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Corso di Laurea Magistrale in
Biomedical Engineering

Integration of a Virtual Reality Environment for Percutaneous Renal Puncture in the Routine Clinical Practice of a Tertiary Department of Interventional Urology: A Feasibility Study

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List of Abbreviations

.dcm: DICOM Format File

.mhd: MetaImage Format File

.obj: Objects Format File

.raw: RAW Format File

.stl: Stereo-Lithography Format File

.**zraw**: Compressed RAW Format File

AR: Augmented Reality

AS: Ascension

ASST: Aziende Socio Sanitarie Territoriali

BPD: Business Process Diagrams

BPMN: Business Process Modelling Notation

BPMS: Business Process Management Software

BPR: Business Process Reengineering

CardioCT: Cardiac CT

CEI: Comitato Elettrotecnico Italiano

CT: Computerized Tomography

MDD: Medical Device Directive

EEC: European Economic Community

GUI: Graphical User Interface

HTA: Health Technology Assessment

HU: Hounsfield Unit

IEC: International Electrotechnical Commission

InfRAs: Inferior Supernumeraries Renal Arteries

ISO: International Organization for Standardization

L3: Third Lumbar Vertebra

MEDDEV: Collection of Medical Device Guidelines

MRI: Magnetic Resonance Image

PCA: Percutaneous Renal Access

PSVR: Patient-Specific Virtual Reality Simulator

QH: Quick Haptics

RSS: Robust Statistics Segmenter

VRE: Virtual Reality Environment

ROI: Region of Interest

T12: Twelfth Thoracic Vertebra

UroCT: Urological CT

VL: Visualization Library

WF: Workflow

WK: Wykoby

Sommario

La tesi, affiliata al NearLAB del Politecnico di Milano, è stata realizzata in collaborazione con:

- *il Dipartimento di scienze biomediche e cliniche "Luigi Sacco", Università degli studi di Milano presso ASST Sacco Fatebenefratelli, Milano;*
- *i Reparti di Radiologia e Radiologia interventistica del Dipartimento di tecnologie terapeutiche diagnostiche avanzate presso l'ASST Grande Ospedale Metropolitano Niguarda, Milano.*

Oggigiorno numerose patologie richiedono come terapia un intervento chirurgico di tipo mini-invasivo per poter garantire al paziente un migliore *outcome* clinico.
Con il passare del tempo infatti le procedure chirurgiche sono diventate sempre più precise e mirate a ridurre il cosiddetto "trauma chirurgico" al quale il paziente è sottoposto al fine di potergli permettere nel post-operatorio lo stile di vita migliore possibile.
Sono state sviluppate quindi tecniche basate sull'utilizzo di strumenti che permettano la possibilità di operare su campo operatorio ridotto rispetto a quello delle tecniche di chirurgia *open* strumenti che tuttavia richiedono una maggiore abilità del chirurgo difficile da ottenere poiché molto diversa da quella tradizionale insegnata durante gli anni accademici (basti pensare alla differenza che vi è tra il classico bisturi e gli strumenti di chirurgia laparoscopica).

In questo contesto, uno degli strumenti che ha preso più piede in ambito medico per il training e il supporto dei chirurghi, è quello dell'utilizzo di un simulatore in realtà virtuale su cui il chirurgo stesso possa fare esperienza prima di effettuare l'intervento.

Partendo da queste ipotesi, mi è stato chiesto di analizzare questo aspetto in termini di utilizzo in clinica di simulatori in realtà virtuale, andando per un periodo di circa due mesi ad assistere in sala operatoria a interventi chirurgici di diverse specialità (Appendix 1) in alcuni ospedali di Milano e interfacciandomi con i chirurghi stessi per capire il loro parere riguardo a questo approccio.

Questa tesi rappresenta quindi il lavoro relativo all'elaborazione di una soluzione ad un problema identificato attraverso questa esperienza.

Tra tutti i diversi tipi di chirurgia ai quali ho potuto assistere, infatti, è stato evidente come effettivamente procedure di radiologia interventistica possano beneficiare dell'utilizzo di un simulatore chirurgico. In questo senso, questo progetto vuole fornire un soluzione che possa rappresentare un supporto all'attività dei professionisti di una specifica procedura chiamata Puntura Percutanea per la Biopsia Renale.
Numerosi infatti sono i pazienti affetti da patologie renali che richiedono quindi l'analisi di un campione dell'organo necessario per poterne effettuare una diagnosi.
Molte degli interventi su questo organo inoltre richiedono un accesso di tipo mini-invasivo, che tuttavia non è di facile realizzazione a causa della posizione complessa di questo organo all'interno della cavità addominale e dell'elevata variabilità anatomica inter-soggetto.

L'accesso all'organo avviene mediante la Puntura Percutanea e viene realizzato posteriormente introducendo attraverso la cavità toracica l'ago per la biopsia (necessariamente lungo) tra l'undicesima e la dodicesima costa.

Trattandosi di una manovra estremamente pericolosa, a causa del rischio di perforazione degli organi vicini o di un eventuale emorragia causata dell'elevata concentrazione di sangue all'interno dell'organo, questa viene realizzata esclusivamente dai chirurghi esperti.

Per tutte queste ragioni, si è ritenuto che l'utilizzo di un simulatore chirurgico in realtà virtuale per la puntura percutanea del rene, in ambito pre-operatorio, possa aiutare il chirurgo nello studio dell'anatomia del paziente che si troverà davanti nel momento in cui dovrà effettuare la procedura, e supportarlo nel momento più complesso dell'intervento avendo già fatto esperienza precedentemente sul simulatore.

Seppur i simulatori siano degli strumenti didattici e di supporto molto richiesti e apprezzati (infatti esistono tantissimi studi nei quali sono stati realizzati dei simulatori chirurgici), questi poi non vengano utilizzati effettivamente in ambito clinico. La ragione per cui questo accade è ritenuta essere l'impossibilità di lavorare su modelli tridimensionali paziente specifici. Inoltre, è stato evidente come un simulatore chirurgico (in realtà virtuale e paziente specifico) relativo a questo particolare tipo di procedura non è mai stato realmente studiato.

Si è deciso quindi, a partire da un simulatore (LACE) che era già stato realizzato in un precedente lavoro in letteratura e che comprendeva anche l'applicazione, seppur generica,

della puntura percutanea renale, di sviluppare questo lavoro rendendone possibile l'utilizzo in un contesto paziente-specifico e andando a studiare come questo potesse essere poi realmente utilizzato in clinica.

Per fare ciò è stato necessario:

- studiare in maniera approfondita il simulatore;
- ottimizzare e standardizzare il processo di simulazione;
- analizzare il tradizionale flusso di lavoro a livello pre-operatorio per verificare la fattibilità di utilizzo del simulatore in termini di tempistiche;
- sviluppare un flusso di lavoro ottimizzato e standardizzato che possa essere eseguito dal chirurgo al fine di utilizzare il simulatore nella pratica 'routinale';
- sviluppare un protocollo sperimentale da sottoporre ai chirurghi dell'ASST Grande Ospedale Metropolitano Niguarda, Milano per la sperimentazione del workflow;
- analizzare i dati relativi alla validazione.

Abbiamo ritenuto inoltre necessario verificare se tale simulatore potesse essere classificato come un dispositivo medico secondo la definizione che ne viene date nelle normative in vigore.

Questo lavoro quindi vuole rappresentare un primo esempio di studio di fattibilità di utilizzo in clinica di un simulatore in realtà virtuale paziente-specifico, realizzato in ambito accademico e validato in collaborazione a un team di medici e chirurghi.

Infatti si ritiene che, la mescolanze e la confluenza di problemi ingegneristici e chirurgici, guideranno la transizione dall'ambiente di realizzazione (bench) all'utilizzo clinico di questo simulatore paziente-sicuro in modo rapido ed efficiente.

In questo senso, il progetto vuole rappresentare anche una piccola parte di un campo più ampio che è la valutazione delle tecnologie per l'uso clinico (HTA, Health Technology Assessment).

Abstract

The thesis, affiliated to the NearLAB of the Politecnico di Milano, was created in collaboration with:

- *the Department of Biomedical Sciences and Clinics "Luigi Sacco", University of Milan at ASST Sacco Fatebenefratelli, Milan;*
- *the Departments of Radiology and Interventional Radiology of the Department of Advanced Diagnostic Therapeutic Technologies at the ASST Grande Metropolitan Hospital Niguarda, Milan.*

Nowadays many pathologies require a minimally invasive surgical approach, in order to guarantee the patient better clinical outcome.
Over time, in fact, the surgical procedures have become increasingly precise and aimed at reducing the so-called surgical trauma to which the patient is subjected, in order to allow him in post-surgery the best possible lifestyle.
Therefore, techniques based on the use of instruments that allow the possibility of operating on a reduced operative field compared to open surgery techniques have been developed.
However, they require a greater ability of the surgeon difficult to obtain because very different from the traditional one taught during the academic years (just think of the difference between the classic scalpel and the laparoscopic surgery instruments).

In this sense, one of the tools that has taken more place in the medical field for the training and support of surgeons, is the use of a virtual reality simulator (VR simulator) on which the surgeon himself can experience before performing the operation.

Starting from these hypotheses, I was asked to analyse this aspect by considering the use of virtual reality simulators in the clinical practice, going for a period of about two months to assist to surgical operations of different specialties (Appendix 1) in some hospitals in Milan and in the operating theatre. I was asked also to interface with the surgeons themselves to understand their opinion regarding this approach.

This thesis therefore represents the work related to the elaboration of a solution to a problem identified through this experience.

Among all the different types of surgery I have been able to witness, it has been evident that actually interventional radiology procedures can benefit from the use of a surgical simulator. In this sense, this project aims to provide a solution that can support the activity of professionals in a specific procedure called Percutaneous Puncture for Renal Biopsy.
In fact, many patients suffer from renal diseases that therefore require the analysis of a sample of the organ necessary to be able to make a diagnosis.
Many of the interventions on this organ also require a minimally invasive access, which is not easy to carry out due to the complex position of this organ inside the abdominal cavity and the high inter-subject anatomical variability.
Access to the organ is performed by Percutaneous Puncture Access (PCA) and is made posteriorly by introducing through the thoracic cavity the needle for biopsy (necessarily long) between the eleventh and twelfth ribs.

It must be considered that this is a potential dangerous manoeuvre, due to the risk of perforation of the nearby organs or of a possible bleeding caused by the high concentration of blood inside the organ. By this way, this procedure requires experienced surgeons.

For all these reasons, it was considered that the use of a VR surgical simulator for percutaneous puncture of the kidney (in the pre-operative setting) can help the surgeon in the study of the patient's anatomy and in the most complex moment of the intervention, having already previously had experience on the simulator.

Even if the simulators are requested and appreciated educational and support tools (there are many studies in which surgical simulators were made), these are not actually used in the clinical field.
The reason why this happens, it was considered the impossibility of working on patient-specific three-dimensional models. Furthermore, it was evident that a VR patient-specific surgical simulator related to PCA has never really been studied.

Starting from a simulator (LACE) which had already been done in a previous work in the literature and which also included the application (albeit generic) of PCA, it was decided to carry on this work making it possible to use in the patient-specific configuration and going to study how this could then be really used in the clinical practice.

In brief, the following steps were followed:

- study the simulator in depth;
- optimize and standardize the simulation process;
- analyse the traditional workflow at pre-operative level to verify the feasibility of using the simulator in terms of timing;
- develop an optimized and standardized workflow that can be performed by the surgeon in order to use the simulator in routine practice;
- develop an experimental protocol to be submitted to the surgeons of the ASST Grande Niguarda Metropolitan Hospital, Milan for the experimentation of the workflow;
- analyse the data related to the validation.

We also considered necessary to evaluate if this simulator could be classified as a medical device according to the definition that is given in the regulations in force.

This work therefore represents a first example of a feasibility study for the use of a patient-specific VR simulator in clinical practice, carried out in the academic field and validated in collaboration with a team of doctors and surgeons. In fact, it is believed that the mixing and the confluence of engineering and surgical problems will guide the transition from bench to bedside of this patient-safe simulator in a quick and efficient way.

In this sense, the project also wants to represent a small part of a wider field that is the evaluation of technologies for clinical use (*HTA, Health Technology Assessment*).

Chapter 1

Clinical Background

1.1 Upper Urinary Tract: Anatomy

The upper urinary tract is the part of the urinary system which is located inside the abdomen. The organs of the upper urinary tract, kidneys and ureters (Figure 1), are classified as retroperitoneal organs, in close contact with the posterior abdominal wall. (Keith L. Moore, 2012)

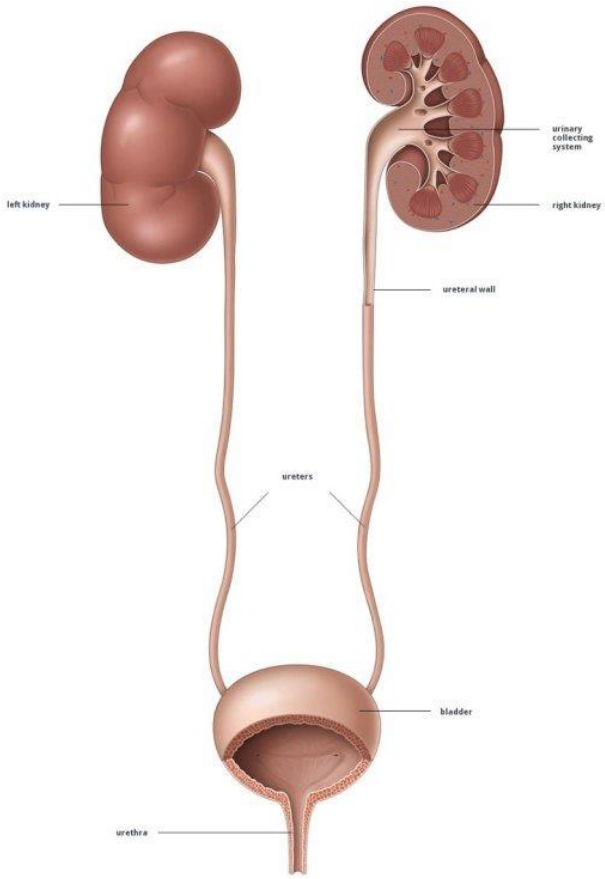


FIGURE 1 The upper urinary tract

1.1.1 Kidney: Macroscopic Anatomy

Kidneys are parenchymal excretory organs, bean-shaped, mainly composed by two components: renal cortex and medulla.

When sectioned, the kidney show different areas with peculiar architectural structure: renal pyramids, renal calyces (majors and minors) and renal pelvis (Figure 2).

The tasks of kidneys are to maintain the correct hydro-saline balance in the body and to assure daily, through nephrons, constant blood purification.

Waste products are excreted as urine, which is transported by ureters to urinary bladder.

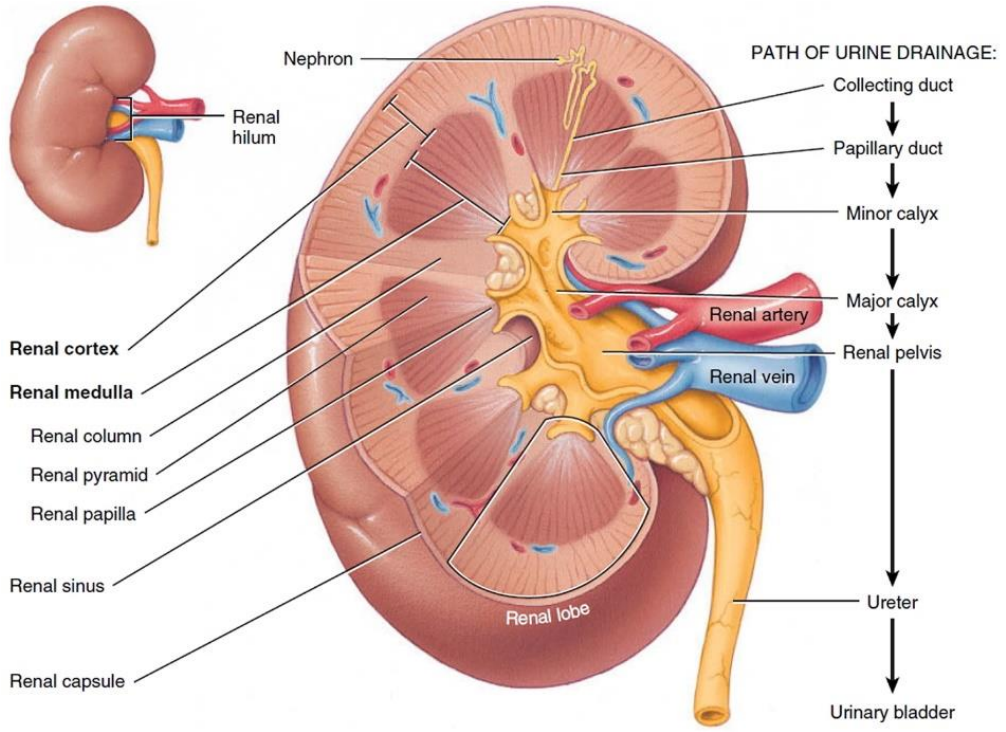


FIGURE 2 Anatomy of the kidney and urine drainage path

The kidneys are pair organs, one on the left and one on the right of the vertebral column, at the level of T12 and L3 vertebras and measure approximately 12 cm in length, 5 cm in width and 2.5 cm in thickness.

They lie posteriorly to the perineum, on the posterior abdominal wall. The upper part of the kidneys is close to the diaphragm that separates them from the pleural cavity at the level of the twelfth rib.

The right kidney, normally, is slightly lower the left one, probably because of the topographic ratio with the liver.

Right kidney is in relation to the liver, colon and duodenum whereas left one is in relation to the stomach, spleen, pancreas and ascending colon (Figure 3).

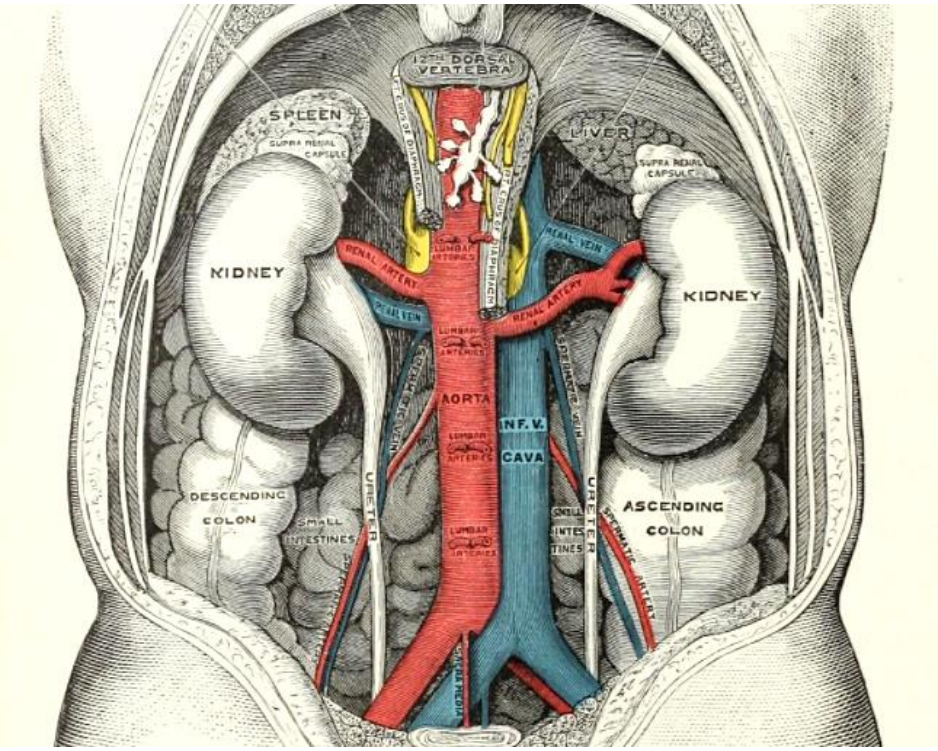


FIGURE 3 Relation of the viscera and large vessels of abdomen (GREY)

Both kidneys receive a high blood supply (i.e., about 20% of the cardiac output) with an average of 1.1 litres of blood flows per minute in the kidneys); they have a rich vascularisation that develop in total for about 160 kilometres in length. The major arterial kidney vessels are the two renal, left and right arteries, two large-sized vessels (5-7 mm) that detach from the abdominal aorta slightly below the upper mesenteric artery and fall behind the renal veins.

Renal artery divides into a branch in front of the kidney and in the back. The front branch divides into 4 further branches, called segmental arteries, which span the apical, upper, middle and lower portions of each kidney, while the back artery divides into branches that vascularize all one posterior segment. Each segmental artery divides into some lobar and interlobular arteries: each of these acts on a renal pyramid in its vertex. Here, at the level of the cortical substance, they supply blood to the glomerulus whom, together with renal tubules, constitute the nephrons, which are the ones responsible for the filtration.

After filtration, the blood moves through a small network of little veins converging into interlobular veins. As with the distribution of arterioles, the veins follow the same pattern: the interlobular blood supply to the lobar and interlobular veins, which form the renal vein coming out of the kidney for blood transfusions.

1.1.2 Kidney: Microscopic Anatomy

The principal structures of the kidney are the connective tissue capsule, the cortex and medulla. Interlobar vessel branches to form arcuate vessels that travel along the boundary between the cortex and medulla. The nephron is the structural and functional unit of the kidney. Each adult kidney contains around one million nephrons. The nephron utilizes four processes to alter the blood plasma, which flows to it: filtration, reabsorption, secretion, and excretion. Via one or more of these mechanisms, the kidney participates in the control of the volume of various body fluid compartments, fluid osmolality, acid-base balance, various electrolyte concentrations, and removal of toxins. Filtration occurs in the glomerulus: one-fifth of the blood volume that enters the kidneys is filtered.

1.1.3 Anatomical Variabilities

Further considerations are needed because the abdominal cavity anatomy and, more precisely, the renal ones is characterized by some differences between different individuals (intersubjective variabilities or anatomical variabilities), especially for vascularization.

The renal parenchyma normally is subdivided in five segments (apical, upper, middle, lower and posterior), each supplied by its own branch originated from the main renal artery, according to the classical Graves classification (Macchi, 2017).

However, recent radiologic studies reported the presence of different anatomical variabilities, such the so-called pre-segmental arteries (originating between the main artery and the segmental branches), or the presence of supernumerary renal arteries (a non-normal bifurcation of the abdominal aorta that imply a duplication of renal arteries, more common on the right side (Klatte, 2015)).

For a better understanding of the entity of the problems in terms of diffusion, it is reported below a table extracted by the study of Keishi Okamotoa et al. (Keishi Okamotoa, 2006).

In this table (Table 1), there are highlighted different types of inferior supernumerary renal arteries evaluated on a sample of 270 subjects and their relative incidence: it is clearly evident the high percentage of incidence of these variabilities, whom is about of 9%.

Table 1 Incidence, Levels of origin and Branches of the Inferior Supernumeraries Renal Arteries (InfRAs) (KEISHI OKAMOTOA, 2006)

Type	Right				Left			
	Number of cases	Level of origin	Branches		Number of cases	Level of origin	Branches	
			TA/OA	Ub			TA/OA	Ub
Type I (pre-ureteral)					14	Upper L2 (1)		
Ia (postcaval)	6	Upper L2 (1) Mid L2 (5)	4	0		Mid L2 (5) Lower L2 (3)	8	0
Ib (precaval)	10	Lower L2 (3) Upper L3 (4) Mid L3 (3)	3	1		Upper L3 (3) Mid L3 (2)		
Type II (post-ureteral)	8	Lower L3 (1) Upper L4 (3) Mid L4 (4)	0	4	4	Lower L3 (3) Mid L4 (1)	0	1
Total	24/270				18/270			

OA, ovarian artery; TA, testicular artery; Ub, ureteric branch.

By this way, it could be resumed that there is not an ideal patient: such intersubjective variabilities of renal vessels network can be considered a sort of digital fingerprint of the subject; each patient is unique. Thus, it is very important for surgeons to conduct an in-depth study of the diagnostic images before perform the surgical intervention.

However, it often happens that some anatomical variabilities are not reported on the radiologic reports whom are discovered during the course of the procedure: this, in some conditions, can be extremely dangerous for the patient, as in a procedure like percutaneous renal puncture of which I will explain better later.

1.2 Percutaneous Renal Puncture for Renal Biopsy

Numerous diseases affect kidneys, many of which require a surgery approach.
The most diffused pathology is probably kidney stones disease (also named urolithiasis).
It is a clinical condition characterized by the presence of one or more variable-size stones (normally of around 4-5 mm) contained within the excretory cavities of the urinary system, the chalices, the kidneys, and the urethra (C.Türk, 2015).

If a kidney stone becomes larger than 5 millimeters (Figure 4), it can cause ureter to block, resulting in severe pain in the lower back or abdomen (known renal colic). The surgical procedure for the removal of stones is called lithotripsy.

FIGURE 4 Kidney Stones with dimension of around 4-5 mm

Between 1% and 15% of people in the world have been hit by urinary calculus at some point in their life (Figure 5). In 2013, 49 million cases were reported, causing about 15,000 deaths (GBD, 2014).

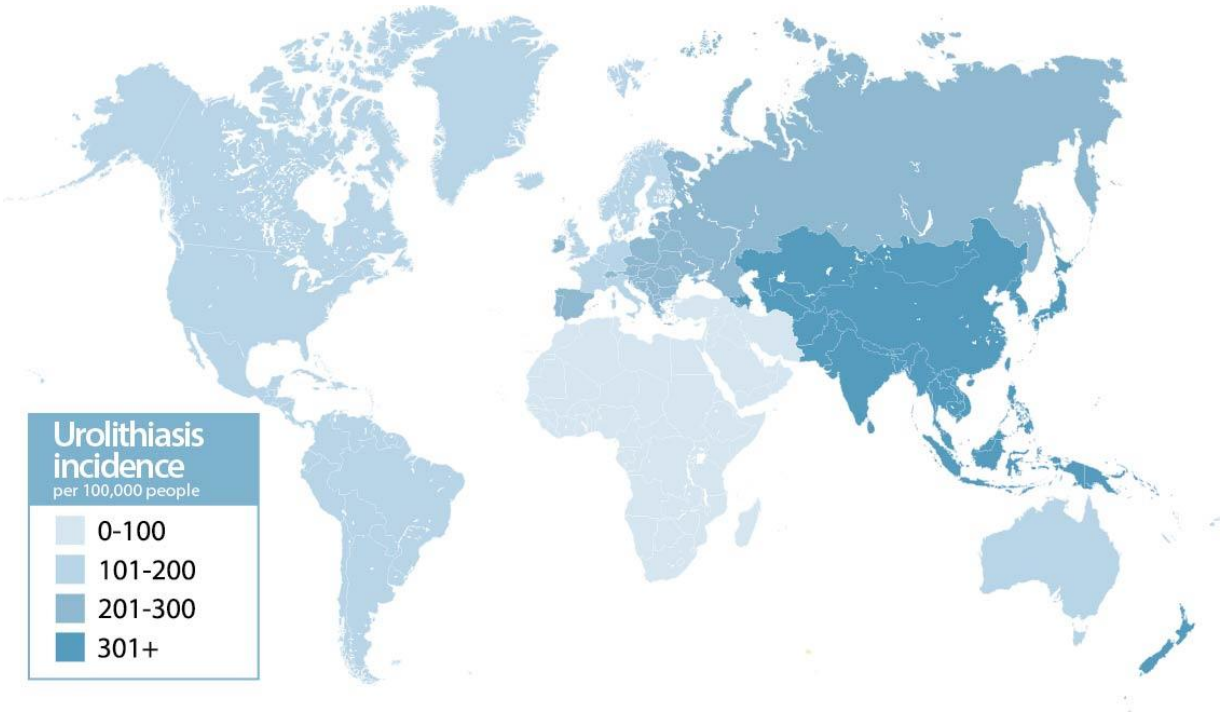


FIGURE 5 Global incidence of kidney stones disease (WORLD KIDNEY DAY: A GLOBAL LOOK AT A GROWING CONCERN, S.D.)

Another widespread disease is that of renal tumours that affects about 330 thousand new cases every year in the world.
There are several cancers that affect this organ, some that develop inside the calix, while others (easier to operate) that develop near the cortex (Figure 6).

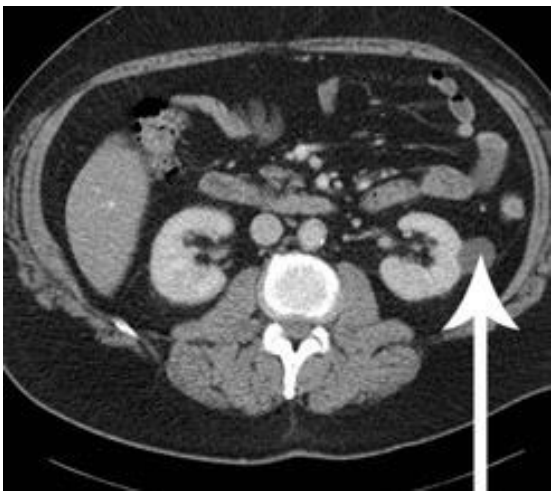


FIGURE 6 CT Scan showing small Left Kidney Tumour

Currently, numerous surgical procedures for the treatment this various kidney diseases require mini-invasive access to the organ as Renal Biopsy: a mini-invasive approach is clearly preferred to minimize the surgical trauma that the patient has to undergo.
This can be guaranteed through the realization of a percutaneous renal puncture.

This manoeuvre represents a mainstay of urological and radiology clinical practice, because of the epidemiology of involved diseases, as highlighted previously. This procedure is performed in general anaesthesia with the supine or prone patient, slightly inclined to the opposite side respect to the area to be treated eventually.
The position of the patient is a choice of surgeons.
The prone position represents a standard because of the advantage of a larger surface area.
However, the main disadvantage was the surgeon fatigue due to the position necessary to the surgeon to use the instruments that require outstretched arms. Also prone position requires a careful positioning of padding to protect support points.
Supine positioning, indeed, has numerous advantages. First, it does not require repositioning after induction of anaesthesia and it is a safer positioning with regard to neuro-musculoskeletal complications, but also has some disadvantages (J. Stuart Wolf).

Because of this duality, we will handle the prone positioning coherently with the literature studied by us (Figure 7).

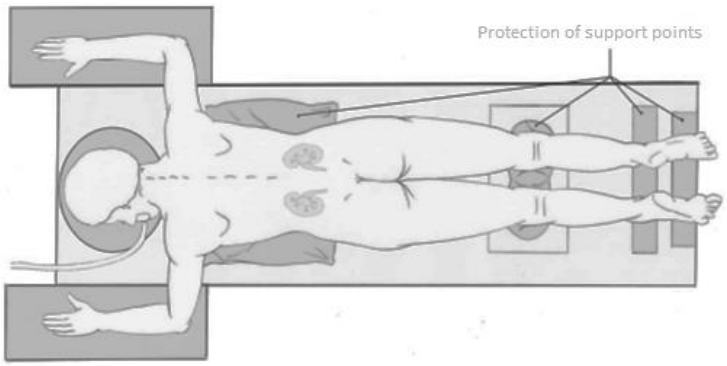


FIGURE 7 Position of the patient during Percutaneous Renal Puncture (B. MAKHOUL, 2004)

Three steps constitute the procedure:

1. Cystoscopy and retrograde positioning of a urethral catheter;
2. Percutaneous puncture of kidney cavities;
3. Dilation of percutaneous medium.

The first step serves to better define the anatomy of the renal cavities by irrigating them with a physiological solution. The aim of this phase is to clearly visualize the renal cavities, thus facilitating subsequent percutaneous access, and ultimately to eventually drain the kidney cavities at the end of the procedure. After inserting the urethral catheter, a bladder catheter is placed and the second phase begins (Kartalas-Goumas, s.d.).

Within the needle, a special guide (Figure 8) is introduced to guide the dilators and the working cannula until they reach the kidney cavities.

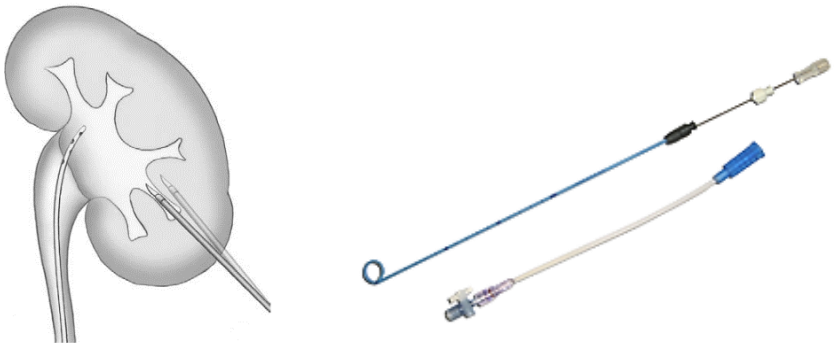


FIGURE 8 Needle used for Percutaneous Renal Puncture

The access to kidney is realized piercing the skin with a very thin needle, behind the axillary axis and immediately above the twelfth rib (Figure 9), until it reaches a calyx in the kidney cavities. Normally is performed the lower calyx puncture.

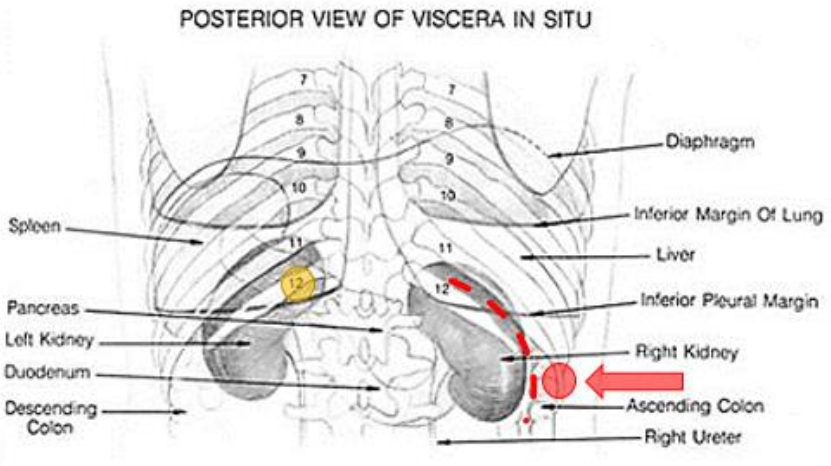


FIGURE 9 Access point for the Puncture respect to 12th rib

The procedure is performed using a dual guide: the ultrasound one for the identification of the possible anatomical structures of passage that the needle can meet and the radiological one for the identification of the position of the needle with respect to the point of interest to be reached (Figure 10). In particular, the X-ray tube is positioned as far as possible perpendicular to the patient to avoid the overlapping of the kidney with the vertebral column, due to the slightly inclined position. The voltage of the X-ray tube is low (70-80 kV) to try to have the greatest possible contrast between the organs of this district, which have very similar densities on average.

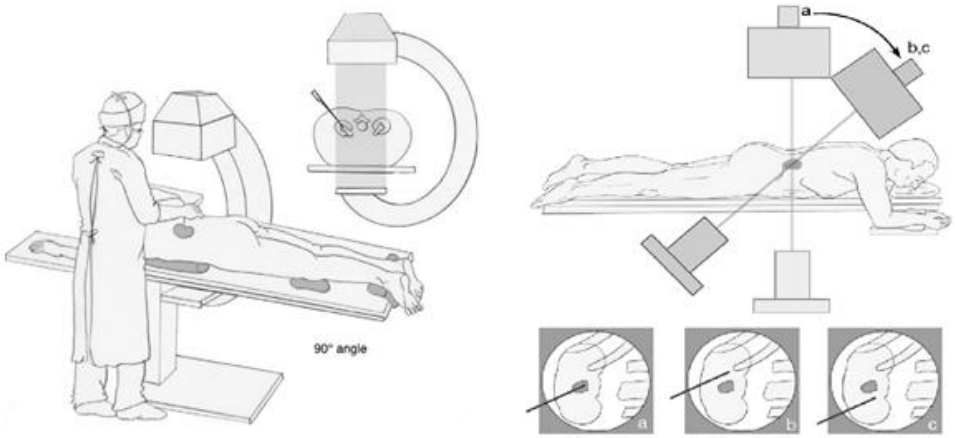


FIGURE 10 X-ray tube positioning (B. MAKHOUL, 2004)

Percutaneous renal access is a very complex and difficult procedure. The difficulty is due to the possible associated adverse effects, which sometimes may be fatal. Let's list some of these:

- acute and/or delayed haemorrhage;
- collecting system injury or obstruction;
- visceral or pleural injury with consequently risk of pneumothorax;
- venous thromboembolism;
- loss of renal function;
- metabolic and physiologic complications;
- post-operative fever and sepsis.

Because of potential complications, trainees have difficulty gaining experience and they usually end their academic curriculum performing just few percutaneous renal punctures.

Chapter 2
State of the Art of Simulators

As previously reported, there are many severe complications related to the percutaneous renal puncture, making difficulty to surgeons to perform the surgical intervention and leading to a severe inexperience of trainees in interventional radiological surgery before starting to perform their profession.

In our opinion, due to the diffusion of the pathologies involved, it is necessary to face these problems and find a way to solve it.

A virtual reality simulator (VR-Simulator) for a percutaneous renal puncture might be an appropriate solution because it permits to surgeons to known the anatomical structure of the patient himself before operate and also it may gradually expose trainee interventional radiologists and interventional urologists to this procedure in a patient-safe way, reducing also the learning curve.

In this contest, virtual reality simulation could have the potential to become an essential piece of surgical education curriculum. In this sense, numerous medical simulators were developed in the last 25 years.

2.1 Medical Simulators

Simulation in the medical field has become necessary over time to try to reduce human errors as much as possible and educate the new generations of health professionals in order to improve clinical outcomes.

The simulation is used in many branches of medicine (from paramedics to anaesthesiologists-resuscitators, up to surgeons) to support the activity of the professionals. Moreover, because of the need to satisfy different needs, different types of simulators (in terms of exploited technologies) are used.

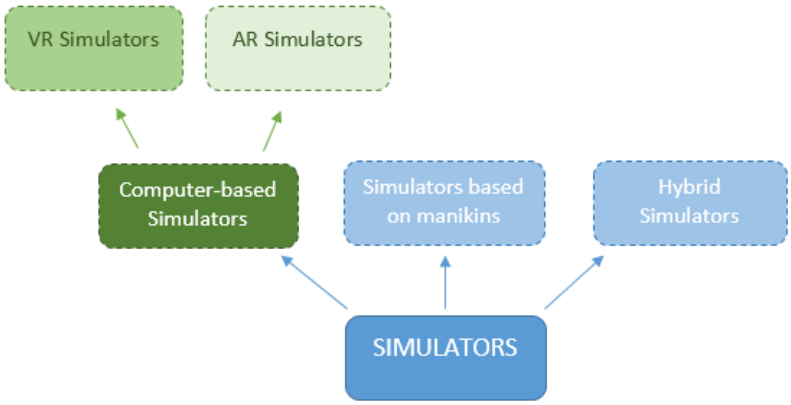


FIGURE 11 Simple classification of different types of simulator

Figure 11 provides a simple classification of these, of which we focalized only on the VR-Simulators.

2.1.1 Virtual Reality Medical Simulators

Already in the early 80's it was catching on the idea that a safe-patient way to approach the surgical interventions was needed. The turning point was the transition from using a simple manikin to using computer science techniques, up to using image-based computer simulation, in particular virtual reality.

One of the founding fathers of this type of overture to surgery was Richard M. Satava, Emeritus Professor of Surgery at the University of Washington.
His activity in the field of the surgical simulation started around 1993 with the development of the first surgical simulator for general surgery, and the publication of his article "*Virtual reality surgical simulator: the first steps*" on the Surgical Endoscopic Journal. In this article, he explained how the simulation already represented a mainstay in other fields like aviation and how a surgical simulation can improve some aspects of surgery.

He outlined two main application: anatomy lesson and surgical procedure simulation.

Regarding the first application, he explained: "*Virtual reality provides the first opportunity to combine 3-D visual imagery with interactivity at a level that would permit realistic simulation of complex anatomic dissection or performance of surgical procedures. It can make learning surgical anatomy easier by allowing the student to explore the interrelations of various organ systems in perspectives not available through other standard teaching techniques*" (Satava, 1993).

Moreover, he underlined that the simulation of a surgical procedure was still primitive.

Obviously, from that moment, the generic technology of VR has undergone a remarkable development: just think of gaming software.

In surgical VR development, we have moved from the first-generation simulation that was discovering flight simulators and developing equivalent simulations for surgery, passing through the second-generation involved in learning that it was about the curriculum and the next transition to criterion-based training (instead of training for a fixed time or number of trials), until arrive to the current generation (Figure 12). These simulators are to more intelligent, with embedded training and assessment of judgment, in addition to psychomotor skills (Satava, 2008).

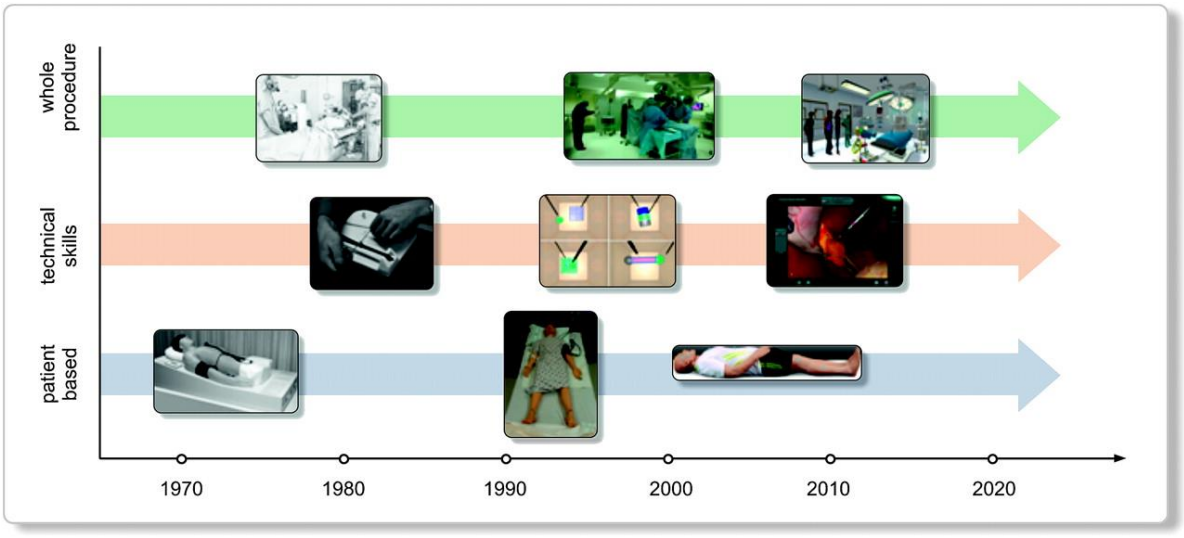


FIGURE 12 Historical change of medical simulation (AGGARWAL R, 2010)

However, why use simulators and why use VR ones?
VR-Simulation is defined as a technique to replace or amplify real experiences with guided experiences, often immersive in nature, that evoke or replicate substantial aspects of the real world in a fully interactive manner (Riaz A. Agha, 2015).

In this contest, the connection between the virtual and the real is what allows us to use the simulation to learn something about reality (Pensieri, 2015). The simulation performs a specific pedagogical function. It introduces the user to reality in the best possible way,

anticipating and limiting the risks associated with something unexpected, which in certain situations require the maximum attention and preparation (Pensieri, 2015).

Thus, with this in mind, numerous are the simulators developed during the years. Citing all of the studies would be difficult, so I summarise in the table (Table 2) below references of some articles reporting the experiences of development and use of different VR simulators in different fields of medicine.

Table 2 State of the art of simulators already developed

R.M. Satava	**Virtual reality surgical simulator-First steps**	*Surg Endoscopy; 203-205*	**1993**
P.J. Gorman, A.H. Meier, T.M. Krummel	**Simulation and virtual reality in surgical education: real or unreal?**	*Arch Surg ; 134:1203-8*	1999
V.M. Tronnier, A. Staubert, M.M. Bonsanto, et al.	**Virtual reality in neurosurgery**	*Radiologe ; 40:211-7*	2000
R.M. Satava	**Surgical education and surgical simulation**	*World J Surg; 25:1484-9.*	2001
A. Jackson, N.W. John, N.A. Thacker, et al.	**Developing a virtual reality environment in petrous bone surgery: a state-of-the-art review**	*Otol Neurotol; 23:111-21*	2002
J.M. Albani, D.I. Lee	**Virtual reality-assisted robotic surgery simulation**	*J Endourol; 21:285-7*	2007
G.M. Jr Lemole, P.P. Banerjee, C. Luciano et al.	**Virtual reality in neurosurgical education: part-task ventriculostomy simulation with dynamic visual and haptic feedback**	*Neurosurgery; 61:142-8;*	2007
R. Hart, K. Karthigasu	**The benefits of virtual reality simulator training for laparoscopic surgery**	*Curr Opin Obstet Gynecol; 19:297-302*	2007
J. Stern, I.S. Zeltser, M.S. Pearle	**Percutaneous Renal Access Simulators**	*J Endourol; 21:270-273*	2007
F.P. Vidal, A.E. Healey, N.W. John, D.A. Gould	**Simulation of ultrasound guided needle puncture using patient specific data with 3D textures and volume haptics.**	*Computer Animation and Virtual Worlds; 19: 111-127*	2008
A.G. Papatsoris, T. Shaikh, D. Patel, A. Bourdoumis, C. Bach, N. Buchholz, J. Masood, I. Junaid	**Use of a Virtual Reality Simulator to Improve Percutaneous Renal Access Skills: A Prospective Study in Urology Trainees**	*Urol Int; 89:185–190*	2012
F. King, J. Jayender, S.K. Bhagavatula, P.B. Shyn, S. Pieper, T. Kapur, A. Lasso, G. Fichtinger	**An Immersive Virtual Reality Environment for Diagnostic Imaging**	*J Medical Robotics Research; 1*	2016
G. Sampogna, R. Pugliese, M. Elli, A. Vanzulli, A. Forgione	**Routine clinical application of virtual reality in abdominal surgery**	*Minimally Invasive Therapy & Allied Technologies*	**2017**

Also, if they are only a small part of the entire literature, it is immediately evident the interest over the years to this type of approach.

From the literature the benefits of using virtual reality, which I have already mentioned above, are clear but also are clear the different limits of the simulators already developed.

The fundamental characteristics of a simulators, in particular of VR one, must be the reliability and the realism of the scene visualized by the users.

Obviously from the 1993 to 2017 there have been numerous and important improvements in this sense. The latest simulators developed gives not only a visible feedback, but also audible and tactile ones, improving enormously the experience of the users.

Nevertheless, these simulators still have two consistent limits:

- lack of possibility of uploading the 3D model of the specific patient, whom the clinician is surgically approaching;
- lack attempts of their integration into routine clinical practice, as highlighted in the article “Routine clinical application of virtual reality in abdominal surgery” of G. Sampogna, R. Pugliese, M. Elli, A. Vanzulli and A. Forgione, even if the transition from bench to bedside represents the basis for improvements of quality care.

Furthermore, it is important to stress that the live relationship with experiences is never replaceable, as the interpersonal relationship that the doctor has with his patients, as far as you can train in the simulation (Pensieri, 2015), which must represent a technology to support the surgeon's activity.

Haptics Simulators

In the previous paragraph I talked about VR simulators, that gives a tactile feedback. This characteristic is very important to submit to necessity of an instrument that is as realistic as possible.

Vision and haptic are the principal sensory inputs employed by humans in object manipulation tasks. While visual display technology has reached an advanced stage, haptic feedback has remained rather underutilized because of practical challenges such as control loop stability (Enayati, 2016). However, the majority of the conducted studies suggest that

realistic procedural simulations with haptic feedback lead to better performances and more rapid learning curves (P. Lamata, 2006).

To perform tactile feedback it is necessary to use a haptic controller. There are different types of haptic controller on the market: the most diffuse are the gloves and joystick types.

A haptic controller is not only a device that gives you a force feedback (kinaesthetic feedback), but also a tactile sensation. Normally the perception of a resistance is simulated with the vibration of the device, proportional to the resistance of the touching object in the scene.

To understand the potential of this technology let's take us, as example, the most common procedures in modern clinical practice that is insertion of needles and catheters.

Perceiving the needle interaction forces could allow the surgeon to better estimate the position of the needle inside the tissue, enhance the accuracy in soft tissue identification and therefore contribute to significant safety improvements (Enayati, 2016).

Thus, the tactile feedback is essential because is one of the tools that surgeon uses as a guide to understand with which anatomical structures he/she are interfacing.

2.2 Percutaneous Renal Puncture Simulators

The only Percutaneous Renal Puncture Simulator that we have found in literature is the PERC Mentor™. It is developed by Simbionix; Lod, Israel.

The PERC Mentor is a VR simulator specifically developed for training in percutaneous renal access. It consists of "flank" box for percutaneous renal puncture (J. Stern, 2007): the flank model mimics a human flank and has corresponding haptics for skin, muscle, connective tissue and ribs (Buchholz, 2012). There is a personal computer system located under a workstation: the central software system includes a proprietary visualization engine, which allows real-time simulation by offering a high-level object-orientated application program interface.

It incorporates tactile feedback, organ displacement with breathing, real-time fluoroscopy, and mock angiographic instruments. A needle with metal sensor is used to achieve percutaneous access into a digitally projected renal collecting system. It can deliver contrast

medium on demand via a retrograde ureteral catheter, and fluoroscopic imaging can be controlled with a foot pedal. Real-time feedback confirming puncture is available by way of aspiration from the needle (Mishra, 2010).

However, this simulator is expensive and there is little evidence of its educational impact. Therefore, more studies are needed to validate the available simulators and assess their educational impact for urology trainees (Yasser A. Noureldin, 2017).

Another limitation of this simulator is that it takes no account of the patient's actual situation and this does not allow a possible integration in clinical practice.

2.2.1 LACE Virtual Reality Environment

The LACE is a virtual reality environment developed by four students of Politecnico di Milano, in collaboration with the Professor Cristian Luciano at the Bioengineering Department of University of Chicago.

It is an integrated platform created for simulation of different medical procedures: in this sense is born to be a multitasking simulator.

His development occurred from the need for virtual reality based applications with a robust highly defined graphic interface and haptics device.

The workstation is constituted by:

- a computer running with a Windows operative system that must be sufficiently powerful to allow a correct visualization of the graphics especially in terms of the haptic controller fluidity;
- a 3D monitor to exploit the possibility of performing a stereoscopic visualization;
- a mouse and a keyboard;
- a haptic device to perform the needle.

It is clear how this configuration makes the global simulator easily accessible to different types of users.

FIGURE 13 Touch™ 3D-Stylus of the 3D Systems Geomagic® (SYSTEMS, S.D.)

The haptic device, used to simulate the needle of Percutaneous Renal Puncture, is the Touch™ 3D Stylus of the 3D Systems Geomagic® Figure 13).

LACE integrates and manages the interactions between four different software-hardware environments:

- Visualization Library (VL) is an OpenGL based open-source library for 2D and 3D graphics application. It is responsible for the graphics rendering of the virtual scene;
- QuickHaptics (QH) is a haptic library developed in C++. QH is used to manage the force feedback;
- Wykobi Library (WK) is a C++ 2D-3D computational geometry library for fast mathematical calculation;
- Ascension 3D Guidance (AS) is a 3D electro-magnetic tracking system, which allows the easy communication with a tracking unit (Faso, 2017).

When compared to PERC Mentor™, this simulator has a complete realistic component given by the fact that you can work on a 3D model reconstructed by the CT scans of a patient.
The reconstruction is made using different types of 3D-reconstruction software and, after backup in the form of a .stl file, the volume scene is uploaded on the LACE so that users (surgeons or radiologists) can simulate the puncture in a patient-safety way.

The user can define as many scenes as he/she desires and choose or to render them on a texture attached to geometries in the main rendering or to a sub-rendering by dividing the screen in multiple viewports.

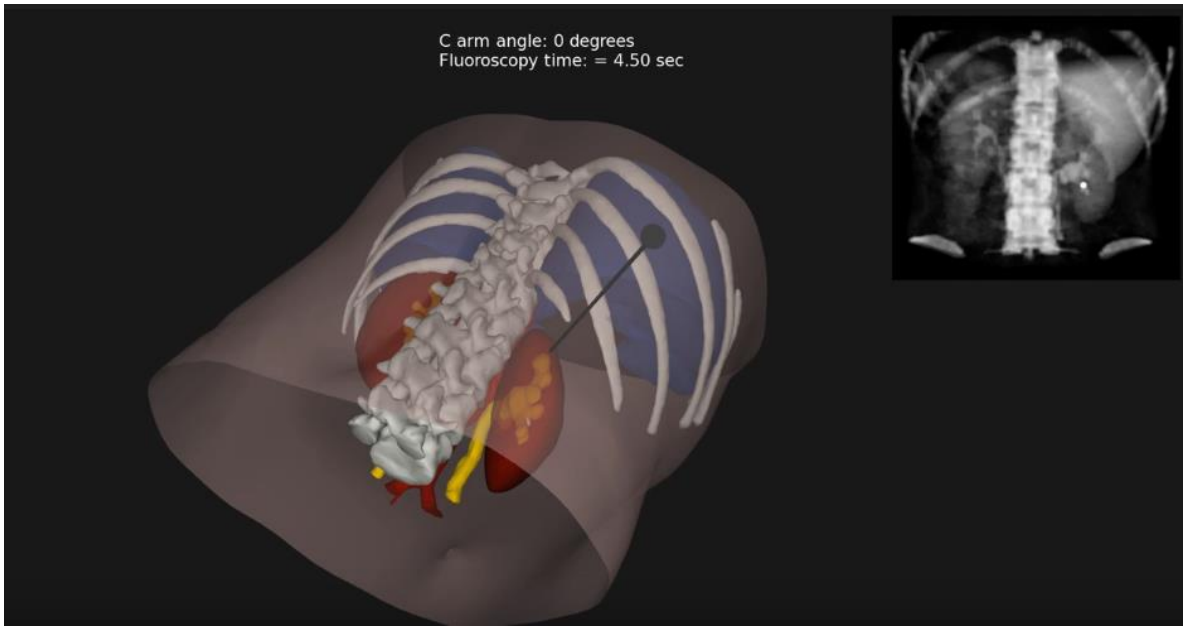


FIGURE 14 A main screen of the lace-based simulator during his use

The trainee can practice on the desired access technique under a real time fluoroscopy guidance (Figure 14). As in real surgeries, the emulated C arm can be moved all around the models, showing the correspondent fluoroscopy image on the screen: rotations, translations and zooming are enabled to give the trainee a reliable and realistic navigation system, by which keeping track of the position, depth and orientation of the puncture needle inside the body structures (Faso, 2017). The parameters modification can be obtained using a graphic user interface (GUI) implemented in the simulator code.

However, the simulator it has been validated only using a volume-scene obtained by an available web database of CT. Furthermore, it can be found a lack of a user-friendly GUI to upload the patient-specific 3D models and of an alarm-system to provide a more immediate evaluation indicator of success during performance.

2.3 Patient-Specific Simulators and Use of Simulator Technology in Clinical Practice

As previously highlighted in §2.1.1 (Table 2), it is evident the high interest in simulation and, consequently, in development of simulators prototypes for medical purposes. Therefore, numerous medical simulators have been created thanks to the collaboration between the scientific faculties (mainly medicine schools, engineering and computational science faculties) of different universities all over the world.

Although these simulators have been developed starting from an obvious interest, most of them are general ones and not patient-specific. Consequently, only a very small percentage can be used in clinical practice.

A not patient-specific simulator has an important limit that is the possibility to perform only a generalized surgical procedure, which not described realistically the condition of the patient who must be operated. This involves only partial reliability and justifies, in my opinion, the hesitancy of surgeons in not using these tools in the routine of the procedures.

A patient-specific virtual reality simulation (PSVR), on the contrary, allows practice to upcoming real operations and complements the established role of VR simulation (already discussed in §2.1.1) not only as a generic training tool.

A revision of the state of the art of PSVR, in which a haptic device was used during the simulation process, was done by William I.M. Willaert et al. in 2012.

They highlighted the two main potential advantages of a PSVR technology: the contribution on both training and pre-operative preparation (coherently with the rest of analysis of the state of the art done previously).

In particular, PSVR technology can effectively constitute an ideal instrument for trainees, which can perform some procedures under the evaluation of a mentor, and shorten the learning curve for more difficult procedures. From a training perspective, patient-specific simulations also can be considered as a growing library of cases that can be practiced and analysed, providing realistic variants.

An overview of their work is reported in the table below (Table 3).

Table 3 Overview of Willaert et al. review of the state of the art inherent to PSVR (W. I. M. WILLAERT, 2012)

Study	Year	Procedure	Device name	Status	Primary input	Volume rendering	Haptics	Primary potential
Wildermuth et al	2001	Colonoscopy	–	Prototype	CT/ MRI	y	Laparoscopic Impulse Engine (Immersion)	Training
Agus et al	2002	Mastoidectomy	–	Prototype	CT	y	SensAble PHANToM	Training
Schendel et al	2005	Plastic surgery: Cleft lip reconstruction	–	Prototype	CT	y	SensAble PHANToM	Planning Training
Meehan et al	2006	Craniofacial bone distraction surgery	–	Prototype	CT	y	SensAble PHANToM	Planning
Suzuki et al	2007	Laparoscopic colectomy	–	Prototype	N/A	N/A	SensAble PHANToM	Planning Rehearsal
Sierra et al	2007	Cranial Ventriculostomy	–	Prototype	CT/ MRI	y	N/A	Training Rehearsal
Soler et al	2008	Laparoscopic Organ manipulation	ULIS	Prototype	CT/ MRI	Automated + manual	KSFFB	Planning Rehearsal
Soler et al	2008	Percutaneous biopsy	HORUS	Prototype	CT/ MRI	Automated	SensAble PHANToM	Training Planning
Peterson et al	2008	Hip fracture Surgery	–	Prototype	CT	y	SensAble PHANToM	Planning Rehearsal
Clark et al	2009	Brain tumor resection	Neurotouch	Prototype	MRI	y	Proprietary	Training Rehearsal
Parikh et al	2009	Sinus surgery	VSE	Prototype	CT	Automated	SensAble PHANToM	Planning Rehearsal
Willaert et al Roguin et al Cates et al Hislop et al	2008–2011	Carotid artery Stenting	AngioMentor	Commercially available	CT/ MRI	y	Proprietary	Training Planning Rehearsal

The benefits of patient-specific rehearsal, however, are not limited to trainees as experienced practitioners may benefit as well. This is in part because structured tools to aid the immediate preoperative preparation, other than a thorough review of medical imagery do not exist (or, if they exist, only in some application fields).

Patient-specific technology also can be used as a debriefing tool when complications or adverse events occur and, because it allows a detailed case review, it seems an ideal tool to assess patient suitability for specific operations and guide treatment by identifying high-risks patients (W. I. M. Willaert, 2012).

VR simulators have the potential to be used for procedure prototyping acting as an escamotage to test new operative techniques, and approaches and, as such, guide the process of device engineering and product refinement.

Nevertheless, William I.M. Willaert et al. underlined also that “major developments are still necessary, because the majority of simulators providing patient-specific rehearsal are still prototypes. Cooperation between academic research groups, medical professionals, and

simulator companies will be vital to commercialize patient-specific VR simulation and make it accessible to a wide group of practitioners in different medical specialties. […] Just as generic simulation had been scientifically validated for the purpose of physician training, patient-specific rehearsal will have to undergo the same scrutiny and be validated for its role as a rehearsal, planning, and team training tool".

Since 2012, some progress has been made in the implementation of the simulators, but their use in clinical practice is still almost null (Gianluca Sampogna et al., 2017).

If one limit was the accessibility of the devices, both economically and fidelity, now this problem does not exist.

In fact, their work has the aim of explore the feasibility, the appreciation by users and the related clinical impact of the routine clinical application of VR in a high-volume department of surgery, acquiring competencies and understanding major organizational and technical limits.

They underlined that their work was still a preliminary study and that reported their experience to overcome the limits of that work, highlighting that a well established workflow, which can be adopted by any department of surgery with a minimum investment of resources, may be the solution to them.

After this in-depth analysis of the literature, we believe that to integrate medical simulators in the clinical practice there is the necessity to:

- make an evaluation of the changes in traditional workflow of clinical practice (with the introduction of ulterior steps) in order to verify that the tight timing of the surgical room are not affected;
- make an evaluation of advantages (costs-benefits) that this technology can introduce;
- and, obviously, make an evaluation of the technology and his performances for clinical use.

Chapter 3

Materials and Methods

3.1 Materials

This thesis work wants to focus on the Percutaneous Renal Puncture procedure and going to develop a workflow to upload a patient-specific 3D reconstruction into a VRE to integrate into routine clinical practice. In this way, the clinicians can become confident with the procedure before performing it, providing also an important tool for future surgeons training.

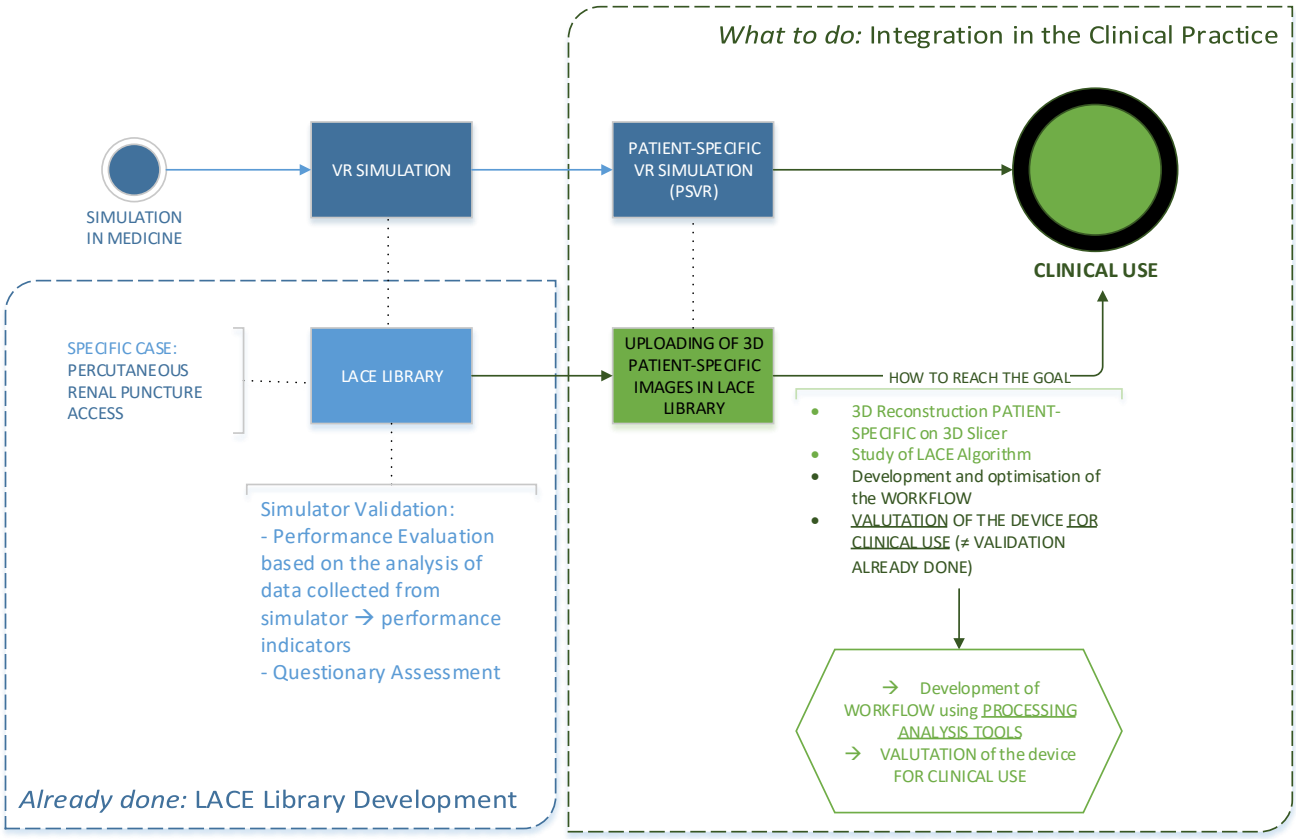


FIGURE 15 Overview of the thesis work on his background

To reach this goal it was necessary to (Figure 15):

- take in hand CT of patient that must be submitted to Percutaneous Renal Puncture;
- work on patient-specific CTs to perform 3D reconstructions and obtain patient specific 3D models;

- take in hand a simulator studied during the analysis of the literature (LACE) and study his possible use as patient-specific simulator;
- develop of a workflow to standardize the simulation process and to analyse the feasibility of simulator integration in clinical practice use;
- perform an evaluation of the simulator in terms of clinical outcomes;
- and, if possible, analyse the chosen simulator in terms of medical device.

3.1.1 CT Images

CT Images provide detailed, cross-sectional views of all types of tissue. CT are obtained by Computerized Tomography, that, like traditional x-rays, produces multiple images or pictures of the inside of the body.

These images can also be used to perform a three-dimensional reconstruction of it obtaining a 3D model of the anatomy of the patient.

The acquisition is performed along three direction, axial, sagittal, and frontal, coherently with the anatomical planes and thanks to the rotation of the x-ray source tube around the patient.

Each material has a proper x-ray attenuation coefficient, and so the different biological tissues. In other words, when an x-rays beam crosses an organ, the organ itself stops some of these radiations. Thus, the value of the x-rays beam after this transition will be attenuated of a certain percentage proportional to attenuation coefficient, according to the absorption law:

$$I(t) = I_0 e^{-\mu t}$$

where I_0 is the initial intensity and μ is the mass attenuation coefficient.

In this way, it is possible to obtain for each anatomic section, along a certain direction and at a certain angle, the profile (variation) of the attenuation coefficient that is proportional to the quantity of radiation attenuated and so to the tissues material properties.

Thanks to some complex algorithms (the most used is the Filtered Back Projection), it is possible to reconstruct the third dimension to obtain a 3D model. In fact, after applying the reconstruction algorithms, we obtain a digital image that represents the distribution of the

density of the object in an internal section (slice) and whose smallest element is called voxel, as it is a volume element: the smaller the volume represented by a voxel, the greater the spatial resolution.

Thus, it is possible to obtain CT Images with a certain value of spatial resolution going to modify the value of the gap between two successive slices. Normally, CT with 3mm of spatial resolution are performed, except for some exams that require a more defined image as in CardioCT.

The value of each voxel represents an average intensity (proportional to the density of the object) on a grey scale called Hounsfield Scale (Figure 16).

The number inside the voxel is called 'CT number' and is measured in HU (Hounsfield Unit) if suitably calibrated according to the following relation:

$$CT\ number = 1000\ \frac{\mu - \mu_{H_2O}}{\mu_{H_2O}}$$

The formula for the calculation of HU shows how water is taken as a reference.

The water CT number is obviously 0 HU; the air density is considered null μ= 0 and therefore the CT number of the air assumes a value of -1000 HU; for the bone, which has a density roughly double that of water, the CT number is +1000 HU.

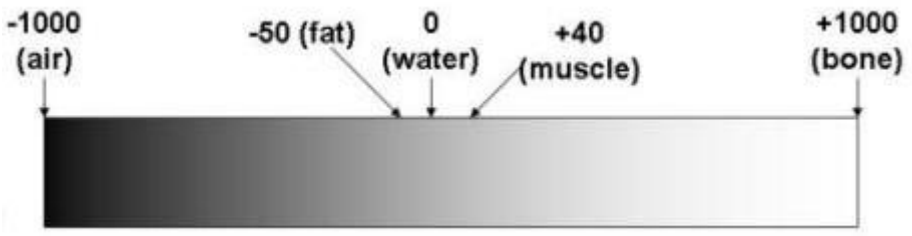


FIGURE 16 Hounsfield Scale

Contrast Medium and Different CT Phases

A medical contrast medium (or contrast agent) is a substance used to enhance the contrast of structures (with different densities) or fluids within the body in medical imaging. Contrast media absorb or alter external electromagnetism; it is commonly used to enhance the

visibility of blood vessels. For radiography, iodine and barium are the most common types of contrast media.

Different iodinated contrast media exist, with variations occurring between the osmolality, viscosity and absolute iodine content of different media.

It is supplied intravenously (bolus) using the injector, which provides also physiological solution to wash the vessels from the contrast agent that is sticky.

The two substances have the same flow: 1 m/s for brain, 3-3 m/s for most tests, 4 m/s for liver, 5 m/s for aorta.

Thanks to this technique, during the CT exam it is possible to enhance different phases, related to the circulation of contrast medium inside the body. These phases are:

- Basal Phase: without use of contrast medium, immediately available.
  The usefulness of the basal depends on what I am looking for: for example, it is possible to see the kidney stones (composed of calcium, they will result white as the bone), or haemorrhagic blood (it is denser due to high concentration of iron).
  If possible, it is better to take advantage of this phase since to get it the patient is less exposed to radiation, and since I do not have to use the contrast medium (it fatigues the kidneys).
- Arterial Phase: with injection of contrast medium, after 30 seconds.
  All that is perfused by the arterial circle is highlighted. For example, it is possible to see better the kidney distinguishing between the medullary phase and the cortical phase.
- Venous Phase: after 1 minute.
  It is a little more washed out than the arterial, since it has been more time since the insertion of the contrast medium.
- Late Phase: after 5 minutes.
  There is a balance between parenchymal and vessels, so it is possible to see the much-sprayed organs: brain, heart, kidney and liver. It primarily evaluates renal excretion.

The exam time depends on what we want to obtain: obviously, we try to give the patient the least amount of radiation.

Split Bolus Technique in UroCT

In CT for urological purpose, one modality to reduce the radiations dose amount is to split the bolus injection. The patient receives about 50 ml of contrast followed by an additional 50 ml eight minutes later: images are then acquired 55 seconds following the second dose of contrast. By this way, it is possible to acquire, at the same time, the Arterial Phase and the Late one, reducing the exam time and so the absorbed dose.

3.1.2 3D Slicer

To realize the 3D reconstruction of the patient starting from CT images, we have chosen to take in hand the 3D Slicer software.

It is a freely available open-source platform (BSD-style license) for segmentation, registration and 3D visualization of medical imaging data.

In 1997, Slicer started as a research project between the Surgical Planning Lab (Harvard) and the CSAIL (MIT); it is a multi-institutional effort supported by the National Institute of Health. Nowadays the infrastructure grants fund the platform, while collaborative projects (e.g. Canada, Japan, Australia, and Italy) fund the application packages. Slicer contributions derived also from the Open Community, 80 authors are developers of the software (Kikinis, 2007).

3D Slicer has a modular organization that allows the addition of new functionality and provides a number of generic features not available in competing tools. In this sense, is a software platform constantly evolving and updating.

It works on Windows, Linux, and Mac and this allows the possibility of work and exchange of information between different users.

Standard image file formats (e.g. DICOM, Metadata Image) are supported (both CT and MRI images) and the application integrates interface capabilities to biomedical research software (Community Users, 2008).

From a technical point of view, Slicer's capabilities include:

- three-dimensional visualization of multimodal image data handling DICOM images and reading/writing a variety of other formats;
- interactive visualization of volumetric Voxel images, polygonal meshes, and volume renderings;

- manual editing;
- fusion and co-registering of data using rigid and non-rigid algorithms;
- automatic image segmentation;
- advanced image analysis and visualization of diffusion tensor imaging data;
- functional magnetic resonance imaging;
- tracking of devices for image-guided procedures, in particular image-guided radiation therapy.

Slicer has been used in a many clinical researches. In neurosurgery, for example, Slicer is frequently used to construct and visualize MRI data that are available pre- and intra-operatively to allow for the acquiring of spatial coordinates for instrument tracking as explained me (during my experience in hospital surgery) by Dr. Cardinale, primary surgeon at Centro Munari Chirurgia dell'Epilessia e del Parkinson, ASST Grande Ospedale Metropolitano Niguarda.

3.1.3 LACE

The VRE that we have taken in hand to integrate in the clinical practice is the LACE.
We have chosen this VRE because:

- to carry on their thesis work;
- this VRE can easily be transformed into a patient-specific simulator;
- this thesis work want to be an example of feasibility study of integration of a VR simulator with the clinical practice.

WHAT IS?

LACE is an anatomically accurate, low-cost, haptics-based virtual reality surgical simulator for percutaneous renal access, developed by four students of the NearLAB of Politecnico di Milano, in collaboration with the professor Cristian Luciano of the Bioengineering Department of University of Chicago.

It is an integrated platform with a robust graphic interface and haptics rendering that provides a powerful and efficient virtual-reality scene.

This platform is developed as a C++ code using Visual Studio 2010 Professional® software: in this sense, it has the form of a 'solution' on Visual Studio, composed by five projects:

- the main code LACE Library: it constitute the real VRE platform based on the interaction of different external libraries;
- the Prostate Biopsy Application;
- the Percutaneous Renal Access (PCA) Application;
- the Psychomotor Skill Learning Test bed Application;
- and finally, the Model of Prostate Application.

Potentially, it has the capacity to simulate a larger number of procedures.

HOW IS DONE?

Physical Configuration

The workstation is composed by four hardware components:

- a computer running with a Windows-based operative system (it can be fixed or portable, the important thing is that it has a sufficiently powerful processor and graphics card);
- a 3D monitor (stereoscopic display), to provide the user with depth perception using a stereoscopic visualization;
- a mouse and a keyboard, to interact with the GUI;
- the haptic device Touch™ 3D-Stylus of the 3D Systems Geomagic® (Figure 13), to convey the sense of touch in the virtual environment to the user, as shown below (Figure 17).

FIGURE 17 LACE workstation

Five types of data can be displayed on the screen:

- CT Images, volumetric image used to extract the virtual models;
- Fluoroscopic Images, use as surgical intervention guidance;
- Virtual Models, segmented and extracted from the CT Images;
- Virtual Needle, imported in the scene as a .obj file;
- Text Files, that contain the initial values of the haptic and graphic features of the virtual models and the parameters for the visualization of the volumetric image (Faso, 2017).

Implementation Configuration

LACE Library integrates and manages the interactions between four different software-hardware environments (Figure 18):

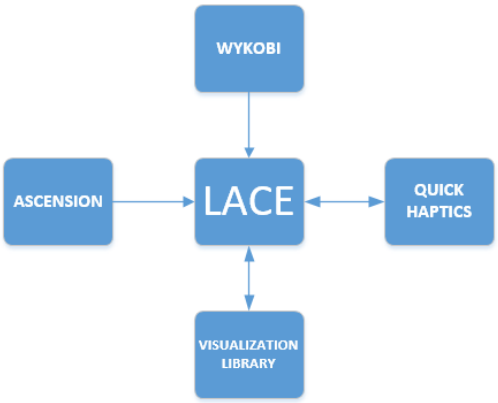


FIGURE 18 Libraries interaction

- Visualization Library (VL): is an OpenGL based open-source library for 2D and 3D graphics application. It is responsible for the graphics rendering of the virtual scene;
- QuickHaptics (QH) is a haptic library developed in C++. QH is used to manage the force feedback;
- Wykobi Library (WK) is a C++ 2D-3D computational geometry library for fast mathematical calculation;
- Ascension 3D Guidance (AS) is a 3D electro-magnetic tracking system, which allows the easy communication with a tracking unit.

Main feature of the C ++ language is the use of 'class' object (object-oriented language) and this implies that LACE Library leans on many classes implemented for its purpose.
In each of them, the variables and the functions used to permit the virtual simulation are declared. Classes of each four library can interact with each other in a similar way to the one reported below (Figure 19):

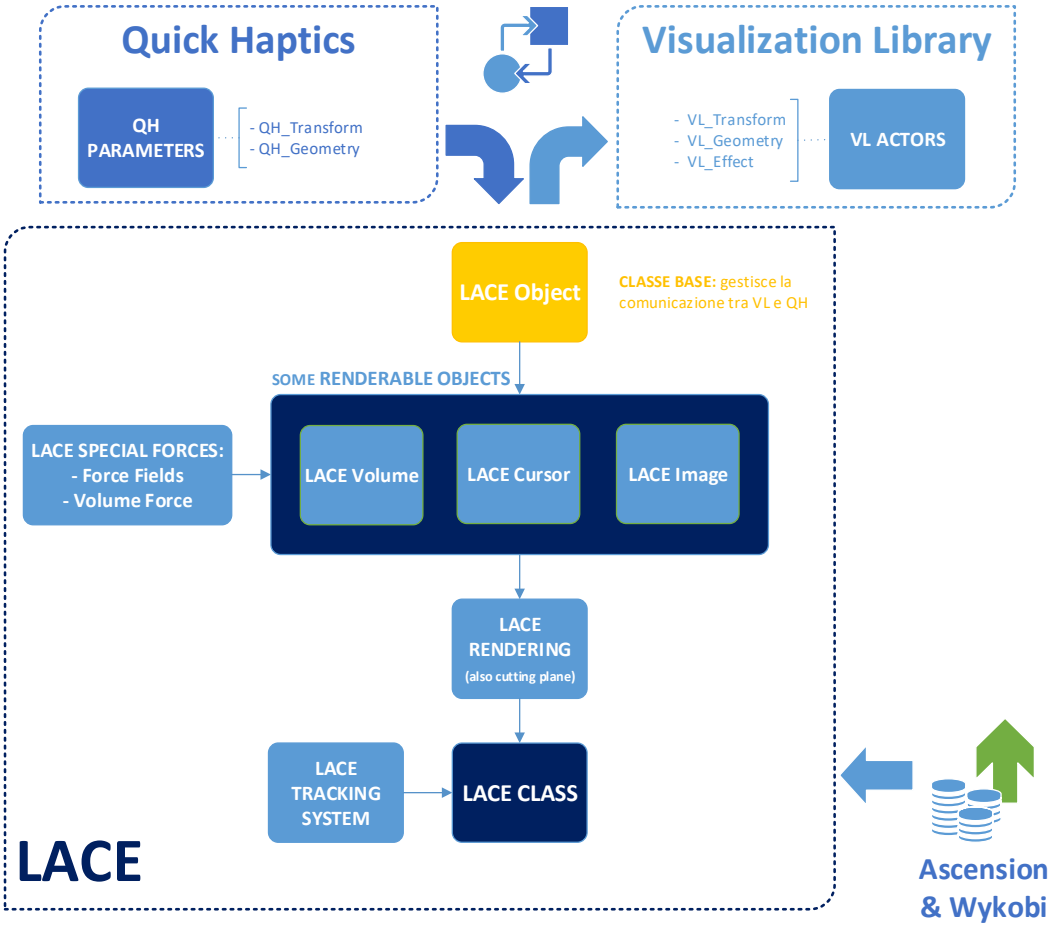


FIGURE 19 LACE Classes

Pointers to all the classes are stored in LACE Class, a class that must be defined in each program based on LACE Library. This is the most important class, as it handles the initialization and update processes, and contains many functions available for the users to customize their executables.

The presence of a base class common to all the objects, containing shape-specific variables and parameters, was needed to properly render the scene and its components and to allow the communication between VL and QH.

Finally, in addition, a stereoscopic view of the scene was implemented to permit users to visualize the scene with the depth perception information.

It has been obtained through a method called stereo-pairs in the off-axis projections: the two views are perspective projections of the virtual environment with parallel cameras.

The user is required to run the application on a 3D monitor that supports the side-by-side mode, and interact with the screen with proper 3D glasses.

How does it work?

The way in which the four libraries work together can be summarize in two main processes:

- Graphic rendering: it comprises those steps related to the visual aspects of the simulation. It handles the reading of the data for the visualization of the virtual models and the fluoroscopy image. The graphic thread is totally supported by Visualization Library;
- Haptics rendering: handled by Quick Haptics, it includes the reading from text file of the values of the haptic properties to be rendered, and most importantly, it is responsible for the tracing of the haptic device in the space, which is essential in the detection of the collision and in the computation of the forces.

Due to LACE Library organisation, two different processes (VL e QH) run concurrently on the computer system: the graphics visualization is rendered at 60 Hz (30 Hz for the left and the right views when the stereo modality is active), while the haptic device process cycles at 1000 Hz (Faso, 2017).

Inputs come from Mouse, Keyboard and the Haptic Device.
Mouse and keyboard are related directly to the Visualization process while haptic device first needs to pass through the Haptic Rendering Process and secondly, through the *LACE Library* the haptic rendering is correlated to a graphic rendering to be display in terms of actions on the 3D model. This correlation is possible because, as said previously, in *LACE Library* are implemented different classes.

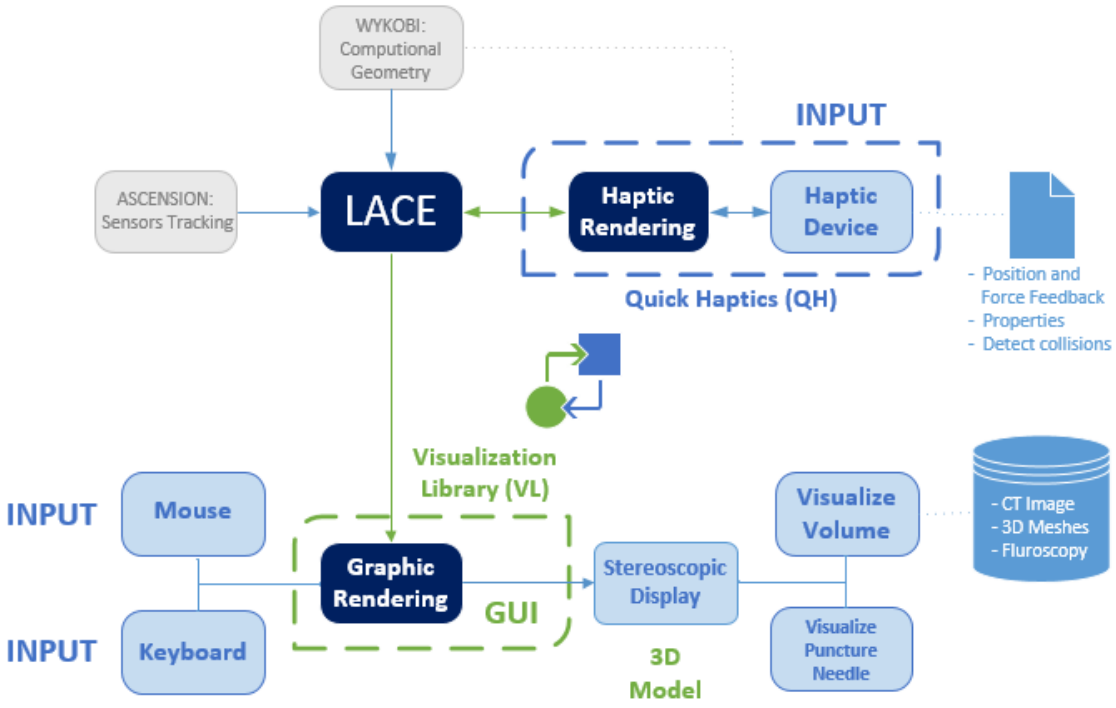


FIGURE 20 General implementation of LACE and communication between the parts

To clarify, a general implementation of LACE is reported in the figure above (Figure 20).

All the objects that can be graphically created in *LACE Library* inherit from a base class called LACE Object. Each LACE Object has an associated actor (VL Actor) which is linked to a geometry (VL Geometry), a transform (VL Transform) and an effect (VL Effect). LACE Object also contains the pointer to the corresponding QH shape (QH Geometry), so that the haptic properties of the specific shape could be directly modified using QH functions.

LACE Volume is the Class in which are defined all the function necessary to create a volume in the VRE. LACE Volume Class works principally calling the VL classes (in which are defined all settings and parameters needed) and including the LACE Object Class that is the class that defines all objects that are visualized in the scene.
It is possible, exploiting LACE Volume Class, to upload the CT image inside the VRE.
This class allows the user to load and display DICOM images and MHD files, which are the most common format for storing medical volumes such CTs and MRIs.
Three ways of volume visualization were implemented in the simulator:

- Volume SLICED, is made up from slicing the volumetric data and then reassemble the cuts into an image, the user can choose the number of slices;

- volume RAYCAST, takes advantage of the Raycasting technique to render a volume;
- and volume ORTHOGONAL, consists in the reconstruction of the three orthogonal planes that are commonly visible in software and applications for the exploration of medical images (sagittal, coronal and axial planes).

We have decided to render the volume in the volume RAYCAST visualization mode to optimize and lighten the graphics rendering.

The other important Class is LACE Mesh one. In this class all those functions that deal with the creation and the management of the meshes are defined. Therefore, through it, it is possible to upload and visualize meshes of the VL supported formats: .3ds, .stl, .obj.
A polygonal mesh in LACE Library can be associated to the volume from which it has been segmented. As a LACE Object, textures or colours can be assigned to the LACE Mesh.

PERCUTANEOUS RENAL PUNCTURE ACCESS (PCA) APPLICATION

We have worked with the PCA Application.

Each model visible in the scene has specific haptic properties of stiffness, damping, static and dynamic friction and pop through.
It is possible to perform the puncture through the simulation in VRE of the needle using the haptic device. Navigating in the VRE needle interact with the 3D model in the space.
When a collision between 3D model and needle is detected, a proxy algorithm based on a spring-damper model, computes the forces to be sent to the haptic device as the distance between p (current stylus position onto the fulcrum line) and p' (desired stylus position) multiplied by a pre-set gain, as highlighted in the following formula:

$$\overline{Force(n)} = \left(\overline{Position\ (n)} - \overline{Position(n-1)}\right) \times Gain\ [N]$$

This force value are calculated depending on the object material properties and on the penetration depth, therefore on the disparity between proxy position and haptic device position: the reaction force is proportional to the penetration depth. The proxy is a point, which closely shadows the position of the haptic device.

The haptic rendering engine continuously updates the position of the proxy. While the actual position of the haptic device may be inside an object, the proxy will always be outside.

The haptic effects that were implemented in the application could be divided in two groups:

- shape-related effects, that are related to the material properties of the objects;
- event-related effects, that are activated when the haptic device is inside the skin or inside the kidney.

The detection of a collision is the basis for both the classes of haptic effects, as the onset of a specific feedback is caused by the interaction of the device with the rendered shapes.

Graphical User Interface

A graphical user interface (GUI), implemented with GLUI, a GLUT-based C++ library has been created to permit the user to modify the features of the 3D model.

The Virtual Reality Environment is constituted by a window on the monitor in which is visible the patient-specific 3D models, a fluoroscopic image and his data, and a drop down menu in which are expressed all parameters for each organs that can be modify by the user.
The user can interact with the VRE with mouse, keyboard and haptic controller.
The last one, as said previously, is the instrument used to perform the puncture, while user can change some aspects of the scene on the GUI by using mouse and keyboard.
In fact, GUI allows the user to pick a particular shape within the scene and change its material properties, whose values are absolute numbers in a range between zero and one.
The user can practice also on the desired access technique under a real-time fluoroscopy guidance. A view of the VRE in which is highlighted the GUI is reported below (Figure 21).

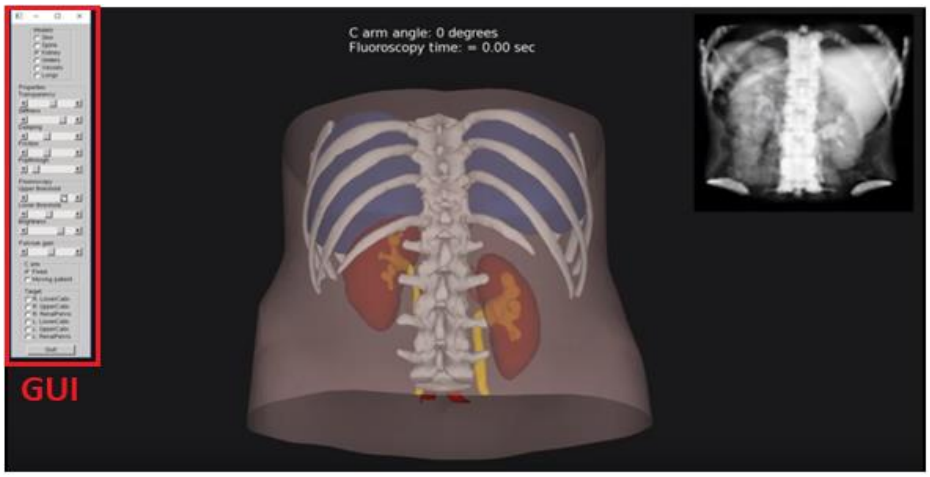


FIGURE 21 Screenshot of the VRE in which is highlighted the GUI

3.1.4 BPMN Language

When we talk about to integrate a new technology for surgeon decision preparation we have to consider that we are modifying the traditional pre-operative workflow.

Therefore, it is necessary to redefine this workflow and analyse deeply the feasibility of this process through a Business Processing Reengineering (BPR).

With the term 'process' we mean 'a set of activities linked together in a logical and temporal sequence, carried out by one or more organizational units. It is not limited to individual functions/departments, but is defined by the production of a final output.

One of the support methodologies used to perform BPR are some support software called Business Process Management Software (BPMS) that are based on Business Process Modelling Notation Language (BPMN Language), in particular, on Business Process Diagrams (BPDs).
This graphical representation is a standard developed in 2004 by the Business Process Management Initiative. It was necessary a notation comprehensible to all starting from the business analyst to technicians, up to managers who manage and monitor processes (Object Management Group, 2009).
Through BPDs, business processes are visually represented as a workflow that, in this way, can be easily analysed in all its parts (e.g. actors, timing, I/O, etc.).

They are composed by four main components:

- Swimlanes: highlight the division of flows between the various actors in a process;
- Flow Objects: main elements that constitute the flow of the process;
- Connecting Objects: they relate flow objects to each other;
- Artefacts: enrich the BPD.

SWIMLANES

Swimlane objects in BPMN are rectangular boxes that represent participants of a process. Swimlanes may be arranged horizontally or vertically. They are semantically the same but just different in representation. For horizontal swimlanes, process flows from left to right, while process in vertical swimlanes flow from top to bottom.
There are two kinds of swimlanes: Pools and Lanes (Figure 22).

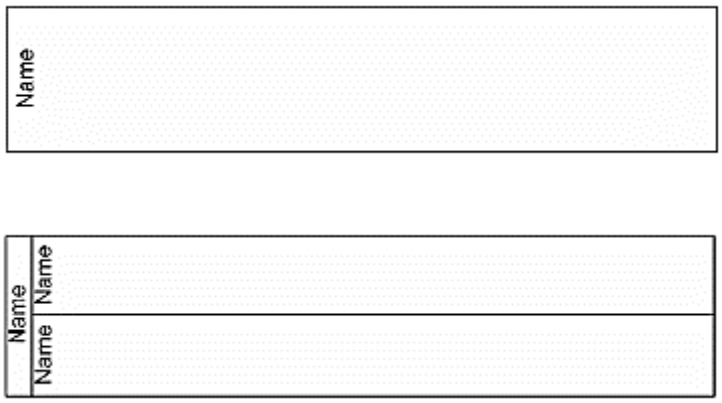


FIGURE 22 Pool (above) and Lanes (below)

Pools represent participants in a process. It can be a specific entity (e.g. department) or a role (e.g. assistant manager, doctor, student, or vendor).

Inside a pool, there are flow elements. They represent the works that the pool needs to perform under the process being modelled.

However, there is one kind of pool that has no content at all: it is known as the black-box pool. Black-box pool is often used when modelling entities external to the process. As it is external, its internal flow does not have any impact on the process being modelled, hence can be skipped, producing a black-box.

Lanes instead are sub-partition of pools. Same as pools, you can use lanes to represent specific entities or roles who are involved in the process.

Lanes may contain other lanes to form a nested structure when needed (BPMN, 2014).

FLOW OBJECTS

Flow elements are elements that connect with each other to form workflows.

Flow elements are the primary elements that define the behaviour of a process. There are three kinds of flow elements: Events, Activities and Gateways.

1) Events are something that happen and may have impacts on a process. An event can be either external or internal. They are shown as circles but in some cases, there are icons within the circles to represent the type of the event trigger.

There are three types of events: Start Event, Intermediate Event and End Event. Trigger can be specified for each of them to indicate under what condition an event is being triggered as shown below (Figure 23).

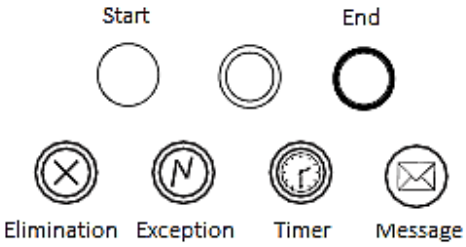


FIGURE 23 Different types of events that can occur in a BPD

Every process should have a start event to show the beginning of process.

2) Activities are works that are performed within a process. They are shown as rounded-rectangle, with names describing the works to perform.

   There are two types of activities: Task and Sub-Process (Figure 24).

FIGURE 24 Difference between Task and Sub-Process representation

   When we want to model an atomic work, which cannot be further broken down or makes no sense to do so, we use a task.

   On the other hand, when we want to model a non-atomic, complex work that can be elaborated into smaller works, we use a sub-process. A sub-process can be broken down into another level of details. For this reason, a sub-process usually contains another BPD modelling its details.

3) Gateways are responsible for controlling how a process flows; they are shown as diamond shapes. In a process, the work to do and the output may vary under different external or internal conditions. Gateway is where conditions are evaluated and the decision is made.

   Some typical types of gateways are:

- Data-Based Exclusive Gateway (A), also known as exclusive gateway is used to control process flow based on given process data.
  Each outgoing flow, which is connected from gateway, corresponds to a condition. The flow with satisfied condition is traversed: only one flow will be traversed.
- Inclusive Gateway (B) can be used to create parallel paths.
  The conditions of all outgoing flow are evaluated. All flows with positive result will be traversed. Therefore, it may result in executing multiple flows if multiple conditions are satisfied.
- Parallel Gateway (C) is used to model the execution of parallel flows without the need of checking any conditions. In other words, all outgoing flows must be executed at the same time.
- Event-Based Gateway (D) is used to model alternative paths that are based on events. For example, to wait for someone's reply, either Yes or No is needed to determine the path to traverse (Figure 25) (BPMN, 2014).

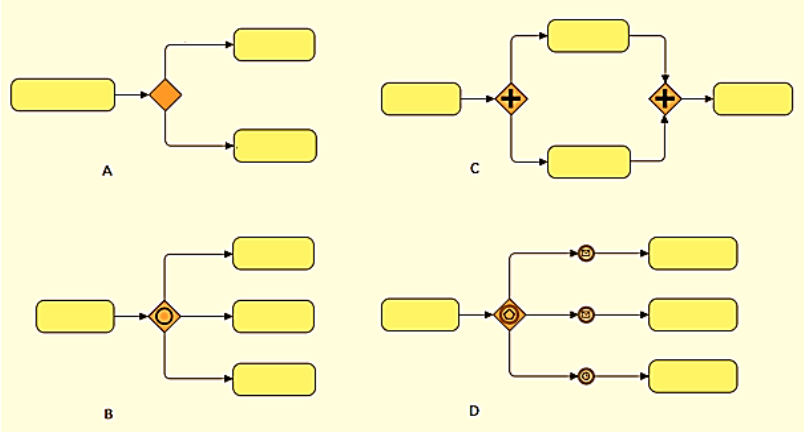


FIGURE 25 Different types of Gateway boxes: A) Data-Based Exclusive Gateway, B) Inlcusive Gateway, C) Parallel Gateway, D) Event-Based Gateway

CONNECTING OBJECTS

Connecting Objects (or Connectors) are used to link the flow elements.

There are mainly three kinds of connecting objects: Sequence Flows, Message Flows and Association Flows.

Sequence Flows are used to show the sequence of occurrence of the activities carried out in a process. It is shown in solid line with an arrowhead. It shows the order of flow elements. You can only use sequence flow to connect flow elements within the same pool: either within the same pool/lane or across lanes in the same pool. If you want to connect elements across pools, you cannot use sequence flow but message flow instead.

In BPMN, the communication between pools (flow of information exchanged between the actors of the process) is achieved by the use of message.
Message flow is used to show the flow of messages between pools or flow elements between pools. A message flow is shown in dotted line with an arrowhead.

Association Flows, finally, are used to associate flow objects and artefacts (e.g. data, text, etc.) and to show input and output of activity (Figure 26) (BPMN, 2014).

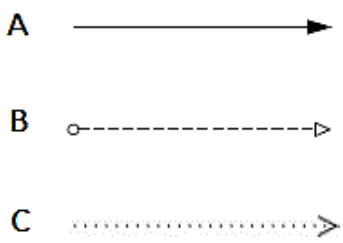


FIGURE 26 Types of Connecting Objects: A) Sequence Flows, B) Message Flows, C) Association Flows

DATA AND ARTEFACTS

BPMN also provides several artefact notations for modeller to describe a process in more detail. Artefacts are additional content suitable for specific modelling situations.

The Data Objects represent the information contents of the process mechanism to show how the data are collected or produced by activities (Figure 27).

FIGURE 27 Representation of Data Objects

Groups, instead, are boxes with dotted line border, providing modellers a mechanism to group shapes by different categories also for analysis and purposes documentation.

Finally, Annotations are notes that can be used to provide additional detail to flow objects in a BPD. They are useful for defining information resources used by each activity and does not affect the flow (Figure 28).

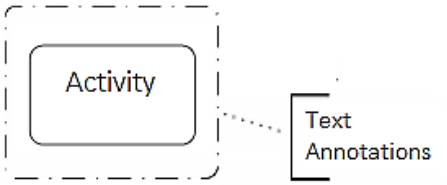


FIGURE 28 Group (dotted line border) and Text Annotations

3.2 What we have done: LACE as a Patient-Specific Simulator

Right now, we are going to explain in details our work.

We have focalized our work on the necessity of a usability of users, and so what we have done with LACE was to analyse deeply that part of simulator use that concern post-processing, upload of the images on the simulator and study of the clinical outcomes.

It has been necessary to study the simulation process in the previous work on LACE and re-define an optimized and standardized one to perform a patient-specific simulation.

To work with the LACE code was necessary to use Visual Studio 2010 Professional®, Microsoft Corporation (Microsoft Corporation, s.d.). As said previously, we have worked with the PCA Application. We have managed principally those classes inherent to volumes and meshes: the CT image is loaded as a LACE Volume instance, while the 3D models extracted from the volumetric image through 3D Slicer are added to the scene as LACE Mesh instances.

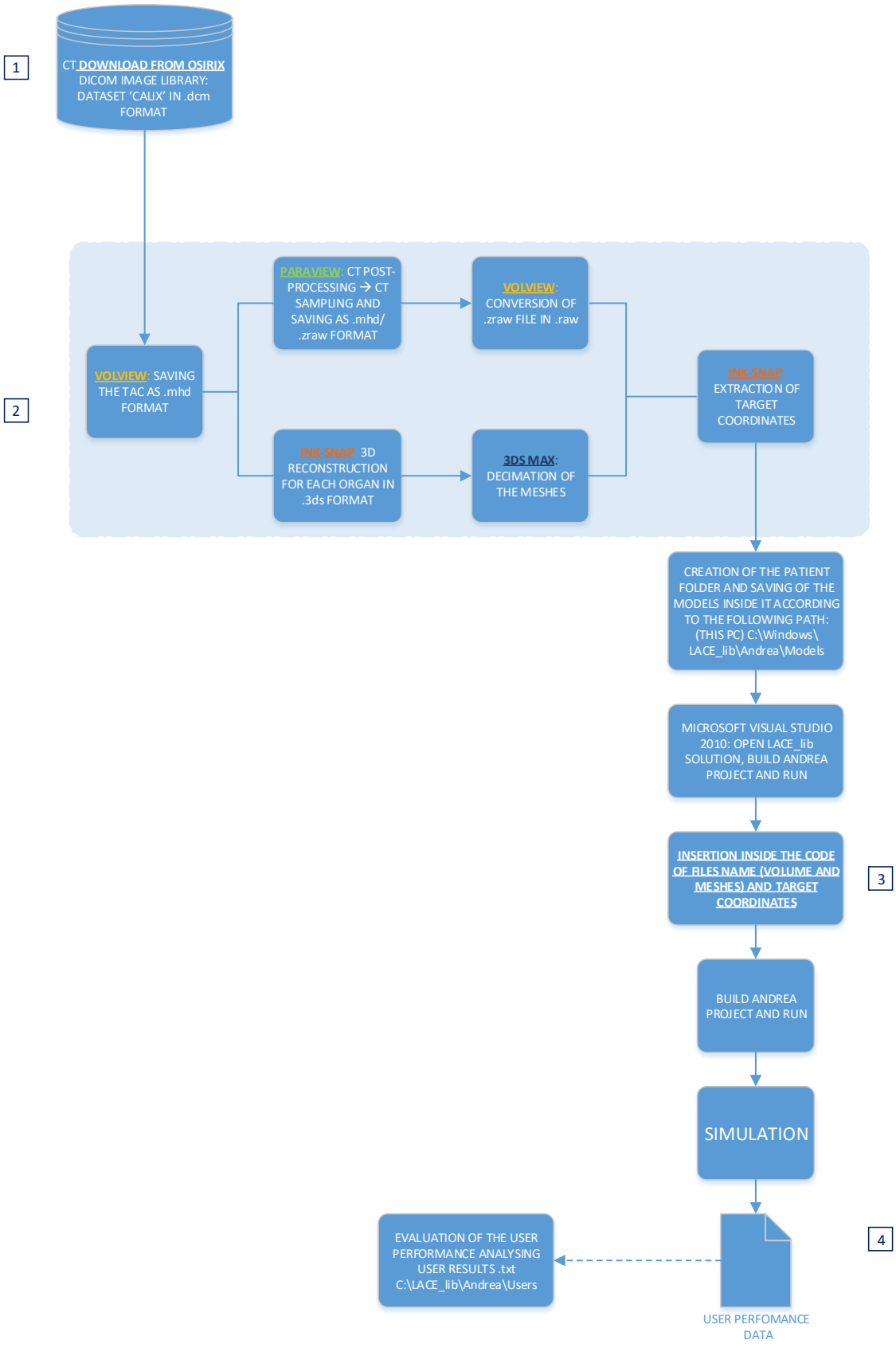
The code extract below, taken from the main function, shows how files are uploaded inside the simulator.

```
////////////////VOLUME/////////////////
data.Volume = new LACE_Volume("Models/CT2.mhd", true, true, -2);

////////////////MESHES/////////////////
data.NeedleFluoro = new LACE_Mesh("Models/Needle1.3DS");

data.Kidney = new LACE_Mesh("Models/kidneys.stl","Models/CT.mhd");
data.Skin = new LACE_Mesh("Models/skin.stl","Models/CT.mhd");
data.Spleen = new LACE_Mesh("Models/spleen.stl","Models/CT.mhd");
data.Bone = new LACE_Mesh("Models/bone.stl","Models/CT.mhd");
data.Lungs = new LACE_Mesh("Models/lungs.stl","Models/CT.mhd");
data.Vasculature = new LACE_Mesh("Models/circulation.stl","Models/CT.mhd");
```

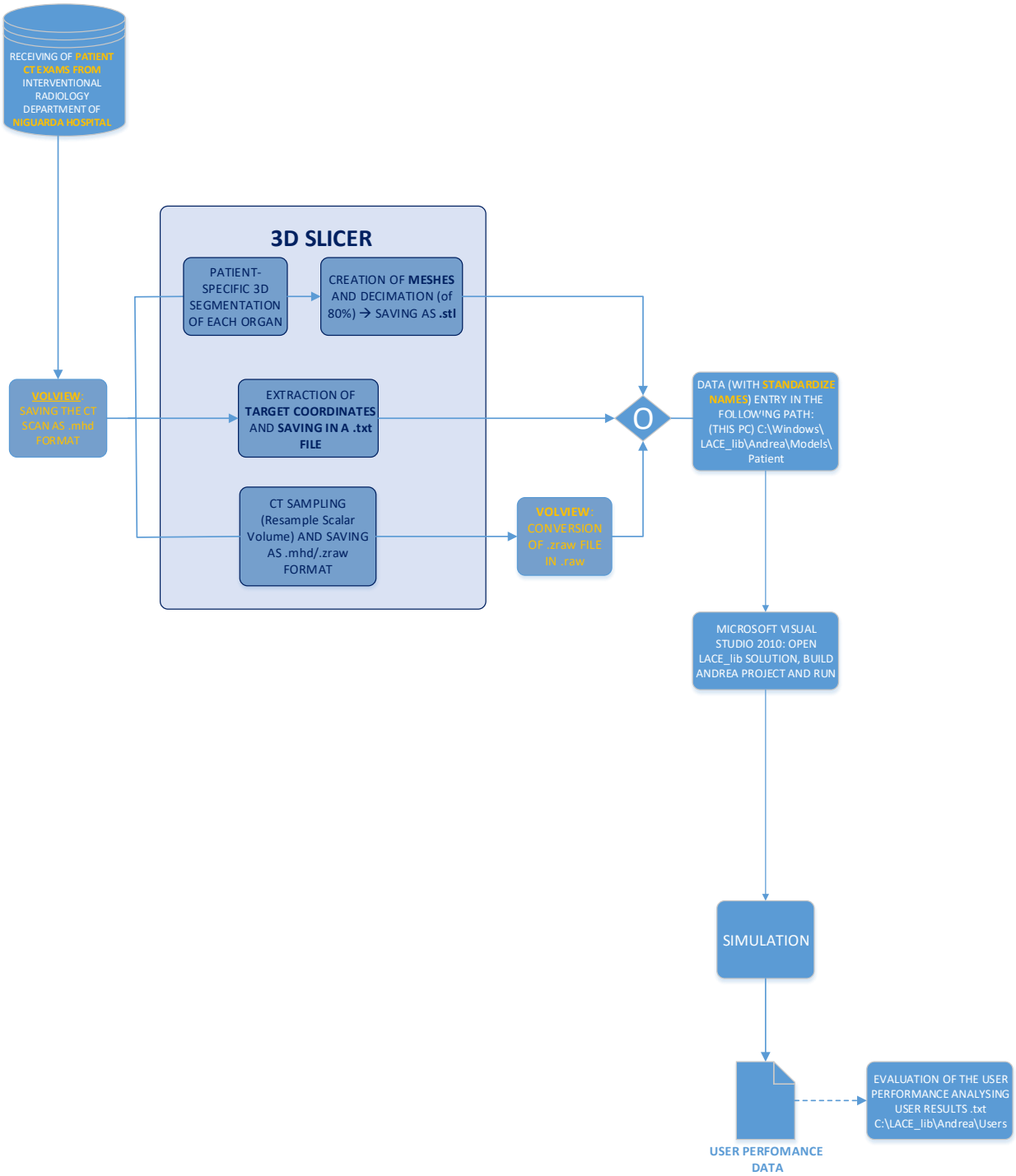
However, the uploading of files are only the tip of the iceberg of our work.

As a first step, we studied accurately the work done previously, starting from the taking in hand of the CT until the uploading itself, and reconstruct a workflow of the simulation process. This has been analysed and described in detail in each passages so that, in such way, limits of LACE VRE were highlighted.

WORKFLOW 1 Reconstruction of previous work: LACE as a generic PCA simulator



WORKFLOW 2 Our work: LACE Optimisation and Standardization for patient-specific simulator use



The reconstructed simulation workflow of the previous work, performed by us, is reported above as also the optimized simulation workflow to show the starting point of our work and what we have obtained.

Starting from the reconstructed workflow of the previous work in fact, we have analysed it entirely, focusing mainly on the four aspects enhanced in the Workflow 1 :

- 1. CT Image Collection;
- 2. Data Processing and Extraction of Target Coordinates;
- 3. LACE VRE;
- 4. Simulation and Outcomes.

This analysis is important because as said previously it highlights the limits, (as a first glance is enough to understand some of that, in particular number of steps to be carried out) and so, after that, the process of simulation could be standardized to make possible the use of the specific patient type simulator.

However, each of the parts that constitute the workflow will be described and explained basing on our analysis. We will then explain how we thought about optimizing and standardizing the procedure (Workflow 2).

3.2.1 CT Image Collection

The first problem that we have met approaching the previous work of LACE was the fact that the simulator validation was done only on a single CT image downloaded by the web archive 'Calix' of OsiriX (Pixmeo, s.d.). This represents an important limitation since, to be a specific patient simulator, it must be guaranteed a generalization possibility by being able to load different images. Also in this sense, a standardization has proved necessary.

What we did then, was to foresee, in our work, the collection of CT images of different patients that must be submitted to Percutaneous Renal Puncture Access.

Going in details of the work done on the CT images, we can say that it is necessary to have a certain clinical eye to identify any regions of interest. For this reason, I had to acquire some skills in term of anatomical skills and in reading of a CT Image attending some anatomy lessons and laboratories and through the many times pass to follow surgeons in operating rooms.

In CT images, each region has usually a grey level, which is different from those surrounding, as points belongings to the same structure possess the same degree of

absorption of the radiation and so each grey value is associated to a certain Hounsfield Unit between -1000 and +1000 coherently with explained above in § 3.1.1.

The value -1000 corresponds to air and it is represented as black tones because is hypodense, while the value +1000 is related to bone and it is displayed as white tones due to the fact that it is strongly hyperdense as well as blood. Those means that tissue with a strong sprinkling of blood can be easily recognized (for example kidneys) and so also that, for example, kidney stones, that are strongly constituted by calcium as well as bone, are highlighted with this method.

Another aspect that a study of anatomy can bring and so facilitate the recognition of different organs is the fact that each organ have specified forms that a trained eye can easily recognize by exploiting the projections of the different plans of the CT. For example, kidneys have a bean form, while liver is a sort of wedge.

All these skills are important to perform a segmentation for 3D reconstruction, as can be shown in the figure below (Figure 29), in which are represented the segmentation phase of the spleen in an abdominal cavity CT before create his 3D model.

Segmentation will be discussed in more detail in the following section.

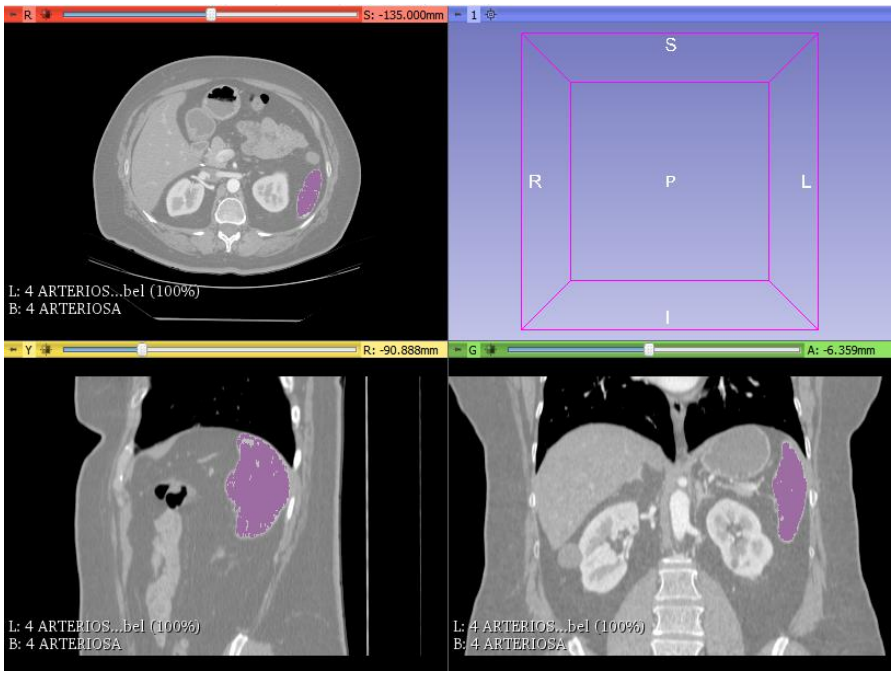


FIGURE 29 The segmentation phase of the spleen in an abdominal cavity CT

3.2.2 Data Processing

One of the focal points of our work, to be able to use it as a specific patient simulator, was the comprehension, analysis and the consequent optimization of the post-processing phase in the simulation protocol, of which little was said in the previous work that had been done on LACE.

VOLVIEW

After taking in hand some patients CT images, we have compared them with the CT image used in the previous work on LACE. Studying the code and the inserted volumes, we realized that CT images on LACE can be uploaded only in .mhd format while normally the CT images are provided in .dcm format file.

To solve this format problem it has been decided to use the Volview® software of the Kitware Inc (Kitware, Volview, s.d.).

This software manage CT images, allowing different functionalities: in our case what interested us was the possibility of converting a .dcm file (more larger) in a .mhd file.

This format conversion phase must be performed with the original CT but also, as we will highlighted below, after the CT sampling. In fact, once saved the sampled CT, it will assume the .zraw file format, a type of compressed format file for image data that, nevertheless, is not supported by the LACE simulator. So, it will be necessary to perform a second conversion with Volview to convert the .zraw file into his uncompressed correspondent .raw.

3D SLICER

The strong point of our work is the radical optimization of the post-processing phase. In fact, we were able to streamline dramatically the process by halving the number of software that must be used to perform the simulation. With the exception of the file conversion software (VolView) (required for the limits imposed by the simulator's implementation choices), now the user can use a single software for processing (3D Slicer), compared to the three used in the previous work of LACE (ITK-Snap for 3D reconstruction, ParaView for the CT sampling and 3DS MAX for meshes).

Referring to Appendix 1, in fact, it is possible to see how the whole simulation process is affected positively by this optimization.

Figure 30 clearly highlights what we have previously said, and therefore allows you to appreciate the advantages of the workflow studied that turns out to be easily usable by a surgeon.

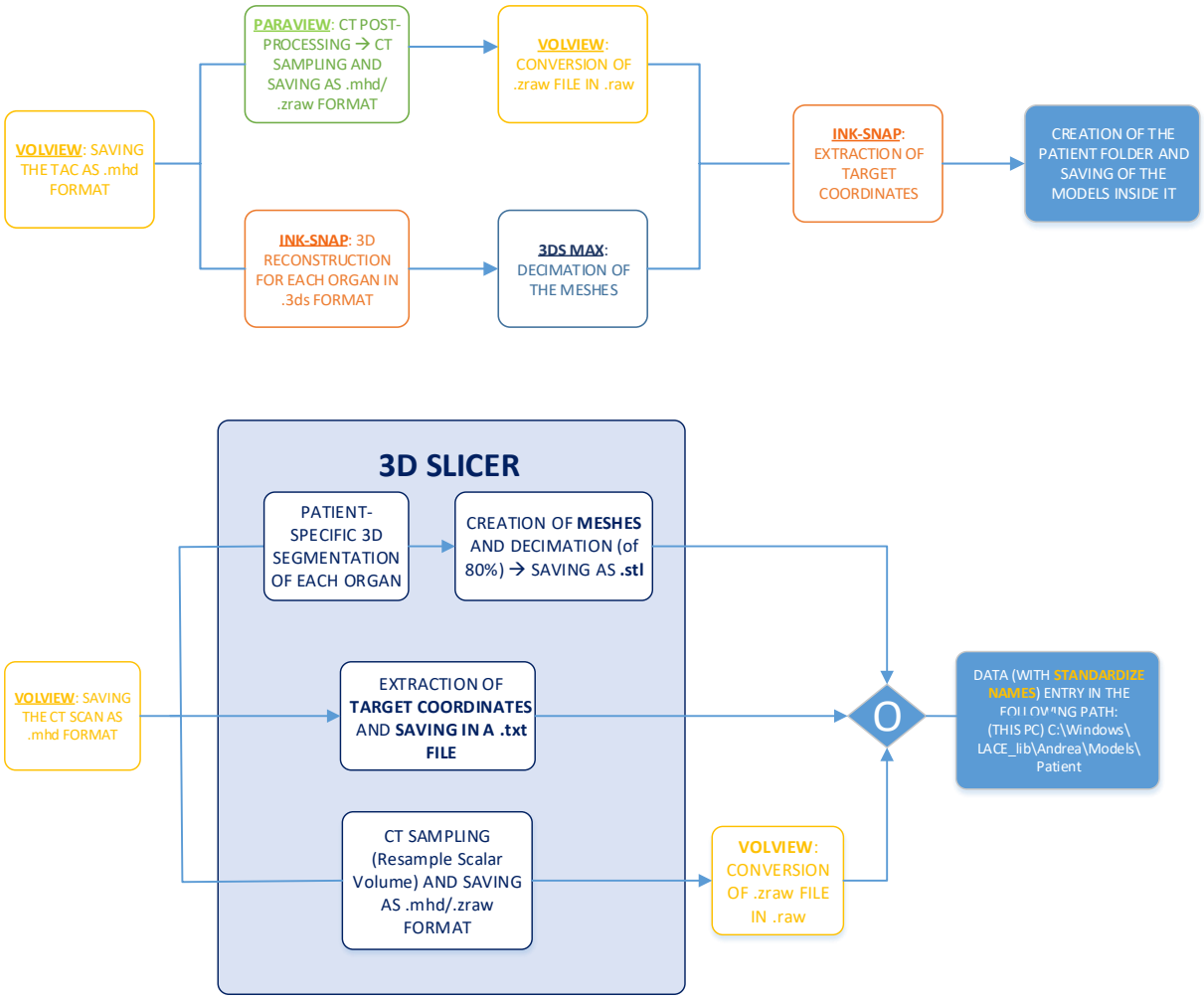


FIGURE 30 Comparison between previous work simulation process and our simulation process

The software that we have used to perform the post-processing phase is the 3D Slicer.

In 3D Slicer we can divide three different sub-phases:

- The 3D reconstruction phase;
- The Extraction of target coordinates;
- The CT Sampling.

3D Reconstruction Phase

The crucial point of the study related to the workflow of the simulation process, it was represented by the 3D models reconstruction. In fact, we have noticed that this part of the post-processing phase was the least optimized of the simulation process.

In the previous work with LACE, as highlighted in the reconstructed workflow, it has been necessary to use two different software to perform the 3D reconstruction of the organs and the subsequent extraction of target coordinates needed to evaluate the simulator performance. In particular, it has been used the ITK-Snap software for the extrapolation of organs meshes, that is a free, open-source, and multi-platform software application used to segment structures in 3D medical images, produced by a collaboration between the University of Pennsylvania and the University of Utah (ITK-Snap Team, s.d.).

However, it has been necessary a second software to reduce also in this case the dimensions of the models (decimation process), limitation even in this case due to a LACE library, this time of Quick Haptics Library.

In our work, we had already decided to use 3D Slicer software as an ideal prosecution of the work of Gianluca Sampogna et al. (2017).
Nevertheless, we have carried out a careful study on this software in order to exploit its full potential and, in order to optimize the process, we have decided to carry out with this software the phases of decimation of created organs meshes and extraction of target coordinates.

To perform 3D reconstructions, it is necessary to upload CT on 3D Slicer (Figure 31).
The anatomy is visible layer by layer by moving the cursor to scroll the slices. The user is able to change the image contrast using mouse buttons.

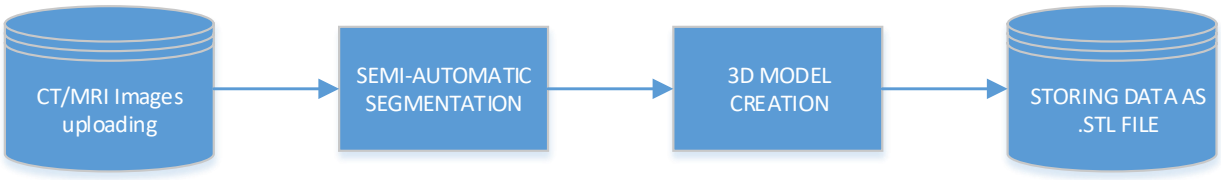


FIGURE 31 Principal phases of a generic 3D reconstruction

The next step was the segmentation: it is an important phase for the reconstruction outcome. There are numerous ways to perform a segmentation: it can be performed manually or automatically. The former is more accurate but it is extremely time-consuming, as the user is responsible for contouring the region of interest (ROI) in each slice of the medical image. The latter instead allows the user to obtain an extremely faster segmentation, but it is not as precise as the manual one.

We have decided to use a middle of the two approaches called semi-automatic segmentation. The automatic approach is used to define clumsily the ROI, and a manual approach is used to improve the contours: it is necessary to have a certain clinical eye to read images and recognize the anatomical structures.

Automatic one can be performed with different method: for different organs, some methods are more effective than others, as for the liver segmentation are (of which is necessary to outline the edges for all slices).

The most used tool for perform automatic segmentation is the Thresholding effect: it goes to work on each voxel and on their intensity manipulating the spectrum of the grey for selecting the anatomical structures. The ends of the scale can be modified to take a smaller range of values and thus reduce the probability of considering anatomical structures not within the region of interest.

Manual segmentation, instead, is performed with the editor of 3D Slicer, constituted by different tools and is used to adjust the automatic selection performed by the Thresholding Effect. The real segmentation process (e.g. the algorithm that perform the calculation of the entire areas starting the selected ones) is performed with the Robust Statistic Segmenter Method.

After segmentation process, the user have only to select the volume-rendering tool to allow the software to elaborate the 3D model.

3D Slicer offers the possibility to use different types of volume rendering effect tools. The choice of the user it must fall back on what provides a better result consistently with the use it must then make.

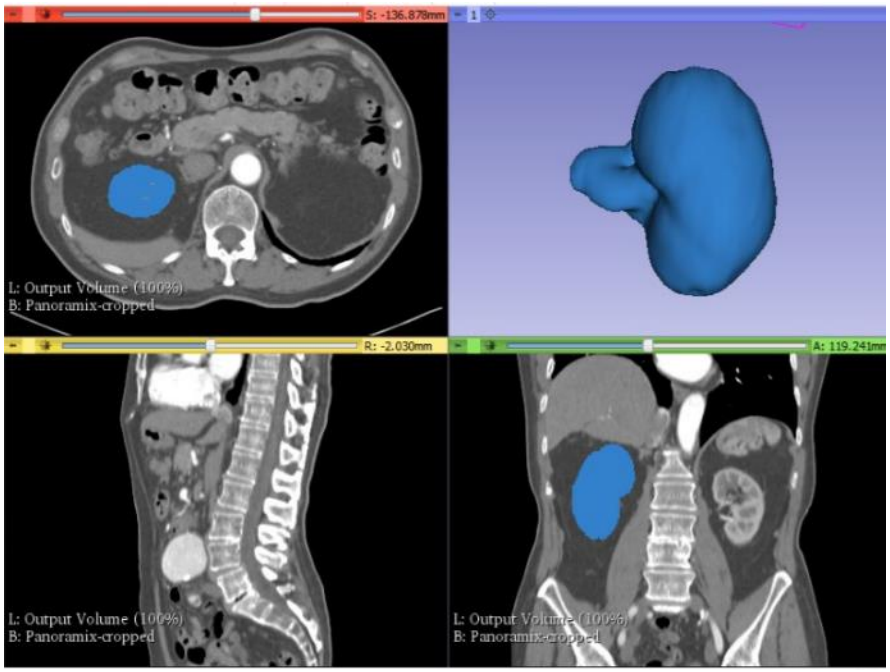


FIGURE 32 Screen of 3D Slicer work window

We have decided to use the Surface Model _Model Maker Tool (Figure 32) of which we had to set some parameters: we have chosen to set the smoothing parameter at 30 and to select the Laplacian Filter with 0.8 decimation parameter (i.e. number of triangles that constitute the surface of the organs that is the mesh).

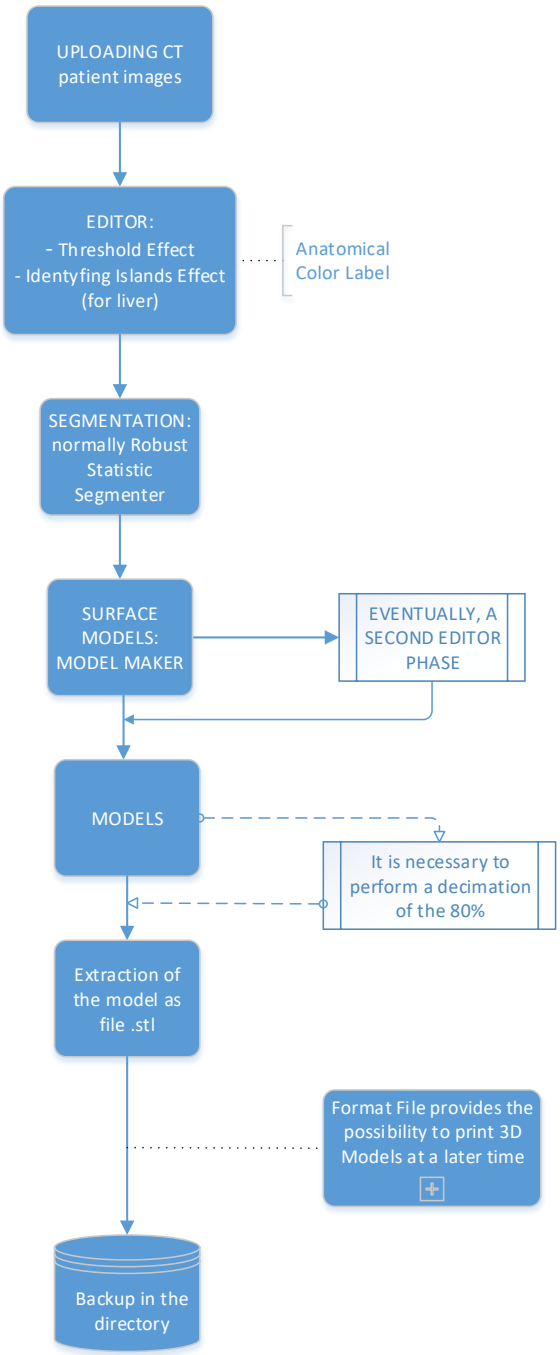
The choice of these values, in particular the value of decimation, is related to the fact that organ model (under the form of a mesh) must undergo some limitations in terms of size to be uploading inside LACE, due to the particular libraries chosen for the implementation of the simulator.

At the end of the elaboration, organ model can easily storage in the directory as different type of file. The most used format file for the mesh is .stl. A STL file ("Stereo-Lithography") allows describing and representing a three-dimensional surface through its discretization with a series of triangles. Essentially, the STL file consists of a list of data that uniquely identifies the triangular faces covering the surface by means of the spatial coordinates of its vertices and of the normal to the triangle. Consequently, each triangle that forms the mesh will add to the STL file twelve coordinates. Each triangle of the mesh must necessarily be connected to the next by sharing two of its vertices, and all the coordinates that constitute the file must be positive (Faso, 2017).

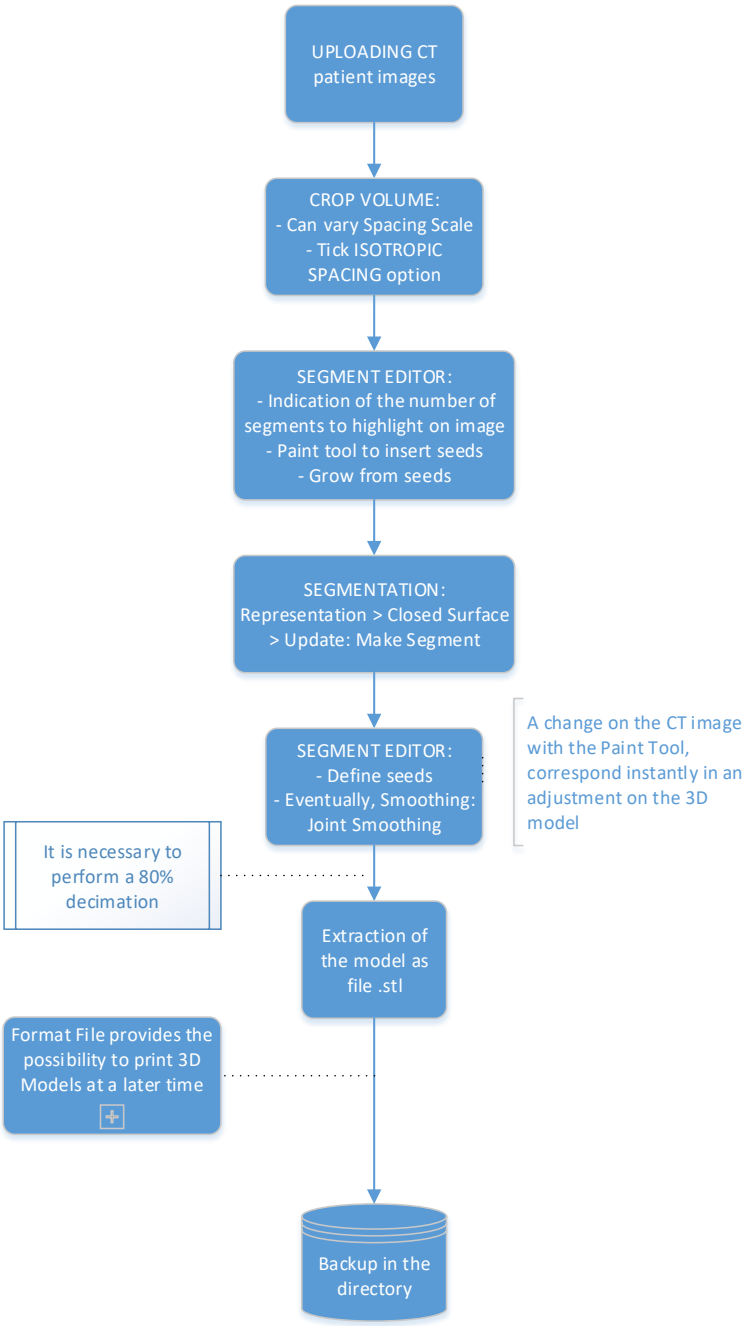
We have chosen to use this file format because owns the advantage of be largely used for 3D printing and prototyping. Therefore, it would be possible later, if necessary, to retrieve the patient's 3D model from the directory and proceed with its 3D printing.

Following two of the most used workflows for image segmentation are reported (Workflow 3, Workflow 4).

WORKFLOW 3 First Type 3D reconstruction with 3D Slicer, the most used



WORKFLOW 4 Second Type of 3D reconstruction with 3D Slicer



We have reported also the second workflow (Workflow 4) to highlight the 'crop' function, which is useful when the dimension of the CT image uploaded is huge and does not allow the PC to work smoothly. As evidenced by the diagrams, there is not a specific guided procedure to perform the 3D reconstruction; it is more a choice of the user, coherently with his/her knowledges and applications.

In addition, it is reported below a table (Table 4) in which are specified some algorithm and some parameters that are considered the best choice for 3D reconstruction for each organ: we have deduced them during some tries in 3D Slicer use.

The RSS abbreviation means Robust Statistics Segmenter method and the following values refer to some RSS parameters: Approximate Volume (mL), Intensity Homogeneity (range between 0 and 1), Boundary Smoothness (range between 0 and 1).

TABLE 4 Algorithms and values that can be used in 3D Slicer for each organs of abdomen

Objective: To assess the most efficient and effective way to segment anatomical structures indicated below by comparing different contrast phases and algorithms.

Imaging: Datasets given during the course including head MRI, head CT, thorax CT, abdomen and pelvis CT.

Abdomen and Pelvis	
Organs	**Algorithms and values**
Bones	Threshold +180/+max
Arteries	Arterial Phase: Threshold +200/+max
Veins	Venous Phase: Threshold +200/+max
Liver	RSS 1700; 0.7; 0.4
Kidneys	RSS 200; 0.7; 0.6
Renal Cyst	GrowCut / RSS x ml; 0.9; 0.9
Ureters	Delayed Phase: Threshold +165/+max
Spleen	RSS 250; 0.9; 0.7
Pancreas	RSS 75 ml; 0.8; 0.1
Stomach	RSS 200; 0.7; 0.1 + manual refinement

e.g. RSS 150 ml; 0.9; 0.7

The main advantage of the use of this software is the possibility to create a 3D model for each organ and to save it as distinct and separated files. Later, the user can create a scene with the structures necessary to perform the simulation (e.g. for the right kidney is sufficient to have a reconstruction of it, of the liver, of the arteries and veins, and of the ribs).

This aspect therefore allows to work, subsequently in a simulation environment, on the properties (physical and rendering) of each reconstructed organ, in order to make it as similar as possible to the real one.

In this way, for example, if it is necessary a change in transparency of the kidney to verify the outcome of the simulation, it is possible to do it.

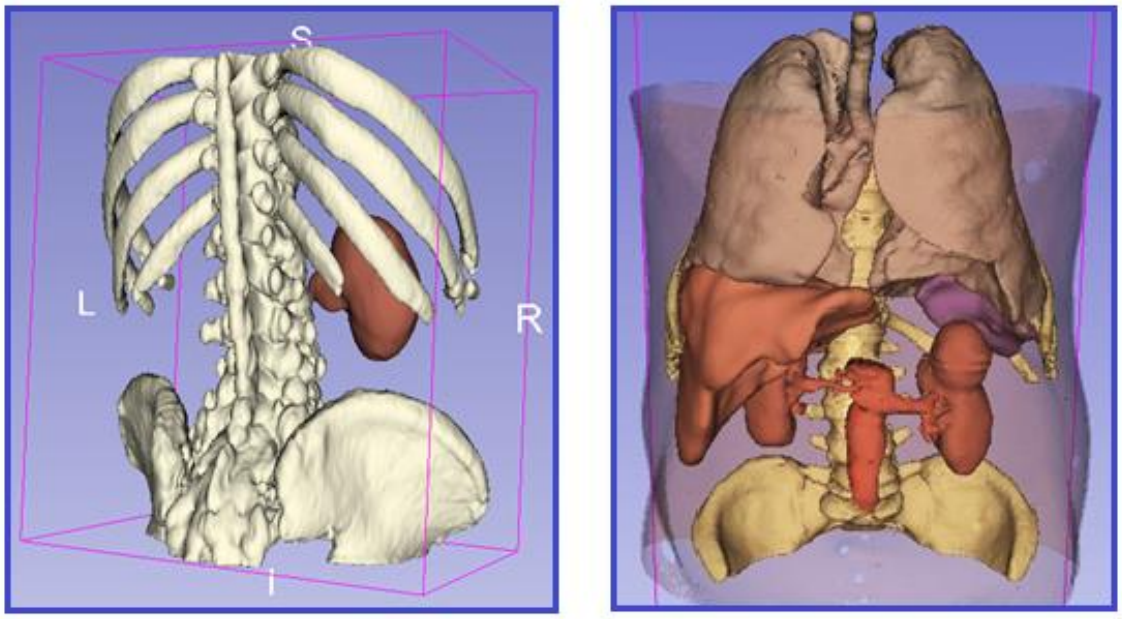


FIGURE 33 Example of scene creation and a complete 3D Abdominal Model reconstructed by a CT image given us by Niguarda Hospital

Overall, thanks to the experience carried out, it is estimated that a user, with a fair knowledge of the software, can carry out the reconstruction of the anatomical district procedure (Figure 33) in a time equal to at most an hour and a half (about 15 minutes for every anatomical structure).

Extraction of Target Coordinates

To perform a Percutaneous Renal Puncture, in particular for Renal Biopsy use, it is necessary to identify a target inside the 3D models. Obviously, the operative target is different according to the patient of his pathology.
This is necessary also to evaluate the performance realized with the simulator.

For the target identification, LACE requires the insertion of the target coordinates that in previous work with LACE they were entered manually into the code.
First of all, how can we get these coordinates?

In the previous work, the extraction has been done visualizing the CT on ITK-Snap and noting down the coordinates that can be visualized on the drop down menu when the user move with the cursor to the point of interest.

In our work, to allow the realization of this extraction that is obligatory but at the same time obsolete in terms of optimization of the process for how it was done previously, we have used the function 'Create and Place Fiducials' presents inside 3D Slicer in the Markups Tool.

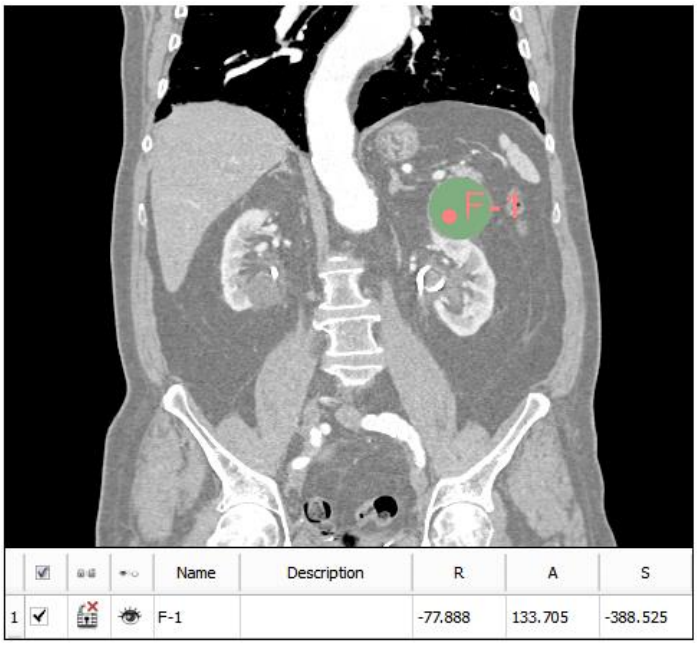


FIGURE 34 Location of the fiducial points

When located and marked with the cursor the fiducial points (F-1 in the figure reported above, Figure 34) on the slices, it is possible to extract and save the point coordinates in mm, as required for the visualization on the defined LACE space.

CT Sampling

Studying the code and the inserted volumes in fact, we realized that the dimension of the uploaded fluoroscopic image (i.e. the CT image with contrast medium) is of about 100x100x100, comparing to that of original CT image that is about 512x512x512. Therefore, it was necessary to proceed to a sampling of the CT image. This is because one of the libraries

used to create LACE (the Visualization Library) does not adequately support the very large size of the CT files, representing an ulterior limitation.

There are different ways to perform a sampling. We decided to perform the Resample Scalar Volume tool of 3D Slicer because guarantees a good ratio between reduction in dimensions and quality of the image.
The user must choose the Spacing Parameter between each new slices in the three spatial dimensions: this means that, by varying the three value, we take the information of the image each gap of that value, obtaining a CT image sampled with the reduced dimension. For the interpolation parameter, we have decided to perform a linear interpolation.
After the sampling, we had save the file again as a .mhd file.

The advantages of the simulation workflow developed are:

- first of all, as highlighted many times, we can identify an optimization of the process in terms of number of software used. This reduction has been necessary to make it more user-friendly to be use by user like surgeons for which it would be difficult to learn to use five different software each of which has many functions and requires some training time to understand how it can be used;
- secondly, it is performed also an optimization in term of timing of the simulation process which is then also reflected on the total time of the whole process of using the simulator in clinical practice.

  In the study and implementation of the workflow inherent to the previous work, we realized how the simulation process is perhaps too high. In effect, for the sampling with ParaView we realized that a time of 2 hours was needed for processing of the image time that, respect to the time that we believe that the surgeon can possess to dedicate himself to this activity during his normal daily tasks, is excessively burdensome. In fact, we have estimated that the surgeon can take care of the reconstruction and the simulation for a time not exceeding two hours, based on the assumption that it has a certain confidence with the software.

  To estimate this timing we had considered that a the reconstruction and creation of meshes process take it can be done in about an hour and a half, as previously mentioned, and that the remaining half an hour can be used for the extraction of the coordinates of the target and for the sampling.

In conclusion, from these evaluations it is clearly evident how the previously work was little optimized and not standardized as regards the post-processing phase, which however represents a critical phase for the patient-specific use of the simulator.
The optimization of this phase in our work has been achieved by making the most of the 3D Slicer software. On this, in fact, it is possible to perform almost all the steps needed, thus reducing the number of software used and therefore also the steps to be performed as it is possible to see in the underlying flowchart, obtained zooming the optimize simulation process developed.

We also want to underline that it could be interesting to create a figure (as it could be that of the biomedical engineer) inside the team, which, besides its normal duties, can be called or consulted if necessary to carry out a support activity to the clinician in the data processing phase.

3.2.3 LACE VRE

In order to standardize the process, it was necessary to make some modifications to LACE and to the use made of it before, in order to make the procedure more automated.
We chose not to make excessive changes, which would denaturalize LACE for what it was meant to be, since we want to demonstrate the possibility of its use in the clinic.

The first modification was to standardize the name of the files to be uploaded inside the code and create a folder named ‘patient’ in the path to which the code refers in which the users can insert volume, needle mesh (default and named ‘needle.3DS’) and organs meshes previously saved. This allows the doctor to open the VRE on Visual Studio and only having to run the PCA Application without having to touch the code and thus making everything more user-friendly.
Moreover, as previously mentioned for the target identification, LACE requires the insertion of the target coordinates that in previous work with LACE they were entered into the code in the following lines present inside the ClassAndre.cpp file.

```
vl::fvec3 PCA::RL = vl::fvec3(3.81, -3.0, 0.15); vl::fvec3 PCA::RU =
     vl::fvec3(3.72, -1.03, 1.79); vl::fvec3 PCA::RP = vl::fvec3(2.99, -1.98,
     0.49);
```

```
vl::fvec3 PCA::LL = vl::fvec3(-4.61, -0.27, 2.36); vl::fvec3 PCA::LU = vl::fvec3(
    -4.50,1.83, 3.39); vl::fvec3 PCA::LP = vl::fvec3(-4.20, 1.00, 1.90);
```

Here we can see that users declare the data of the target inserting the coordinates (highlighted in red) of the right and of the left kidney manually. In addition, we want to point out that the target within the virtual reality environment is implemented as a small sphere with origin in the entered coordinates.

After the upload of the volume and meshes in the main, in the code is implemented a for-cycle in which the target coordinates are recalled and a target volume is generated through the LACE Sphere class after the selection of the user of the wanted target in the GUI.
It is possible to see six different possibilities for the target:

- Right Upper Calix;
- Right Lower Calix;
- Right Renal Pelvis;
- Left Upper Calix;
- Left Lower Calix;
- Left Renal Pelvis.

```
for(int i=0; i<6; i++)
     {data.Target[i] = new LACE_Sphere(0.3);
     data.Target[i]->LACE_SetColor(vl::white);
     data.Target[i]->LACE_SetCompletelyVisible(false);
     data.Target[i]->VL_Actor->setRenderRank(0);
     data.Target[i]->QH_Geometry->setVisible(false,false);
     }
     data.Target[0]->LACE_SetTranslation(data.RL.x(),data.RL.y(),data.RL.z());
     data.Target[1]->LACE_SetTranslation(data.RU.x(),data.RU.y(),data.RU.z());
     data.Target[2]->LACE_SetTranslation(data.RP.x(),data.RP.y(),data.RP.z());
     data.Target[3]->LACE_SetTranslation(data.LL.x(),data.LL.y(),data.LL.z());
     data.Target[4]->LACE_SetTranslation(data.LU.x(),data.LU.y(),data.LU.z());
     data.Target[5]->LACE_SetTranslation(data.LP.x(),data.LP.y(),data.LP.z());
```

However, the manual insertion of the target coordinates is a very important limit of the previous work because it means that when the fluoroscopic image and the meshes uploaded are changed, the user must change also the coordinates of the patient coherently with the target that it is necessary to operate on.

To overcome this limit we have decided to implement the possibility for the user to save the target coordinates (also more than one) in a .txt file that the code, once run, provides to search in the path and read each row of the .txt going to insert the coordinates automatically in the code. In this way it is not necessary to implement the possibility of having six targets, but only the one of clinical interest is displayed.

In addition, we have to set the SetRotation and SetTranslation function to display the 3D model coherent to the fluoroscopic image, so that when the surgeons stings the model by using the haptic controller, the anatomical location of the needle in the 3D model and in the fluoroscopic image is the same.

3.2.4 Simulation and Outcomes

Before opening the VRE, the user has to locate the files created previously inside the folder 'Patient' present in the following path:

C:\Windows\LACE_lib\Andrea\Models\Patient

The VRE requires the access to ten different files:

- the sampled CT that will have to be called CT sampled.mhd (file format), needed to visualize the fluoroscopic image as guidance;
- the original CT that will have to be called CT.mhd, needed to tell the program what volume the meshes are referring to;
- the needle mesh that will be present in the Patient folder by default and will be called Needle.3ds (another type of format for meshes in addition to .stl), needed to view the needle to perform the puncture and that will be displayed as angle of 30° respect to the C-arm (i.e. x-ray tube used in surgical room to perform real-time fluoroscopic guidance);
- and the organ meshes of the abdominal cavity that must be those of:
    - the kidneys, named kidneys.stl;
    - the spleen, named spleen.stl;
    - the lungs, named lungs.stl;
    - the skin, named skin.stl;
    - the liver, named liver.stl;

- the ribs, named bone.stl;
- and the circulation pathway, named circulation.stl.

Each file will be associated different properties of material, which have been set previously by us coherently to the real properties of material of the organs with which the surgeons could interact during procedure.

After this phase of uploading of the files in the simulator folder, to simulate the Percutaneous Renal Puncture Access the user have to open Visual Studio 2010 and open the PCA Application (Andrea project) searching it inside the directory.

Subsequently to the opening of this, the user has to build the 'Andrea project' and proceed to run the solution for open the simulation window.

At this point the user will display a window called a command line interface where the user can see the uploading the file status and in which he will be asked to enter the name of the user who is using the simulator.

Once inserted, the simulation window comes into view and the user can use mouse, keyboard or the haptic device to interact with the simulation window.
The figure above (Figure 35) shows one of our 3D models which have been reconstructed by a CT given us by Niguarda Hospital.

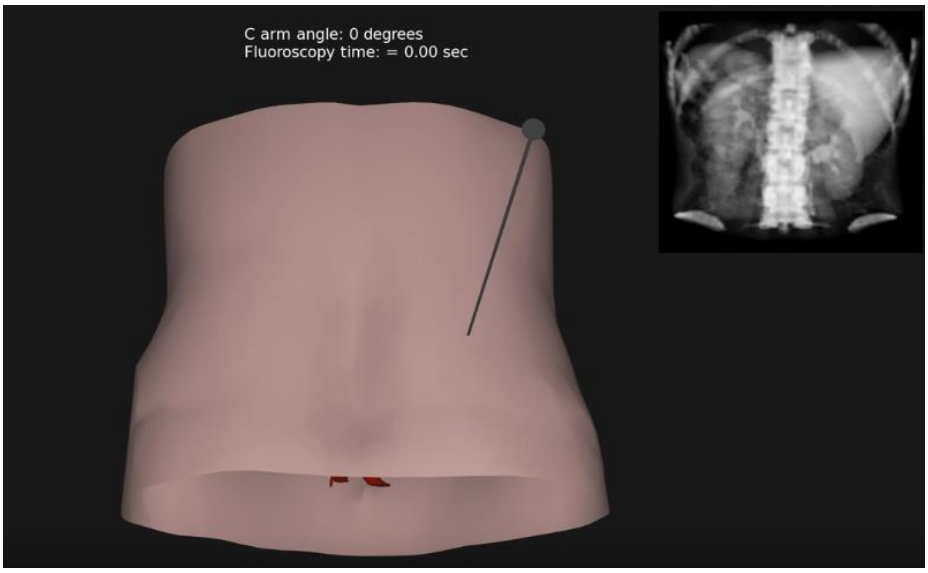


FIGURE 35 One of our 3D model reconstructed by a CT given us by Niguarda

Several are the actions that can be performed by the user, in particular it is possible to:

- visualize and interact with the fluoroscopic image in the upper part of the screen on the right;
- start the time of fluoroscopy and visualize it on the screen;
- visualize the C-arm angle orientation;
- visualize and interact with the 3D model of the abdominal cavity;
- visualize the GUI to modify the properties of each organ (like stiffness, transparency, etc. that at the first use of the user are standard), set up the fluoroscopic image range on grey levels, and choose the type of simulation that the user needs to perform, training or trial;
- perform the puncture and control in different way (also written on the top of the screen) the distance from the target.

All the functions reported above can be performed by using the following main commands:

- F1: to exit the simulator display window and return to the development environment;
- Space-bar: to freeze the performed puncture and analyse the performance of simulation observing the distance from the target;
- C: to use a plane for cut the 3D model;
- T: to move from the fluoroscopic image window to the 3D model one
- +/- : to zoom in and out the fluoroscopic image;
- ↑/↓/→/← : to shift the fluoroscopic image;
- Right click: to show the GUI;
- Mouse wheel: to rotate the fluoroscopic image.

The 3D models can be dragged, translated and rotated by pressing a button on the haptic device: the user is able to move freely the objects in the virtual environment, therefore always obtaining the desired view of the scene.

After the user performance, a .txt file named as the user insert in the command line interface is generated in the ‘Users’ folder inside the path *C:\Windows\LACE_lib\Andrea\Users*. In this .txt file, different information related to the user setting of the simulator are reported, in terms of, for example, properties of material chosen, but also index like distance from the target that can be used to evaluate the performance.

In fact, we find reported:

- UpperThreshold of the fluoroscopic image transfer function;
- LowerThreshold of the fluoroscopic image transfer function;
- Brightness of the fluoroscopic image;
- EyeSeparation of the camera that is default to 1/30;
- FulcrumGain, that is the force gain related to the fulcrum point (tip of the needle);
- Transparency of the organs in the same order as they are listed in the drop-down menu;
- Stiffness of the organs;
- Damping parameter of the organs related to the haptic force feedback;
- Friction parameter of the organs related to the haptic force feedback;
- Pop Through parameter of the organs, that is the force threshold value that which indicates whether the user has passed the organ or not;
- Distance from the target;
- Fluoroscopic Time;
- Procedure Time.

In particular, with the last three parameters, we can evaluate the performance of the user in doing the simulation, as previously said.

However, we are also interested in understanding if the simulation can help and support the surgeon in performing the surgical intervention basing on what he has experienced with the simulator. We want to clarify that this is not a tool for preoperative planning but we believe that a surgeon who has already seen the patient's anatomy to be operated can be facilitated in the intervention by improving some clinical outcomes.

In fact, we believe that some parameters in the operative room like operative time, and some clinical outcomes that can be measured on the patient in the immediate post-operative period can benefit and therefore improve because of using LACE for this procedure.

3.2.5 Pre-Operative Workflow Development

At this point, it was necessary to understand if the use of simulation in clinical practice can be sustained inside a Tertiary Department of Interventional Urology. Therefore, we have

studied a workflow of clinical processes to check, especially in terms of timing, if this were possible comparing it with the traditional one, and to outline a standard workflow for its real use.

To develop the workflow, basing on the BPMN Language, we have decided to use Visio 2013®, a software of Microsoft Office®.
The workflow has been developed mainly by interviewing surgeons who deal with the type of intervention we talked about previously. This activity was fundamental in order to develop a workflow that was as precise and coherent as possible with the real workflow that is followed by the surgeons in the different phases. In fact, we asked to surgeons to highlight which processes could have been taken into account in order to develop a workflow that can then be effectively used in clinical practice. We therefore wanted to focus not only on the preoperative phase, but also on the operative and on the post-operative one, in order to have an overall vision as much as possible.
As it is possible to view in the workflow reported in the Appendix 3, we can identify two pools, the Clinical Activity and the Surgical Unit Activity, divided in three different phases, the Pre-Operative Phase, the Operative Phase and the Post-Operative Phase.

For simplicity of analysis of the developed workflow, we can divide it in three main parts:

- 1° part, in green, corresponds to the arrival of the patient and decision making inherent to surgical intervention, which we have corresponded, from a temporal point of view, to day zero (T=0);
- 2° part, in blue, corresponds to the 3D reconstruction and simulation process, which can be performed n days after the arrival of the patient and the day before the intervention (T=n);
- 3° part, in yellow and orange, corresponds to the surgical intervention (T = n+1) and to the day immediately following it (T= n+2).

Going into the details of each of these parts, we are now going to explain how it was developed.

The 1° part, as previously mentioned, is related to the acceptance phase in which patient arrives at the Niguarda hospital. We deemed it appropriate to switch patients in two types:

those that arrives with his/her personal CT previously done in another centre, and who arrives without CT (Figure 36).

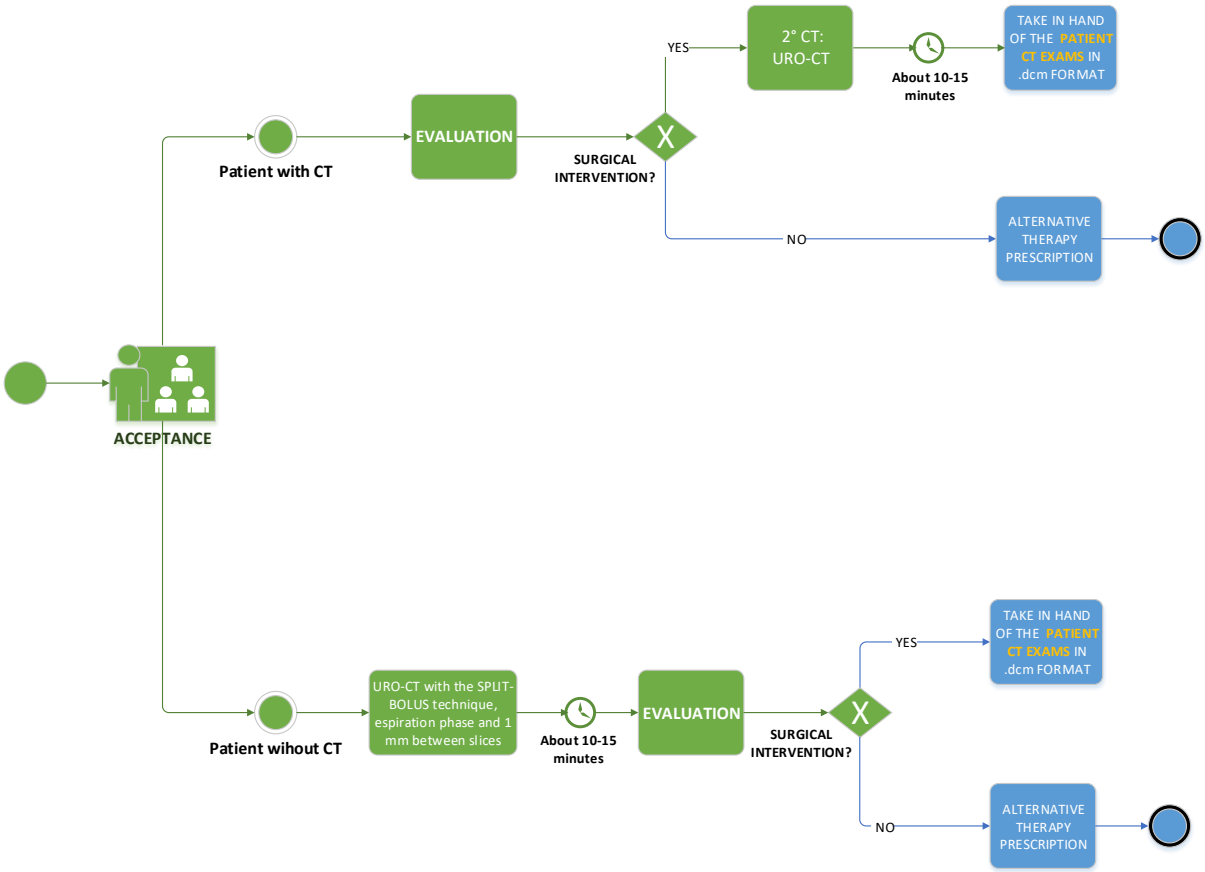


FIGURE 36 First part of the developed workflow: patient acceptance

In the first case, the surgeon must evaluate the patient CT to make a decision of surgical intervention or not. If it is decided to carry out the intervention, it is necessary to perform a second UroCT with Split-Bolus method. The CT must be performed with a distance of 1 mm between the slices and in prone position to facilitate the 3D reconstruction of the abdominal cavity. After a time delay due to the waiting for the CT scan report (which we can consider of about 10 minutes), surgeon can proceed with the post-processing and 3D Slicer phase.
If the surgeon evaluates that the patient does not undergo to surgery, to the patient will be evaluated and prescribed another therapeutic path.

In case of patients without CT, it is necessary to perform the CT exam, with the same characteristics of the one just described, wait the time necessary for the production of the

CT scan report and only at this point proceed to the evaluation of a possible intervention. Also in this case, if the surgeon decides to carry out surgical procedure, he/her can advance to the post-processing/3D Slicer stage.
In both cases, to proceed with the post-processing and 3D reconstruction phase (the same in both) it is necessary to acquire the CT image in the .dcm format.

Before performing the next stage of the workflow it is necessary to perform a conversion of the CT image from .dcm format to .mhd one with Volview®.
The post-processing phase, as highlighted previously in the paragraph relative to the simulation, is necessary to reduce the dimension of the CT image and can be performed on 3D Slicer. The user must perform the elaboration of the image into a 3D models with the creation of the meshes.

As it has been extensively described above, the major advantage of the use of 3D Slicer is the fact that all the most important steps can be obtain with this software:

- sampling of the CT image;
- the segmentation of the patient CT image;
- the creation of the meshes relative to abdominal cavity organs;
- the extraction of the target coordinates.

We underline the time estimation for the complete phase of about two hours that is reported in the box.

At this point, only after the processes of these steps have been carried out, data can be saved in the folder ‘Patient’ on the directory to which LACE refers: this, in fact, is necessary to permit to the simulator to open the patient 3D image. To perform the simulation, the user must to open the Microsoft Visual Studio® software, upload the LACE library solution, build and run the PCA Application (Andrea’s project). Data relative to the performance will be saved in the .txt file which can be analysed to carry out an evaluation.
This phase is the same for the two branches relative to patient with CT image and patient without CT image.
For this reason, we have reported it only one time and is visible in the following scheme (Figure 37).

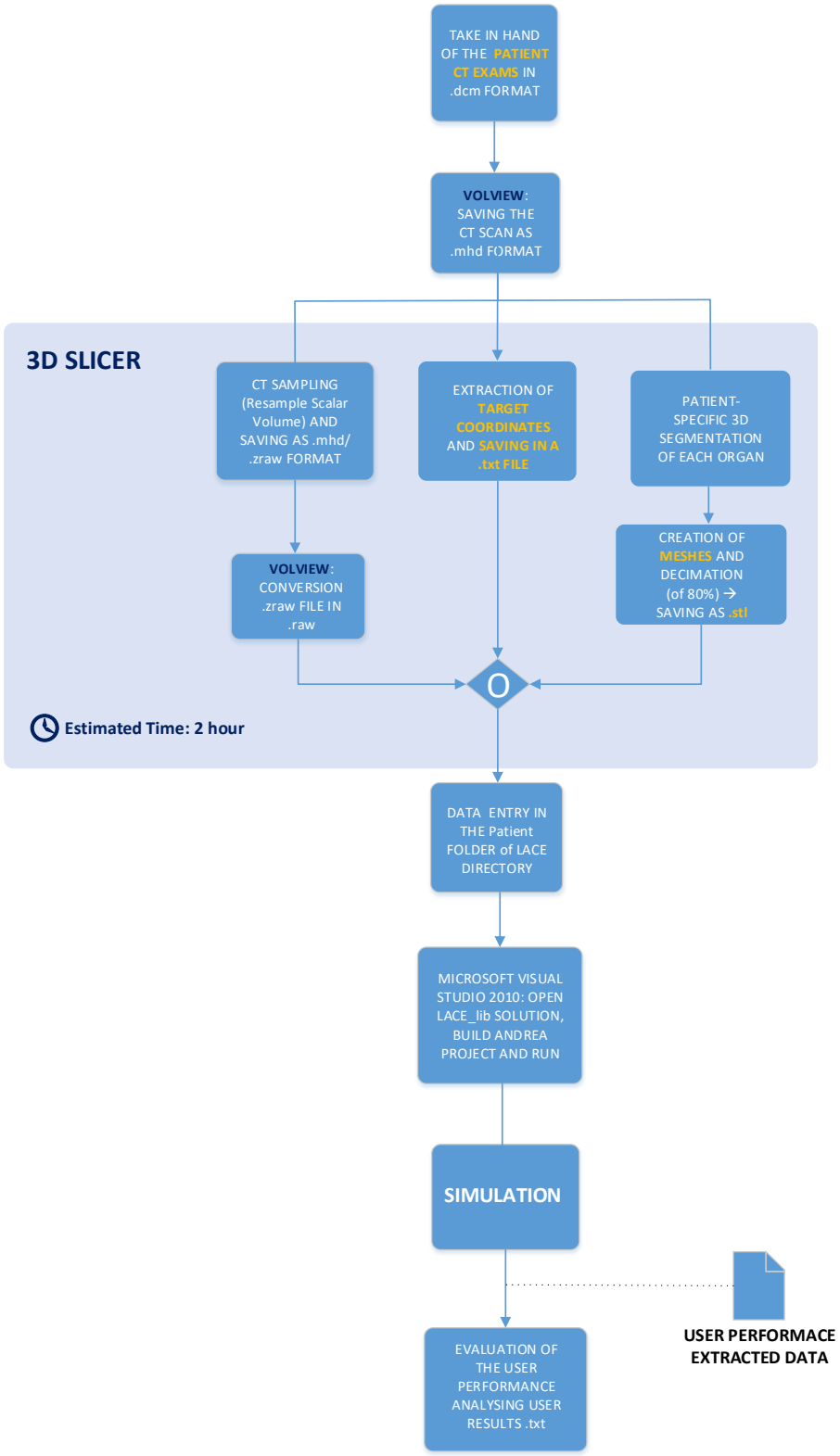


FIGURE 37 Second part of the developed workflow: post-processing, 3D reconstruction and simulation process

The last part of the workflow (Figure 38) is the description of those activities that are related to the real percutaneous renal puncture surgery (yellow) and to the immediate post-operative period (orange). In particular, we have highlighted three basic steps: the preparation of the patient (positioning and local anaesthesia, the sterilization of the operative field and, finally, the preparation for performing the radiological guidance during the procedure.

When the procedure can be considered completed, immediately operative time and loss of blood are annotated because they, with clinical outcome parameters of the patient, indices will be analysed later.

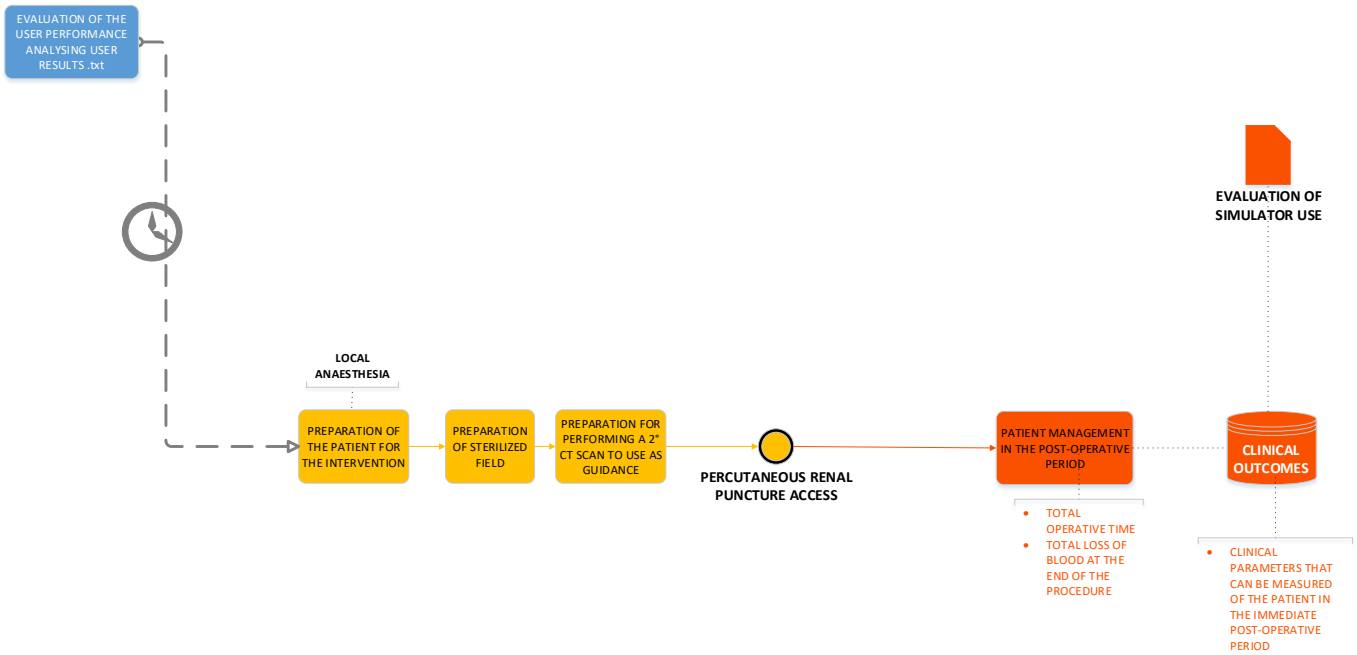


FIGURE 38 Third part of the developed workflow: surgery and post-operative period

There are different actors that act inside the workflow that we have studied:

- surgeons (interventional radiologists or even urologists interventional radiologists);
- urologists;
- radiologists;
- resuscitative anaesthesiologists;
- nurses.

The surgeons are the users most interested in the described process because are the professional figures that perform the percutaneous renal puncture while urologists may be present in the operating room to support the surgeon or take measurements inherent kidneys. Radiologists are those who are in charge of fluoroscopy during the operation while the tasks of are of resuscitative anaesthesiologists and nurses are of obvious nature.

We also believe that the professional figure of a biomedical engineer, already present in the structure and to which the task of supporting the surgeon during the phase of the simulator (2nd part) would also be assigned, may not only facilitate and speed up the procedure of post-processing, but also represents an example of direct cooperation between engineer and doctor.

3.2.6 Experimental Protocol Development

To perform an experimentation of the workflow it has been necessary to develop an experimental protocol to be presented to surgeons.

This experimental protocol was developed with the collaboration of Prof. Vertemati, Department of Biomedical and Clinical Sciences "L.Sacco", University of Milan, ASST Sacco Fatebenefratelli, Milano.

We have decided to propose this experimental protocol to Dr. Vanzulli, Director of Radiology, Department of Advanced Diagnostic Therapeutic Technologies at ASST Grande Ospedale Metropolitano Niguarda, Milano, and to Dr. Rampoldi, Director of Interventionist Radiology, Department of Advanced Diagnostic Therapeutic Technologies at ASST Grande Ospedale Metropolitano Niguarda, Milano, essentially for two reasons:

- I was followed by them during my clinical experience at Niguarda Hospital;
- and there was the necessity that patient was in prone position during the surgical intervention which, in Milan, in this position is done only at Niguarda Hospital.

In development of experimental protocol, we have analysed principally three aspects: the patient typology, the CT exam setting before intervention, and we have done some observations correlated to the surgery preparation of the patient.

Relatively to the patient typology, we could subdivided the analysis in five points:

- age of the patient;
- sex of the patient;
- physical characteristics;
- pathology;
- number of subjects.

Starting from the first point, the ideal age range, without distinction of sex, is 30-65 years because, in case of older patients, there could be more complications due to the age. The patient has not to be obese for problems related to standardization of the protocol.
We aim to consider patients that must be submitted to percutaneous renal puncture due to a renal biopsy.
We had also to study deeply the CT exam setting because an important part of our study is related to the possibility of reconstruct a patient-specific 3D model on which simulate the surgical procedure. In particular, we have focused attention to these considerations:

- type of exam;
- method;
- setting parameters of the image;
- position of the patient;
- CT Phases;
- breath.

We believe that patient must be submitted to an UroCT examination in prone position because in this way organs in the 3D reconstruction have a the same attitude of the of organs during surgical intervention.

In addition, we consider it appropriate to perform UroCT with a Split Bolus method for radioprotection needs. This is because, through the injection of contrast medium in two different moments and knowing the timing of diffusion in the body, it is possible to obtain the Arterial Phase and the Late one performing the exam with half of the radiations dose.

We are interesting, in fact, to all CT phases (Basal, Arterial, Venous and Late Phases), phases that will have to be well highlighted, especially the Arterial one, to allow a better 3D reconstruction of circulatory pathways on 3D Slicer. Furthermore, to guarantee this better

3D reconstruction will be useful to have CT image characterized by slices of a 1 mm of distance between each other's.

Therefore, we believe that Arterial Phase, for his importance, must be obtained during expiration phase, to minimize the impact of the breath on organs displacement.

These considerations are important because perform a simulation on a 3D model reconstructed by a such CT permit to simulate a realistic surgical intervention on LACE because patient positioning and breath pattern are, for the most, the same of surgical intervention since the patient is under local anaesthesia.

Then, it will be necessary to make a comparison between the interventions carried out with the prior support of the simulation experience and interventions carried out without being able to evaluate the actual usefulness and benefits.

We therefore intend to measure in surgical room some clinical outcomes of the surgical room in both processes and then to compare them, thus having the opportunity to evaluate in a scientific and not empirical way some performance-related indices.

The indices that we thought to consider, during the development of the experimental protocol, are mainly:

- operating time;
- loss of blood;
- some measurable parameters on the patient in the immediate post-operative period.

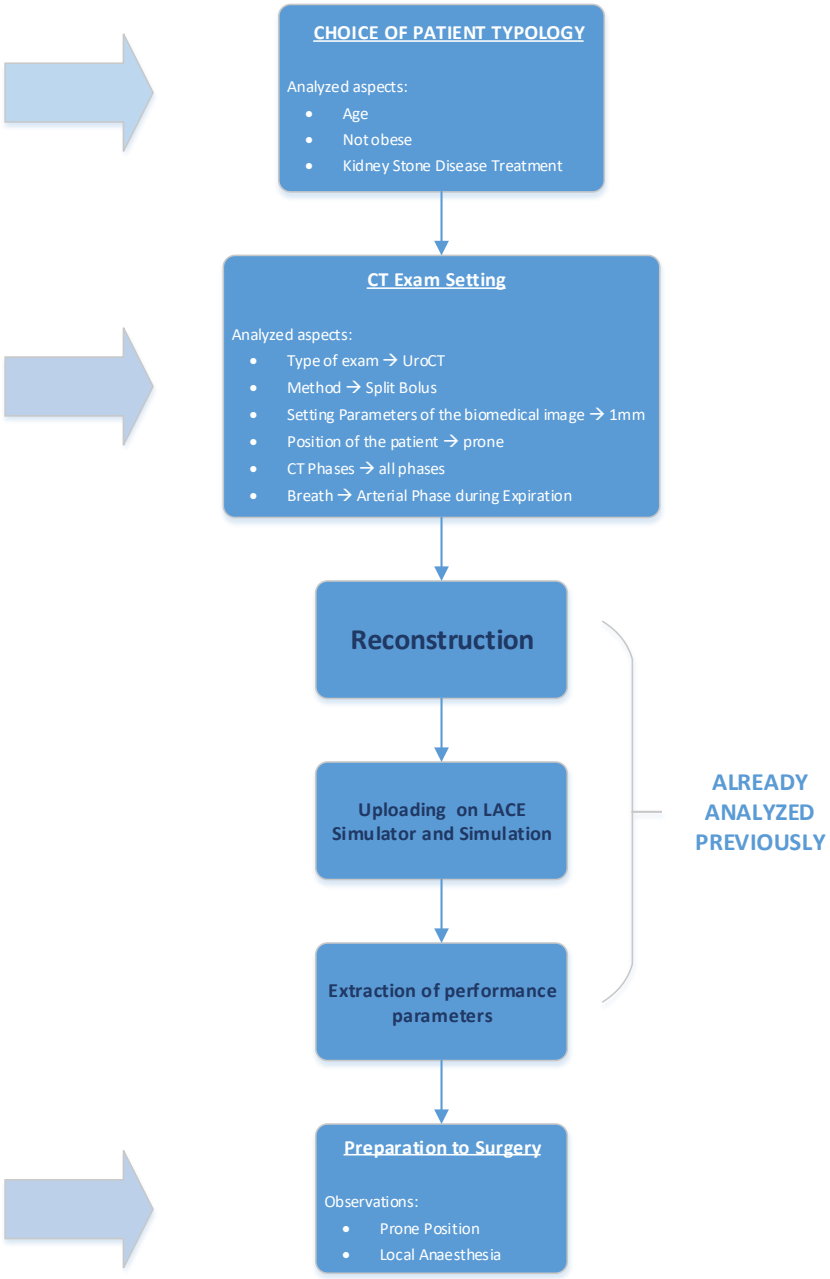
We expect the use of the simulator to improve these indices for a number of reasons:

- knowledge of the patient's anatomy, which must be operated before surgery, can facilitate the surgeon during the perforation phase. In fact, a perforation carried out in an easier way involves a decrease in the number of attempts necessary to make them and therefore a decrease in the time necessary to perform the procedure.
- what is reported also implies a total time of the intervention lower or in any case a saving of time regarding the PCA that could prove valuable in the case of complications. The time in fact the patient is subjected during the operation is strictly correlated also to the time of recovery that will be necessary after the intervention and this also because of a greater time spent under anaesthesia.

- last but not least, we believe that a reduction in parameters such as time in the room, less blood loss and less patient recovery time (with better parameters in the immediate post-operative) can also benefit in economic terms of the operative block.

This last aspect, however, we did not consider it possible to evaluate it since it would require more data than expected for the experimental protocol developed by us. Nevertheless, we felt it necessary to mention it since it would be a quite relevant benefit in operating block management. We report the workflow for experimental protocol.

WORKFLOW 5 Experimental protocol



Chapter 4

Experimental Validation Protocol

In the previous chapter has been described deeply the development of different workflows. Going in details of the experimental protocol, if what we have reported can be considered the ideal experimental protocol developed by us by trials and errors, it was then necessary, once presented to the surgeons, to re-evaluate it according to available resources.

As emerged from the first meeting with Dr. Rampoldi, it was necessary to make some changes to the protocol. In particular, while at first we thought it was essential to have the patient during the UroCT in the prone position, Dr. Rampoldi showed how most of the patients come from centres outside the Niguarda, and then they arrive with the CT already done normally in a supine position. The necessity of having patients with an UroCT in prone position was because, as outlined above, also PCA is performed in the same position.

Those implies that the 3D reconstruction made on an UroCT in prone position can guarantee a major fidelity of representation of the real abdominal configuration of the patient during the surgical intervention.

Nevertheless, we have also specified that the simulator serves as a tool to support the surgeon's activity and not for the planning, so that the error in the arrangement of the different organs, passing from one position of the patient to the other, can be considered negligible since then the operation is performed under radiological guidance.

We also decided to consider not only patients who underwent renal biopsy, but also those who underwent to percutaneous puncture for thermal ablation: this to try, at the beginning, to increase the casuistry.

At the end of this meeting, we made arrangements with Dr. Rampoldi to be contacted when a patient, who should undergo to this intervention, was presented to Niguarda Hospital.

However, at a later time, it was communicated to us that no intervention of this type was planned during the period of our interest for validation.

What we did then was to redefine the validation process of this work by analysing the different possibilities presented to us and taking advantage of the opportunity to work with the interventional radiologists of Niguarda.

From what emerged, we decided to articulate the validation of the work in two main strands:

- the verification of the possibility of using the simulator as a patient-specific simulator;
- the verification of the integration in the clinical field, going to evaluate the utility of the simulator and the workflow developed through an interview with 5 interventional radiologists.

The first verification was done by taking in hand from the Niguarda Hospital the CT images of four patients who had been previously subjected to this type of surgery: obviously, the patient's sensitive data were obscured.
We considered four subjects, which we will call anonymously Subject 1, Subject 2, Subject 3 and Subject 4, and of these, we report some data (Table 5) to show the consistency with the type of patient we researched according to what is reported in the experimental protocol developed:

TABLE 5 Subject for experimental protocol

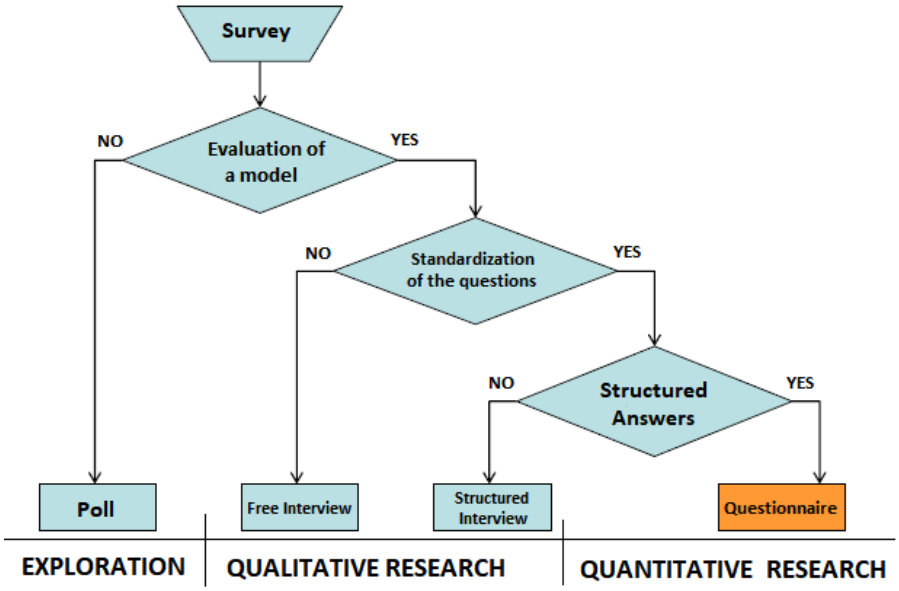
	Subject 1	***Subject 2***	***Subject 3***	***Subject 4***
Sex	Male	Male	Female	Male
Age	62	64	63	57
Pathology	Tumour of the left kidney: Upper Calix	Suspected Right Renal Neoplasm: Lower Calix	Hypodense alteration of the Right Kidney to the Middle third	Tumour of the Right Kidney
Intervention	Thermo-ablation	Renal Biopsy	Renal Biopsy	Thermo-ablation
File Dimension (# slices along longitudinal axis)	916	156	138	145

Of these, by applying the workflow of the simulation process developed by us, we carried out the 3D reconstruction and verified the possibility of loading inside the simulator.

In fact it was necessary to verify that the implementation choices made to realize the workflow of the simulation process (tools used in 3D Slicer and settings of parameters chosen) could be valid for different types of CT images characterized by different dimensions (in terms of number of slices), different machines that produced them and therefore possible different reference systems.

For the second verification instead, we have decided to subject the interventional radiologists of Niguarda Hospital to a sample survey and, according to the indications of the underlying workflow (Workflow 6), we decided to create a questionnaire.

WORKFLOW 6 Choice of the sample survey method



Going in details of it, we have produced a 13-points questionnaire based on a Likert Scale. The Likert scale provides for a list of statements, semantically linked to the attitudes on which we want to investigate, is submitted to a group of individuals together 4-7 possible alternative answers. We have decided to fix the number of answers to five different possibilities:

- 1: in no way;
- 2: not much;
- 3: enough;
- 4: very;
- 5: very much.

We asked questions related to everything that has been studied in this work, paying particular attention to asking their opinion on the different workflows developed.

Our questionnaire is reported below.

FIGURE 39. Questionnaire submitted to the Niguarda Staff

What is your current position?	Trainees in Intervention Radiology				Interventionist Radiologist
	1 In no way	2 Not much	3 Enough	4 Much	5 Very Much
1. *How familiar are you with percutaneous renal surgery?*					
2. *How familiar are you with virtual reality simulations with tactile feedback?*					
3. *Can a 3D model be useful to interact with?*					
4. *How useful do you think the simulator could be in learning percutaneous access techniques to the kidney?*					
5. *In particular, can it be useful in the preparatory moment when the access point must be decided?*					
6. *Do you think it can be useful for the training of trainees?*					
7. *Is it an advantage that the simulator is a specific patient?*					
8. *Do you think it gives an easier comprehension of patient-specific anatomy?*					
9. *Do you think the simulation process workflow is easy to understand?*					
10. *Compared to the previous work do you think it is optimized?*					
11. *Can it be useful for other types of intervention?*					
12. *Is the integration process workflow clear?*					
13. *Is the integration process workflow feasible?*					
14. *Tips*					

Chapter 5

Results and Discussion

The discussion of the results of the validation of this feasibility study can be subdivided in two different aspects:

- evaluation of LACE as a patient-specific simulator based on the optimized simulation process developed;
- evaluation of the work (in particular the study of the different workflows) in terms of ease of use for the user and utility.

5.1 LACE as a Patient-Specific Simulator

At first use of the virtual reality environment with a different model from that of the previous work, in fact, it was evident that it was necessary to study adequately the whole simulation process to make sure that any files tried to load in the code were not rejected by the code itself but displayed correctly.
To do this we have devised in detail the whole simulation process described above, paying particular attention to each phase of this. Making a test with a sample CT, it was evident that the main problem was the size of the CT file and the size of the meshes created due to the implementation choices of the simulator itself in terms of maximum size of loaded CT files and of number of triangles of the meshes of the organs.

After standardizing the workflow of the simulation process and having completed the study, we have validated this by going to load several CTs and associated meshes in order to verify that all the study done was not in any way 'sewn on' to the CT sample and meshes dimension that we had taken for its development. The entire test was tried by two students.

As highlighted in the previous chapter, we have taken the CT of four subjects with different problems, of which among these we see that Subject 1 has particularly high dimensions compared to the others due to a greater portion of the body taken into consideration during the CT exam (almost total body).

By applying the simulation process workflow to all four subjects, we created the sampled CTs and the meshes.

Proceeding to the loading, we managed to show how the implementation choices made are suitable for CT images of different sizes and produced by different machines with different reference systems. In fact, the file upload is done correctly even if there are differences in file size of the four patients, as it is possible to view in the figure below which represents the simulation environment of the Subject 1, the largest CT file (Figure 40).

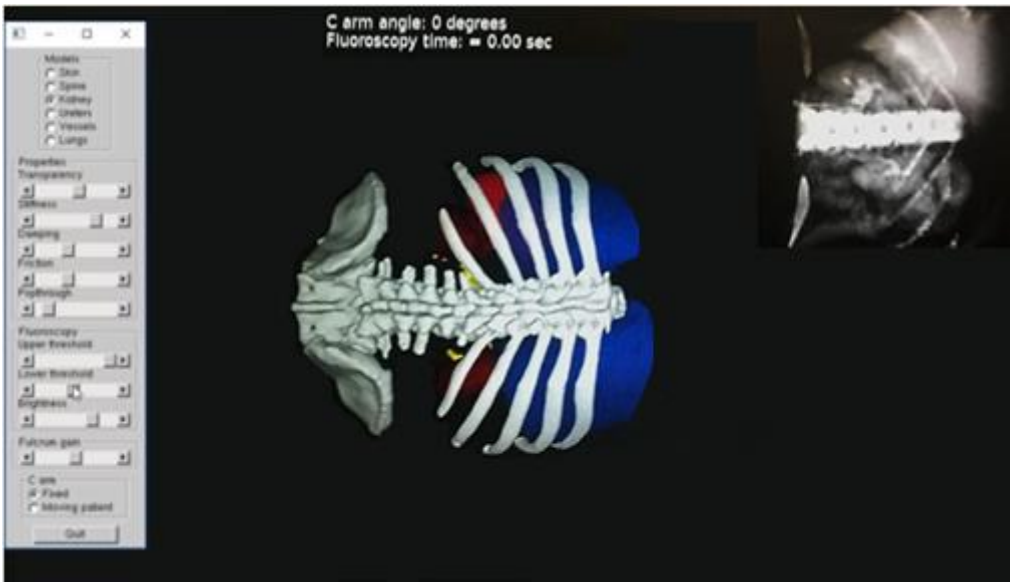


FIGURE 40 Simulation of Subject 1

In particular, all the files (meshes and fluoroscopic image) are displayed in the correct position within the viewing environment with good quality 3D models and above all with a coherence between the fluoroscopic image orientation and the meshes. This coherence is identifiable going to use the device haptic within the environment and, making 'proof' bites, verifying that the anatomical structures perforated in the 3D model coincide with those indicated in the fluoroscopic image.

This is guaranteed by using a single software for the realization of all the phases of the simulation process (3D Slicer). By this way, the reference system is the same both for the meshes and for the CT.

Above all, the fact that the files of the Subject 1 (much larger) have been correctly visualized, guarantees that any other file of smaller dimensions produced following the indications of the workflow can be used.

5.2 Evaluation of the Work in terms of Ease of Use and Utility

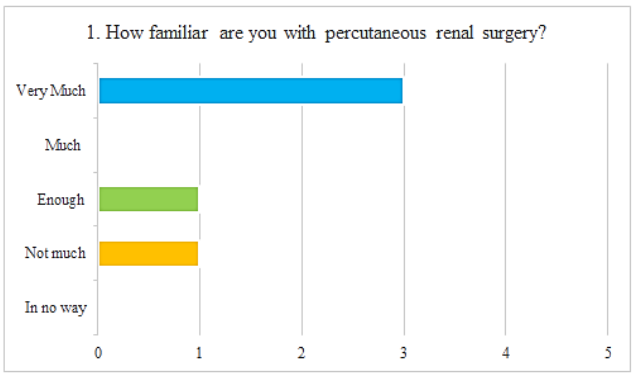
This evaluation was performed on the base of the questionnaire developed by us, described previously. The questionnaire takes into account different aspects, in particular wants to highlight the analysis of three main instances:

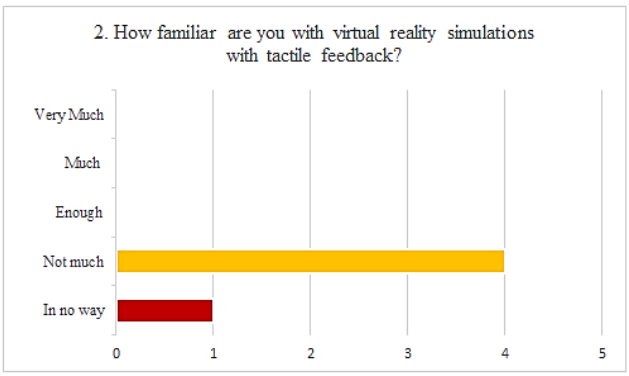
- evaluation of the simulation workflow;
- utility of the simulator for percutaneous renal puncture within the Tertiary Department of Interventional Radiology of Niguarda Hospital;
- evaluation of the workflow for integration in clinical practice.

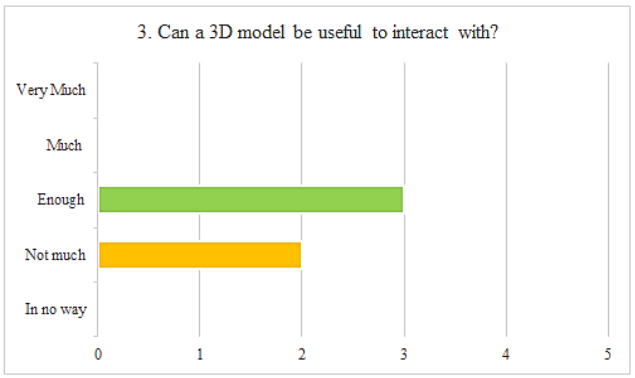
After a long and in-depth explanation of the work, we submitted the questionnaire to five interventional radiologists, three experts and two who have just finished their specialization and we have analyse their answers.

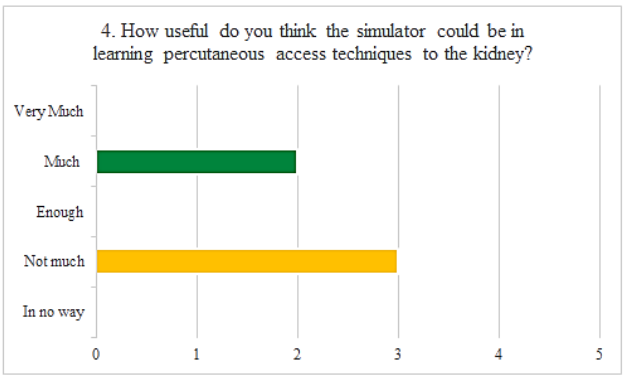
Obviously, the difference between an experienced interventional radiologists and a beginner one is that the former have more experience in the field, so it is easier for them to make a puncture (which therefore implies a certain access blindly to the patient's internal organs) without the risk of damaging any anatomical structures.

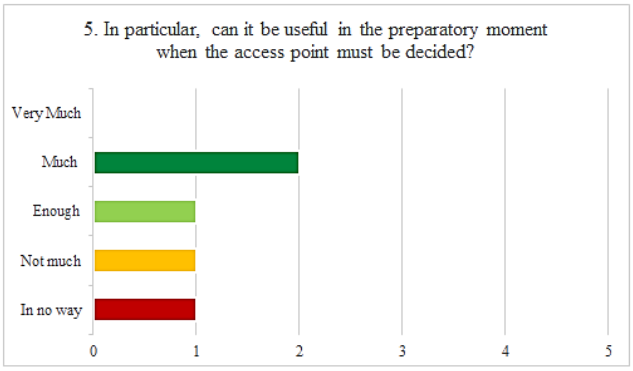
Once the answers have been received, we have made an analysis based on the frequency that each answer has obtained with respect to the specific question and, at the end of it, we have evaluated overall the percentage of positive responses to the questionnaire. Results of this analysis are shown in the bar charts below (Figure 41).

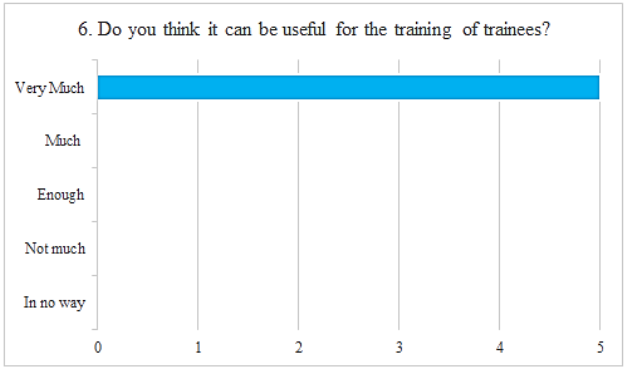


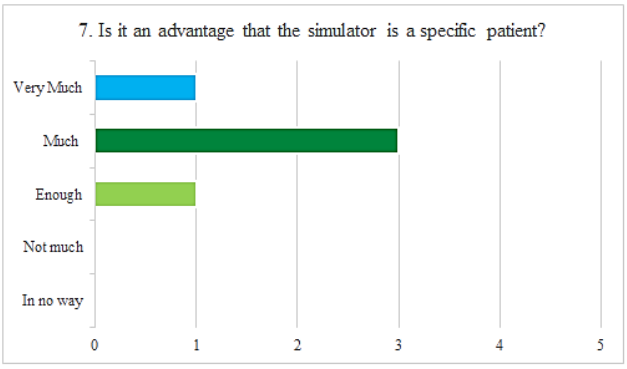


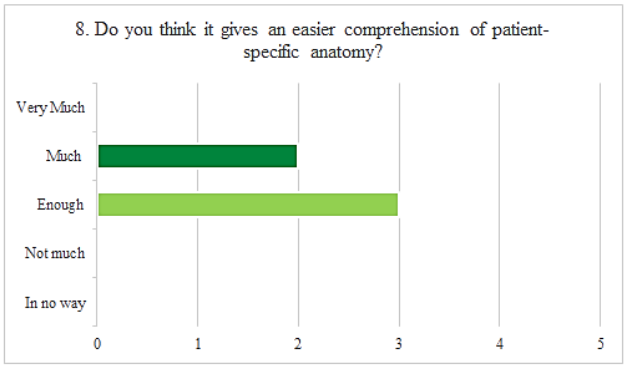

3. Can a 3D model be useful to interact with?
Very Much
Much
Enough
Not much
In no way
0
1
2
3
4
5

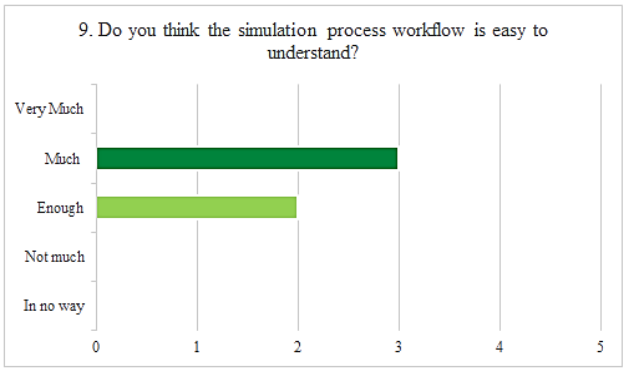

4. How useful do you think the simulator could be in learning percutaneous access techniques to the kidney?
Very Much
Much
Enough
Not much
In no way
0
1
2
3
4
5


5. In particular, can it be useful in the preparatory moment when the access point must be decided?
Very Much
Much
Enough
Not much
In no way
0
1
2
3
4
5


6. Do you think it can be useful for the training of trainees?
Very Much
Much
Enough
Not much
In no way
0
1
2
3
4
5


7. Is it an advantage that the simulator is a specific patient?
Very Much
Much
Enough
Not much
In no way
0
1
2
3
4
5


8. Do you think it gives an easier comprehension of patient-specific anatomy?
Very Much
Much
Enough
Not much
In no way
0
1
2
3
4
5


9. Do you think the simulation process workflow is easy to understand?
Very Much
Much
Enough
Not much
In no way
0
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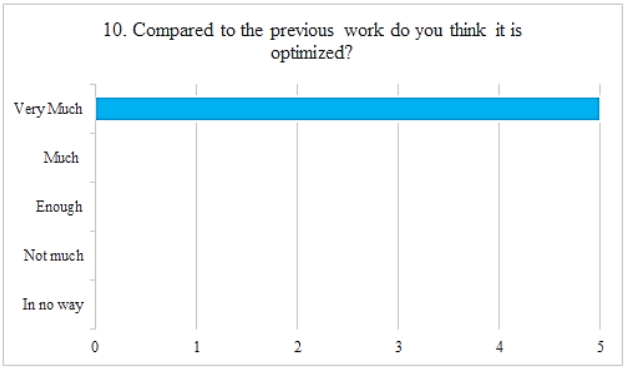
10. Compared to the previous work do you think it is optimized?
Very Much
Much
Enough
Not much
In no way
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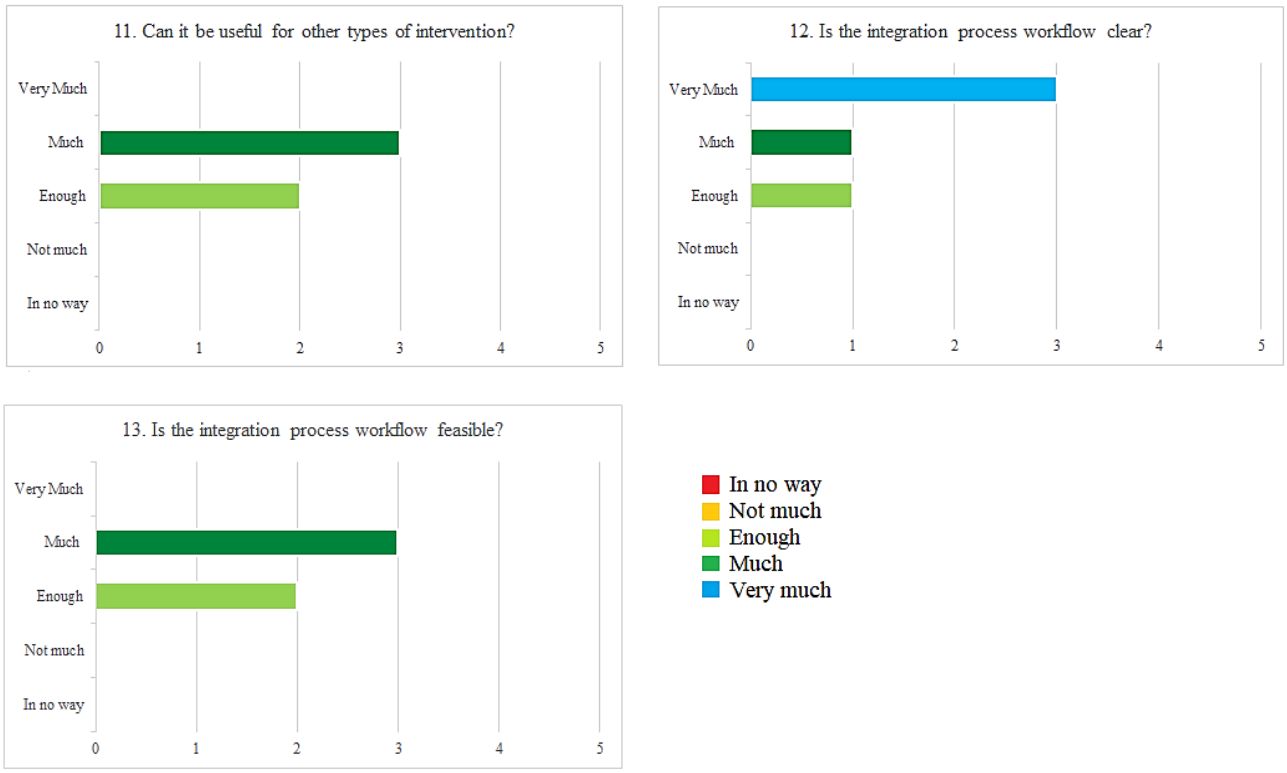


FIGURE 41 Bar charts of the frequencies of the answers for each question

The questionnaire was created in order to have an overall opinion on all the work.
The first three questions (1-3) are used for 'probing the ground' and understanding what the skills of the person answering the questionnaire are.
The next five questions (4-8) provide an evaluation of the simulator and its usefulness in this particular type of procedure.
Finally, questions 9 and 10 concern the workflow of the simulation process, while the last three (11-13) are related to the integration of the technology.

From the bar charts, it is evident how on average the answers are positive (‘very much’, ‘much’) or possibly neutral ('enough'): we have calculated in fact that the positive answers are around the 80% of the total ones.

When considering the evaluation and usefulness of the simulator, data show a fairly neutral trend. This is because, as has been indicated in several comments, for this particular type of procedure an experienced intervention radiologist (for the training he possesses) does not need any particular supports besides considering the CT before the intervention. However, as can be seen from the chart on question 5 (*In particular, can it be useful in the preparatory*

moment when the access point must be decided?), 80% of respondents answered that it could be very useful in the pre-operation stage of access planning. This data is important because professionals who have just completed the period of specialization provided 80% of the answers.

This means, as confirmed by those more experienced (100% of the answers at the question 6), that for this type of procedure, the possibility of a simulator of this type would be very important for the training of trainees (reducing operating time and increasing the goodness of the sample taken), as it would ensure a safe and non-generic tool on the which to practice.

In fact, there has been highlighted by the answers to the question 7 (*Is it an advantage that the simulator is a specific patient?*) how important it is that the simulator is patient-specific.

In fact, the 90% of the answers is positive while the remaining 10% (gives by the most experienced professional) is neutral. This means that generally, it is still a highly appreciated work.

This has also been highlighted by the answers that have been regarding the developed workflows: in fact, it emerges from the bar chart regarding question 9 that 80% said that the simulation process is easy to understand, while 20% answered 'enough'.

However, we believe that the lack of understanding must be referred to the low level of knowledge of the software, in particular of 3D Slicer (with which most of the work is done), but we see there is a general interest mainly deduced from the number of comments and suggestions that have been provided to us of which we will talk about later.

However, it was highlighted how the workflow was totally optimized and standardized compared to the previous work on LACE thanks to 100% of affirmative answer to question 10.

This same judgment was also given to what is the workflow developed for the integration of technology into clinical practice. In particular, professionals have confirmed to us how the described process is achievable in terms of timing.

As far as clinical outcomes on the other hand have suggested, in addition to taking into account the operating time, to take also the goodness of the sample taken during biopsy.

In conclusion, with regard to the comments and suggestions given to us, a good deal has already been highlighted as we have analysed the data on the various questions, but we have not yet shown how most of the interventional radiologists have spurred us on and advised to

look at other types of intervention. In particular, we have been suggested to look at some procedures related to liver lesions using ultrasound guidance, since these are not visible on the CT (as opposed to the kidney) without the use of a contrast medium, which during the intervention is not used. In fact, having previously viewed the CT with contrast, reconstructed the affected anatomical district and having simulated the procedure before the intervention with the before identification of the target, could help a lot the interventional radiologists.
This is certainly an advice we will take into account for future developments of this project, together with the possible application of the device in the thoracic-abdominal field.

Being a feasibility study, the sample of the subjects taken into consideration is not high both in terms of the number of patients and in terms of the number of professionals, and it can certainly be increased.
However, we are still satisfied with the results since we have seen that there is a wide interest both by surgeons to propose possible developments, both in the scientific community (thanks to the various professionals with whom I have interfaced) for regarding the integration of a technology within clinical practice.

Chapter 6

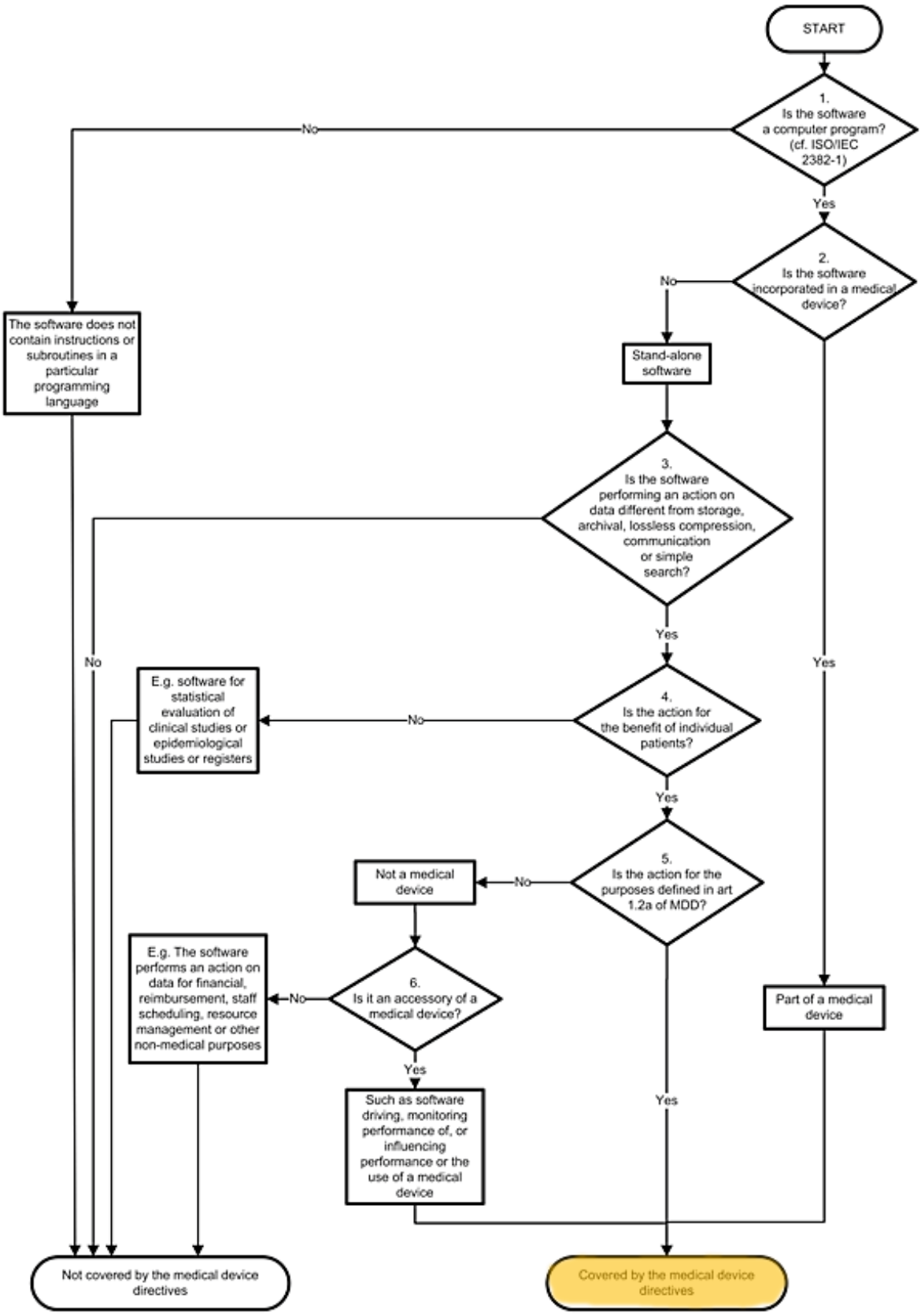
Evaluation of LACE as Medical Device

As completion of the work, we thought it was necessary for the clinical integration of LACE to understand if this technology could be classified as a medical device.
To perform this analysis, we have decided to refer to two basic documents for the Italian regulations concerning medical devices: the Italian standard CEI 62/237 ‘Guida alla gestione del software e delle reti IT-medicali nel contesto sanitario’ (CEI, 2015) and ‘Le indagini cliniche dei dispositivi medici’ (Direzione generale dei dispositivi medici e del servizio, 2015). What we did then was to classify the software we used according to current regulations. For completeness, the definition of a medical device according to the regulations is reported:

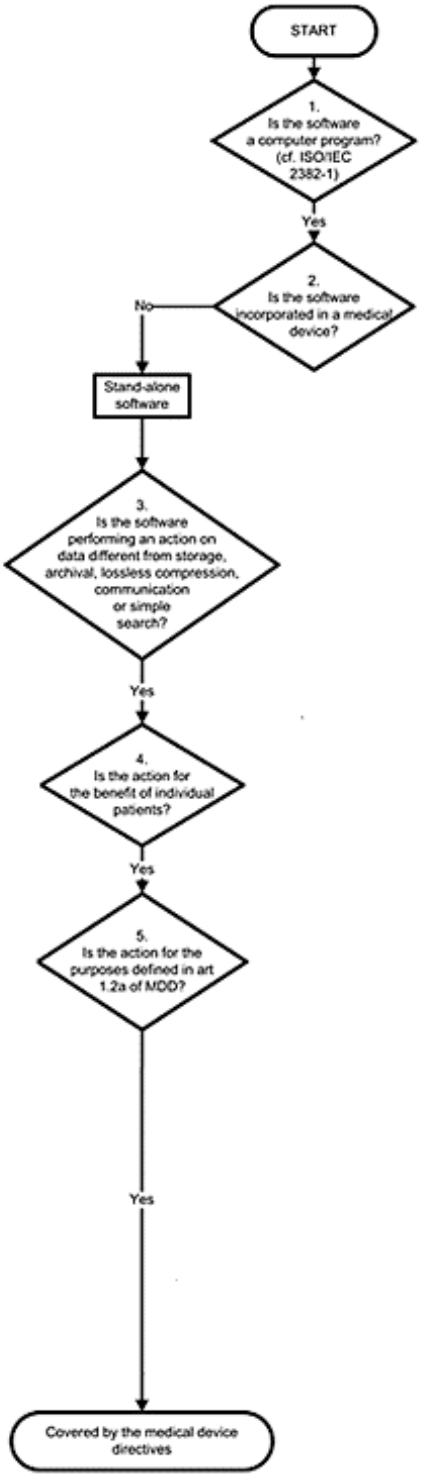
*"A medical device, according to the definition of Directive 93/42/EEC (MDD) is any instrument, apparatus, plant, substance or other product, used alone or in combination (**including computer software used for correct operation**) and intended by the manufacturer to be used in humans for the purpose of diagnosis, prevention, control, therapy or attenuation of a disease; diagnosis, control, therapy, attenuation or compensation of a wound or handicap; of study, replacement or modification of the anatomy or of a physiological process; of intervention on conception, which product does not exercise the main action, in or on the human body, for which it is intended, with pharmacological or immunological means through metabolic process but whose function can be assisted by such means".*

First of all, it is fundamental to consider the difference between a software integrated into a medical device, an accessory software and a 'standalone' (independent) software.
An integrated software, being 'on board' of the device, must follow the regulatory requirements of the host device and must be classified in its own class if it is necessary for its operation or affects its use. In the second case (accessory software), being an adjunct of a medical device in turn a medical device, it must follow the regulatory provisions of the MDD and have to be classified. In fact, by Directive 93/42/EEC, an accessory is a product, which, although not a device, is specifically necessary to be used with a device to allow the use envisaged by the manufacturer itself.
Standalone software is instead considered an active medical device according to definition 1.4 of Annex IX of the aforementioned Directive.

WORKFLOW 7 MEDDEV 2.1/6 workflow to classify standalone software



In the case of standalone software, the manufacturer can classify and qualify it using the MEDDEV 2.1/6 "Qualification and Classification of standalone software" guideline so we proceeded with the classification according to this legislation. Following the scheme reported in the previous page (Workflow 7), we have conducted this analysis:



1. *"A computer program is defined as a syntactic unit that conforms to the rules of a particular Programming language and that is composed of declarations and statements or instructions needed to solve a certain function, task or problem"* (ISO/IEC 2382-1). Is the software (LACE) a computer program? Yes.

2. Is the software incorporated in a medical device? No, because of the physical configuration of LACE (§3.1.1) → Standalone Software

3. Is the software performing an action on data different from storage, archival, lossless compression, communication or simple search? Yes, because it is a simulator.

4. Is the action for the benefit of individual patients? Yes, it is patient specific.

5. *" […] intended by the manufacturer to be used in humans for the purpose of diagnosis, prevention, control, therapy or attenuation of a disease; diagnosis, control, therapy, attenuation or compensation of a wound or handicap; of study, replacement or modification of the anatomy or of a physiological process; of intervention on conception, which product does not exercise the main action, in or on the human body, for which it is intended, with pharmacological or immunological means through metabolic process but whose function can be assisted by such means".*
Is the action for the purposes defined in art 1.2a of MDD? Yes

LACE can be covered by the Medical Device Directives

When established that it is a medical device, it is necessary to assign a risk class according to the current regulations.

Medical devices are grouped according to their complexity and potential risk for the patient in four classes.

The classification depends on the intended use indicated by the manufacturer and must be assigned by consulting the classification rules in Annex IX.

The classification is basically taking into account the invasiveness of the device, its dependence on a source of energy (active device) and the duration of contact time with the body. The classes are:

- I: generic non-electrically powered (non-active) equipment that does not penetrate the body or surgically non-invasive equipment for transient use (less than 60 minutes) and electrically powered (active) equipment with low risk for diagnostic or patient support.
- IIa: active therapeutic and diagnostic devices generally not risky and surgically invasive low risk equipment for transient use or short-term use (up to 30 days).
- IIb: active therapeutic and diagnostic devices that are generally potentially hazardous (for example X-ray sources), equipment with higher surgical-invasive risk for transient or short-term use and surgically invasive long-term or implantable (non-active) devices (no more than 30 days).
- III: all equipment that can be in contact with the central circulatory system of the heart or the central nervous system and all long-term or implantable invasive devices that have a biological effect on the body or are absorbed in it.

Consistently with what has been reported, we believe that LACE can be classified as a class I medical device, since it is not a tool for operative planning, but rather a tool to support the surgeon's activity, as it helps him, through an interactive experience, in the analysis of patient reports.

In addition to this analysis, it is possible to evaluate the potential use of the software in a health context.

FIGURE 42 Classification of the software basing on the health context (CEI 62/237)

As shown in the scheme (Figure 42), extracted by the text of the CEI 62/237, a software (A) can be used in a health context (B) and assumed (D) or not (C) health purposes.

It is therefore possible to subdivide the C and D group into different subgroups, but since LACE is part of the D group, we are going deeper into this category.
D group can be subdivided into four different groups:

- D1 group: are part of this group the software declared by the manufacturer as medical devices, regardless of the risk class to which they belong according to the Classification established according to the sector Directives.
- D2 group: are part of this group that software, for which the manufacturer has indicated a context of health destination, has indicated health purposes, but that the manufacturer does not declare.

- D3 group: in this group are included those software for which the manufacturer has indicated a health destination, which does not have indicated healthcare purposes and for which it can be reasonably assumed, based on actual use and context of use, that they can assume sanitized purposes or ability to have an impact on health
- D4 group: part of this group includes software for which the manufacturer has not indicated a specific intended use related to health and/or health destination, for which we can reasonably assume, based on actual use and context of use that the software can assume sanitary purposes or ability to have impact on health.

Obviously, for what we have previously said, LACE is part of the D1 group in this category.

In conclusion, we have established that the simulator of our work, LACE, can be classified as a medical device for percutaneous renal puncture simulation. As medical device without the CE mark, it cannot be used as a planning tool in routine surgical procedures, but it can anyway represent a good instrument for surgeon activity support.

In case there was the desire to use the simulator for planning, surely a process must be activated to obtain the CE marking.
However, we believe that before to undertake this type of use, it should be perfected and studied on a larger sample.

To do this, since it is a medical technology in development, the most appropriate thing to do for us could be to set up a clinical ‘non-profit’ investigation of this device building it on the indications shown in the document ‘Le indagini cliniche dei dispositivi medici’ (Direzione generale dei dispositivi medici e del servizio, 2015). In fact, in this way, a much more structured clinical study can be conducted through the notification to the Ministry of Health.

Chapter 7

Conclusions and Future Developments

This work represents a study of feasibility for the integration of a VR patient-specific simulator in the clinical practice of a Tertiary Department of Interventional Urology.

Starting from an accurate study of the background and state of the art, also thanks to a clinical experience 'on the field', we have decided to take in hands LACE as simulator with which work.
We have studied deeply the simulator itself by providing a standardization to allow the professionals to perform a patient-specific and user-friendly simulation.
We have optimized the simulation process allowing its realization using only one software (3D Slicer) to make the 3D reconstruction, the CT sampling and the extraction of the target coordinates. The workflow has been described in a very accurate way to enable interventional radiologists and urologists to perform it without the help of an external figure. We believe that, in any case, the figure of a biomedical engineer can help train users, especially as regards software, guaranteeing a faster learning curve.
A workflow was then developed that allows the integration of the simulator within the traditional clinical practice taking into account time as the main factor within a hospital department.

The validation of this work was done verifying two main aspects:

- the patient-specific use of LACE;
- the ease use and utility of the workflows developed.

What emerged from our analysis, regarding the first point, is the possibility of use LACE as a patient-specific simulator thanks to the standardization and optimization of the simulation process performed by us (in particular for our implementation choices).
As regards instead of the second point, we have interviewed the professionals that routinely have to perform this type of intervention thanks to a collaboration with the Interventional Radiology Department of the ASST Grande Ospedale Metropolitano Niguarda, Milano.

From the data that we have obtained, it has been evident that there is a good interest on their part and on the scientific world in a work of this kind.

In particular, inherent the actual use of the simulator, we have been given a good feedback, especially as regards the training of specializing students. It has also been pointed out that the fact that the simulator is patient-specific can potentially help even the most experienced surgeons in the planning of other types of intervention such as those of liver lesions.

As far as the management of workflows is concerned, the potentials of those developed by us are clear, since the optimization of the processes is objective, especially for simulation processes, with reference to the work previously done with LACE.

A very big advantage of this work is the standardization of processes.
In fact, thanks to this work we can deduce that:

- the simulation workflow can be used for many other surgical applications that can be developed on LACE VRE;
- the integration workflow can be used for the integration of other simulation technologies inside the clinical practice.

In particular, this second aspect is not only due to the developed workflow, but also to the analysis that was then made of the simulator as a medical device, since in this way all aspects of the introduction of an instrument like this have been considered (not being a pre-operative planning device).
Despite the economic aspect of the device has not been considered we believe that it does not represent a limitation of the work since the cost is quite small, attributable only to the purchase of the haptic controller.

7.1 Future Developments

According to these reflections, there are still two main aspects that can be further explored: the one inherent to the simulator and that of the clinical trial.

As regards to LACE simulator there are some improvements that can be made to make the simulator more complete, such as the implementation of an ultrasound guide, widely used in the field of interventional radiology, in order to make the simulation similar to all effects to the real procedure. In addition, the implementation of the possibility of simulation with the use of glasses for virtual reality (like the Oculus) could provide added value, ensuring the possibility of a totally immersive environment.

To further optimize the process and remove the required file conversion step you should be able to load directly the CT in DICOM format, even if this presupposes the need for a very powerful computer, since to not burden the speed of the simulation experience, was already chosen to perform a sampling of the CT.

As far as the development of the workflow is concerned, the natural continuation of this work would be to apply the developed experimental protocol to all effects, something that we could not do for a patient availability problem.
In particular, we believe that it would be useful to modify the protocol using the advices provided us by professionals, carrying out the clinical trial on patients with hepatic injuries, and considering the operative time and the goodness of the sample taken as clinical outcomes.

Finally, given the need to expand the patient sample, it may be useful to proceed with a much more structured clinical study conducted through the notification to the Ministry of Health.

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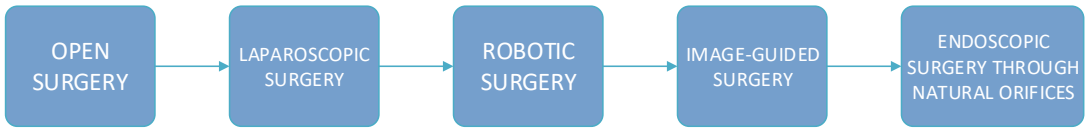
Appendix 1

Activity in the operating room for the evaluation of the background

As highlighted in the abstract, to understand completely the background I was asked to attend some surgical interventions of various specialties around some hospitals in Milan.
The purpose of this activity was to understand how the surgery is evolving and, interfacing with the surgeons, to understand where the use of a simulator could be adequate. What I did was therefore 'interviewing them' to find out what their needs were.

In this appendix we describe this activity as a completeness of the work I have done since we believe it can be an added value and to better explain how we arrived at the choices that were made for the thesis work.
The evolution of the surgery can be summarized by the scheme below:



Following this trend, my activity "in the field" has touched all these phases and now it is our intention to describe them briefly highlighting the usefulness for the work that each experience has brought and reporting in the following table a list of the type of intervention to which I have assisted.

1. OPEN SURGERY	• Abdominal Wall Surgery
2. LAPAROSCOPIC SURGERY	• Laparoscopic Colecistectomy • Partial Nephrectomy with and without Ureterectomy • Total Nephrectomy • Pyeloplasty: Stenosis of the Ureteral Joint

3. ROBOTIC SURGERY	• Robotic Radical Prostatectomy according to Bocciardi • Prostatectomy with removal of Pelvic Lymphnodes
4. IMAGE-GUIDED SURGERY	• Temporal Lobectomy with Craniotomy • Trans-arterial Chemioembolization • Transjugular Intrahepatic Portosystem Shunt on a Cirrhotic patient • Electrode Implant for Stereoelectro-Encephalography (SEEG) • Embolization bleeding Pancreatic Prosthesis (emergency intervention) • Percutaneous Renal Puncture for Renal Biopsy
5. NATURAL ORIFICIES SURGERY	• Endoscopic Resection of Bladder Polyps • Embolization of the Prostate

Referring to the table above, it is possible to realize that I was also able to attend interventions of disciplines very far from the urological field, such as those of neurosurgery. The reason for this was the fact that in particular disciplines, the use of a particular surgical technique is much more evident.

1. Open Surgery

Seeing an open surgical intervention was **fundamental to understand the main problems that led to the use of increasingly minimally invasive and precise surgical techniques**. Although it is clear that not all procedures can be carried out in a minimally invasive manner and therefore that the open technique retains its validity and importance, it is however to be underlined that this type of technique certainly causes a major surgical trauma in the patient. It was fundamental to see how access to the organs of the abdominal cavity is made.

2. Laparoscopic Surgery

Viewing the laparoscopic technique **was fundamental to understand the difficulty of a very complex technique and to interrogate the surgeons about how they learned it when they were "beginners".** The difficulty and the complexity of the technique are given by the fact that the instruments with which the surgeons operate are very long and the movement to be done to use them is unnatural with respect to the scalpels, even if they have the advantage of providing the surgeon with a return of strength. In fact, there is the problem of the fulcrum (too much resistance, if it yields there is the risk of burning surrounding tissue, no abrupt movements), that gives little freedom of movement. There are many problems which trainees have to face, because they have to do everything 'in the dark', because of surgical field is not visible as in the case of open surgery, but is determined by the manoeuvre area available within the patient based on where the trocars (are medical devices that allow the insertion of the laparoscopic instruments inside the abdomen) are positioned.

Compared to the traditional method, the laparoscopic procedure has a limited invasiveness (due to the fact that the only incisions that are made are those for the trocars), reduction of post-operative pain, short stay, rapid return to normal life, minor complications and sequelae (infections, post-laparotomy hernia, adhesions), better aesthetic outcomes.

It was fundamental to see how some urological pathologies are treated.

3. Robotic Surgery

The advantage of robotic surgery compared to laparoscopic is the fact that the instrument has a greater number of degrees of freedom, so it can also reproduce the movement of the wrist. This is much easier to use than laparoscopic instruments, as the **hand-piece performs perfectly the movement of the hand**. It should be noted that the magnitude of the amplitude of the hand-piece movement and that of the instrument inside the patient is 6 to 1.

With the robot, however, you lose the tactile sensation that you have with the laparoscope instrument, because the surgeon does not physically hold the instrument with which he operates: an expert surgeon is able however to cope with this lack using the possibility to see the depth through the **stereoscopic vision** of the robot.

Also in this case, it has been useful to learn some pathologies that can affect the urinary system.

4. Image-guided Surgery

As said previously, surgery is increasingly focusing on the most precise and targeted interventions possible: it was therefore essential to see some images-guided interventions. Two were the disciplines on which I focused: neurosurgery interventions and interventional radiology procedures.

The first ones were important because I had the opportunity to see interventions based on a preoperative study of 3D models reconstructed through the use of 3D Slicer, going to the Center for the 'Munari' epilepsy of Niguarda where Dr.Cardinale works.
This experience was important to **understand the potential of 3D Slicer**, in particular as regards the possibility of reconstruction of separate anatomical areas.
The second ones were important instead to learn many notions related the interventional radiology. Interventional radiology is a branch of medical radiology that includes all invasive or minimally invasive diagnostic and therapeutic procedures performed by guiding and controlling radiological methods, such as fluoroscopy, computed tomography, magnetic resonance, and ultrasound. The goal of interventional radiology is to obtain results equal to or better than the corresponding surgical interventions.
Interventional radiology today is a discipline characterized by an ever-increasing clinical focus on patients; the radiologist interventionist is a specialist physician able to guarantee not only **minimally invasive procedures** but to follow the patient in the pre-operative period and in the post-operative follow-up through dedicated clinics.
In this case, most operations are performed through the use of catheters. These are very fine and precise manoeuvres, which are used for different purposes, from simple biopsy to the removal of certain tumours via chemotherapy.
Given the difficulty of performing these manoeuvres, it is **not easy for the trainees to learn** them.

5. Natural Orifices Surgery

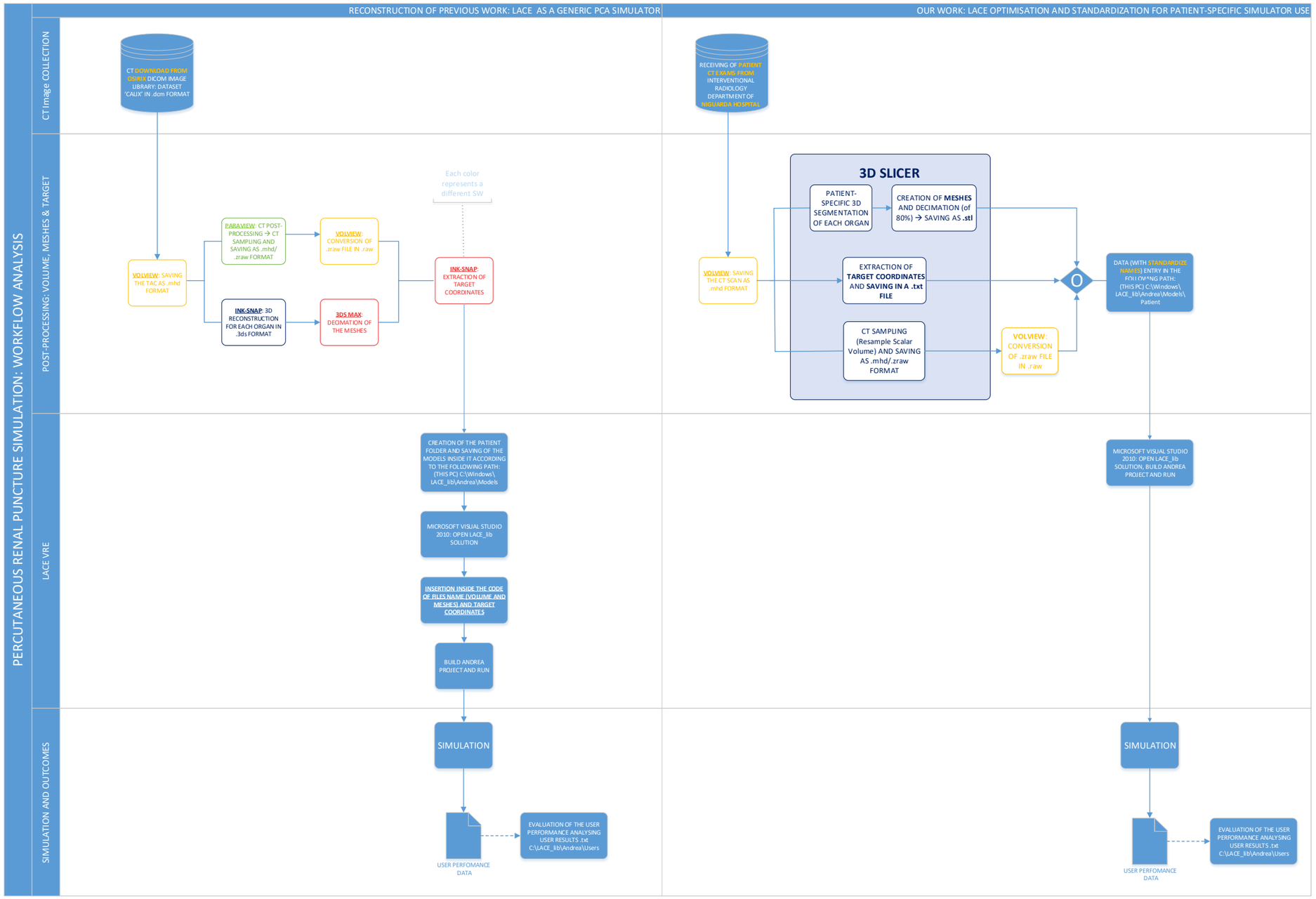
Surgery based on natural orifices is a surgical technique based on the possibility of using anatomical openings as access to the site on which the surgeon must work. It was also important to see this type of technique as it will surely be the **future of many surgical**

procedures, since it provides the advantage of generating a **very limited surgical trauma** (when compared with the open technique).
However, it will be increasingly difficult for those who want to do this work to learn these techniques.

It is evident from all considerations, how there is the necessity to support the surgeons work and found ways to teach to trainees, increasingly complex procedures. In this sense, the idea of a patient-specific virtual reality simulator is developed to provide the surgeon with a safe, interactive and potentially total immersive tool.

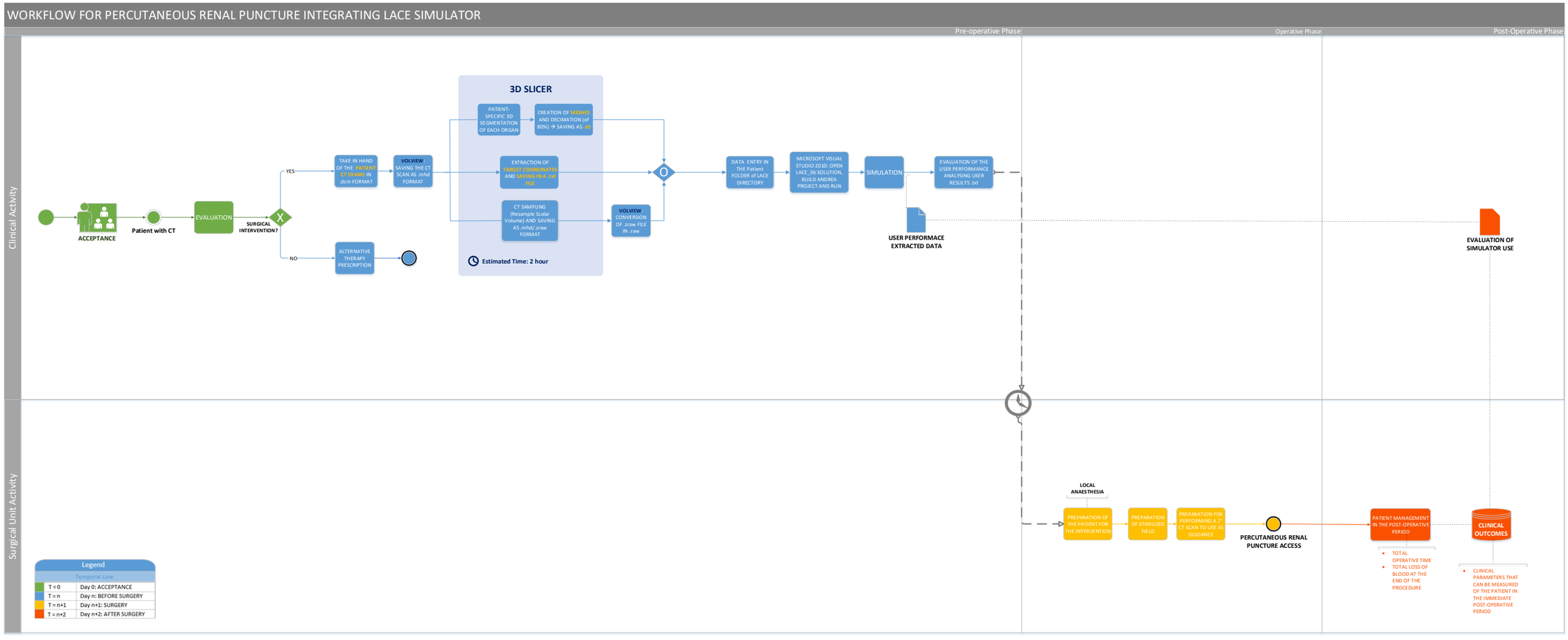
Appendix 2

Simulation Process comparison between Previous Work and Our Work



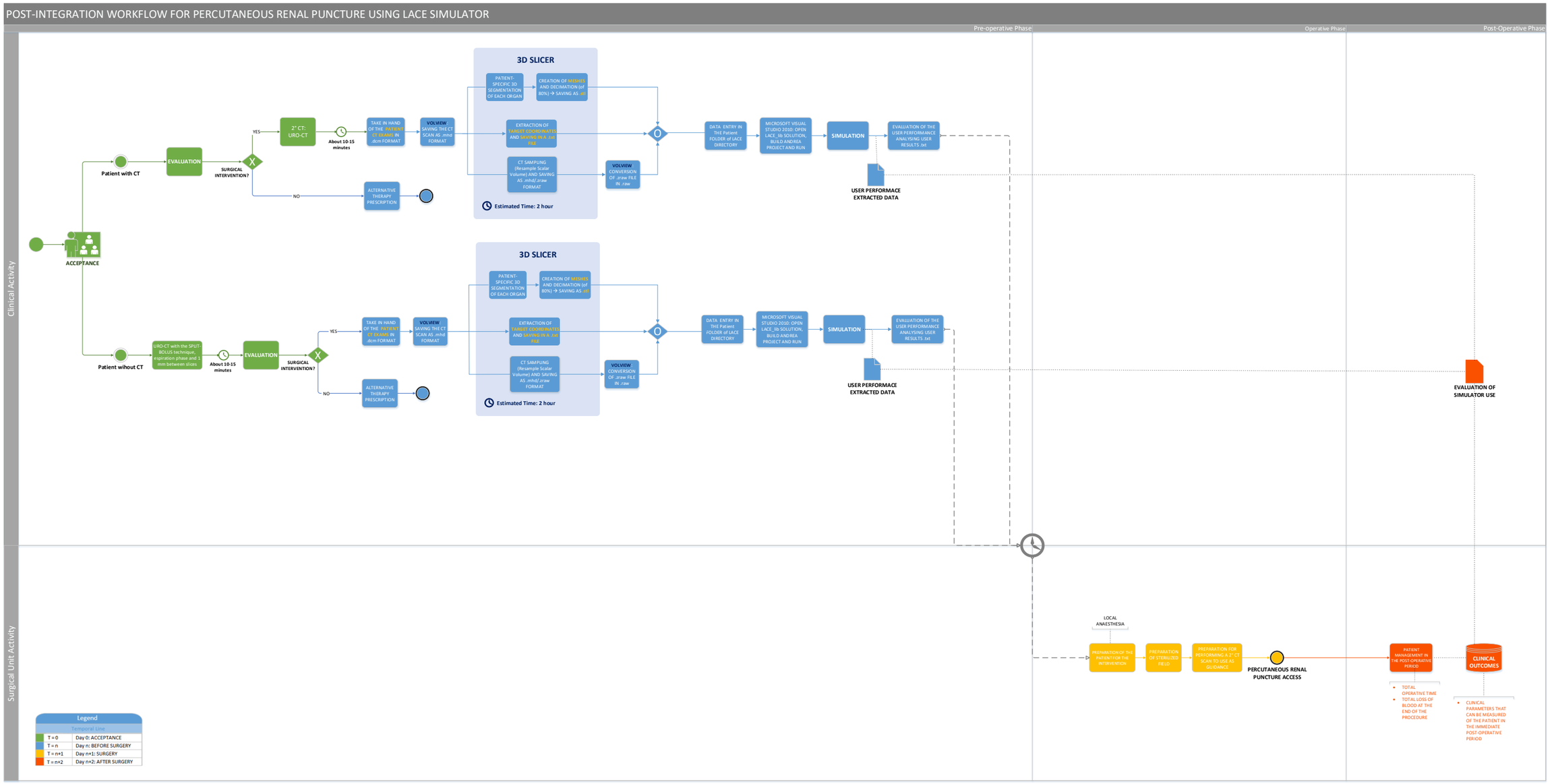
Appendix 3

Workflow for Integration of LACE Simulator in Percutaneous Renal Puncture Practice



Appendix 4

Post-integration Workflow for using of LACE Simulator in Routine Clinical Practice



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