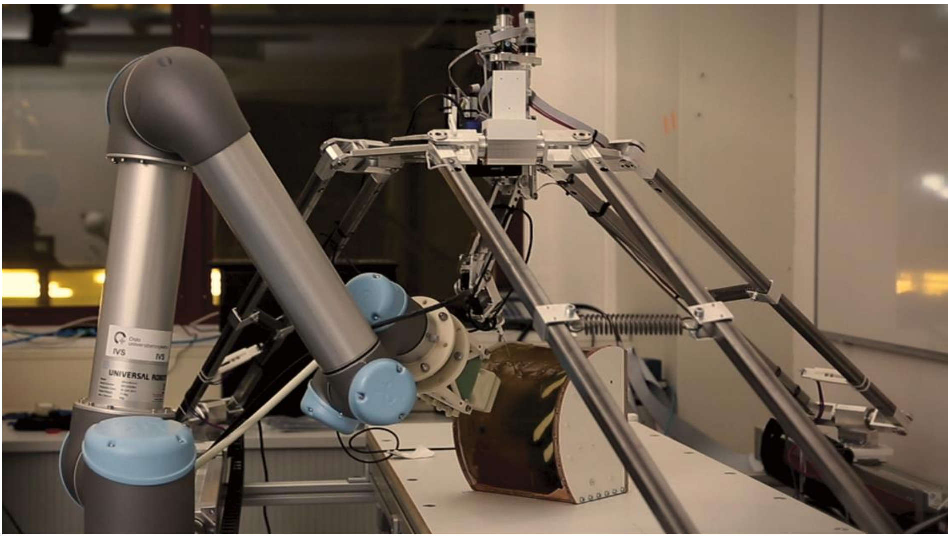

Figure 2.9 Kidney box phantom used in experimenting automated needle guidance with US probe handling done with UR5 robotic arm and needle guided with ISUR robot developed in ETH

2.4 Conclusion

In this chapter two phantoms were demonstrated as examples of testing materials in robotic surgery. In the SAFROS project pig abdominal phantom helped to reduce and avoid animal experiments whereas percutaneous puncturing phantoms in I-SUR project where the bases for development of new automated surgical techniques.

In the SAFROS project a realistic phantom pig abdomen was developed for testing safety features on two robotic platforms. The features of the phantom in general, and of the two pancreatic models (silicone and gelatin), allowed testing of the overall robotic procedure and the intraoperative US guidance. The phantom had two other major advantages:

- First, the phantom offered consistent and more-standardized conditions. When creating the phantom, the anatomy and all of the anatomical variations, including pathological variations, can be controlled.
- Secondly, the phantom permitted savings in terms of money and time. The use of animals has a high cost, as it requires not only the cost of purchase, but also the cost of maintaining a dedicated facility for housing and surgical procedures.

As the phantom had a modular design, it was possible to replace the damaged organ or structure within the abdomen between single tests, as required, making the whole process more efficient and less expensive. Of course the pig abdominal phantom’s anatomical reality could have been more complete. For example the phantom lacked bleeding functionality in the organs and blood vessels which is important for mimicking hazardous situations during surgery. Also the need use organs from different materials for cutting (silicone) and intraoperative US imaging (gelatin) interrupted the experiments and did not allow to test surgical procedures with their natural pace.

In conclusion the pig abdominal phantom filled its purpose as no known artificial animal models for surgical experimentation are available on the market and the human phantom counterparts are too expensive and with limited usability. We can say that the results set a robust basis for eliminating the need for animal experiments in the development phase of MIRS systems, where modifications to the system are usually necessary, before continuing with animal experiments in the final development stages.

In the I-SUR project the percutaneous kidney puncturing phantom was developed to test different technologies separately for the automation of cryoablation procedure of kidney tumors. The designed puncturing phantom filled the set goals by having modular design that allowed to carry out repeatable experiments in short intervals. The low price allowed supplying the project partners with new phantoms throughout the project and if needed change the phantom design which would be not possible with phantoms found on the market.

The low cost of the phantoms set a limit to the anatomical reality of the puncturing phantom. For example the simplified layer of fat, muscles and skin could have reduced the sensibility of the puncturing robot's awareness. The missing features like nerves between ribs, vessels under and in the kidney would have constrained the entry points of the needles and therefore make the simulation environment more realistic. But as the project was aimed to demonstrate the possibility of automated surgery then the reduced anatomical actuality was not considered as a limiting factor. Therefore it can be concluded that the percutaneous kidney puncturing phantom filled its needs in the I-SUR project as a standardized testing platform for different project parts integrated into one autonomous surgical platform.

In conclusion the two phantoms in SAFROS and I-SUR project demonstrated the virtues of using phantoms in testing robotic surgery systems that potentially decrease the cost of experiments, decrease the time between experiments, allow to experiment on the same anatomical environment repeatedly and also have pathologies that are not always available in animal or cadaver experiments.

The need for phantom organ validation instigated co-operation with radiologists that ended up in small-scale production and commercialization of medical training tools. The kidney phantoms usage as training tools in radiology is covered in the following chapter.

3 Phantoms in radiology education

The need of organ phantoms' validation in the SAFROS and I-SUR projects initiated co-operation with radiology department at the East-Tallinn Central Hospital. The collaboration with radiologists brought out, that the phantoms can be applied in training residents in the field of interventional radiology. The following chapter describes the integration of kidney phantoms into training of radiology residents, which lead to commercialization activities in the form of a *spin-off* company producing affordable simulation tools for improving patient safety.

3.1 Introduction

Interventional radiology originated from diagnostic radiology as an invasive diagnostic subspecialty. Interventional radiology is now a diagnostic and therapeutic specialty that has a wide range of minimally invasive image guided therapeutic procedures as well as invasive diagnostic imaging. As part of interventional radiology practice, interventional radiology physicians provide patient evaluation and management relevant to image-guided interventions in collaboration with other physicians or independently [79].

The variety of procedures, both diagnostic and treatment, that interventional radiologist must learn and practice throughout their career makes them unique and irreplaceable in the medical field [80]. The number of different procedures that interventional radiologists can carry out has increased mainly due to the progress in technology, more precisely in medical imaging [81]. The improvement of technology has allowed to cut down costs and at the same time maintain and increase efficiency in medicine [82]. Trends of replacing conventional surgical techniques with minimally invasive procedures mean that the curriculum of interventional radiology has become more difficult and concise. The improvement of curricula and new training methods of interventional radiology might not keep up with the new involving technologies or methods and could therefore pose a direct risk for patient safety and to overall healthcare quality.

Lately, Cardiovascular and Interventional Radiological Society of Europe (CIRSE) introduced a set of training standards (European curriculum and syllabus for interventional radiology) for interventional radiology [83] which aims to unify the training and assure that interventional radiologists provide top-quality safe treatment for their patients within EU. The document describes the knowledge and skills that the practitioner should have after residency but leaves the methods of how the training is implemented free to decide for each country and institution. Training and self-learning is usually a part of the performance improvement programs [84] that hospitals are entitled to carry out. Interventional radiologist come often in contact with new techniques and equipment that cannot be adopted in a short period [85]. Training of staff and residents must be carried out within the hospital and operated by appropriately credentialed and board-certified interventional radiologists. This means that radiologists have to share their time between everyday work, keeping up with new technologies and training.

The traditions of teaching practical skills in interventional radiology vary between countries and between institutions. For long time teaching has followed the “master-apprentice” model where the residents could train on patients. In today’s medical climate this model is neither sufficient nor ethical any more. The trends of reducing the time of patient hospital stay and time-constraints on working hours mean that residents’ possibilities of training on patients to get enough practical experience are diminishing [86]–[88]. So other ways of acquiring practical skills are needed. One possible solution is to use phantoms for in early training phases. Evidence of the effectiveness of training on simulated environments has been shown in studies using endovascular simulators both within and outside radiology [89]–[91]. There are also examples of phantoms being used in the training of interventional radiologists. For example Mendiratta-Lala et al [92] included simple commercial part-task trainer to teach biopsy in simulation based curriculum where the results indicated improvement of the performance both in written and practical examinations after the training.

The high price (see Table 1 for phantoms suitable for various interventional kidney procedures) or simplified anatomy of phantoms for interventional radiology training on the market could result in dismissal of training of a new procedure. There are many studies that have tried to find affordable counterparts for commercial phantoms in interventional radiology training. For example porcine kidneys and turkey breasts have been proposed for training ultrasound-guided biopsy [93]–[95], home-made phantoms made from gelatin or agar have been proposed for learning various ultrasound procedures [96]–[101]. Using phantoms with unrealistic anatomy (parts of animals, or, even worse, fruits and vegetables) might cause risk for patients as the residents might not be ready to work with US visualized human anatomy. Demand for affordable anatomically realistic phantoms is therefore eminent.

In this work the author proposes to improve patient safety by introducing affordable kidney phantoms with realistic anatomy for radiology training. The first motivation for this work came through the need to provide affordable training phantoms for the radiologists, and also find practical output for the phantom development outside and after the SAFROS and I-SUR projects. The second motivation came through the need to introduce qualitative evaluation methods into the training of radiologists, which would assure that the trainees understand the anatomical structures and perform the procedures on a correct spatial spot.

The description of the phantoms development for radiologist, overview of the training, phantom’s evaluation and results in form of opinions of trainees and radiologists are presented in the following sections.

3.2 Integration of phantoms in radiology training

3.2.1 Goals of the study

At the time we introduced phantoms for the radiologists in East-Tallinn Central hospital, the training of residents was following the “master-apprentice” model where the trainees performed procedures with radiologists’ supervision on patients. In some cases the residents prepared gelatin or agar based phantoms themselves to practice US guided procedures to get first experience and confidence before acting on patients. This training model allows the trainee to practice in real clinical environment and the radiologists consider it to be safe as they can intervene whenever a dangerous situation occurs. Although this training model is considered safe, it is still expensive as it is likely to extend the procedures’ times because the radiologists needs supervise and guide the unexperienced residents. Also training on patients might prolong training cycles as the patients with specific procedures are always not be available.

To improve training effectiveness in clinical trials with patients, residents’ readiness for the clinical training and the quality of pre-patient training, we propose to use anatomically correct phantoms in early training phases of interventional radiology. The goal of the study was to develop anatomically correct kidney phantoms for radiology training, which could also be used for procedures’ quality assessment and residents’ examination, and to evaluate their suitability for training.

3.2.2 Training overview

The kidney phantoms were developed for interventional radiology training in the East-Tallinn Central hospital. The usefulness of anatomically correct kidney phantoms was evaluated by second year interventional radiology residents over 3 years (2011 to 2013) in an introductory course to interventional radiology, where kidney phantoms were used to gain practical skills in various US guided needle procedures before acting on real patients.

Through-out the three years of practical evaluation studies the training in the hospital stayed similar. The introductory course to interventional radiology began with an overview lecture where topics concerning patient safety, communication with the patient, procedural principles and safety were covered. The usage of different imaging equipment with practical examples of different procedures on the phantoms or if possible on patients were demonstrated to the residents. The procedures involved thin needle aspiration (*type of biopsy procedure where a thin needle is inserted into an area of abnormal-appearing tissue or body fluid* [102]), tru-cut biopsies (*collecting tissue samples with a disposable needle with outer cannula and inner, notched rod in which a tissue specimen is cut, trapped and withdrawn* [103]) and nephrostomy (*passageway maintained by a tube, stent, or catheter that perforates the skin, passes through the body wall and renal* *parenchyma, and terminates in the renal pelvis or a calyx* [104]) under US or fluoroscopy guidance.

After the introductory part the training continued with practical work where residents gained hands-on experience on phantoms. During the first training year the residents were training in parallel on the traditional hand-made training phantoms and on the kidney phantoms [42]. After completing the training residents were asked to fill in a questionnaire to evaluate the importance of the kidney training phantom in radiology training, its suitability for practicing various tasks and its anatomical correctness.

During the second training year a case study was conducted in addition to the survey where kidney phantoms were used to evaluate residents' psychomotor skills, accuracy and time in performing a needle guided procedure in US. During the second training year we compared performances of two group of students out of whom one trained on home-made phantoms and the second group on the kidney phantoms developed by us [105].

The training plan was developed and training was carried out by Dr. Peeter Ross from the East-Tallinn Central hospital. Dr. Ross also contributed in designing of the phantoms by describing the desired functionalities of the kidney phantoms and also was the first evaluator of the kidney phantoms (moreover, Dr. Ross was also the evaluator of the segmentation accuracy during the reconstruction process of the organs).

3.2.3 Training phantoms

Kidney phantoms

The needle guided procedures in radiology are in essence guidance tasks where it is important to understand the spatial motion of the needle in two-dimensional images. The procedures aim usually at puncturing small targets (diameter less or equal to 5mm) which means that also the simulated targets in the phantoms needed to be small. The anatomy of kidney (see Figure 3.1) provides various chances for reconstruction of small objects that can be used as puncturing targets.

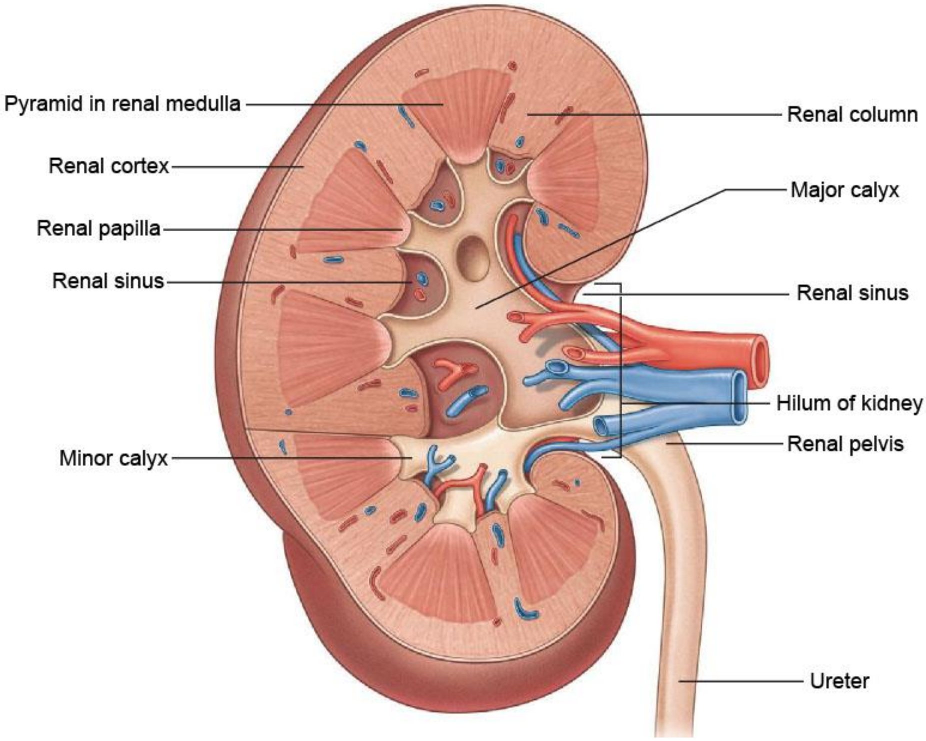

Figure 3.1 Anatomy of the right kidney[4]

During the first training cycle it was decided to add colored solid tumors (with cyst-like appearance) into the uniform body of the kidney phantom as puncturing targets [42]. This allowed the trainees to learn and practice needle guidance under ultrasound and perform thick and thin needle biopsy from the tumors and the body of the kidney (renal cortex). The phantom used in training during the first year is shown in Figure 3.2 on the upper image.

Besides biopsy training biopsy, kidney related procedures also involve drainage and catheter placement procedures. The possibilities for practicing nephrostomy are scarce, as the cases are rare and are usually performed by experienced physicians. To create a possibility for drainage training for the trainees it was decided to reconstruct minor calyces in the kidney phantoms. During the second training cycle 3 large calyces or cysts were added to the kidney phantoms [105]. During the third training cycle in total six calyxes were included in the kidney phantom. By connecting the calyces separately to reservoirs filled with differently colored liquids outside of the phantom a qualitative feedback

[4] This image was published in Gray's Atlas of Anatomy, Drake et al, page 188, Copyright Elsevier (2014).

mechanism was created[5]. The free flow of colored liquids allowed the supervisors to control whether the resident punctured the correct calyx and allowed the residents to get immediate feedback about the placement of needle tip when aspirating with the syringe. The kidney phantoms used for the training in the second and third training cycle are shown in Figure 3.2.

Home-made phantoms

In the comparative study we included also phantoms prepared by the residents that were traditionally used for training US guided needle procedures in our test-hospital. The self-made phantoms consisted of vegetables, fruits and pieces of meat casted into a bowl of gelatin covered with a thin opaque plastic sheet. The objects placed into the gel represented areas of interest and allowed verifying the correctness of the procedure by investigating the biopsy material content.

[5] A patent application was applied for the last version of the kidney phantom (patent application nr. PCT/EP2014/054448).

Figure 3.2 Different versions of kidney phantoms used in the interventional radiology training (upper image: simple kidney phantom with puncturing targets made from clear gelatin; middle image: kidney phantom with three drainable calyces; lower image: kidney phantom with six calyces connected to outer reservoirs with hoses aligned under the kidney as a descending ureter)

3.2.4 Integration results

The evaluation of the phantoms covered suitability for training US guided interventions, realism of medical imaging and durability of the phantoms. The suitability for training was evaluated by the residents after the 5 day introductory course to interventional radiology. Overall 35 residents participated on the training course on our kidney phantoms in the East-Tallinn Central hospital, out of who 25 were included in the evaluation process over the 3 training years (7 residents in 2011, 9 residents in 2012 and 9 residents in 2013).

Figure 3.3 Resident practicing drainage on the kidney phantom

The questionnaire over 3 years clearly indicated that phantoms are an important part of the training. Residents strongly agreed that phantoms are an essential part of the interventional radiology training (4.96 in five-level Likert scale), that they help to improve manual coordination of needle in the US plane (4.96), help to understand how to prepare for the intervention (4.40), what are the properties of the US machine (4.36) and help to understand the movement of the needle during the intervention (4.76).

The size of the kidney phantoms was unchanged trough-out the training and was also suitable according to the residents (4.72). Residents also indicated that the consistency (4.72), anatomical similarity of the structures/pathologies (4.44) and the size of the structures (4.60) in the kidney phantoms were suitable for puncture training. The objects in the kidney phantoms also helped to verify that the puncture was performed at the right location (4.25). The suitability for different procedures e.g. thin needle aspirations (4.20), tru-cut biopsies (4.33) and drainages (4.33) was also highly evaluated by the residents. The only downside marked by the residents was the change of US properties (3.88) (visible needle marks in the phantom) over the training period. Despite this shortcoming the residents found that the kidney phantoms should be available in addition to training sessions also in radiologists' every-day work (4.75).

The importance of phantoms in training was also evaluated by 10 professional radiologists who were anonymously enlisted in an internet poll. The radiologist agreed that the usage of phantoms in the training increases patient safety (4.70) and would increase residents' confidence before working with patients (4.60). The phantoms would reduce the time that the radiologists spend on teaching and the residents spend on learning (4.40) and would help to find out good interventional executers sooner (3.70). The radiologists also agreed that phantoms should be available in addition to training in everyday work of radiologists (e.g. in skill evaluation of radiologists) (4.10). The radiologist were also asked in an open form which phantoms in addition to kidney phantoms should be used in the interventional radiology training – the most frequently mentioned organs were liver with gallbladder and thyroid.

The small case study on the second training year with 9 residents divided into two groups indicated that students practicing on the kidney phantoms achieve the same level of expertise of skills as professional radiologist faster than those who practice on home-made phantoms [105].

3.3 Commercialization

As the kidney phantoms were well accepted in the radiology community, the author among with Dr. Peeter Ross and Prof. Maarja Kruusmaa decided to start a joint venture to start commercialization of the developed phantoms in Estonia and abroad. Tallinn University of Technology was also included in the company as small shareholder and owner of the patent application of the kidney phantom with 6 calyces.

To give a proper appearance for the product, simplify and standardize the assembly of the kidney phantom, a new casing was designed in co-operation with a product development bureau (Ten Twelve Ltd, with support from Enterprise Estonia). More about the design of the commercial kidney phantom can be seen in the user manual shown in Appendix D.

Figure 3.4 Commercial version of the kidney phantom and its US images

3.4 Conclusion and future work

The increasing number of minimally invasive procedures that radiologists are performing increases the need to improve the training quality. The necessity to learn and test new procedures are not just important for residents but also for professional radiologists who every once in a while come in contact with new procedure, equipment or need to rehearse and remind a complex procedure before actually acting on patient.

In this chapter we demonstrated that the developed phantoms can also be applied outside of robotic surgery. The kidney phantoms applicability for radiology training was evaluated in 3 training courses by 2nd year interventional radiology residents. The trainings carried out on anatomically correct kidney phantoms showed, that the phantoms can be successfully used in acquiring first hands-on skills in interventional radiology without threatening the health of a patient. The small number of residents and radiologist included in the survey suspends us from making general conclusions but the first evaluation results indicate that phantoms are an important part of the training and should also be used outside of training in radiologist’s everyday work.

In order to evaluate the phantoms effect of the training effectiveness more test subjects from numerous training centers should be included in the future studies. The preliminary case study indicated that students who train on anatomically correctly constructed phantoms gain experience faster. In the future studies the author would like to research whether the phantoms would allow to conduct the introductory course to interventional radiology partially in a self-study form and how would it influence the effectiveness of the training.

Some changes in the kidney phantom could improve the training quality. For example, the US image quality of the phantom could be improved by increasing the attenuation of the surrounding medium of the kidney, the problem with needle marks left after needle extraction need attention, and the reality of the phantom could be increased for example by introducing pulsating blood vessels, movement of kidney due to the breathing, added surrounded structures like liver, ribs etc. Whether the added features make the training more realistic or just distracts the student in the training a specific procedure need answers from the studies conducted in the future.

The successful integration of phantoms in radiology training encouraged the author and CO to start a joint venture (SafeToAct Ltd.) to enter medical training market with affordable training tools. By the time the thesis is submitted the company has entered the market with an anatomically correct kidney phantom for puncture and drainage training and has found its first customers at the hospitals in Estonia, Finland and USA. The work done in this thesis will be continued by the author at SafeToAct Ltd. where new training tools along with training methods will be designed and developed for radiology and beyond.

The venture has widened possibilities for future projects. The cooperation with radiologists and electronics have initiated a joint project with Technology Competence Centre in Electronics-, Info- and Communication Technologies (ELIKO) to localize needle in the phantoms with impedance (Impedance sensing for artificial organs) or with other ways (e.g. 3D visual tracking) and to develop a software for training of interventional radiology and image guided minimal invasive surgical procedures. The project will start in the second half of 2015.

To widen variation of product portfolio, improve the materials of the phantoms and scale up the production negotiations are ongoing with Competence Center of Food and Fermentation Technologies (CCFFT). At the moment the production in smaller scale is currently already ongoing at the CCFFT.

In conclusion the phantoms were well received by the radiological community and the successful integration of kidney phantoms into training program of radiology residents initiated a *spin-off* company that will continue the work that is described in this thesis.

4 Conclusions

The work in this thesis was motivated by two European Framework 7 projects I-SUR and SAFROS. In both of these projects experiments with new methods of treatment and awareness of robotic surgery was planned to be carried first in an artificial environment that imitates real anatomy. In this thesis we demonstrate a method of producing affordable artificial organs i.e. phantoms and demonstrated their usage in testing robotic surgery and tested them also in training radiology residents.

The first part of the work concentrated on the reconstruction of the phantoms from medical images. Human kidneys were taken as a basis for the reconstruction work for their small size and simple shape. The reconstruction work had two parts. First the materials used to reconstruct organs had to mimic soft tissue properties in ultrasound, in computed tomography and also have soft-tissue-like mechanical properties. It was found that gelatin gels fill all of the criteria. The main benefits found using gelatin gels were the simple and harmless manufacturing process and low price of the mixtures (50€/kg including working labor). The influence of the gelatin mixtures components were mapped to evaluate their effect on mechanical, US and CT properties. The results indicated that the properties can be tuned separately. The US and CT properties of the gelatin gel's well matched those in real tissues, although the US images of the phantoms still indicated, that in order get correct gray-scale images in US we have to tune also the attenuation of the space surrounding the phantom organ. The gelatin gels mechanical properties allowed to reproduce stiffer healthy kidneys and a range of diseased kidneys. Unfortunately the gelatin gels did not allow to reproduce soft organs (with Young's modulus below 10kPa) as the gelatin gel became fragile and the gelatin gels keep hardening over 100 days [32], which means that the phantoms needed to be used short after manufacturing. Secondly the organs had to mimic the anatomical shape of the real organs. Today's imaging technologies (CT and MRI) in medicine allow us to have three dimensional view of the patient's inner structures. So the phantom organs' shape reconstruction was done using anonymized patient's CT scans. The developed reconstruction method was validated first by radiologists who assessed the segmentation of CT scans and secondly a study was carried out with cadaver kidneys that were prepared by pathologist from patients who had died within 2 weeks after having a CT scan taken from their abdomen. It was shown that the average volumetric reconstruction error of the kidneys was less than 5%.

The calibrated tissue mimicking material and organ reconstruction methods were then used in two robotic surgery projects to develop pig abdominal laparoscopy phantom [71] for the SAFROS project and partial human abdominal kidney puncture phantom in the I-SUR project [78].

In the SAFROS project a realistic phantom pig abdomen was developed for testing safety features on two robotic platforms. With the pig abdominal phantom in SAFROS project we reduced animal experimentation following 3Rs principle of reducing, replacing and refining animal experiments [106]. In fact the animal experiments in the SAFROS project were completely replaced with experiments on the pig abdominal phantom. The features of the phantom in general, and of the two pancreatic models (silicone and gelatin), allowed testing of the overall robotic procedure and the intraoperative US guidance. The downside of using gelatin gel in this phantom was its fragility. Larger organs e.g. liver, stomach, spleen with heavy weight where therefore casted from silicone rubber as they would crumble on their own weight if built form gelatin gel. So only pancreas, the organ that was the operable organ, was reproduced from gelatin for intraoperative US experiments. As the gelatin gel cannot withstand cuts and pressure from the graspers the pancreas from gelatin needed to be replaced with silicone counterpart for nucleating the tumors from the pancreas. So it was not possible to follow the procedures natural pace as it was necessary to use different materials for cutting (silicone) and intraoperative US imaging (gelatin). Of course the pig abdominal phantom’s anatomical reality could have been more complete. The phantom lacked bleeding functionality in the organs and blood vessels which is important for mimicking hazardous situations during surgery. The solid abdominal wall permitted simulating pressurization of the abdomen.

In conclusion the pig abdominal phantom filled its purpose as no known artificial animal models for surgical experimentation are available on the market and the human phantom counterparts are too expensive and with limited usability. The SAFROS project benefited from pig abdominal phantom by reduced time for preparing experiments and time between repeated experiments (fast replacement of damaged organs), allowing to control the anatomy and pathologies (e.g. size, shape and position of tumors were tailored for the needs of the project) and to reduce costs as experiments on live animals are expensive. We can say that the results set a robust basis for eliminating the need for animal experiments in the development phase of MIRS systems, where modifications to the system are usually necessary, before continuing with animal experiments in the final development stages.

In the I-SUR project we used the gelatin recipes to build partial human abdominal phantom representing the right kidney and its surrounding space to test different technologies separately for the automation of cryoablation procedure of kidney tumors. The designed puncturing phantom filled the set goals in the project by having modular design that allowed to carry out repeatable experiments in short intervals. The low price allowed supplying the project partners with new phantoms throughout the project and if needed change the phantom design which would be not possible with phantoms found on the market. The low cost of the phantoms set a limit to the anatomical reality of the puncturing phantom. For example the simplified layer of fat, muscles and skin could have reduced the sensibility of the puncturing robot's awareness. The missing features like nerves between ribs, vessels under and in the kidney would have constrained the entry points of the needles and therefore make the simulation environment more realistic. But as the project was aimed to demonstrate the possibility of automated surgery then the reduced anatomical actuality was not considered as a limiting factor. Therefore it can be concluded that the percutaneous kidney puncturing phantom met the requirements of the I-SUR project as a standardized testing platform for different project parts integrated into one autonomous surgical platform.

The cooperation with radiologists that began with validation of phantom kidneys led to applying the kidney phantoms in radiology training. Over 3 years the kidney phantoms were used in introductory courses to interventional radiology to train ultrasound guided needle procedures to second year radiology residents. The kidney phantoms were used in training and evaluated by 25 residents and also 10 radiologists. The results indicated that the phantoms are needed in training and also in radiologists' everyday work. The phantoms allow the trainees to practice and learn procedures safely in a stress free situation without threatening the patient. The phantoms also showed to be useful in practicing more difficult procedures and would therefore help radiologists gain confidence before acting on patients. The results from the study are preliminary and need more test subjects to make general conclusions about the effects that the phantoms have in the training. The kidney phantoms that we used in this study were with simple design. Of course we could enhance the kidney phantom realism to improve the training quality. For example, the US image quality of the phantom could be improved by increasing the attenuation of the surrounding medium of the kidney, the problem with needle marks left after needle extraction need attention, and the reality of the phantom could be increased for example by introducing pulsating blood vessels, movement of kidney due to the breathing, added surrounded structures like liver, ribs etc.

In conclusion the phantoms were well received by the radiological community and as a result the successful integration of kidney phantoms initiated a *spin-off* company.

The successful integration of the anatomically correct training devices encouraged the author along with Prof. Maarja Kruusmaa and Dr. Peeter Ross to start a joint venture for commercialization of the phantoms in and outside Estonia. The venture has already widened possibilities for future projects. The cooperation with radiologists and electronics have initiated a joint project with Technology Competence Centre in Electronics-, Info- and Communication Technologies (ELIKO) to develop needle tracking methods for improving training quality and qualitative feedback systems. To improve the materials of the phantoms and scale up the production negotiations are ongoing with Competence Center of Food and

Fermentation Technologies (CCFFT). At the moment the production on a small scale is currently already ongoing at the CCFFT.

To emphasize, the relevant conclusion of the thesis are following:

- The tissue mimicking material calibrated and used in this thesis, gelatin gels, are inexpensive, harmless to handle, allow to recreate a range of soft tissues and the physical properties (radiodensity, US properties and elasticity) can be tuned separately.
- The developed reconstruction method of phantoms from CT scans allows accurate recreation of organs. A cadaveric study showed that the volumetric difference between CT reconstructed kidneys and post-mortem scans of kidneys was less than 5%.
- The reconstruction methods and tissue mimicking material was used to develop phantoms for 2 robotic surgery projects SAFROS and I-SUR. It was shown that the phantoms are useful for experimentation in the early development phase of robotic surgery systems. The projects benefited used phantoms as standardized test-platform that helped to reduce time for preparing experiments, time between repeated experiments (fast replacement of damaged organs), allowed to control the anatomy and pathologies (e.g. size, shape and position of tumors were tailored for the needs of the projects), reduce costs and avoid animal experiments.
- The implementation of anatomically correct kidney phantoms in interventional radiology training indicated that the phantoms are needed in training and also in radiologists' everyday work. The phantoms allowed the trainees to practice and learn procedures safely in a stress free situation without threatening the patient. The phantoms also showed to be useful in practicing more difficult procedures and would therefore help radiologists gain confidence before acting on patients.
- The successful integration of the anatomically correct training devices encouraged the author and CO to start a joint venture for commercialization of the phantoms in and outside Estonia. The venture has already widened possibilities for future projects and as a results of this thesis a product is launched onto the market and used to train residents and training centers and hospitals.

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Abstract

The late developments in medicine have been aimed to reduce post procedure recovery time of the patients, pain for the patients, minimize tissue damage during the procedures etc. It has been made possible due to introduction of minimally invasive procedures and improved medical imaging possibilities. One of the latest enhancements to minimally invasive surgery has involved robotics that have improved the capabilities of the surgeon and have helped overcome the limitations of laparoscopic surgery. But before new procedures or devices can be applied to patients they need to go through thorough validation process. In this work we demonstrated that in the early phase of robotic surgery platform development, when the systems are unreliable, phantoms offer a good standard model for repeatable experimentation and it is possible to avoid animal experimentation by replacing them with custom made affordable anatomically correct phantoms.

Today's medical imaging devices (CT, MRI and also US) allow to reconstruct the patient's inner anatomy's volumetric composition with submillimeter accuracy. In this work we used patients' anonymized CT scans to reconstruct artificial organs' i.e. phantoms' anatomical shape. To evaluate the reconstruction quality a cadaver study was performed where post-mortem human kidney scans were compared with corresponding patient's kidney models reconstructed from CT scans. The anatomically correct shape of the organ is as important of its substance. To mimic the soft tissue properties of real organs a material research was performed. Gelatin gels were chosen as they represent US, CT and also mechanical properties in similar range of real soft tissues. The gelatin gels components effect on the tissue properties were mapped and the recipes were used to build phantoms for two projects.

In the SAFROS project (Patient Safety in Robotics Surgery) pig abdominal phantom was developed to reduce the number of animal experiments that were planned at the end of the project. In fact the animal experiments in the SAFROS project were completely replaced with experiments on the pig abdominal phantom. The pig abdominal phantom helped to reduce the time for preparing experiments, time between repeated experiments (fast replacement of damaged organs), control the anatomy and pathologies (e.g. size, shape and position of tumors) and reduce costs as experiments on live animals are high. Another project I-SUR (Intelligent SUrgical Robotics) benefited by having partial human abdominal phantoms for automation of kidney puncturing task under US guidance through low cost of the phantoms, standardized anatomical testing environment for different project partners and also through short time interval between experiments. Both of the projects were finished successfully and the phantoms were appreciated by the reviewers. As the phantoms served as good standard models in testing robotic surgery, other applications were searched for in order to continue the work with phantoms after the two projects.

The alternative applications for the phantoms came through cooperation with radiologists who found usage for the phantoms in radiology training. In the introductory course to interventional radiology where ultrasound guided needle procedures where taught for second year radiology residents was performed on kidney phantoms developed and prepared by the author. The kidney phantoms were used in training and evaluated over 3 years by 25 residents and also 10 radiologists. The results indicated that the phantoms are needed in training and also in radiologists' everyday work. The phantoms allow the trainees to practice and learn procedures safely without threating the patient in a stress free situation. The phantoms also showed to be useful in practicing more difficult procedures and would therefore help radiologists gain confidence before acting on patients. The successful integration of the anatomically correct kidney phantoms in radiology training encouraged the author along with Prof. Kruusmaa and Dr. Ross to start a *spin-off* company that would commercialize the phantoms in and outside Estonia.

To emphasize, the main results of this thesis are as follows:

- Calibrated tissue mimicking materials, gelatin gels, and a method for reconstruction of organs from CT scans.
- Demonstration of applications of the phantoms in robotic surgery, where the phantoms reduced time and costs of repetitive experiments, helped to avoid animal experimentation, allowed to control the anatomical and pathological conditions.
- Implementation of phantoms in radiology education and evaluation their usage in training interventional radiology procedures to residents and others.
- A market ready product, kidney phantom that is being used to train residents in and outside Estonia.

Kokkuvõte

Meditsiini viimased trendid on olnud suunatud kulude kokkuhoiule, sealhulgas patsientide kiiremale operatsioonijärgsele taastumisele, patsientide raviprotseduuride aja lühendamisele, koekahjustuse minimaliseerimisele operatsioonidel jne. See kõik on realiseerunud tänu minimaalse invasiivsusega ravi- ja analüüsimeetodite kasutuselevõtule ning paremate meditsiiniliste pildistusseadmete arengule. Viimase 15 aasta jooksul on minimaalse invasiivsusega laparoskoopilisi protseduuride kvaliteedi tõstmiseks kasutusele võetud kirurgide poolt juhitavad robottööriistad, mis on aidanud ületada laparoskoopiliste operatsioonide puudujääke. Robotkirurgia süsteemide rakendamiseks patsientidel peavad nad läbima põhjaliku kontrolli. Käesolevas töös näidatakse tehisorganite ehk fantoomide rakendatavust arendusfaasis olevate robotkirurgia süsteemide testimisel. Eriotstarbeliste taskukohaste anatoomiliselt korrektsete fantoomide rakendamisega on võimalik läbi viia võrreldavaid korduskatseid ning vältida loomkatseid robotkirurgia süsteemi varajases arengufaasis, kus süsteemi töös esineb tihti katkestusi ning tõrkeid.

Tänapäeval kasutusel olevad erinevad meditsiinilised pildistusmodaalsused (kompuutertomograafia, magnetresonantstomograafia, ultraheli) võimaldavad kujutada patsiendi sisemisi anatoomilisi struktuure alla millimeetrise resolutsiooniga. Antud töös rekonstrueeriti fantoomorganite kuju anonüümsete patsientide kompuutertomograafia uuringute alusel. Rekonstrueerimiskvaliteedi hindamiseks viidi läbi võrdlusuuring, kus võrreldi omavahel patsiendi surmale eelnenud kompuutertomograafia uuringu alusel rekonstrueeritud neerumudeleid patoloogiakeskuses skanneritud vastava surnud patsiendi neerudega. Anatoomiliselt korrektne kuju on fantoomide puhul niisama oluline kui nende sisu. Pehmete kudede füüsikaliste omaduste matkimiseks fantoomorganites viidi läbi materjali uuring. Uuringu tulemustes selgus, et sobivaks materjaliks valmistamiskeerukuse, hinna ning füüsikaliste omaduste (ultraheli, kompuutertomograafia ning elastsuse) poolest on želatiinil baseeruvad segud. Želatiinisegude komponentide mõju koostisele kaardistati ning saadud retsepte kasutati fantoomide ehitamiseks kahes Euroopa Komisjoni 7. Raamprogrammi projektis.

Projektis SAFROS (Patsiendi ohutus robotkirurgias) arendati välja sea kõhufantoom vähendamaks loomkatseid viimases projekti faasis. Antud fantoomi kasutamisega aga jäeti loomkatsed projekti lõppedes üldse kõrvale. Sea kõhufantoomi abil vähendati eksperimentide ettevalmistusaega, lühendati aega korduskatsete vahel (kuna vigastatud organid olid lihtsasti vahetatavad), seadistati anatoomilisi struktuure vastavalt vajadustele (näiteks tuumorite suuruse ning paigutuse muutmine vastavalt vajadusele) ning alandati ka katsete hinda kuna loomkatsed on oma loomult oluliselt kallimad kui arendatud tehisorganid. Teises 7. Raamprogrammi projektis I-SUR (Arukad kirurgiarobotid) arendati välja osaline inimese kõhufantoom, millel viidi läbi eksperimente neerupunktsiooni protseduuri automatiseerimiseks. Kõhufantoomi kasutamisega I-SUR projektis hoiti kokku aega korduskatsete vahel, pakuti erinevatele projektipartneritele standardset testplatvormi ning omati kontrolli anatoomiliste struktuuride üle, mis poleks võimalik kommertslike fantoomidega. Mõlemad projektid lõppesid heade tulemustega ning mõlemas projektis hinnati fantoome kõrgelt. Et fantoomid leidsid head tagasisidet robotkirurgia testimisel ning et mitte tööd fantoomidega seisma jätta, otsiti fantoomiarendusele alternatiivseid rakendusi.

Alternatiivina leiti fantoomidel rakendust koostöös radioloogidega, kes leidsid fantoomidele kasutuse menetlusradioloogia õpetamisel. Menetlusradioloogia sissejuhataval kursusel teise aasta radioloogia residentidele võeti kasutusele neerufantoomid, millel õpetati erinevate nõelprotseduuride teostamist. Neerufantoome kasutati treeningutel ning hinnati 3 aasta jooksul 25 residendi ning 10 radioloogi poolt. Hindamistulemused kinnitasid, et fantoomidel harjutamine on oluline osa treeningust ning nad võiksid olla saadaval ka radioloogide igapäevatöös. Fantoomid võimaldavad residentidel õppida ning harjutada protseduure stressivabalt ilma patsiente ohustamata. Neerufantoome kasutamisel on võimalik radioloogidel meelde tuletada keerulisemaid protseduure ning seeläbi tõsta ka enda enesekindlust enne patsiendi peal praktiseerimist.

Anatoomiliselt korrektsete odavate neerufantoomide edukas rakendamine radioloogide õppetöösse julgustas autorit koos professor Kruusmaa ning doktor Rossiga alustama *spin-off* ettevõtet, mille eesmärgiks on fantoomide arendamine ja kommertsialiseerimine haiglates, treeningkeskustes ja ülikoolides Eestis ning mujal.

Rõhutamaks veelkord antud töö põhitulemusi on nad ära toodud alljärgnevas loetelus:

- Kalibreeritud omadustega želatiinigeelid ning organite rekonstrueerimise metoodika kompuutertomograafia uuringu baasil.
- Fantoomide rakendamine robotkirurgia testimisel, kus fantoomide rakendamine aitas vähendada eksperimentide korduvkatsete ettevalmistusaega ning kulutusi, aitasid vältida loomkatseid, võimaldasid muuta anatoomilisi ning patoloogilisi struktuure fantoomides vastavalt projektide nõuetele ning vajadustele.
- Fantoomide rakendamine radioloogia õppetöös ning fantoomide sobivuse hindamine menetlusradioloogia protseduuride õpetamisel radioloogia residentidele.
- Toode, neerufantoom, mis on valmis meditsiiniliste õppevahendite turule sisenemiseks ning mille esimesed eksemplarid on juba kasutusel radioloogia residentide õpetamisel Eestis ning mujal.

Appendix A

Hunt A, Ristolainen A, Ross P, Opik R, Krumme A, Kruusmaa M. Low cost anatomically realistic renal biopsy phantoms for interventional radiology trainees. European Journal of Radiology. Elsevier Ireland Ltd; 2013; 82:594–600.

Appendix B

Ristolainen A, Colucci G, Kruusmaa M. A phantom pig abdomen as an alternative for testing robotic surgical systems: our experience. Alternatives to laboratory animals. 2013; 41: 359–367

Appendix C

Ristolainen A, Ross P, Gavšin J, Semjonov E, Kruusmaa M. Economically affordable anatomical kidney phantom with calyxes for puncture and drainage training in interventional urology and radiology. Acta Radiology Short Reports. 2014; 3: 1–7.

Appendix D

Kidney phantom user manual. SafeToAct Ltd.

CURRICULUM VITAE

Personal data

Name:	Asko Ristolainen
Date of birth:	27.12.1985
Place of birth:	Tallinn, Estonia
Citizenship:	Estonian

Contact data

Address:	Laagri, Kuuse 18a-11, Saue vald, 76401, Harjumaa, Estonia
Phone:	+372 52 68 094
E-mail:	ristolainen.asko@gmail.com

Education

2011 – 2015	Tallinn University of Technology	PhD
2008 – 2010	Tallinn University of Technology	MSC in Mechatronics, *Cum Laude*
2005 – 2008	Tallinn University of Technology	BSc in Mechatronics
1993 – 2005	Tallinna Pääsküla Gümnaasium	Highschool

Language competence

Estonian	Native
English	Fluent
German	Average

Professional employment

2012 -…	Tallinn University of Technology, Centre for Biorobotics	Junior Researcher
2010 - 2012	Tallinn University of Technology, Centre for Biorobotics	Engineer
2009 - …	Steelmet OÜ (0.1 work load since 2010)	Engineer

ELULOOKIRJELDUS

Isikuandmed

Nimi:	Asko Ristolainen
Sünniaeg:	27.12.1985
Sünnikoht:	Tallinn, Eesti
Kodakondsus:	Eesti

Kontaktandmed

Aadress:	Laagri, Kuuse 18a-11, Saue vald, 76401, Harjumaa, Eesti
Telefon:	+372 52 68 094
E-mail:	ristolainen.asko@gmail.com

Hariduskäik

2011 – 2015	Tallinna Tehnikaülikool	PhD
2008 – 2010	Tallinna Tehnikaülikool	MSC, Mehhatroonika, *Cum Laude*
2005 – 2008	Tallinna Tehnikaülikool	BSc, Mehhatroonika
1993 – 2005	Tallinna Pääsküla Gümnaasium	Keskharidus

Keelteoskus

Eesti keel	Emakeel
Inglise keel	Kõrgtase
Saksa keel	Kesktase

Teenistuskäik

2013 - ...	Tallinna Tehnikaülikool Biorobootika keskus	Nooremteadur
2010 – 2013	Tallinna Tehnikaülikool Biorobootika keskus	Insener
2009 - …	Steelmet OÜ (0.1 töökoormus alates 2010)	Insener