

IMPACT

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State-of-art in medical robotics and navigation for liver and lung interventions



Project number:	ITEA 17021
Document version no.:	v 1.0
Edited by:	Pieter Wiskerke (DEMCON), Dominique Clevers (DEMCON)
Date:	September 27, 2019

ITEA Roadmap domains:

Major: Group

ITEA Roadmap categories:

Major: Content & knowledge

Minor: Interaction



History

Document version #	Date	Remarks
V0.1	2019-01-01	Starting version, template
V0.2	2019-03-28	Definition of ToC
V0.3	2019-05-20	Draft version, contributions by partners
V0.4	2019-06-21	Updated draft
V0.5	2019-09-06	Final draft to sign of by PMT members
V1.0	2019-09-27	Final Version (Approved by PMT)

Deliverable review procedure:

- **2 weeks before due date:** deliverable owner sends deliverable –approved by WP leader– to Project Manager
- **Upfront** PM assigns a co-reviewer from the PMT group to cross check the deliverable
- **1 week before due date:** co-reviewer provides input to deliverable owner
- **Due date:** deliverable owner sends the final version of the deliverable to PM and co-reviewer



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1. Glossary

AR	Augmented Reality
CT	Computed Tomography
EMG	Electromyography
MIS	Minimally Invasive Surgery
MRI	Magnetic Resonance Imaging
PET	Positron Emission Tomography
WP	Work Package
IUS	Intraoperative Ultrasound
NIR	Near Infrared
HCC	Hepatocellular Carcinoma
DRF	Dynamic Reference Frame
LAAO	Left Atrium Appendage Occlusion
US	Ultrasound
VR	Virtual Reality

2. Introduction

2.1 Aim of Activity

The goal of this document is to provide an overview of the current state of the art in medical robotics for minimally invasive liver and lung interventions from a technical (navigation technology, augmented reality, needle intervention systems, steerable catheters and guidewires), medical (clinical procedures using robotics and navigation technology), and business perspective. The objective of this work package (WP4) is to pave the way to an industrialized treatment of liver and lung tumors, which will improve the patient outcome by reducing preventable medical error and improving predictability and efficiency of clinical procedures. The state-of-the-art descriptions lie at the basis of this report and determine the further development of the techniques within this work package.

The next chapter focusses on the usage of medical robotics and navigation technologies in clinical practice in the lung and liver. Every subsequent chapter describes a technology in a standardized way. First, an introduction to the topic is given describing the background and context. Secondly, the state of the art of the technology is given followed by the business aspects. Lastly, a discussion is given with a conclusion based on the state of the art in terms of opportunities for improvement within this work package of the IMPACT project

2.2 Contributors

Several authors contributed to the production of this document. Each of those authors was responsible for either technical (DEMCON, Philips, UT), clinical (LUMC), or business (DEMCON, Philips) contribution. An overview is shown in Table 1.

Table 1 Contribution of every author to this report

#	Section	Authors
1	Clinical procedures using medical robotics and navigation technology	LUMC
2	Navigation technology	UT, Philips, DEMCON
3	Augmented reality	UT, Philips
4	Needle intervention systems under image guidance for usage in thorax and abdomen	UT, Philips, DEMCON
5	Steerable catheter and guidewire technology	DEMCON
	Global editor	DEMCON



4. Clinical Procedures Using Medical Robotics and Navigation Technology

4.1 Clinical Procedures in Lung Oncology

4.1.1 Introduction

Despite advances in diagnostic modalities, supportive care and novel treatment options, the prognosis of lung cancer patients remains poor. When diagnosed with non-small cell lung cancer, the 5-year survival rate for patients with all stages of the disease combined is 23%. Even when the tumor is staged as local disease, without lymph node or distant metastases, despite curative intended treatment, 5-year survival rate is only 60%. To improve the prognosis of lung cancer patients, all facets of diagnosis and treatment are currently being studied. Recent literature demonstrates the benefit of lung cancer screening in high-risk patient groups. This leads to earlier diagnosis of the disease, at a lower stage, increasing the possibility of curative intended treatment. Surgical treatment of smaller tumors can be challenging, as exact tumor localization can be difficult. Especially in the light of minimally invasive, lung parenchyma sparing resections, there is a clinical need for intra-operative tumor identification tools. Tumor-targeted imaging using near-infrared fluorescence has the potential to identify tumors in real-time during surgery.

Various treatment modalities are available for lung cancer treatment. In the past, curative treatment consisted of major surgery, and treatment in a palliative setting included chemotherapy and/or radiotherapy. In recent decades, stereotactic ablative radiotherapy (SABR) has been added as a curative intended treatment option. However, long-term results in comparison to surgery are still unclear. Furthermore, in recent years targeted therapies have entered the field. These include therapies targeting a driver mutation, such as anaplastic lymphoma kinase (ALK) inhibitors and endothelial growth factor receptor (EGFR) inhibitors, and immunotherapy, including immune checkpoint inhibitors targeting the programmable death receptor 1 (PD-1) and its ligand (PDL-1). Although these therapies were initially studied in palliative patients with metastasized disease, the extraordinary outcomes have resulted in new clinical trials studying these therapies in patient with lower stages of lung cancer. However, despite all these options, surgery remains the cornerstone of curative treatment in lung cancer.

4.1.2 Clinical State of the Art in Robotics for Lung Oncology

Ongoing clinical trials provide positive data on lung cancer screening. Lung cancer screening programs are being implemented across U.S.A. and expected in Europe. Due to increased screening and quality of diagnostic tools, more patients are diagnosed with a small, early stage lung tumor. Current literature suggests that a parenchyma sparing, sublobar resection (i.e. anatomic segmentectomy), has similar oncologic outcomes in comparison to conventional lobectomy. Intraoperative identification of these smaller lesions and the anatomical relation to hilar structures such as segmental pulmonary arteries and segmental bronchi can be challenging. In recent years, intraoperative imaging using near-infrared fluorescence has been used in clinical studies for tumor localization in other cancer types, such as ovarian cancer and colorectal cancer.

Preoperative planning of a resection using the currently available imaging modalities (contrast enhanced CT scan and PET/CT) and 3D anatomical models based on available imaging data can be challenging. Intraoperative access to these models in combination with intraoperative, tumor-targeted near-infrared fluorescence imaging, may support the treating physicians in performing the least invasive, most optimal treatment for each patient. Alternatively, tumors can be marked by



radiopaque fiducials under guidance of Cone Beam CT imaging and surgically removed in the same session in a hybrid X-ray – surgery room.

Apart from surgical resection tumors can be biopsied and removed by ablation via a needle or catheter. Tumors close to the big airways (bronchi) can be approached via a catheter. Using 2D and 3D image guidance (US, X-ray fluoroscopy and Cone Beam CT, CT), overlay of pre-interventional images and/or electromagnetic navigation of the catheter (Pritchett, 2017) the physician can target the tumor to take biopsies or destroy it by heat or freezing it. Recently the FDA has approved a robotic system to navigate a steerable catheter through the bronchi to a lung tumor. Tumors in the periphery of the lung can be approached from the outside by needle puncturing through the skin.

4.1.3 Potential Clinical Applications in Lung Oncology

Several techniques of robot-assisted thoracic surgery (RATS) for lobectomy and segmentectomy have been described. Park in 2006 introduced a technique that reproduces the patient and port positions of the anterior video-assisted thoracoscopic surgery (VATS) approach with a utility incision of 3–4 cm in the IV intercostal space on the mid axillary line, and uses two more trocars for the camera port and for the second instrument; as a result no CO₂ insufflation is necessary, and the surgical steps reproduce those of VATS lobectomy, with anterior-to-posterior hilum isolation. This approach was modified by Veronesi et al. during the first comparison between open, muscle-sparing thoracotomy and RATS lobectomy (four-arm technique with a 3 cm access port) [1], [2]. This technique introduced the use of a fourth arm, positioned posteriorly, and was mainly utilized to place the lung parenchyma in the correct fixed position and obtain good exposure of the surgical field. A similar four-arm technique was described by Cerfolio [3]. They positioned the four arms along the same intercostal space (usually the 7th), between the mid-axillary and paravertebral lines, at the minimum distance of 9 cm, with no utility incision. CO₂ insufflation was standardized and resections were removed within a plastic bag via enlargement of the trocar incision in the VIII i.c.space. A posterior-to-anterior approach to the hilum was described, with vein resection as the final step of the lobectomy. The results were good in terms of duration of surgery and speed of postoperative discharge. A study by Dylewski et al. on 200 robotic resections has been reported using a three-arm approach in which pulmonary resection was performed only through ports with CO₂-induced pneumothorax (complete portal robotic lobectomy, CPRL) [4]. At the end of the procedure, the resections were extracted via a subcostal, trans diaphragmatic approach, and the diaphragm subsequently repaired. With this technique, re-admission rate was around 10%, usually for effusion requiring drainage or post-operative pneumothorax. Other technical variants have been described. Gharagozloo reported on 100 consecutive cases operated on with a hybrid, two-phase procedure: robotic isolation of hilar elements and mediastinal lymph-node dissection, followed by stapling of the hilar structures using a manual VATS approach [5]. The authors suggested that a robot-assisted approach was best for fine dissection of lymph nodes and vascular structures, whereas the established VATS procedure was superior for the lobectomy phase. Other papers describe the use of a three-arm technique, with the camera placed in the 6th or 7th intercostal space along the posterior axillary line, and the other one positioned through a utility incision made at the 5th intercostal space along the sub mammary line. The main advantages of using the utility port from the beginning instead of at the end of the procedure are: i) the possibility of palpating the lung and removing a specimen in the case of a diagnostic wedge resection of small nodules before lobectomy is confirmed; ii) the use of only four ports instead of five. iii) the possibility of enlarging the same utility incision in case of conversion, avoiding an additional thoracotomy; iv) comfortable access with a sponge in the case of emergency bleeding; and v) no need for CO₂ insufflation. The benefit of complete portal robotic procedures is avoidance of the cold 22°C ambient air of the



operating room interfering with the 37°C temperature within the chest preventing potential tissue desiccation and further inflammation.

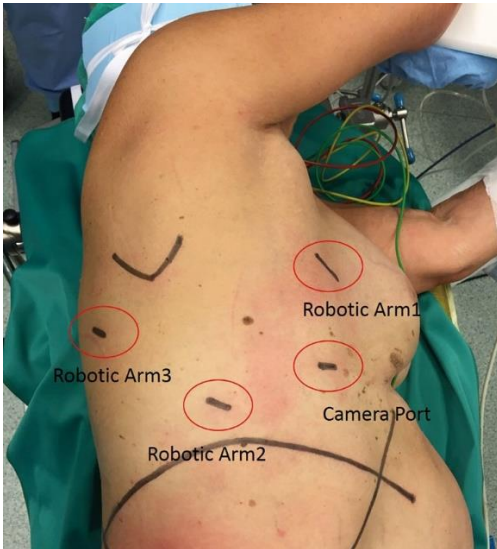


Figure 1 Patient positioning and port placement



Figure 2 Right middle lobe carcinoid

4.1.4 Discussion

The use of the robot is constantly growing throughout the world. With the spread of robotic systems amongst health facilities, the number of procedures performed with this technology is growing exponentially. Robotic technology has made enormous strides to date, but in the near future improvements beyond the actual use of robot-assisted are expected. Thoracoscopic surgery is undergoing a rapid increase in the development and use of uniportal techniques. Robot-assisted surgeons cannot avoid facing the rise of this type of procedure. Through one 4–6cm-long incision, very skilled VAT surgeons can perform a number of procedures in the chest, such as major lung resections with vascular reconstruction and lymph node dissection. This approach is becoming more and more attractive to patients as it is less invasive than traditional 3-port video-assisted surgery. As a result, robotic technologies have started to be developed towards uniportal interventions too, namely the Single-Site da Vinci platform.

Robot-assisted technology has indisputable technical advantages over traditional video-assisted surgery. The robotic approach combines benefits of minimally invasive surgery with precision of movements, comfort and three-dimensional views of the surgical visual field. The learning curve for robot-assisted thoracic surgery necessitates work on 20 cases, but improvements continue up to the completion of 90 cases. According to recent studies, for early stage non-small-cell lung carcinoma, perioperative outcome appears superior after robotic-assisted surgery when compared to open and VATS approaches, and lymph node upstaging and intraoperative safety seem to improve with RATS. Different studies show higher costs of RATS vs. VATS. The diffusion of robotics in the operating room seems destined to spread further on account of the widening of implications to include locally advanced disease, the improvements being made to the instrumentation and underlying technology, and reductions to the implementation costs.



4.2 Clinical Procedures in Liver Oncology

4.2.1 Introduction

Liver tumors are caused by primary or secondary liver cancer. The most common form of primary liver cancer in adults is hepatocellular carcinoma (HCC). HCC can be caused by a viral infection with Hepatitis B or C or by cirrhosis, a disease that causes chronic liver damage due to non-alcoholic fatty liver disease and abuse [6], [7]. Patients with HCCs often do not show symptoms other than caused by the underlying liver disease, and thus these tumors are detected in a late stage, which gives poor survival rates for patients diagnosed with HCCs (5-year survival of 12%, and median survival ranging from 6 – 20 months). Early detection and adequate treatment options thus are required. Secondary liver cancer implies liver tumors are metastatic, most commonly from primary colorectal cancer, but also from lung or breast cancer.

The introduction of minimally invasive surgery (laparoscopic and robotic) have shown many advantages for the quality of the surgical care, such as shorter hospital stay, less perioperative mortality and technically more complicated resections could be performed, for instance in the field of hepatobiliary surgery [8], [9]. However, the lack of tactile feedback made surgery less convenient. Visualization of the surgical field with a camera, sometimes in combination with near infrared (NIR) fluorescence imaging, and the presence of haptic feedback in case of robotic surgery showed potential to improve surgical outcomes [8], [10]. However, anatomical three-dimensional (3D) orientation is still difficult during minimally invasive surgery, caused by limited depth perception, especially for liver surgery, which is one of the most complex abdominal surgeries. Due to the complex anatomy of the liver, the high risk for bleeding, and the difficulty to approach sensitive structures and some liver segments, implementation of laparoscopic surgery normally takes long time. Today, laparoscopic liver surgery is world-wide performed, however intraoperative navigation for determination of resection planes, which is based on the vasculature (portal branches and hepatic veins), is still difficult, sometimes resulting in larger resections than necessary.

Currently, surgical navigation in liver surgery is mainly based on preoperative computed tomography (CT)/magnetic resonance imaging (MRI) and intraoperative ultrasound (IUS). Intraoperative laparoscopic ultrasound is useful in providing real-time information about the tumor location, although it has been shown that IUS lacked sensitivity when patients are treated with chemotherapy or abnormal liver parenchyma [11]. Another intraoperative imaging technique is NIR fluorescence, which showed promising results for liver tumor detection [12]. However both IUS and NIR fluorescence imaging lack the capacity of real-time intraoperative 3D orientation of the liver and especially the liver vasculature, which determines the resection planes.

Recently two systems (CAS-One and Explorer) were developed and approved by the Food and Drug Administration for image guided liver surgery [13], [14]. These systems were capable to create accurate 3D models derived from preoperative CT/MRI, and to predict both accurate resection planes and remnant liver volumes. Nicolau et al. used augmented reality to visualize the portal branches and the liver tumor [15]. However, the transition to real-time intraoperative navigation is difficult, because of liver deformation or manipulation during surgery. For instance, electromagnetic (EM) tracking is dependent on interference with metallic objects and the accuracy varies over the working volume of the sensors [11].

Robotics was applied to surgery in the 1970s as a military project endorsed by the National Aeronautics and Space Administration (NASA) and funded by the Defense Advanced Research Project Administration (DARPA), with the aim of replacing the surgeon's physical presence and



providing care to astronauts in spacecrafts or to soldiers in battlefields. In the event of natural catastrophes, remote-controlled robots could work in protected surgical pods [16].

4.2.2 Clinical State of the Art in Robotics for Liver Oncology

Currently the da Vinci® Surgical Robotic System is the state-of-the-art technology. It has been upgraded over recent years to include additional features, such as near-infrared technology. The latest generation, the da Vinci Xi™ system, released in 2014, is less bulky and its arms are arranged more ergonomically. However, it still has major technical drawbacks, such as lack of force/tactile feedback [16]. An increasing number of potential competitors are at different stages of development. Some have developed competitive platforms for general surgery based on a similar global architecture as Intuitive. Others are working on miniaturized platforms.

All-in-one robotic platforms that seemed to be potential competitors of da Vinci® were being developed by Titan Medical (Toronto, Ontario, Canada). The Amadeus Composer™ (equipped with articulated instruments designed for surgery in restricted spaces in thoracic, pelvic, and ear, nose and throat surgery) and the Amadeus Maestro™ (4 arms) featured a proprietary haptic feedback technology (Titan True Touch Technology™). However, the development of these prototypes, which had a configuration very similar to that of the Da Vinci®, has been stopped recently, mainly for potential patent infringement, and the company is now producing a special single-access robotic device.

Another platform is the TELELAP Alf-X® system [13], which has been developed by SOFAR (Milan, Italy) and received the CE mark in 2011. This robotic telemanipulator includes proprietary force-feedback technology that allows realistic perception. In addition, a useful eye-tracking solution allows navigation in the surgical field, which is displayed on a glass-based 3D monitor. It also allows zooming in and out. Arm selection is possible and can be activated by the surgeon's direct vision on specific icons.

AVRA Surgical Robotics (New York, USA) is developing a modular Surgical Robotic System (ASRS), with a wireless surgeon console controlling up to four arms. The modularity allows greater freedom as well as the possibility of adapting to multiple surgical or image-guided percutaneous procedures. In addition, a variety of projects have been launched recently at both academic and corporate levels to develop lightweight, miniaturized, surgical robotic prototypes, showing the increasing complexity and the interest of several companies in sharing the surgical robotics market.

For CT-guided ablations in the liver the Needle Positioning System (NPS) was developed by DEMCON Advanced Mechatronics [17], which consists of a robotic arm that slides on a rail parallel to the CT table. The robotic arm is positioned manually on top of the entry point on the skin, after which a registration CT scan, visualizing the fiducials of the NPS, is performed. The system uses the registration scan together with the position of the selected target to automatically orient the needle guide towards the target. Needle insertion is then performed manually along this calculated path.

The accuracy of the NPS was compared to freehand needle placement in a randomized controlled trial in patients who were scheduled for CT-guided microwave ablation for one or more liver tumors [18]. In the robotic arm (21 tumors), no antenna repositioning was required. In the freehand arm (also 21 tumors), a median of one repositioning was required (range 0-7; $p < 0.001$). For out-of-plane targets, lateral targeting error was $10.1 \text{ mm} \pm 4.0$ and $5.9 \text{ mm} \pm 2.9$ ($p = 0.007$) for freehand and robotic procedures, respectively, and for in-plane targets, lateral targeting error was $6.2 \text{ mm} \pm 2.7$ and $7.7 \text{ mm} \pm 5.9$, respectively ($p = 0.51$). Mean targeting time was 19 minutes (range, 8–55 minutes) and 36 minutes (range, 3–70 minutes; $p = 0.001$) for freehand and robotic procedures, respectively. The number of incomplete ablations (four in total) did not differ between the two groups ($p = 0.34$). There were two complications: one in each group. Robotic antenna guidance with



the NPS reduced the need for antenna repositioning in CT-guided liver microwave ablations to accurately target liver tumors and increases accuracy for targets with complex angulations.

4.2.3 Potential Clinical Applications in Liver Oncology

Oncological outcomes of laparoscopic liver resection are comparable to those of the open approach, with the benefits of minimally invasive surgery [19]. Surgical robots simplify microsurgical dissection of the hepatic pedicle and biliary reconstruction, which are difficult steps in standard laparoscopy. However, the current experience with robot-aided liver resection is limited to several hundred procedures worldwide [20]–[24]. Some centers undertake the majority of minor hepatectomies using robotic assistance, complemented by preoperative simulation and intraoperative augmented-reality navigation [16].

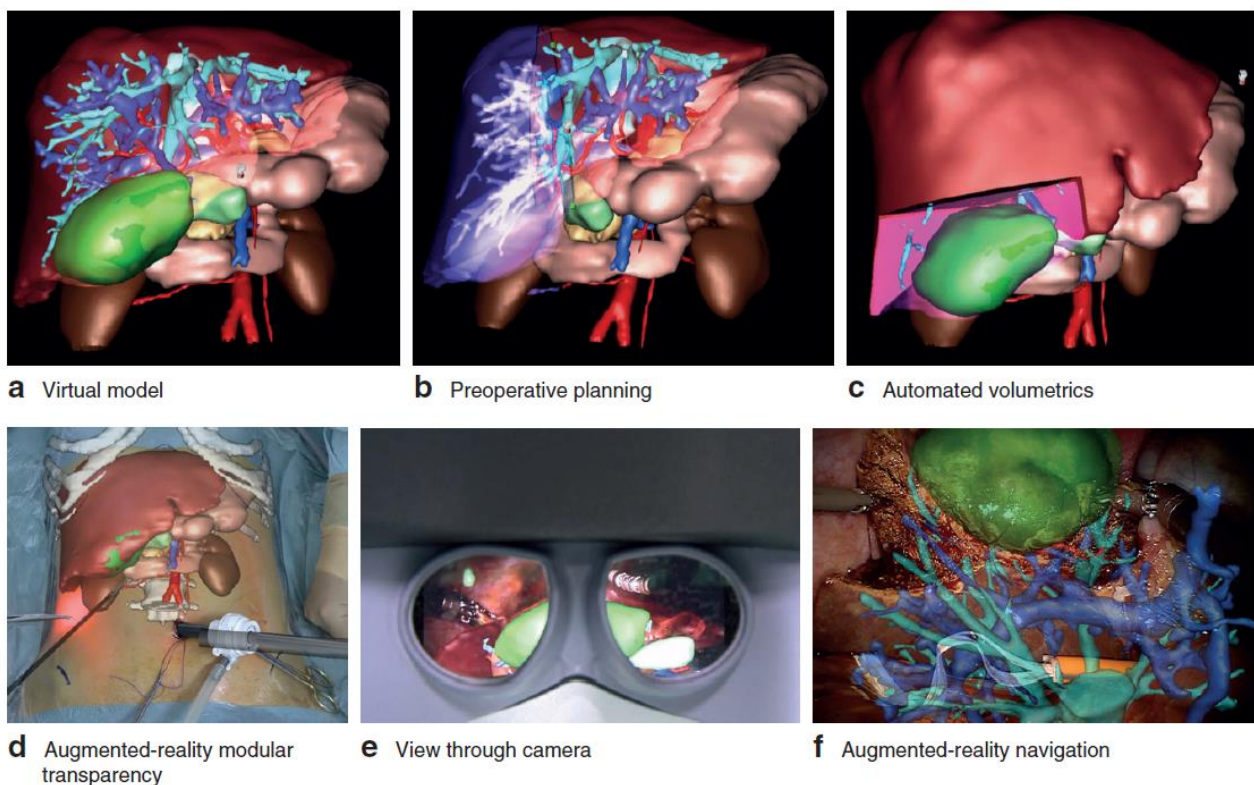


Figure 3 Robotically assisted image-guided liver resection. a) Three-dimensional patient-specific virtual model demonstrating a large tumor in liver segment V. b,c) Preoperative planning and automated volumetrics. d) Optimal port placement through augmented-reality modular transparency. e) Augmented reality seen through the robotic stereoscopic camera. f) Augmented-reality navigation during robotically assisted liver resection, from [16]

4.2.4 Discussion

Although most reports to date show that robotic hepatectomy are safe, feasible and effective, most of these studies are case reports and case series from high volume centers. There are relatively few case-control studies with large sample sizes, and high-quality randomized controlled studies are lacking. According to the findings of current studies, the effectiveness of robotic hepatectomy is essentially identical to that of open surgery and traditional laparoscopic hepatectomy. However, conclusions on operative time, intraoperative blood loss, conversion rate, incidence of postoperative complications, and overall cost-benefit ratio remain divided in different reports. These factors severely limit the application of robotic hepatectomy. Some researchers have



pointed out that it is undesirable to simply increase economic expenses and aggressively apply robot-assisted laparoscopic surgical system for procedures such as living-donor hepatectomy while therapeutic efficacy is not improved. Other opinions point out that as a developing and advancing surgical technology, robotic surgery will become effective enough to allow us to correct any complications with its own techniques [25].

5. Navigation Technology

5.1 Introduction

Imaging and navigation are the key building blocks of image-guided surgery. Particularly, Minimally Invasive Surgery (MIS) often requires tracking and navigation technology to guide the clinician, due to the limited optical feedback during these interventions. MIS has besides the benefit of less post-operative pain, shorter hospital stay with comparable outcome to open surgery and thus reduced costs [26], [27]. Navigation is commonly realized by registering the patient's anatomy with pre- and intra-operative image data. This image data can then be overlaid in a virtual or augmented representation. See Figure 4.

In order to do real-time registration during the procedure, actual patient tracking and motion compensation is needed.

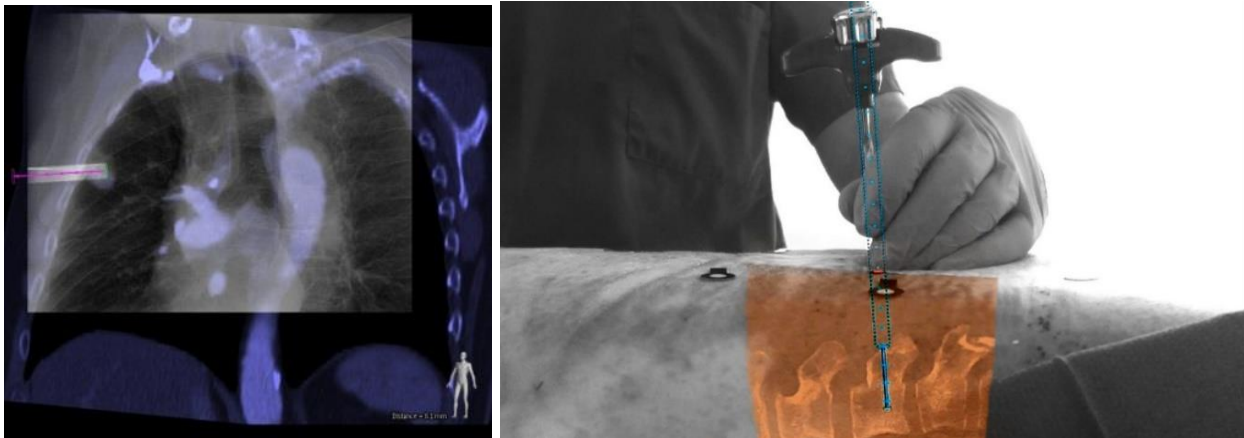


Figure 4 Left: a pre-operative CT registered with live fluoroscopy. Right: Optical imaging augmented with intra-operative cone beam CT

5.2 State of the Art in Clinical Navigation Technologies in General

Navigation, in addition to traditional image guidance, is a technology that has been around for many years. Commercially available state of the art navigation systems are produced by companies like Brainlab, Stryker and Medtronic.

Application areas where these systems are used are spine, ortho, neuro, ear nose throat and crano-maxillofacial fraction surgery.

Typically, in these applications, rigid parts of the patient's anatomy are used to register pre- and intra-operative imaging. Soft tissue deformation can only be taken into account through real time imaging, where ultrasound is used, for instance. In state of the art navigation, the real-time imaging can also be registered to a detectable fiducial or device, e.g. Philips EchoNavigator [28] that automatically detects the ultrasound probe in the X-ray image.



Figure 5 Current state of the art navigation systems. Left, Brainlab for neuro interventions [29]. Right, Medtronic for spine procedures [30]: O-arm with the Stealth Station

The current state of the art in robotics and navigation systems that treat soft tissue areas, such as lung and liver, is described in chapters 4.1.2 and 4.2.2.

5.2.1 Registration

Registration is an essential step of navigation systems. From a navigation perspective, registration involves more than pre- and intra-operative image registration, either 2D-3D or 3D-3D image registration. In addition to the images, actual patient and optional tracked devices should be correlated to the same space. The registration process can be manual or automatic.

A manual registration can be done e.g. by identifying anatomical or artificial added markers (fiducials) in the image set/volume and at the patient in world space coordinates. Other used manual registration methods are based on palpation of the anatomy or the use of a laser scanner for surface matching. See Figure 6.

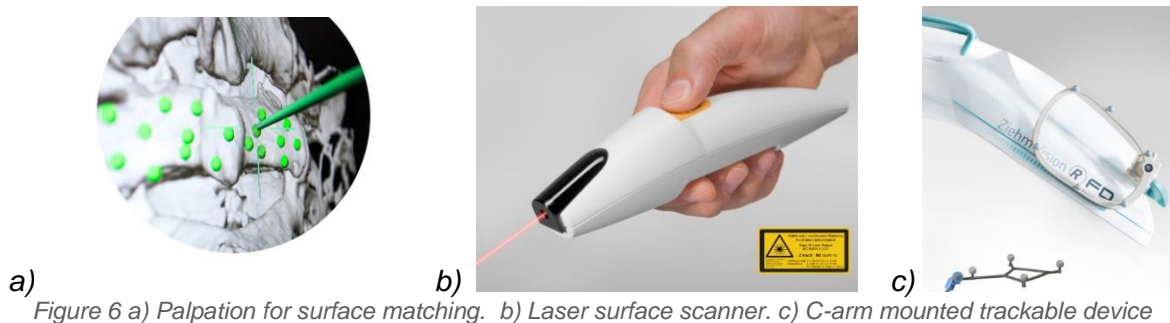
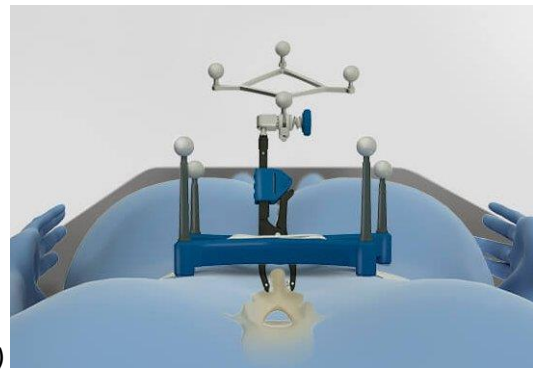
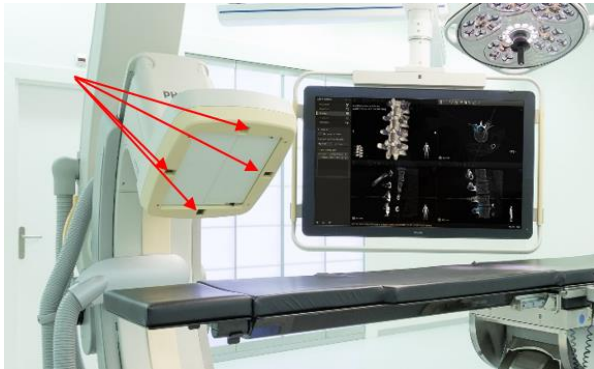


Figure 6 a) Palpation for surface matching. b) Laser surface scanner. c) C-arm mounted trackable device

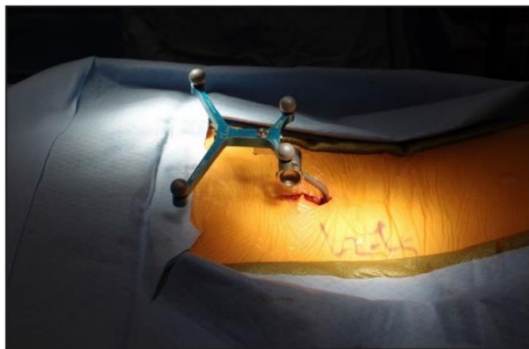
Automatic registration is either done implicitly or explicitly. In implicit automatic registration, the imaging system has a pre-calibrated and tracked position of the scanned image or volume, which is known to the navigation system.

On the other hand, in explicit automatic registration, an external device is attached to the patient which is detected automatically in the images and in navigation coordinates.



a) Philips Allura X-ray system with integrated navigation in the flat panel detector. b) Automatic image and patient registration frame

Patient tracking is considered a must in surgical navigation systems in order to correct for motion. Therefore, a patient tracker (Dynamic Reference Frame (DRF)) or a patient model/mask is often attached to the patient.



a) an example of a spinal DRF for patient motion compensation. b) Stryker SpineMask™, a non-invasive tracker [31]

5.2.2 Tracking

Various tracking technologies exist, but only a few have medical grade and are commonly used in clinical practice.

5.2.2.1 Infrared optical tracking

Most of the market manufacturers of navigation systems, like Brainlab, Medtronic and Stryker, use an infrared stereo camera to track patient and instruments and sometimes C-arms with marker plates. They have over 30 years of experience in the area of 3D localization with near infrared stereo cameras. One prominent manufacturer is Northern Digital Inc. (NDI), which has a special medical division and delivers as original equipment manufacturer (OEM) cameras to a couple of navigation companies.

Infrared cameras can pick up either passive (reflective) or active markers and locate them with sub-mm accuracy at a typical working distance up to 3 m. With a typical 1.8 m by 1.4 m field of view, the NDI Polaris Vega camera claims a volumetric accuracy of 0.12 mm RMS and a 95% confidence interval accuracy to 0.20 mm.



Figure 9 NDI optical infrared tracking camera suitable for active and passive markers

5.2.2.2 Visible light optical tracking

The principle of visible light optical tracking is the same as the infrared optical tracking, as it uses the angle of arrival technique and triangulation to determine marker position.

The use of visible light and thus visible images has the advantage that the camera image can be fused with the medical image, volume or graphics, to provide so-called augmented reality.

5.2.2.3 Electromagnetic tracking

Electromagnetic (EM) tracking systems have been commercially available for nearly three decades. They are capable of tracking multiple flexible instruments in a non-line of sight situation, e.g. in-patient. The operating volume depends on the generated EM field, typically 500 mm x 500 mm x 500 mm and up to 600 mm x 400 mm x 600 mm for a tabletop field generator. The accuracy of the system depends on the sensor/tool design and the presence of metal close to the EM field generator but is typically within 1 mm RMS and 1.5 mm at 95% confidence interval CI.



Figure 10 a) The NDI aurora, one of the most commonly used EM tracking systems. b) Size of EM coils to for instruments

Other existing tracking techniques, but not available as medical grade solution, are:

- Laser
 - o Light Detection and Ranging (LIDAR). It is very popular and becoming cheaper due to the autonomous driving vehicle industry, where it is mainly used to provide a depth information image from a certain point of view, but not much for tracking objects. The range resolution and thus accuracy is still not enough for a medical application.
 - o Structured light. Its resolution is determined by the number of patterns used and currently it is not high enough for sub-centimeter or sub-millimeter tracking of an object.
- Radio Frequency



- Ultra Wideband (UWB). It works with radio wave pulses between 3.1-10.6 GHz and 22-29 GHz and uses the time of flight (TOF) technique to determine the distance between transmitter and receiver. State of the art commercial available systems can provide an accuracy of just less than 2 cm.
- Ultrasound
 - It uses the TOF technique. Literature reported accuracy in lab conditions is of 2 mm for a single tag. Practical 3D accuracy is unknown. Accuracy is influenced by reflections, environmental conditions, and objects in the line of sight between the ultrasound beacon and the tag.

5.3 State of the Art in Movement Compensation

In conscious patients, soft tissue organs, such as the one in the abdomen and thorax have movements that can have different causes:

- Respiration
- Cardiac activities
- Tissue deformation due to treatment
- Patient motion
 - Body displacement
 - Unexpected movements, e.g. coughing and hiccups

To make a navigation system applicable for the situation in which target motion occurs, the system should detect and compensate for target motion. Most patients are asked by the physician to stay still and sometimes the use of equipment, e.g. a vacuum mattress, can help the patient to stay in place. Respiration is the most common cause for inaccurate placement of interventional instruments [32], which is the main focus of this chapter.

5.3.1 Respiratory Motion

Respiration is the expansion and compression of the lungs to maintain normal levels of gas pressure (oxygen and carbon dioxide) in the arterial blood [33]. In low levels of sedation, the action of breathing will continue automatically, due to chemoreceptors regulated by the level of CO₂, O₂ and pH of the arterial blood [33], see Figure 11. However, in deep sedation levels respiration is maintained by a ventilator device. With deep sedation, the patient does not move, and respiration can be controlled by the anaesthesia staff such that generating identical breath holds is possible. Deep sedation is a common practice in most ablation procedures but is barely used in biopsy procedures. Most often only local sedation is used for biopsy. So, especially for biopsy procedures respiratory motion may cause difficulties.



	Minimal sedation (anxiolysis)	Moderate sedation (previously called conscious sedation)	Deep sedation	General anesthesia
Responsiveness	Normal response to verbal stimulation	Purposeful response to verbal or tactile stimulations	Purposeful response following repeated or painful stimulation	Unarousable even with painful stimulation
Airway	Unaffected	No intervention required	Intervention may be required	Intervention required
Spontaneous ventilation	Unaffected	Adequate	May be inadequate	Frequently inadequate
Cardiovascular function	Unaffected	Usually maintained	Usually maintained	May be impaired

Figure 11 Different Levels of Sedation

The respiratory motion is not constant and does not follow a precise rhythm. It is dependent on the posture of the person (upright, lateral, decubitus, supine or prone), the type of breathing (abdominal or chest), and the respiration depth (deep, normal or shallow). The frequency and displacement magnitude of the respiration as well as breath holds can be controlled by the patient him/herself, within limits [33].

The diaphragm is the most important muscle of inhalation. Due to inhalation the diaphragm contracts, descends, and forces the abdomen inferiorly and anteriorly (see Figure 12). During normal breathing, the intercostal muscles are also participating and contract during inhalation. Normal exhalation is passive due to the elasticity of the lung and the chest walls. Only during active exhalation, other ventilation muscles are involved as well [33].

Research has been carried out about the amount of motion of specific organs and tumours in the abdomen and thorax. Imaging techniques (CT, MRI, US or etc.) are often used for these measurements [33], [34]. The amount of movement differs for each organ, and depends on factors like patient position and breathing depth. It also largely varies between different patients, see Figure 13. In most cases, the motion is mainly in the superior-inferior direction while the displacement in anterior-posterior and lateral direction is only 2 mm maximum. However, tumours in the lungs and kidneys often show a wider and more complex trajectory of motion [33].

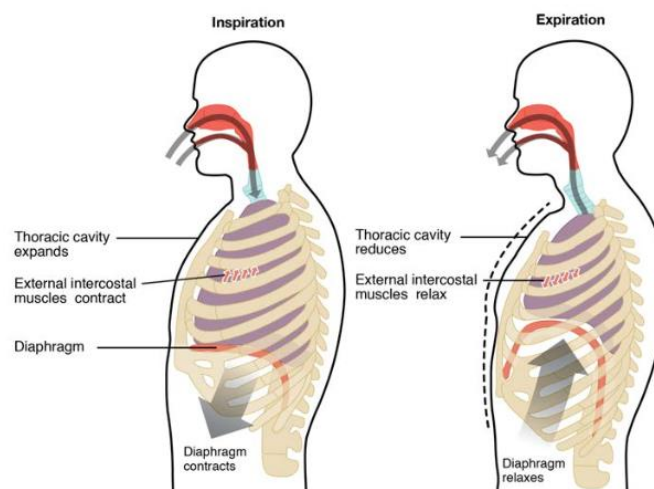


Figure 12 Inspiration and expiration occur due to the expansion and contraction of the thoracic cavity, respectively [35]



Site	Observer	Breathing mode	
		Shallow	Deep
Pancreas	Suramo (Ref. 57)	20 (10–30)	43 (20–80)
	Bryan (Ref. 59)	20 (0–35)	-
Liver	Weiss (Ref. 66)	13±5	-
	Harauz (Ref. 67)	14	-
	Suramo (Ref. 57)	25 (10–40)	55 (30–80)
Kidney	Davies (Ref. 58)	10 (5–17)	37 (21–57)
	Suramo (Ref. 57)	19 (10–40)	40 (20–70)
	Davies (Ref. 58)	11 (5–16)	-
Diaphragm	Wade (Ref. 68)	17	101
	Korin (Ref. 64)	13	39
	Davies (Ref. 58)	12 (7–28)	43 (25–57)
	Weiss (Ref. 66)	13±5	-
	Giraud (Ref. 63)	-	35 (3–95)
	Ford (Ref. 76)	20 (13–31)	-

Figure 13 Abdominal motion data. The mean range of motion and the (min-max) ranges in mm for each site and each cohort of subjects. The motion is in the superior-inferior direction [33]

5.3.2 Surrogate signals

To track whether the target is in the initially registered position or not, imaging can be used. However, this will cause undesirable radiation exposure to the patient and physician in case of fluoroscopy or in case of MRI, this is expensive and time consuming. An alternative for tracking the target is to measure other representative movements that are easier to measure, these are referred to as *surrogate signals*. The surrogate signals should have a strong correlation with the target motion. Different surrogate signals have been investigated in the literature [32], [36]:

1. Volume/flow of the lungs: Spirometer, Electrical Impedance Tomography, CO₂ measurements
2. Displacement of chest or abdomen
 - a. Respiratory inductance plethysmographic (RIP) belts
 - b. Markers (IR, visible, etc.)
 - c. Electromagnetic tracking systems
 - d. Laser tracking systems
 - e. Respiratory belts
 - a. 3D representation of the patient's skin (Structured light plethysmography, laser grid, etc.)
 - f. Accelerometers on the skin
 - g. Depth images: Kinect, Zivid, TOF
 - h. Motion of one or more points on the diaphragm
 - i. 2D images (e.g. Cone-Beam CT (CBCT) projection data) of internal anatomy
 - j. Infrared thermography
 - k. Laser Doppler Vibrometry
 - l. Radar: (FMCW radar, Doppler (pulsed) effect radar, XeThru X4M200 respiration sensor, etc.)
 - m. Respiration detection with Wifi signal
 - n. Ultrasound
 - o. EMG surface sensor
 - p. EMG catheter (esophageal)
 - q. Distance sensor (laser)
3. Tracking the needle: Reference needle with inertial measurement unit (IMU) sensor [32]



5.3.2.1 Correspondence model

The surrogate signal can be used to predict the real target motion with a correspondence model [36], by using the correlation between the measured surrogate signal and the acquired real target motion [37]. For instance, Cyberknife Synchrony (Accuray) [38], is used for radiation therapy and is based on a correspondence model. Before the treatment, a series of rapid X-ray images are made. In the meantime, an optical camera records the movements of markers on a vest worn by the patient. With this information the system builds a correspondence model to predict the tumour location and its motion. During the treatment the system updates the correspondence model by acquiring additional X-ray images and moves with the tumour motion to irradiate the tissue, while avoiding to damage the surrounded healthy tissue [38].



Figure 14 Cyberknife Synchrony system (Accuray) [38]

5.3.2.2 Gating

Another option is to use a surrogate signal for gating. Gating is a method that is already used in radiotherapy [34]. The idea of gating is that the patient is only irradiated during a well-defined interval of the respiratory cycle. Therefore, the respiration cycle has to be monitored during normal breathing and irradiation may occur only when the breathing signal is within this well-defined interval. So, the beam is switched off when the tumour moves outside the initially registered target region, and the beam switches on when the tumour is back in the initially registered target region [36]. The respiratory signal can be tracked by using the phase or the amplitude of the signal (Figure 15) [33], [39].

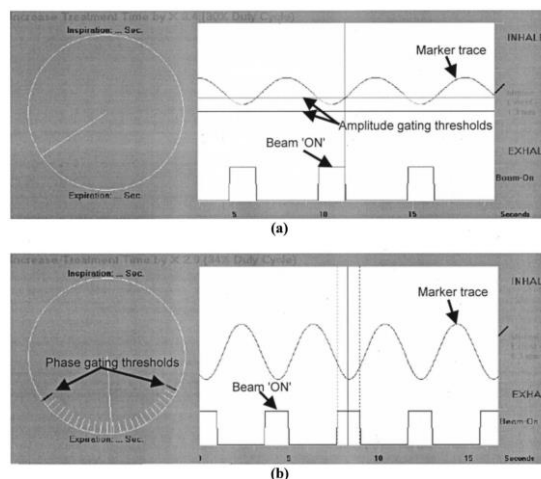


Figure 15 Amplitude and phase gating [39]

5.3.2.3 Breath holds



Breath holds reduces the target motion effectively [34], [39]. Combining gating with breath holds will improve the efficiency of the gating technique. However, not every patient is able to maintain a breath hold for a certain amount of time [39].

5.3.3 Devices

An example of a device that is developed for needle placement and compensate for breathing and patient movement is the XACT™ system [40]. The device is patient mounted, so it moves along with the movements of the patient. This device is CE-marked but no clinical test has been done yet (only pre-clinical test). This and more devices will be discussed further in chapter 7.

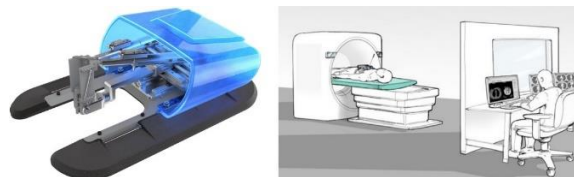


Figure 16 XACT™ system: Patient mounted needle placement system [41]

5.3.4 Patient feedback

According to some research results, the gating can be improved by giving feedback to the patient about the desired breath hold [42], [43]. According to Keall et al. respiratory reproducibility can be improved by audio-visual biofeedback [33]. However, some researches show no statistical difference in the reproducibility of breath holding position with and without a feedback device [44].

5.4 Business Aspects of Navigation Technologies

According to market research, the global surgical navigation system market size was about 730 million USD in 2017. With an expected compound annual growth rate (CAGR) of 7.0%, the forecasted value of the total market size for 2025 is 1.25 billion USD [45], [46]. The current navigation market comprises mainly application areas, such as neuro, orthopaedic, spine, trauma, ENT, dental and cardiac. North America takes a share of 36% of the total market, driven by the developed healthcare system and increasing demand for shorter hospital stay and better patient outcome and thus, the adoption of minimally invasive surgery.

5.4.1 Trends

Traditionally the used tracking technologies are mainly optical and electromagnetic systems. A larger growth of the optical solution is still expected, due to its versatility and proven accuracy. There is a trend to use more and more hybrid solutions to track instruments and devices, including non-rigid devices, inside the body, without line of sight.

The integration of tracking in the imaging equipment to streamline the workflow and to enable real-time navigation on intra-operative imaging is certainly a trend caused by the collaboration amongst the players in the industry. Also instrument and device companies are more and more involved to interface with navigation systems.

The latest key trend is the use and development of augmented reality, where live view of reality (e.g. patient), direct or indirect, is enhanced with virtual- and medical image- information. This presents a more intuitive and understandable image to the physician. For example, critical structures from medical imaging are overlaid on the by navigation system tracked microscope or endoscope image.



5.4.2 Growth Drivers

Various factors can be identified in the growth of the surgical navigation market. One is the aging population, which results in more orthopaedic, spinal and neurological treatments. This is amplified by the demand to do these treatments minimally invasive, with the benefit for the patient of smaller incision wound, less chance of infection and quicker recovery with the economic benefit of shorter hospital stay and outpatient treatment. The economic benefit also creates good base to reimburse MIS with the use of surgical navigation systems.

The demand for more outpatient treatment has increased the number of ambulatory surgery centres (ASCs) and office-based labs (OBLs). ASCs can carry out the same complex procedures as in a hospital in a fully sterile environment. Sometimes they are even part of or located at the hospital campus.

ASCs and OBLs do not offer overnight stay, the operations are done faster, easier, in a more efficient and predictable way, which creates a new market for surgical navigation systems.

5.5 Discussion

For many years, the application areas of surgical navigation systems have been the same. This landscape will change with the upcoming population screening programmes for cancer where more cases in an earlier stage will be detected. Early stage means smaller tumours in mostly soft tissue, such as lung, liver and colon, demanding thus accurate guidance during treatment.

As stated before, most navigation systems rely on registration with rigid anatomical structures, track sturdy instruments and devices, and use a line of sight technology. Although EM tracking is already applied in cardiac procedures, and companies like CAScination [47], offer a resection/ablation solution in the abdominal area based on EM, ultrasound imaging is still needed for correct for motion.

There is still a big opportunity, but also challenge for advanced technologies to be able to guide/navigate and treat soft tissue pathologies and to be able to compensate for motion and deformation.

Another opportunity to improve accuracy and treat the patient with a more predictive outcome is the combination of navigation and robotics. In this case, imaging, navigation and robot/steerable instrument holder should seamless work together in an industrialised manner where standards and open interfaces are key.

6. Augmented Technology

6.1 Introduction

The use of multimodality imaging and image fusion continues to drive medical innovation and promises even further advances with the increasing use of big data and computer science in combination with imaging technologies. Therefore, current technological developments are aiming towards more efficient methods to access and interact with multimodality imaging data in real-time, to improve the efficiency and precision of procedures and the outcome for patients.

One such example is augmented reality (AR), which is an enhanced version of reality whereby computer-generated content (e.g. 2D and 3D graphics, sounds, etc.) is super-imposed over a live view, direct or indirect, of the real-physical environment, thus augmenting the current perception of reality.

In parallel with emerging AR use in other fields such as e.g. gaming, architecture and navigation, innovation in healthcare related AR continues to grow, with multiple AR healthcare applications already developed to date. Some of these applications are educational, others are more collaboration-oriented and the most complex applications are intended for surgical assistance. Most of these applications remain under development with few in clinical practice, given the novelty of AR and challenges that still need to be overcome. However, the latest innovations in head-mounted goggles, such as Microsoft HoloLens and Magic Leap, are helping AR healthcare applications become more interactive, efficient, immersive and realistic, and thus, increasing the acceptance of AR.

The future of AR in healthcare is promising due to two main aspects that make it unique: users do not lose touch with reality (e.g. compared to virtual reality) and it puts relevant information in front of the user's eyes in an accessible and timely way. These distinctive features will enable AR to become a driving force in the future of medicine. The non-occlusive nature of AR makes it perfect to be used during interventions, where the interaction with the rest of the staff and the patient is critical.

6.2 State of the Art

6.2.1 Augmented reality evolution

Augmented reality is a technology under development for more than 50 years. From the possibility to add simple drawings or 3D graphics to videos, the technology has evolved to a more immersive experience with the use of head-mounted displays and space mapping.

The beginning of AR dates back to 1968, when Ivan Sutherland created a broad range of inspirational ideas in computer graphics and interactivity as part of his Ph.D. thesis on Sketchpad [48], a program where the user could draw on a display screen by using a hand-held object, such as a lightpen. Sutherland started working on a Virtual Reality and AR system using a head-mounted display hung from the ceiling with wireframe line-drawing overlay graphics (Figure 17). The technology experienced later advances for virtual features for the Air Forces (Figure 18) and enhanced visual navigation tests for NASA.

However, the term "augmented reality" was first introduced at Boeing in 1990 by researcher Tom Caudell. It was the beginning of AR applications as we know them now. Individual wiring schematics for each plane at the factory floor were displayed on a head-mounted apparatus and projected onto a multipurpose, reusable board. In this way, the instructions could be easily and efficiently altered using a computer system without being manually and physically manufactured.



The growth of AR technology continued in 2009 with the smartphone revolution and it has recently experienced a second growth phase due to the emergence of smart-wearable technology, such as Google Glass, Magic Leap and HoloLens (Figure 17).

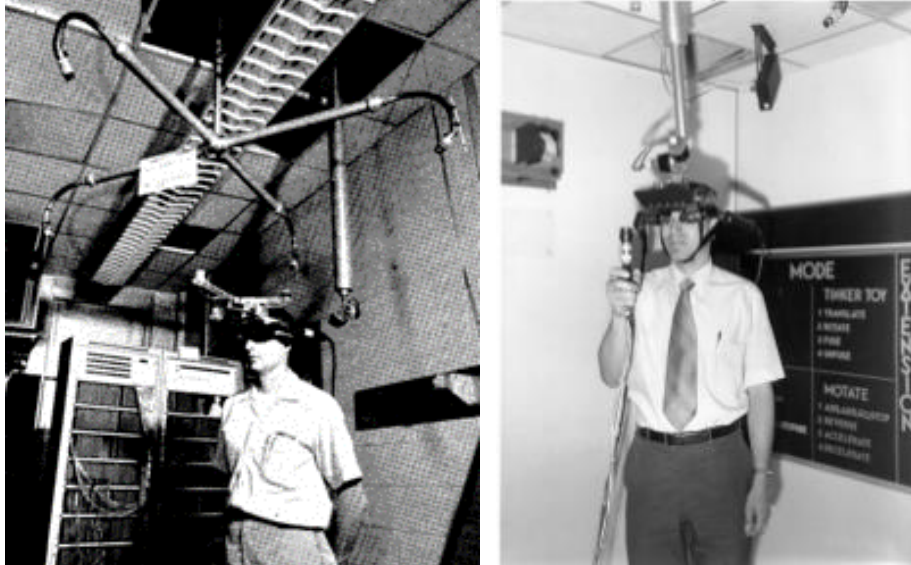


Figure 17 First virtual head-mounted system created by Ivan Sutherland



Figure 18 Head up display used in the F-16 fighter



Figure 19 Augmented reality system introduced in 1990 in Boeing to help technicians to wire different plane's boards



Figure 20 New generation of head-mounted AR devices. Left: Google Glass. Center: Magic Leap Right: HoloLens 2

6.2.2 How do AR devices work?

AR information can be displayed on top of real world objects on a wide range of displays, from screens to handheld devices to wearable smart glasses (Figure 21). Google's Glass, HoloLens, Magic Leap and other head-up displays place AR directly in front of the user's eyes, in the form of glasses. Handheld devices are based on small displays that fit in users' hands, including tablets and smartphones. The virtual models can be directly projected on the patient anatomy using a projector beam instead of a display device. With the evolution of AR devices, smaller and more integrated hardware is expected, such that the form factor will approach the size of contact lenses or virtual retinal displays.

Usually, AR devices are self-contained, consisting of cameras, microphones, depth and motion sensors, display, battery, projectors, processing and graphic units, without the need for being connected to an external computer.

AR devices are often controlled by a touch pad or with voice commands. Touch pads are usually located on the device and easily accessible. Voice commands operate based on verbal keywords and commands detected by a microphone and interpreted by the device itself. In the most advanced devices, such as the Microsoft HoloLens or Magic Leap, it is also possible to interact using hand gestures without the need for a touch pad. Some of the newer and more advanced AR devices are also able to interpret intuitive gestures, making the interaction easier for the user. The new generation of the Microsoft HoloLens, launched in February 2019, includes eye tracking, so that users can also use their eye gaze as a way of interaction.

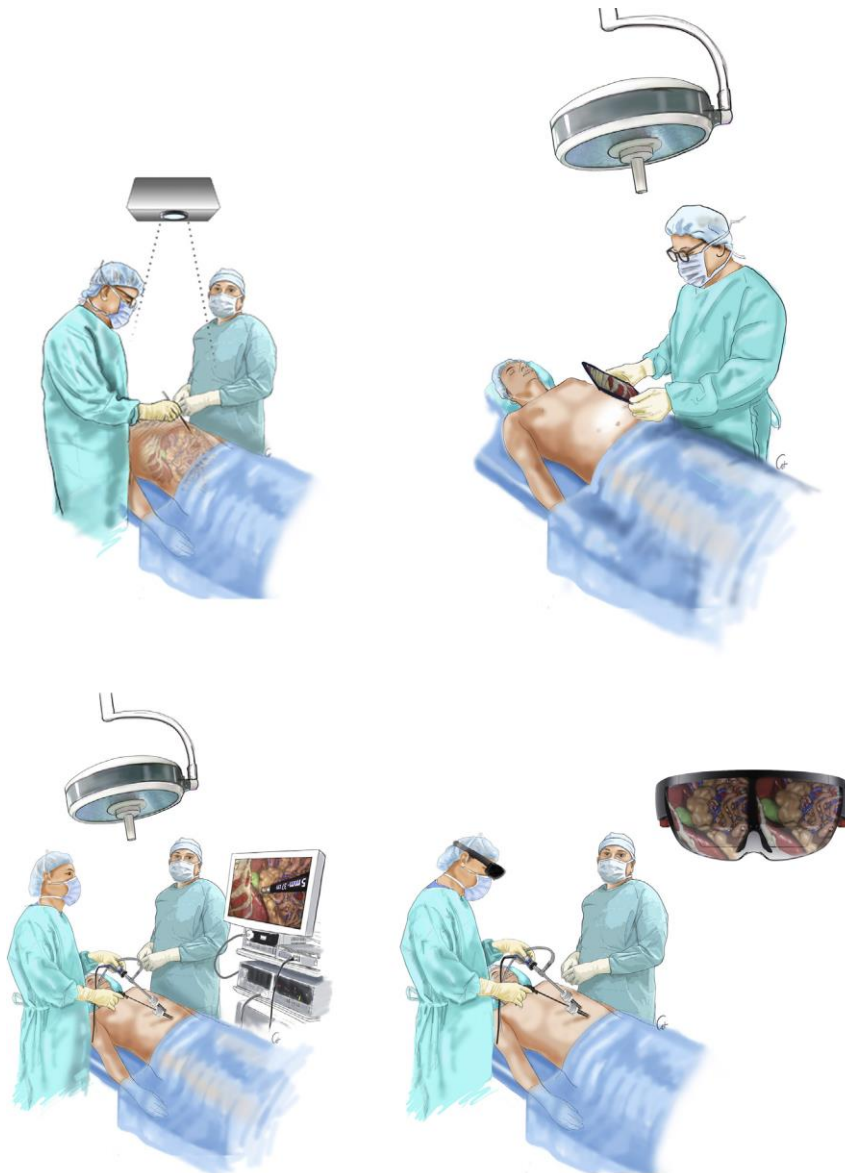


Figure 21 Different flavors of AR: virtual model projected on the patient anatomy using a projector beam (top left); or visualized using a calibrated hand-held device (top right). The virtual model is visualized on a screen in camera-based AR (bottom left), or using a head-mounted device [49]

6.2.3 Main applications in healthcare

From a routine checkup, to a complex surgical procedure, AR can provide enormous benefits to both patients and healthcare professionals. Main applications in the healthcare market are oriented to training/education, collaboration and procedure assistance.

6.2.3.1 Training/education

AR is already being used for the training and skill assessment of students, surgery residents and other medical staff [50]–[52].

The use of AR simulators improves the skills of the trainee in various controlled scenarios, making the learning process faster and more systematic, without the need for experimenting in practice laboratories or long clinical practice. Even improbable scenarios can be included, so that the



trainee is prepared to deal with unexpected and complex procedures where the assistance of an experienced surgeon would be required otherwise.

In addition, presenting 3D stereoscopic information improves depth perception and anatomical understanding, by adding to the orientation and location of anatomical features [53]. Cui et al. 2017 have shown that medical students using virtual 3D stereoscopic models when learning the head and neck vascular anatomy, increased their ability to identify the correct anatomy.

The advantage of training using AR is the ability to combine real time objects with virtual content, resulting in real tactile feedback as opposed to virtual reality simulators. AR has been also shown to increase the enjoyment of surgical training [54].

Finally, AR technologies will also allow experienced medical professionals to continuously observe and give feedback to students during practice.

Touch Surgery [55], CAE LucinaAR and VimedixAR [56], Medivis AnatomyX [57] and laparoscopic surgery simulators [58] are examples of these applications (Figure 22).



Figure 22 Platforms for healthcare education and training: Medivis AnatomyX (left) and CAE LucinaAR (right)

6.2.3.2 Collaboration-oriented applications

A current challenge in the healthcare domain is the access to remote support and expertise of highly skilled physicians during a procedure. Currently, many hospitals use telephone calls or live video for live support. However, the local physician still depends on verbal instructions from the remote physician and in many cases the remote physician cannot exactly access the same field of view of the local physician. This can result in the misinterpretation of instructions and miscommunication between physicians.

AR enables remote physicians to not only see and discuss a procedure from the practitioner's viewpoint but also to interact with the practicing physician, by making annotations in the AR environment. Annotations can include text, images or links to supporting videos, for instance.

Proximie [59] and Skype for AR [60] are some of the solutions already available in the market (Figure 23).

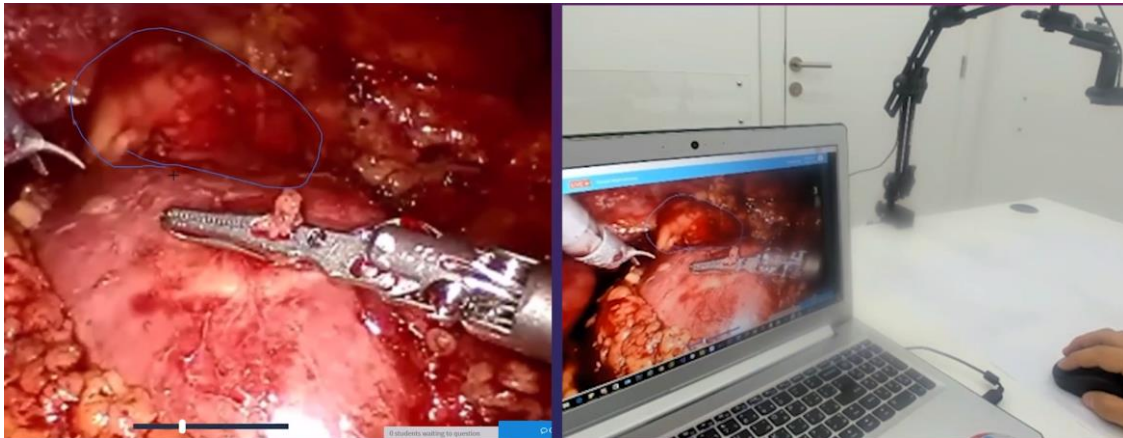


Figure 23 Proximie application in use. Views of the operator (left) and the remote physician (right), respectively [59]

6.2.3.3 Procedure assistance

Existing literature suggests an increasing interest from surgeons to include AR in their procedures to improve efficiency and safety [61].

The advantage of AR is that the surgeon does not need to look away from the surgical site. The use of special head-mounted displays has the additional advantage that there is no obstruction of the surgeon's view when compared to a traditional display, and there is no need for someone else moving the display.

In particular, some of the latest head-mounted AR devices enable the visualization and inspection of complex 3D data in space. 3D reconstructions of preoperative medical images are used for planning a procedure to virtually exploring target areas. Medivis Surgical AR is one the available AR platforms for surgical planning [62]. The 3D reconstructions may be also superimposed on top of the patient for navigation and better orientation during the treatment

Augmented reality applications are easily implementable for surgery of organs with minimal movement and deformation, such as the skull, brain, and pancreas, as less tracking and processing power is required. Conversely, mobile organs, like the bowel, are significantly more complicated to track and display in real time.

Voice commands, eye gaze and air-based gestures are used to interact with the environment, so that the control of the AR device and other equipment can be performed hands-free without the need for assistance or breaking aseptic protocols.

Given the advantages of AR, it can help physicians to become more efficient during interventions. Whether they are conducting a simple invasive procedure or complex surgery, medical AR applications can help treat patients seamlessly.

Below some examples of intra-procedure AR applications in different clinical areas, including liver and lung oncology, are described:

Augmented reality usage in oncologic liver surgery

Despite the current limitations in the accuracy of real time registration between 3D models and the patient, AR assistance has shown potential clinical utility, especially in cases of complex liver surgery [49], [63].

Invasive laparoscopic and robotic liver resections benefit from AR due to the technical challenges of minimally invasive surgery, such as reduced haptic feedback and limited field of view. One example is the use of AR in conjunction with robotic surgical system, such as the da Vinci™ (Intuitive Surgical, Inc., Sunnyvale, CA). The virtual model is projected onto the patient's skin to select the optimal placement of robotic tool and camera port (Figure 24-Left). Using this method,



surgeons can get better sense of tool orientation and triangulation of the surgical ports towards the tumor location.

The use of AR has been also reported to increase the accuracy in tumor localization and resection, and the understanding of the vascular anatomy. The need for precise modeling when assessing the size of the functional liver remnants are particularly important when performing major liver resection. For instance, the virtual model of the liver tumor and liver vascularization are projected into the surgeon's view in real-time during the intraoperative phase (Figure 24-Right). The use of AR allows for a correct dissection of the tumor with enhanced recognition of the major vascular structures. However, an accurate real-time registration of the virtual model remains a challenge for a widespread use of AR in minimally invasive abdominal surgery.

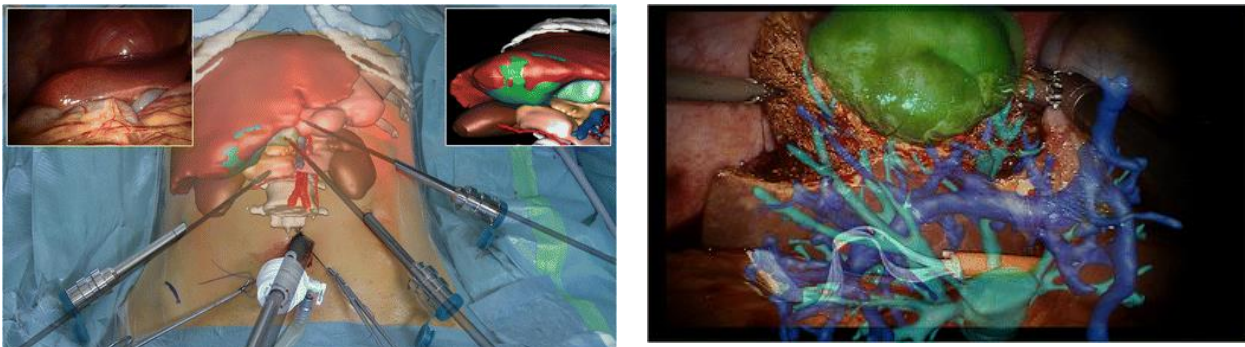


Figure 24 Use of AR for optimal robotic port placement in minimally invasive liver intervention (left), and for dissection of the tumor (right image, displayed in green), with the identification of liver vascularization based on the virtual model generated during preoperative planning [64]

Use of AR in left atrium appendage occlusion (LAAO)

Augmented Reality has been already used during LAAO interventions, using stereographic images and an AR head-mounted display (Figure 25) [65]. Three-dimensional models of the heart were segmented from cardiac CT and displayed using the Microsoft HoloLens. Physicians were able to rotate, magnify, slice and partition the models using gestures and voice commands. The models enabled a comprehensive assessment of the LAA and the adjoining structures, which was essential before the procedure and during the implantation of the device.



Figure 25 Use of AR in LAAO. Stereographic images of the heart are shown on top of the operation room [65]

Augmented reality in spine, cranial and trauma surgery

In 2017 Philips announced the first industrial AR surgical navigation technology designed to help surgeons perform image-guided open and minimally invasive spine surgery [66]. The fully



automatic AR navigation improves procedure planning, surgical tool navigation and implant accuracy, as well as reducing procedure times of surgical procedures.

The technology uses high-resolution optical cameras located on the flat panel of the X-ray detector to obtain live images of the surface of the patient. The external view captured by the cameras is combined with the 3D internal view of the patient acquired by the X-ray system. An AR view of the patient's external and internal anatomy is constructed, including device tracking and path prediction data (Figure 26).



Figure 26 AR in spine surgery. External view of the patient is combined with X-ray images of the spine and device tracking and path prediction and displayed on a big screen

Augmented reality in reconstructive surgery

Researchers and surgeons at Imperial College and St Mary's Hospital in London, have been using the Microsoft HoloLens to provide visual assistance during reconstructive surgery on patients who have suffered severe injuries in the lower limb [67].

Before using AR, surgeons were using handheld ultrasound scanner to locate major vessels under the skin, near wounds. Using AR, CT scans of the patient are overlaid onto the patient's lower limb to easily identify bones and key blood vessels (Figure 27). This allows the surgeon to quickly see "through" the limb of the patient during surgery. The technology may help the surgeons exactly locate and reconnect target blood vessels during surgery and improve the outcome of patients.

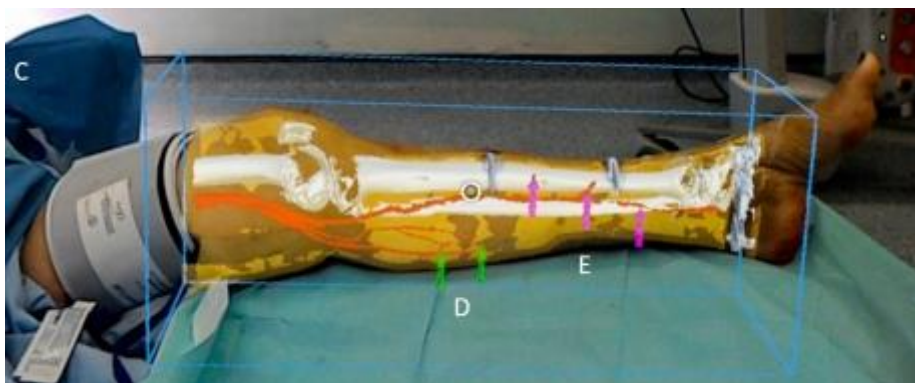


Figure 27 Use of AR with the Microsoft HoloLens to overlap reconstruction of bones and vessels on top of the patient's leg during reconstructive surgery [67]

Augmented reality for planning in electrophysiology



Cardiologists at the Cardiac Magnetic Resonance Center at Beth Israel Deaconess Medical Center have run a pilot animal study to demonstrate the feasibility of AR to visualize and assist the assessment of the complex 3D scar anatomy during electrophysiology studies [68].

Both, operator and mapping specialist found the use of AR useful to assess scar information during a procedure. AR provided an accurate 3D perception and stereoscopic visualization of the complex scar architecture. In addition, the operator was able to access and directly interact with the maps during the procedure, compared to current practice where this possibility does not exist. Sharing the same 3D model with the mapping specialist improved the communication between the electrophysiologists.

Another example is SentiAR [69], which presents real-time visualization of the patient's anatomy combined with the catheter during the treatment and analysis of cardiac arrhythmias (Figure 28).

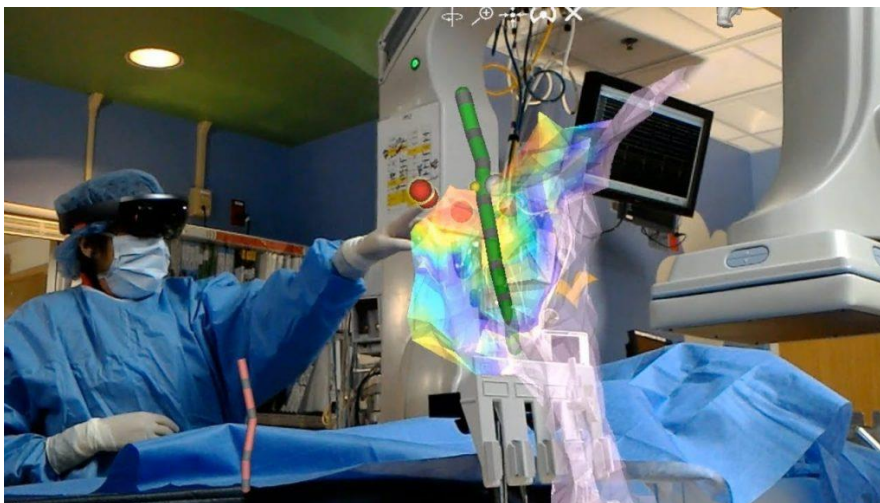


Figure 28 Use of AR to guide treatment of cardiac arrhythmias, showing combined view of the patient's anatomy and the catheter [69]

Use cases in lung interventions

AR has been used to plan transcatheter pulmonary interventions. Stereographic models were used during the procedure as guidance and navigational tool, in order to understand the 3D relationships between the anatomical structures [70].

AR has been also used as a tool before the surgical procedure to improve decision making and surgical planning in a challenging case of video-assisted thoracoscopic surgery lobectomy [71]. The display of patient's 3D data using AR is a useful tool for surgical planning by providing the surgeon with a true and spatially accurate representation of the patient's anatomy.

6.2.4 Challenges in augmented reality

Although the constant improvement of AR technology and the increasing number of applications in the healthcare field, there are still challenges that need to be addressed before widespread adoption.

Fragmentation: The existence of different development platforms, operating systems and hardware impedes the introduction of AR technologies for mainstream audiences. A single integrated platform where everyone can develop, experience and learn from each other will provide a focal point for real AR enterprise applications.

Financial barriers and evidence: The elevated cost of AR headsets remains a barrier for consumers. The financial impacts are even higher for enterprises to adapt AR technology. The cost



of implementation and the subsequent return or increased investment for companies is still unknown. For consumers, it still needs to be proved that the benefits of using AR technology in clinical practice compensates its costs.

Content and education: The amount of information that a physician can access during a procedure continues to increase, creating a possible distraction for the physician [72]. Moreover, the use of AR has been shown to exacerbate these potential distractions, increasing inattentive blindness during procedures [73].

AR solutions need to be built so that they are content-tailored to the environment, context and user. Today applications are still complex and need to evolve to ensure AR technology is more accessible.

Privacy: AR technology may have a big impact on privacy. Data of the user/operator such as location and motion are normally tracked using sensors embedded in AR systems. Even eye tracking and facial expressions can be identified through computer vision technologies. Additionally, audio conversations can be monitored. If the data is saved to a cloud, it will make confidential patient information vulnerable. And as AR smart glasses automatically screen and process a user's environment, the privacy of those around the user can also be affected [146]. Clear rules and regulations will need to set the limit in which these technologies can operate.

Technical barriers: Current head-mounted devices are still heavy and produce excessive heat, factors that affect the long-term wear comfort. AR projections in head-mounted devices also cause simulation sickness in some users.

The latency of the whole system is also a concern because excessive latency may lower precision and reduce comfort for the physician. Excessive latency or delay in the displayed image by the AR devices may inhibit the surgeon's performance during the use in real-time AR use cases. Existing study about effect of latency suggests that delay of more than 86 *milliseconds* will introduce a noticeable decrease in user's performance in pointing and steering tasks [74].

These limitations create a complex engineering challenge in developing medical AR devices, to balance the amount of processing needed for each use-case, the latency performance, and the head-mounted device ergonomics for long-term wear comfort.

AR will reach its full potential when technology and standards in optics, 3D capabilities, motion tracking and CPU power evolve. The next step is to create a powerful CPU that fits within smaller and lighter AR glasses, thus providing improved immersion and ergonomics. The advances in technology will also enable real-time acquisition of high-resolution medical scans and 3D reconstructions, to be used during procedures.

Apart from the technical limitations concerning the AR device itself, the use of fully automatic and accurate registration in soft tissue, between virtual images and the patient remains a major challenge today and is subject to ongoing research [49]. Soft tissues such as the liver or the lung are subject to organ motion and large deformation because of respiration, pneumoperitoneum and surgical manipulation, which affects the AR guidance system performance.

6.3 Business Aspects

Augmented reality was valued at US\$4.21 billion in 2017 and is expected to be worth \$60.55 billion by 2023, growing at a compound annual growth rate (CAGR) of 40% during the forecast period, according to data published by MarketsandMarkets [75]. The head-mounted displays will hold a major share of the AR market. These devices have the greatest potential to drive the growth of the AR market. With advances in computing, AR-enabled devices would be used for applications in consumer, commercial and enterprise.



In particular, healthcare is one of the key applications driving the market. The global use of AR in the healthcare market is expected to grow to USD ~1.32 billion by 2023 at a CAGR of ~23% during the forecast period 2017-2023 (Figure 29) [76].

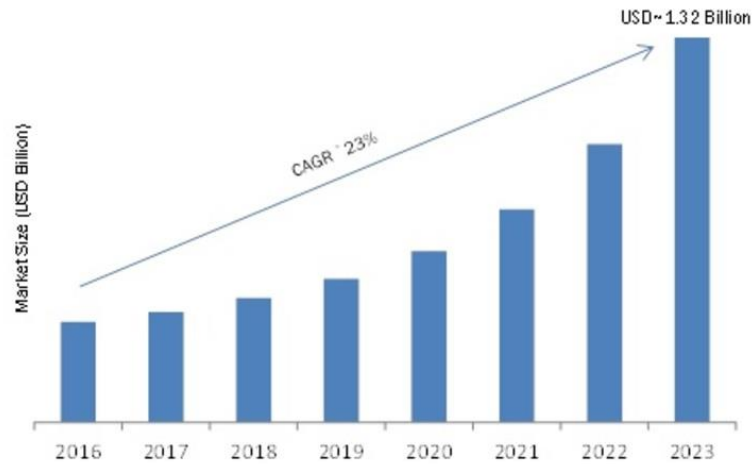


Figure 29 Growth of the global AR market in the healthcare sector [76]

The major drivers for the growth of AR in the healthcare market are [77]:

- The increasing penetration of connected devices in the healthcare sector
- The increased investment in AR and VR healthcare by the major technology companies
- The growing need to reduce the healthcare cost

Given that AR is an emerging technology, there are still limitations and challenges, such as:

- The limited user interface that affects the navigation performance and interaction experience of AR applications
- Limited processing power, battery life, and storage, which are the major limitations of the AR market
- Overcoming the challenge of changing the current way of working to increase the adoption rate

The widespread use of AR in the healthcare industry will provide many new technical and clinical opportunities. The possibility for physicians to efficiently access information during an intervention will help them to conduct minimally invasive procedures that provides better outcomes for patients and increase staff satisfaction.

Healthcare organizations are predicted to spend as much as \$5 billion globally on AR and VR by 2025 [78]. The key use of AR driving the growth of the AR market are: diagnosis and treatment of patients, improving ergonomics, teaching complex subjects to medical students, training doctors, managing logistics (e.g. device and medication inventory) and caring and supporting patients after they leave hospitals.

6.3.1 Key players

Some of the most relevant players in the global AR healthcare market are: Google LLC. (U.S.), Microsoft Corporation (U.S.), DAQRI (U.S.), Mindmaze (Switzerland), Wikitude GmbH (Austria), Medical Realities (U.K), Atheer (U.S.), Augmedix (U.S.), Oculus VR (U.S.), CAE Healthcare (U.S.), Philips Healthcare (Netherlands & U.S.), 3D Systems (U.S.), Blippar (U.K), VirtaMed (Switzerland), HTC (Taiwan), Siemens Healthineers (Germany), Magic Leap, Inc. (U.S.), and Osterhout Design Group (U.S.) and Virtually Better (U.S.), among others [76].



In particular, Philips Healthcare announced its partnership with Microsoft in February 2019, where Microsoft HoloLens will be integrated into the Philips Azurion platform to aid efficiency in minimally image guided therapies [79].

6.3.2 Regional Analysis

North America is one of the leading regions in terms of market share due to the increasing adoption of consumer electronic devices, which is propelling the market growth to a large extent. AR in the healthcare market in Europe is expected to witness rapid growth in the forthcoming period whereas, Asia Pacific countries such as China, Japan, and India are an emerging market, and are expected to grow at the highest CAGR in the coming years [76].

6.4 Discussion

The evolution of medical imaging has provided technologies such as multimodality imaging, image fusion, and advanced segmentation and registration algorithms to improve image guided therapies in the clinical practice. The next step is to integrate artificial intelligence and AR technologies, to facilitate the access and use of that information whilst increasing the efficiency of procedures and decreasing costs.

Although the beginning of AR dates to the 60's, tremendous progress has been made in recent years, due to the available processing power, and largely to the smartphone revolution and the boom in smart-wearable technology. In this respect, innovative products like Google Glass, the Microsoft HoloLens and Magic Leap have attracted the attention of many industrial fields, including the healthcare sector.

Augmented reality and the most immersive head-mounted devices have the promise to revolutionize the clinical industry. The possibility of having quick and seamlessly access to the necessary information during a procedure and that the information is presented in front of the practitioner without external assistance, makes the technology extremely attractive. On the other hand, an interaction system based on hand gestures, voice commands or even eye gaze is compatible with the sterility protocols at the interventional room. The possibility of seeing and interacting with 3D models in space, provides a better understanding, depth perception and orientation of 3D anatomies, which has immense value during training, planning of procedures, and even during real-time procedural guidance. The integration of microphones and cameras creates a perfect collaborative environment, such that the operator has access to the opinion of experts all around the world during a procedure.

Augmented reality applications in healthcare range from educational and training to assistance of surgical procedure.

From a business perspective, AR is predicted to grow at a CAGR of ~23% during the forecasted period 2017-2023. This predicted growth is a consequence of the increase in technological investment by the major technology companies and the increase of AR devices in healthcare, plus the need for decreasing healthcare costs.

Despite the rapid propagation of AR in the healthcare sector and its promises, many challenges, such as technical, financial- and privacy-related, still need to be resolved before widespread adoption. For example, the use of AR in liver and lung treatments is subject to future developments in order to get accurate and real-time registration between patient and virtual 3D reconstructed models. Also, the evidence of the added value of AR in the clinical practice is one of the most essential aspects for successful adoption.



7. Needle Intervention Systems under Image Guidance for Usage in Thorax and Abdomen

7.1 Introduction

Needle intervention systems are used to perform minimally invasive surgery. In order to visualize the target and the location of the needle image guidance (e.g. MRI, CT) is often used. In the past decades, various needle intervention systems were developed for various therapeutic and diagnostic applications. In clinical practice the main application areas of robotic needle intervention systems are the brain and the prostate. This chapter focusses on another application area: the use of needle intervention systems under MRI or CT guidance in the abdomen and thorax. Although many systems have been developed in recent years, only a few are used and the freehand method remains dominant [80]. The freehand method is an iterative process in which the needle is inserted manually, and the insertion point and insertion angle are obtained from the scan. Multiple scans during insertion are needed in order to check if the steered towards the target correctly. The workflow of this method is shown in Figure 30. The main disadvantages of this method are the increase in exposure to radiation of patient and physician when CT is used, tissue damage every time the needle is not inserted correctly, long procedure time leading to high costs and long equipment occupation time [80]. Robotic needle intervention systems can increase the accuracy and efficiency of the procedure, especially for lesions that are difficult to approach.

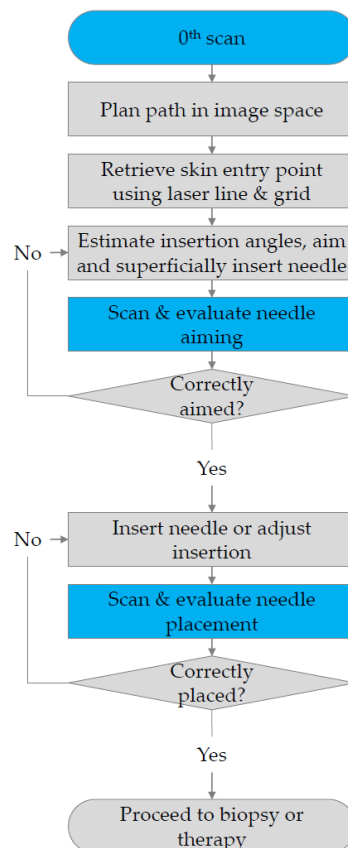


Figure 30 Workflow of the conventional freehand needle placement method [80]



7.2 State of the Art

Arnolli et al. performed a comprehensive study on systems for CT- and MRI-guided percutaneous needle placement in the thorax and abdomen [80]. This section will give a summary of the paper by Arnolli et al. In addition, some more developed systems have been added since the publication of this paper.

Needle placement systems can be divided into two groups: needle feedback systems and needle guidance systems. Needle guidance systems provide physical guidance during needle placement whereas needle feedback systems give feedback on the needle placement. An overview of all needle placement systems discussed in this section is shown in Table 2.

7.2.1 Needle Feedback Systems

As the imaging in the freehand method is not real-time, multiple iterations of imaging and subsequent positioning are required. Feedback from other sources than the imaging modality can improve positioning, thereby reducing the number of iterations, the procedure time, and radiation exposure. Feedback systems can be divided into three groups [80] based on their working principle:

1. Navigation and tracking systems
2. Gravity guided systems
3. Laser guided systems

Navigation and tracking systems use a single image set and continuously track the position of the needle. Both the image set, and the tracking need to be in the same coordinate system. The needle can be tracked mechanically, optically, or electromagnetically. Mechanical systems use the encoders on the joints of the insertion arm to monitor the location of the needle [81], [82]. The base of the arm is fixed with respect to the imaging device. An example of such a system is the Philips Pinpoint system combined with an Immersion MicroScribe-G2X arm [81].

Optical systems use instruments that contain light reflecting or emitting markers which are detected by an infrared laser light. A reference frame is obtained by placing markers on the patient's skin. These markers are detected by the image and the instrument, creating a common coordinate frame [47], [83]–[86]. The line of sight of optical systems should not be obstructed. This could influence the workspace of the physician and the placement of equipment [80].

Electromagnetic systems use an instrument with an electromagnetic sensor containing one or multiple coils. Additionally, a generator of a controlled, changing magnetic field is used. The instrument is tracked with respect to the generator using the electromagnetic induction in the coils [83], [85]. An example of such a system is the CT-NAV by IMACTIS, see Figure 31. A major disadvantage of these kind of systems is that they are influenced by surrounding metals and magnetic fields, which will distort the magnetic field leading to tracking errors [80].

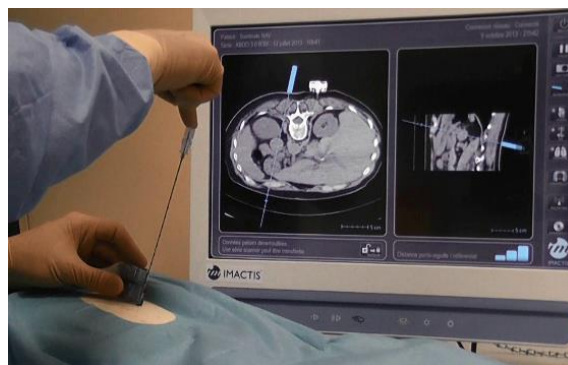


Figure 31 IMACTIS CT-NAV [87]



Gravity guided systems use gravity to position the needle (Figure 32a) [88]–[90]. The direction of gravity is used as a reference vector, guiding the needle in the correct orientation of a planned axial trajectory. Rotation around the gravity vector can be provided by a second reference vector, e.g. the imaging device, the imaging table, etc. These two reference vectors determine the instrument orientation, making it parallel to the planned instrument path. Subsequently, the marked entry point is placed under the instrument and the instrument can be inserted. The insertion depth is monitored by the markings on the needle.

Laser guided systems work similarly to the gravity guided systems. However, instead of using two gravity reference vectors, a laser is used as a reference vector [91]–[98]. The laser is placed in the direction of the planned needle trajectory, see Figure 32b.

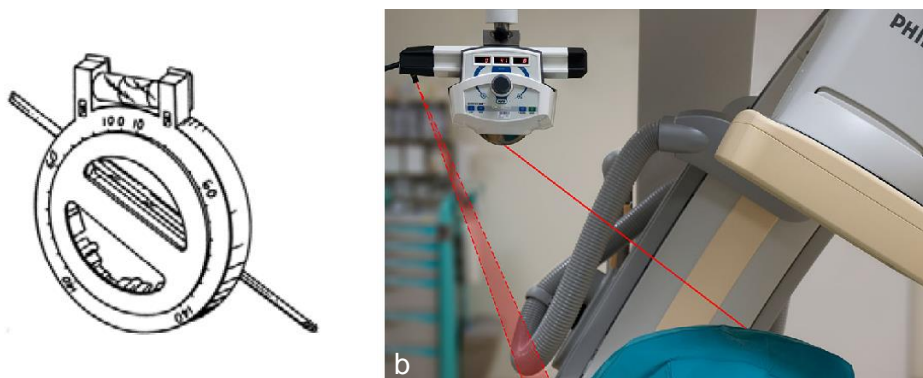


Figure 32 a) The gravity guided system INRAD AccuPlace [90]. b) The laser guided NeoRad system [95]

Examples of navigation and tracking systems, gravity guided systems, and laser guided systems are shown in Table 2.

7.2.2 Needle Guidance Systems

Needle guidance systems physically guide the needle and sometimes even insert the needle. These guidance systems can be divided into two groups: patient mounted systems and surroundings mounted systems. In patient mounted systems the system is placed directly on the patient which reduces errors due to patient movement. Surroundings mounted systems are mounted to the table, floor or gantry.

Patient mounted needle guidance systems enter the imaging device together with the patient [80]. The angle and insertion depth can be modified by either the physician and/or by the device itself depending on the type of system. The angle and insertion depth are determined using path planning, as done in the needle feedback systems. Simple passive mounting systems consist of one or two arcs along which the needle can be rotated to position the desired angle. When the position is correct, the needle is locked in the system and then scanned to check the needle path. As the needle is locked in the system, the physician does not need to hold the needle and radiation exposure is limited. Examples of these systems are the Neorad Simplify system [99] and the Apriomed Seestar [100]. Active systems automatically position the needle in the correct angle. An example for CT is the Robopsy system [101] which uses actuators for positioning and clamping/releasing of the needle. The position cannot be registered yet, but the needle can be controlled remotely using feedback from the CT. The actuators are placed outside the planes of the needle trajectory in order to prevent distortion of the image. Other examples of CT compatible patient mounted needle guidance systems are the CT-Bot [102], [103], the Light Puncture Robot



(LPR) [104], and XACT [40] (Figure 33a). These systems contain actuators to position the instrument and contain fiducials to register the position of the system. The CT-BOT can automatically insert the needle and contain haptic control. The LPR is MRI compatible and can not only position the instrument angle, but also automate movement over the patient's abdomen. A major disadvantage of the CT-BOT and LPR is their sizes, which fills a large part of the imager bore [80]. The XACT can automatically insert the needle as well and its size is smaller than the CT-BOT and LPR. Examples for MRI-guided devices are the systems developed by Wu et al. [105] and Song et al. [106]. In both systems, the needle guidance system is mounted on an MRI loop coil. The position of the systems is registered using fiducials.

Surroundings mounted needle guidance systems can be mounted to the table, the floor or the gantry [80]. Table mounted systems often enter the image device with the patient. Examples of passive CT needle guidance systems are the CT Guide [107], which is table mounted, and the floor mounted stereotactic frames by Onik et al. [108], [109], Koutrouvelis [110], and Bidwell [111]. All these passive systems make use of rulers and protractors to position the needle in the correct direction. In addition, a passive, table mounted, MRI compatible system was developed by Christoforou et al. [112]. This system uses markers to visualise the needle in the MRI image. The markers are attached to the end-effector which is parallel to the needle.

Examples of active table mounted CT compatible systems are a device developed by Siemens [113], the iSYS1 developed by iSYS Medizintechnik [114], the AcuBot [115], the INNOMOTION developed by Innomedic [116], [117], and the needle positioning system (NPS) of Arnolli et al. [17] (Figure 33B). These needle guidance systems can remotely and/or automatically be positioned on the entry point, after which the correct needle angle is determined. The Siemens system, the iSYS1, and the NPS use manual insertion of the needle, whereas the AcuBot and the INNOMOTION have an optional insertion module that can insert the needle automatically. The INNOMOTION system is also MRI compatible and contains markers for visualisation [80].

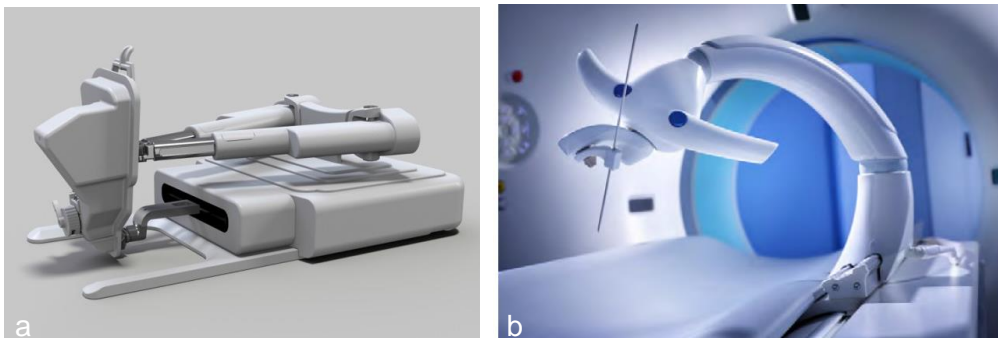


Figure 33 a) The patient mounted XACT by XACT Robotics [40]. b) The table mounted Needle Positioning System (NPS) developed by Arnolli et al. [17] in collaboration with DEMCON

Examples of active floor or gantry mounted CT compatible systems are mobile robots on wheels developed by Perfint [118], [119], the system developed by Yanof et al. [120], the floor mounted robot of Zhou et al. [121], and the system of Tovar-Arriaga et al. [122], [123]. The Perfint system can be placed into a docking station next to the imager. The docking station has the same coordinate systems as the imager and contains fiducials which are recognized by the camera [80]. The insertion of the needle is performed manually as is done in the system developed by Tovar-Arriaga et al. The needle placement systems developed by Yanof et al. and Zhou et al. contain automatic needle insertion.

MRI-guided systems were developed by Hata et al. [124] and Chinzei et al. [125]. Hata et al. create a virtual centre of motion at the target. The physician can manually orientate the needle guide and a XYZ translational stage automatically moves the needle guide in order to maintain the



intersection of the axis of the needle guide with the predetermined target location. The XYZ stage uses the same coordinate system as the imager [80]. The needle is inserted manually. The system by Chinzei et al. is placed in between two vertical MR coils and works similarly to the iSYS1. An overview of all patient and surroundings mounted needle guidance systems mentioned in this section is shown in Table 2.

Table 2 Overview of needle placement systems. Adapted from [80]

Category	Active/ passive	System	Com. Available?	
Needle feedback systems				
Navigation and tracking	Passive	PinPoint stereotactic arm [81]	Yes	
		Claron MicronTracker [82]	Yes	
		Mechanical		
		Optical		
		NDI Polaris [83]	Yes	
		Stryker Navigation System II [84]	Yes	
	Electromagnetic		Stryker eNlite Navigation System [84]	Yes
			Medtronic StealthStation [85]	Yes
			CAScination CAS-ONE [47]	Yes
			ActiViews CT-Guide [86]	Yes
			Medtronic AxiEM [85]	Yes
			NDI Aurora [83]	Yes
			IMACTIS CT-NAV [126]	Yes
Gravity guided systems	Passive	Palestrant I [88]	Yes	
		Palestrant II [88]	No	
		Zhang et al. [89]	No	
		INRAD AccuPlace [90]	Yes	
Laser guided systems	Passive	Frederick et al. [91]	No	
		Ishizaka et al. [92]	No	
		Unger et al. [93]	No	
		LAP Patpos Invent [94]	No	
	Active	NeoRad SimpliCT [95]	Yes	
		Amedo LNS [96]	Yes	
		Yanof et al. [97], [98]	No	
Needle guidance systems				
Patient mounted	Passive	Neorad Simplify system [99]	Yes	
		Apriomed Seestar [100]	Yes	
	Active	Robopsy system [101]	No	
		CT-Bot [102], [103]	No	
		Light Puncture Robot (LPR) [104]	No	
		XACT [40]	No	
		Wu et al. [105]	No	
		Song et al. [106]	No	
Surroundings mounted	Passive	CT Guide [107]	No	
		Onik et al. [108], [109]	No	
		Koutrouvelis [110]	No	
		Bidwell [111]	No	
		Christoforou et al. [112]	No	
	Active	Siemens system [113]	No	
		iSYS Medizintechnik iSYS1 [114]	Yes	
		AcuBot [115]	No	
Innomedic INNOMOTION [116], [117]	No			



	NPS [17]	No
	Perfint [118], [119]	Yes
	Yanof et al. [120]	No
	Zhou et al. [121]	No
	Tovar-Arriaga et al. [122], [123]	No
	Hata et al. [124]	No
	Chinzei et al. [125]	No

7.3 Business Aspects

In general, most information regarding robotic medical systems is about tele-robotic surgical systems. The market leader in this field is Intuitive Surgical Inc. (ISI) which had a revenue of 3,129 million USD in 2017 [127] and an estimated market share of 80% [128]. Current ISI robots cost from 910,000 to 2.5 million USD with annual maintenance contracts of \$125,000. The robotic surgery market is predicted to increase sales of robotic instruments to 18 billion dollars annually within the next few years. In this same article it is concluded that value proposition of these type of robots for Hepato Biliary surgeries is incomplete [128].

Typically, the cost of robotic surgery is compared with manual procedures that are often more invasive and cause more complications and/or longer hospital stay.

In another article [129] on medical tele robotic systems it is concluded that the amount of systems that are commercial available and used in clinical practice is still very limited. In this article the status of reviewed robots is shown in graph below, illustrating that the majority of these robots is in an experimental phase.

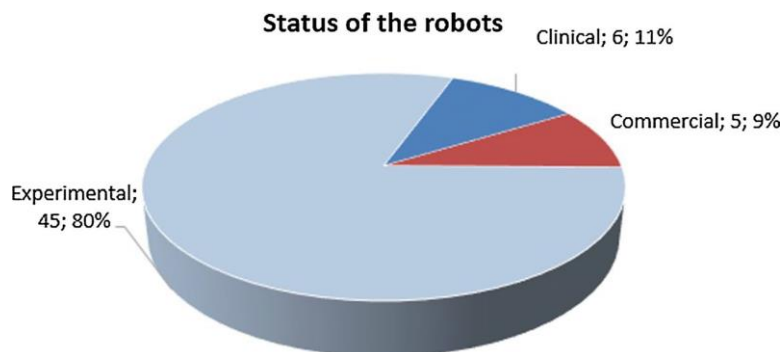


Figure 34 Status of medical telerobotic systems [128]

There is little information to be found about business aspects of the needle guidance systems discussed in the previous section. Interventions that benefit from needle guidance systems are typically performed by interventional radiologists. Based on anecdotal evidence from discussions with Dutch interventional radiologists, the majority of these specialists perform their interventions manually with the aid of ultrasonic diagnostics if feasible. With the aid of the prototype that will be developed in this project, stakeholder input will be gathered, including information that can be used to build a business case for needle guidance systems.

7.4 Discussion

There are many types of needle feedback and needle guidance systems, although not many are used in clinical practice and the freehand method remains the main method being used. Needle

feedback systems provide the correct orientation based on one image set, whereas needle guidance systems can hold the needle and sometimes even place the needle improving the procedure especially for lesions that are difficult to approach. All these needle intervention systems reduce the exposure to radiation for patient and physician.

The XACT patient mounted needle guidance system is a promising device. It is better than their competitor's patient mounted systems due to its size and because it is patient mounted positioning error due to patient movement is low. All surroundings mounted needle guidance systems are still in development stage. The NPS was recently validated in a clinical trial and the accuracy compared to the freehand method was investigated [18]. As mentioned in section 4.2.2, the positioning error is reduced with the NPS. In order to make the NPS applicable for biopsy procedures as well, the NPS must be suitable for patients which are locally sedated. In comparison to the current NPS which is only used on fully anesthetized patients (common in ablation procedures). During the IMPACT project the NPS will be made suitable for locally sedated patients and hence bringing this needle intervention system a step closer to industrialization.



8. Steerable Catheter and Guidewire Technology

8.1 Introduction

The concept of a steerable guidewire has the main advantage that its tip can be actuated, in contrast to existing guidewires. Existing guidewires lack this possibility and passively follow a path. To better understand the concept of a steerable catheter, guidewire and their benefits, the general use will be first explained.

In general, guidewires are used for minimally invasive surgery. A wire is inserted through a small incision in the skin and then navigated through the blood vessels in order to reach the area of the (vascular) disease. These kinds of wires are called guidewires, since they act as guidance for larger catheters or stent delivery systems [130].

Most minimally invasive surgeries involve two kinds of tools: a guidewire and a catheter. The main difference between a guidewire and a catheter is the fact that a catheter is hollow in contrast to a guidewire. During these interventions a combination of a guidewire and a catheter is navigated through the blood vessels. Special X-ray images are taken to guide the surgeon to the desired area. These X-rays will give the surgeon a 2D-image of the position of the guidewire. This entire procedure is called "Image-guided endovascular intervention" [131]. One key aspect for reaching areas which are difficult to access, is the maneuverability of both tools. The ability to remotely steer both the guidewire and the catheter will affect the success rate and the duration of the procedure [132]. The steerability and maneuverability of both tools is in particular dependent on the ability of the tool to transfer movement from the proximal end outside the body to the distal tip inside the body [133].

The steerability of conventional guidewires and catheters is limited by a couple of factors. First, existing tools often have a fixed distal shape which only can be reshaped manually outside the body. Having a fixed distal shape means that the surgeon must extract the catheter or guidewire from the patient several times to change the shape of the distal tip to reach different areas. The repeated extraction and insertion of these tools increases the risk of infection, the procedure time, and it leads to higher costs. On top of that, having a fixed distal tip is directly related to poor usability and a low success rate of reaching the desired position inside the body [134], [135].

Secondly, rotation of the tip can only be achieved by rotating the proximal end of the tool. Rotation of the tool by rotating the proximal end means that the tool should be able to transmit a torque from the proximal end to the distal tip. Moreover, it also means that the catheter or guidewire must be rotated over the entire length which is inside the body. This causes a large amount of friction between the tool and its corresponding wall (catheter or blood vessel wall) [133], [136]. The transmission of a torque between the proximal end and the distal tip of both tools is influenced by the contact friction and the torsional rigidity of the tool. However, the relatively large length will reduce the torsional rigidity of the tool [137]. Due to these factors the rotation at the distal tip will deviate from the rotation at the proximal end, causing a tip which is not in the desired position. Consequently, the accuracy of the rotation of the distal tip is directly affected. Moreover, a deviation in rotation makes the handling of conventional guidewires less intuitive and less efficient [132].

8.2 State of the Art in Steerable Catheters

Special catheters and guidewires are developed to reach the desired location accurately and fast. Catheters with different tips are designed to get in different side branches. There already are some steerable catheters on the market, using manual or robotic actuated bending. An example is the



Swift Ninja of Merit Medical [138]; a micro catheter of 2.4 French (Fr) that can articulate 180° by using the turning wheel at the proximal end as is shown in Figure 35.

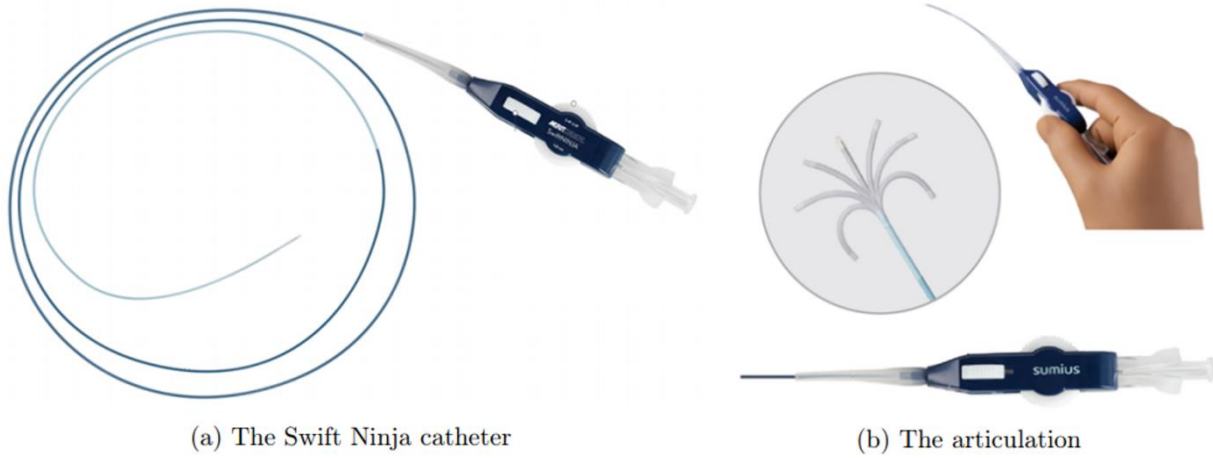


Figure 35 Merit Medical - Swift Ninja

In the assortment of OSCOR Inc., there are three types of steerable guiding sheaths, shown in Figure 36. The diameters of the sheaths range from 6.5 to 13.8 Fr and the tip of the Destino twist can deflect 180° unilateral while the Destino and Destino Reach can deflect 180° bilateral [139].

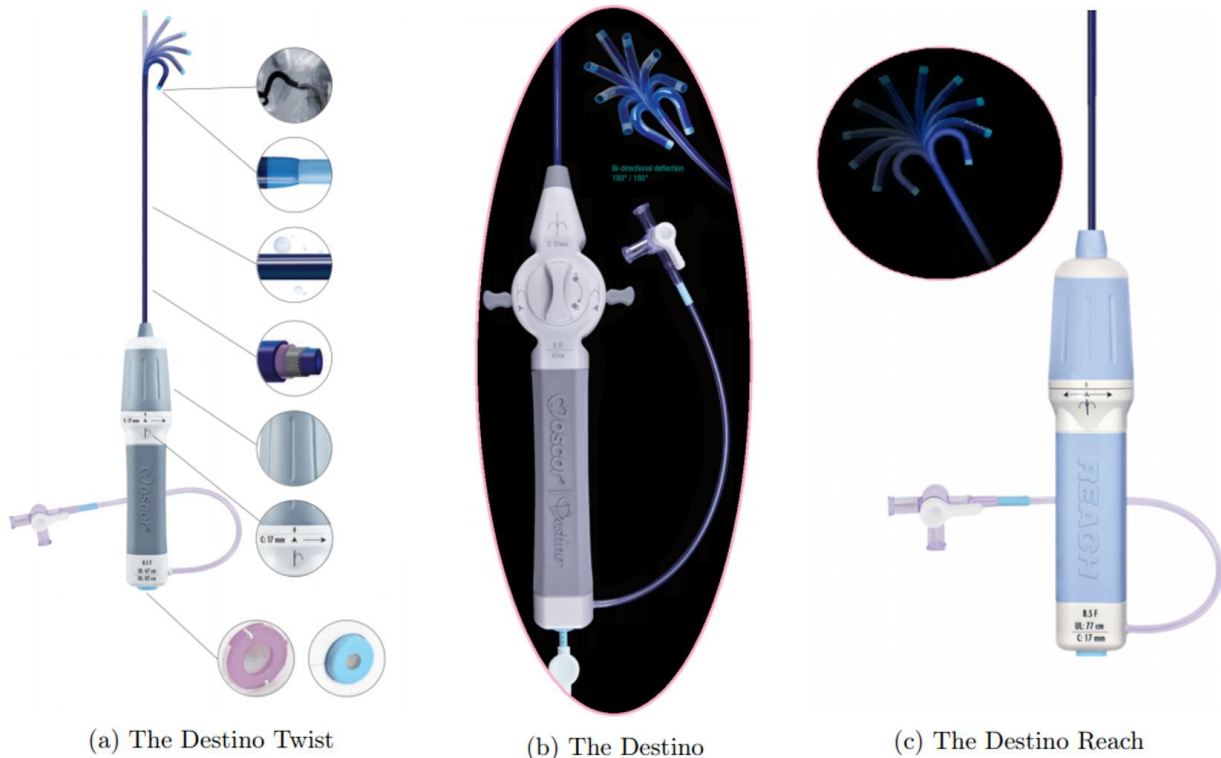


Figure 36 OSCOR Inc. – Destino



Boston Scientific also has several diagnostic steerable catheters of 6 and 7 Fr, including a back steer catheter and a bilateral curvature catheter [140]. Robotic actuated bending is used in the 9 Fr Magellan catheter by Hansen Medical, shown in Figure 37 [141].

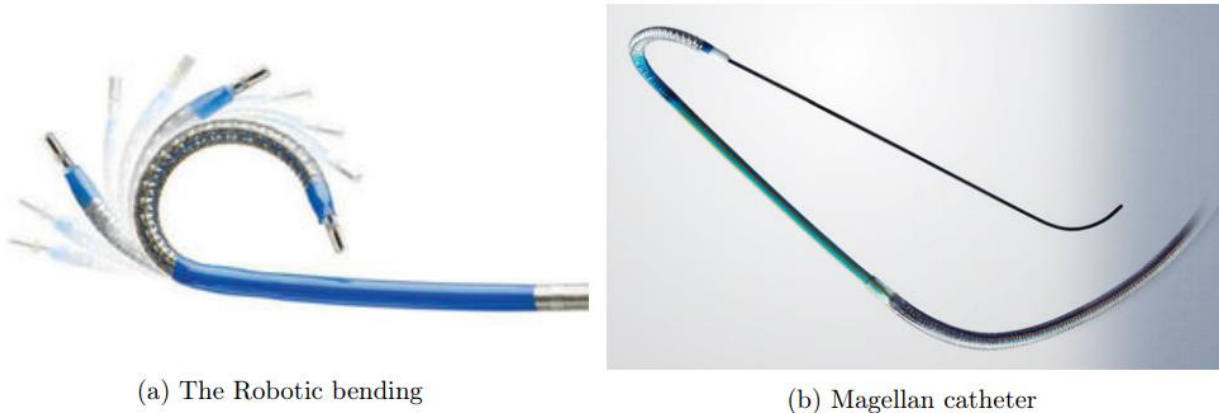


Figure 37 Hansen Medical - Magellan catheter

Another development is a steerable catheter with a magnetic head, which is used for cardiac ablation. A computer and an external field are needed instead of manual steering. Due to the magnetic head, the front part of the catheter can be bent in any direction to steer through complex blood vessel anatomy. The stiffness of the front part can be adjusted through fine copper wires inside the catheter [142].

Currently available techniques for steerable catheters are based on either electrical actuation, thermal actuation, magnetic actuation, hydraulic chamber actuation, or mechanic cable actuation. A schematic representation of the advantages and disadvantages of these techniques is shown in Figure 38 [132].

Mechanical actuation describes the largest and most commercially available group of contemporary catheter actuation technology, based on cable or tendon actuated steering. This technique uses the basic principle in which cables run from the proximal handle through the catheter shaft towards the distal tip where they cause deflection upon push/pull movement of the cables. The more cables and segments implemented in the technique; the more degrees of freedom the catheter obtains. However, increasing the number of cables and segments comes with assembly and control complexities. Furthermore, the design has to deal with mechanical challenges such as preventing friction, buckling, and wedging of cables with each other or with their surroundings. In addition, in the case of a catheter an inner lumen is required to allow for guidewires and interventional tools to be introduced, while the outer diameter must remain small enough for the intended applications.

The vascular surgeons of UMCG already use a steerable guiding sheath that belongs to the category of mechanic actuation techniques. UMCG uses the previously mentioned Destino Twist from Oscor®. In clinical practice the Destino Twist is found functional and intuitive. The response of the handle collar to rotation is accurate and it allows for the use of conventional guidewires. However, due to its large outer diameter it can only be steered through relatively large vessels and it has the potential to disrupt the natural blood flow, which increases the risk of embolization [135]. Hence, it can only be used in a limited range of applications.

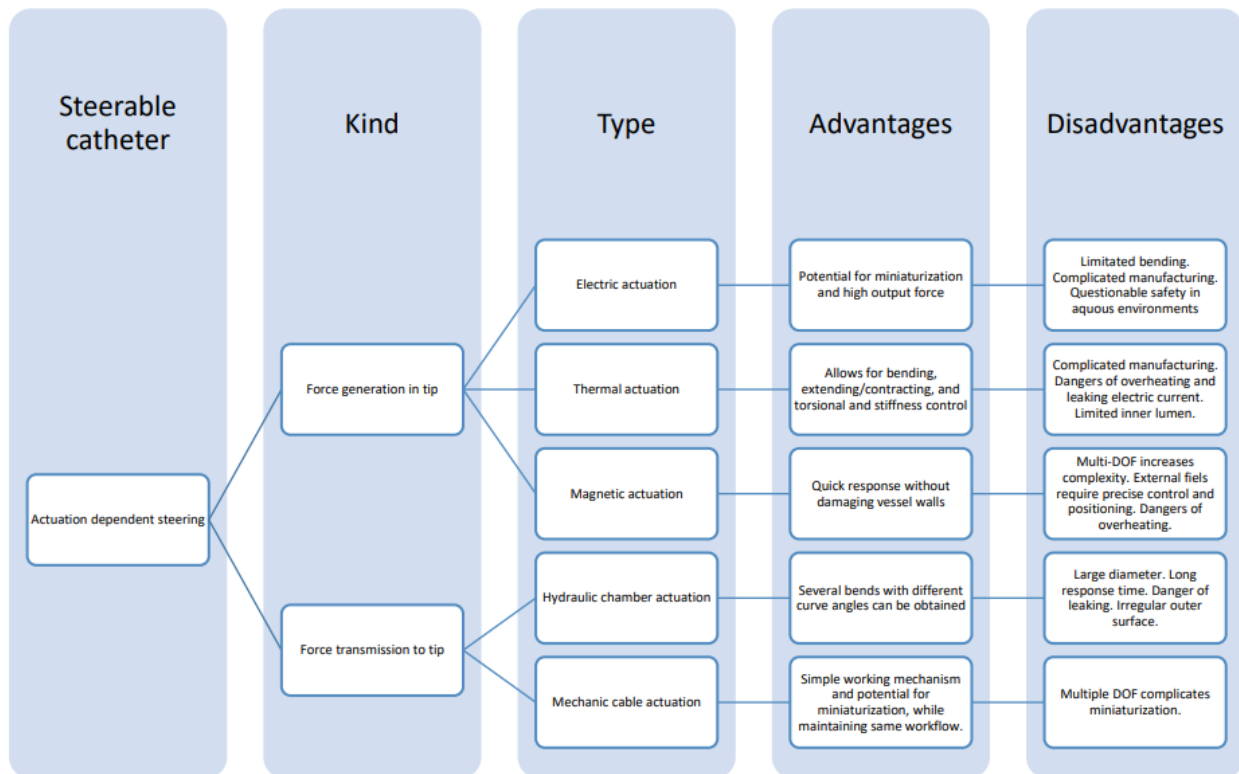


Figure 38 Schematic representation of the advantages and disadvantages of all currently available techniques for steerable catheters (DOF = Degree of Freedom)

8.3 State of the Art in Steerable Guidewires

Currently, only a few steerable guidewires are on the market or in research. There are guidewires available which claim to be steerable. However, when looking closer at the source of this statement it seems that this refers to the torqueability (e.g. the ratio of rotation of the proximal end with respect to the distal tip) of the guidewire. A general guidewire is specified by a number of properties. For a well-defined guidewire the support, tip stiffness, and coating are specified. These properties result in different properties in handling. A large tip stiffness will result in easy passing of a lesion. But has a higher risk of penetrating the vessel walls.

Hence, guidewires are used in different ways. Abbot categorises the guidewires in four divisions making a balance between support stiffness and tip stiffness [143].

- Workhorse guidewires
- Finesse guidewires
- Extra support guidewires
- Specialty guidewires

Supportability is a measure of the capability of the guidewire to slide a catheter over it. The tip stiffness can be defined as the resistance against bending of the tip of the guidewire. A low tip stiffness, or in other words a floppy tip, is required in case of usage in fragile vessels. However, a low stiffness decreases the supportability.

Workhorse guidewires offer a trade-off between tip stiffness and supportability. Therefore, workhorse guidewires are often the first choice of a clinical specialist. If more complicated tasks have to be performed another guidewire might be chosen.



A finesse guidewire offers low support and low tip stiffness. Therefore, it is generally used in cases where the location is difficult to reach. If more support is required a catheter is sled over the finesse guidewire and the wire is replaced with a stiffer guidewire, for example an extra support wire, when the desired location is reached.

Extra support guidewires are used for example when stents have to be placed and the guidewire acts as a trail over which the required material is moved.

Finally, a range of specialty guidewires exists which are made to have good crossability. This means that they can easily cross obstacles. This type of guidewire requires a high tip stiffness and a good torqueability to make it easier to wiggle the tip of the wire.

A guidewire that is actually steerable is the Cordis STEER-IT guidewire, shown in Figure 39. This guidewire has a two-way deflectable tip which can be controlled by a device on the distal end of the guidewire. The control device is fixed on the guidewire and cannot be removed. This limits the usability of the guidewire, which will only be used in areas of difficult anatomy.



Figure 39 Cordis - STEER-IT

8.4 Business Aspects

The total catheter market was 35.1 billion USD in 2017 and expected to grow to 73.5 billion USD in 2024. The largest share is in the area of cardiovascular catheters (37,8%). [144]

The global guidewires market is projected to reach USD 764.0 million by 2022 from USD 605.2 million in 2017, at a CAGR of 4.8%. The growth witnessed by guidewires is mainly driven by the growing target patient population, continuous product launches by major manufacturers, increasing availability of medical reimbursements for guidewires across developed countries, and rising adoption of minimally invasive surgical procedures across major countries.

In 2016, Boston Scientific (U.S), Abbott Laboratories (U.S), Medtronic (Ireland), Terumo Corporation (Japan), and Cook Group (U.S) held the leading position in the global guidewires market. In the past three years, these companies adopted product developments & commercialization, acquisitions, market expansions, and agreements & collaborations as their key business strategies to ensure market dominance. Cardinal Health (U.S), Olympus (Japan), Johnson & Johnson (U.S), B. Braun (Germany), and C.R. Bard (U.S) are some of the other major players in this market [145].

8.5 Discussion

In the field of steerable catheters there is a broad range of products available on the market by established medical technology manufacturers. In the field of steerable guidewires there are only few examples found in research and even less on the market. The commercial available steerable



guidewire from Cordis described in 8.3 is sub-optimal and there is room for improvement on the bending and rotation aspects of the distal end and on the means of control on the proximal end. An improved steerable guidewire will be developed under the IMPACT project.



9. References

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