Needle guidance technology for image-guided percutaneous procedures

Assessment of clinical applicability and feasibility

Master Thesis Technical Medicine

by

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Summary

Image-guided percutaneous approaches are increasingly used during interventional radiologic procedures with either diagnostic purposes, such as biopsies, or therapeutic aims, including ablations and drainages. A freehand manual needle positioning, a step-wise approach is often employed. Research performed within this topic often describes the disadvantages of the iterative approach, each adjustment and reinsertion of the needle leading to increased procedural time, patient radiation exposure and potentially additional soft tissue trauma and complications.

The use of navigation technologies or robotic assistance during image-guided percutaneous procedures could be of added value within clinical practice to improve both the efficiency and effectiveness of these procedures, especially in case of technically challenging target lesions, but widespread clinical adoption has not taken place yet. An overview of (pre-) clinical studies evaluating the performance of robotic assistance or navigation technology was created to formulate hypotheses on why this is the case. In the author's experience, two important factors play a role in this.

First of all, there seems to be a limited amount of high-quality evidence showing the added value within current clinical practice. The disadvantages of the iterative nature of the conventional manual approach are emphasized in research regarding image-guided procedures, but a quantification of these drawbacks and the extent to which these can be improved by needle guidance technologies is lacking. This research has contributed to the knowledge base by evaluating the efficacy of the freehand approach for a broad spectrum of procedures and anatomical targets as performed within a large peripheral center. Based on these results, the relevance of the potential improvements associated with adopting needle guidance technology seems to be limited. However, the high accuracy that is provided by needle guidance technology could improve the procedural success rates, and therefore, the clinical benefit during complex cases.

The second factor that plays an important role in the (lack of) adoption of these techniques is that an adequate method to account for the needle tip positioning errors induced by perprocedural lesion displacements is often lacking, which reduces the feasibility of several (prototypes of) needle guidance devices. A method based on gating and biofeedback was proposed to account for the needle tip positioning errors caused by breathing-induced lesion displacements.

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Chapter 1 – General introduction

Background

Image-guided percutaneous approaches are increasingly used during interventional radiologic procedures with either diagnostic purposes, such as biopsies, or therapeutic aims, including ablations and drainages. [1-4] A manual approach is conventionally adopted during these procedures, which means the physician mentally maps the 3D patient anatomy from pre- and perprocedural 2D images acquired in order to position the surgical instrument according to the planned position and orientation. [3-6]

Adequate positioning of the tool tip at the predefined target tissue is crucial to achieve interventional success, [4, 7, 8] but may be challenging due to small lesion size [9, 10], deep target locations, [9, 10] poor lesion conspicuity, the need to adopt a (double-)oblique approach during lesion targeting. On top of that, the physician experience level plays an important role and, due to the lack of actual real-time tool visualization during CT-guided interventions, [5, 11] any perprocedural patient and target motion would increase the procedural complexity further. [5, 6, 11]

A step-wise approach is often employed during freehand needle positioning. After initial placement, the needle path and the position of the needle tip are checked using CT-imaging. [3, 11] Deviations of the needle course with respect to the planned path lead to an iterative process of estimating the target depth and the required needle orientation, repositioning the tool accordingly and subsequently acquiring a CT-scan to evaluate the current needle position and orientation. Research performed within this topic often describes the disadvantages of the iterative nature of this approach, each adjustment and reinsertion of the needle potentially leading to increased procedural time, patient radiation exposure [12, 13] and soft tissue trauma. [12-14]

The use of navigation technologies or robotic assistance during image-guided percutaneous procedures could be of added value within clinical practice to improve the efficacy of these procedures, [4, 6-8] especially in case of technically challenging target lesions. [7, 11] However, the extent in which these techniques become commercially available and are implemented within clinical practice remains low, despite the fact that several (prototypes of) needle guidance systems have been developed and described in the literature. [3, 6, 15] This is often attributed to drawbacks reducing the clinical applicability of these technologies, including increased procedural complexity, set-up effort, needle targeting time or automation of the tool insertion, [3, 12-14, 16] but the evidence base is limited in quantity and quality.

Objectives

The goal of this research was to assess the clinical applicability and feasibility of needle guidance technology within the daily clinical practice of the radiology department of a large, non-academic hospital located in the Netherlands. At the start of the project, two broad goals were formulated; (i) the implementation of the DEMCON Needle Positioning System (NPS) within the clinical practice of CT-guided procedures at a large non-academic hospital, and (ii) to propose a method to provide perprocedural motion compensation within the workflow.

The first objective was formulated after demonstrating the NPS to radiologists at the Meander Medical Center. The performance of the NPS had been clinically tested during a randomized controlled trial at the University Medical Center Groningen within the area of CT-guided ablation therapy of primary and secondary hepatic malignancies. The initial goal for the current research was to identify whether the use of the NPS would provide added value during CT-guided procedures as performed in the daily clinical practice of a non-academic hospital and to test this in a (pre-)clinical setting. However, after attendance of several procedures and discussions with radiologists at the Meander, it became clear that the method used to perform these procedures was very different from the workflow of the UMCG. Therefore, it was necessary to acquire clinical data for a multitude of diagnostic and therapeutic procedures performed in a broad range of anatomical structures that could act as a benchmark prior to (pre-)clinical testing. The objective was reformulated: identify the window of opportunity for the NPS by quantifying the efficiency and effectiveness of CT-guided procedures.

The second objective was formulated after assessing the assumptions that were made during the design of the NPS. Similar to different (prototypes of) needle guidance systems that have been developed and described in the literature, the provided trajectory guidance is based on the assumption that the target lesion does not deform or displace. Therefore, intraprocedural motion of the patient or the target lesion is not accounted for and needle targeting errors may occur. When patients are generally anesthetized, the respiration-induced target motion can be minimized by temporarily pausing the mechanical ventilation during path planning and needle insertion. However, most image-guided procedures take place under local anesthesia or sedation, during which the patients keep breathing spontaneously. Incorporating a method to encompass or compensate for respiration-induced deformation and displacement of thoracic and abdominal organs could increase the clinical applicability and feasibility of needle guidance devices; the objective was to explore and propose such a method.

Thesis outline

A general introduction to the topic of image-guided percutaneous procedures was provided and the main objectives were formulated. (*Chapter 1*)

The literature published on the topic of systems developed for use during image-guided percutaneous procedures was analyzed to identify the trends in the state-of-the-art. The aim was to expand the knowledge currently available, as presented in published reviews and overviews, and to identify new research on previously existing and newly developed devices over the past few years. An overview was created on the (pre-)clinical experience with needle guidance technology intended for use during CT-guided interventions, focusing on the reported performance measures and the added value of introducing these technologies within clinical practice. (*Chapter 2*)

A single-center, prospective, observational study was conducted to assess the efficacy of CT-guided percutaneous procedures performed at a large peripheral medical center in the Netherlands. The aim was to quantify the efficiency and effectiveness of CT-guided interventions. These results acted as benchmark during the evaluation of the potential merits and disadvantages of adopting needle guidance technology in daily clinical practice. (*Chapter 3*)

An explorative study on the technologies available to compensate for perprocedural (respiration induced) motion of the target lesion and surrounding tissues was performed. The problem was evaluated theoretically by means of literature study and practically through attendance of multiple diagnostic and therapeutic procedures performed in several organ systems. Based on these observations and the received clinical input from radiologists, two use cases were described and a stakeholder analysis was performed, which lead to the formulation of user and system requirements. A concept technology was described, focusing on the clinical applicability and provided added value of the newly envisioned system within the boundaries provided by the current clinical practice. (*Chapter 4*)

The research concludes with a general discussion and the overall conclusions. An outline for future research is provided. (*Chapter 5*)

Chapter 2 – An overview of the (preliminary) experience with systems for CT-guided percutaneous needle positioning

Introduction

Over the last few years, a considerable amount of research has been performed to identify methods to improve conventional percutaneous procedures with a focus on needle guidance and navigation technologies. Several research groups and medical device companies have created instruments, tools and accessories with the goal to facilitate percutaneous needle placement, either by providing real-time navigation or by providing physical support during the needle positioning.

Although the preliminary results and experience of using these technologies during CT-guided interventions are often positive, the extent to which these techniques become adopted within clinical practice remains low. [3, 6, 15] This may be attributed to a lack of high-quality evidence that introducing these technologies within the current clinical practice would offer additional value. [11, 17] Claims regarding this topic are often based on research on phantoms or within strictly defined patient populations, commonly investigating only a single indication within the scope of image-guided interventions. This limits the extent to which the results of these studies may be extrapolated to the clinical practice or to other application areas. Furthermore, the extent to which these researches can be compared to each other is limited because the methods of data acquisition adopted in these studies are often significantly different. Lastly, the impact of introducing these devices within the clinical workflow is often neglected, but plays an important role in the clinical applicability and acceptability.

The work of Arnolli, Hanumara, Franken, Brouwer and Broeders (2015) provides an overview of systems developed for CT- and MRI-guided percutaneous needle placement, in which the trends in the state-of-the-art were analyzed. Although the devices, the provided needle guidance and the underlying methods of operation were described in detail, a qualitative and quantitative comparison of the devices was not provided. The aim of the current paper was to present an overview on the (pre-)clinical experience with robotic systems intended for use during CT-guided interventions, focusing on reported performance measures and the added value that introducing these technologies within clinical practice can provide.

Methods

A literature search was performed in PubMed. The terms 'robot', 'device', 'computed tomography', 'CT', 'CT-guided', 'CT-fluoroscopy guided', 'CTF-guided, 'percutaneous', 'needle positioning', 'needle placement', 'ablation' and 'biopsy' were used as free text words and in different combinations during the search. Additionally, the search was extended by reviewing the references of the found publications. Articles published between 2013 and 2018 were screened on title and abstract to assess eligibility.

The publications on each of the devices were reviewed for (i) the intended/current application area, (ii) the method of needle guidance and the main principles underlying the design, (iii) the suggested workflow, and (iv) preliminary results, including placement accuracy, procedural success rate, complication rate and influence on procedural time or (patient) radiation exposure. Statements regarding the applicability within the daily clinical workflow, such as advantages or disadvantages of the design, and assumptions made during device development, were also reviewed.

An overview was created based on system function and the provided needle guidance, according to the method of categorization as proposed in [3] and that is shown in Figure 1. The devices are categorized based on the type of guidance they provide, the first group provides active, physical guidance during needle placement, whereas the second group of systems provides (passive) feedback on how to position the needle, additional to the imaging data that is conventionally available.

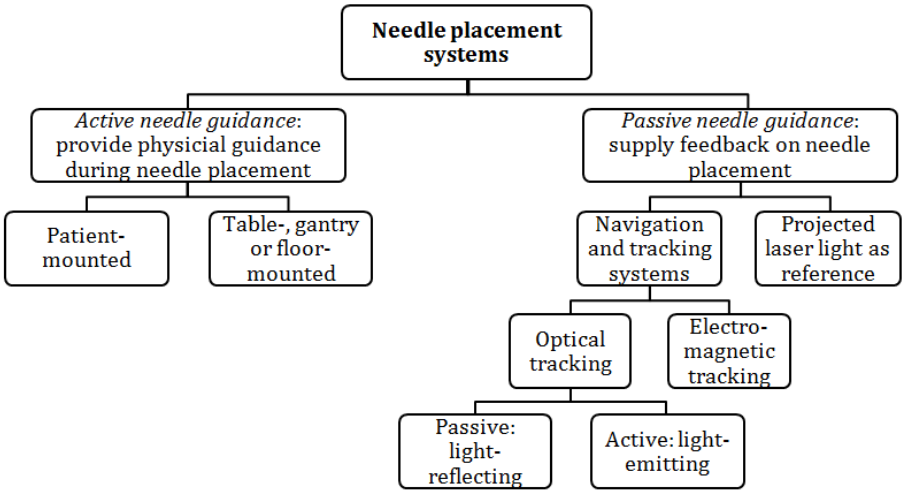

Figure 1. Overview of the method of device categorization, based on system function.

Results

This section presents an overview of the included studies evaluating the performance of robotic assistance or navigation technology during diagnostic or therapeutic image-guided percutaneous interventions. A summary of these studies is provided in Table 1. The results from each of the studies regarding procedural time, target positioning error, patient radiation exposure and clinical outcome are listed in Table 2, Table 3, Table 4, and Table 5 respectively. If the study did not evaluate the outcome measure, then it was not included in the tables.

Active needle guidance

Patient-mounted

These devices are positioned onto the external skin surface of the patient during the procedure. In case of any patient motion, the device will move together with the patient. [3, 18] This includes movements introduced by changes of the patient position and those induced by the respiratory motion. The trajectory guidance hereby automatically alters to the current situation. It is hypothesized that this has a beneficial effect on the precision and accuracy of the needle guidance compared to table-, gantry- or floor-mounted devices, provided that there is no underlying software package used for path planning that accounts for perprocedural motion.

The XACT robotic device (XACT Robotics, Ltd, Caesaria, Israel) is an example of a patient-mounted device. The general workflow is as follows. First, the robot is placed on the patient and secured with four detachable straps that are attached to a rigid body positioned between the patient and the CT-table. Based on CT-imaging and fiducials located within the device, the registration is then performed. The user indicates the needle entry point, the target and checkpoints. The needle is advanced in an end-expiratory window in a stepwise manner, enabling the acquisition of control images and evaluation of the needle path at each checkpoint. Important features of this device include the fact that the robot positioning unit is able to correct the trajectory by steering the needle during the procedure and that respiration-induced motion is taken into account within the workflow. Changes in the thoracic circumference are sensed by a dedicated motion sensor that was coupled to the device.

Currently, a prototype of this device has been evaluated in a pre-clinical animal study by [19]. A total of 45 simulated biopsies were performed in several anatomic locations. Although a technical failure occurred in two cases and needle reinsertion was

required to ensure a safe puncture in four cases, the achieved complication rate was very low with a high targeting accuracy (<3 mm), even for organs susceptible to deformation and respiration-induced motion. These results are promising, but the used device was a prototype and the results were not compared to the conventional method. Additionally, the effect of using this device on the total procedural time, patient and physician radiation dose and procedural success rates were not assessed as the main focus of this study was the accuracy of needle placement. The device has recently been CE-marked, which enables the evaluation of the actual feasibility and applicability of the device in clinical studies, assessing the performance in a broad spectrum of procedures, anatomical target areas and outcome measures.

Table-, gantry- or floor-mounted

The guidance provided by these type of systems is often characterized by the stability of the needle trajectory and therefore high reproducibility, as the devices are fixed to the CT-table, -gantry or the floor. [3] However, an important drawback is that for most of the devices the assumption is made that the patient anatomy remains static throughout the planning and execution of the procedure. The validity of this assumption should be questioned, as patient motion [20], respiration [5, 21, 22] and needle advancement within the body may induce movement of the target lesion, especially for non-rigid target organs. [23, 24]

The ROBIO EX (Perfint Healthcare, Chennai, India) and the MAXIO (Perfint Healthcare, Chennai, India) are examples of floor-mounted devices that provide physical assistance during diagnostic and therapeutic CT-guided interventions. In short, the workflow exists of the following steps. First, the device is positioned on floor-mounted registration plate and a planning CT-scan is acquired of the patient, including the target lesion and needle entry point in the field of view. The user then identifies the location of the target lesion and an adequate needle entry point on the skin. From the provided input, the needle path is automatically calculated. The robot arm then positions and orients the needle guide located on the robot arm accordingly and the physician is enabled to insert the needle manually. [25]

Abdullah and colleagues (2014) have assessed the performance of the ROBIO EX during clinical use in providing robotic assistance during percutaneous thermal ablation of primary and secondary hepatic malignancies. [26] Their evaluation of the ROBIO EX only describes their preliminary experience in the use of robotic assistance during CT-guided intervention, but shows promising results in terms of success,

usability and radiation exposure. The usability, described as assessed performance level, varied between 'good' and 'excellent', with a mean performance level of 4.6/5.0. Also, the patient radiation dose was reduced compared to a historical control group. [26]

Anzidei et al. (2015) have also reported their preliminary clinical experience with the ROBIO EX in providing robotic assistance during CT-guided biopsies of lung lesions, [17] and have evaluated the device in a more quantitative manner. The use of robotic assistance was associated with lower procedural time and patient radiation exposure, but no significant differences were found in the precision of needle placement, the procedural success and the complication rate. [17] Strengths of this study include the study design; the sample size was relatively large and the patients were enrolled in a prospective, randomized and controlled manner. All procedures were performed by a single, highly experienced radiologist, which eliminates potential inter-operator variability. However, the definitions of performance measures procedural time and patient radiation dose were unclear. It was unclear whether the time required to position and dock the system was incorporated or not, which influences the extent to which the use of robotic assistance would decrease the total procedural time. For the measurements of radiation dose, it was unclear whether the DLP was reported for all CT acquisitions, or that only the DLP attributed to CT's acquired during needle positioning was presented. Unfortunately, this limits the extent to which their results can be compared to other studies.

The research group of Abdullah and colleagues has also evaluated the MAXIO, the successor of ROBIO EX. Again, the results achieved with the navigated approach were not compared to a control group, but the authors describe the device to be promising in terms of success, safety and performance. The authors report successful thermal ablation and no procedure related complications in all cases, as well as a mean performance level of 4.4/5.0, which indicates the radiologists rated the navigated approach to be superior to the manual needle insertion technique is most cases. [14] However, multiple factors decrease the extent to which these studies contribute to the evidence base. First of all, the method of patient selection was not described and the results were either not compared to a control group or to historical controls. Second, no definitions were provided on when the lesion targeting, needle positioning and ablation procedure were deemed as adequate or successful. Furthermore, the influence of using robotic assistance on procedural time was not evaluated. Lastly, different ablation

systems were used, which influences the amount of target movement induced by needle insertion, and therefore needle placement accuracy. [23]

Smakic et al. (2018) have also clinically investigated the performance of the MAXIO robotic assistance during CT-guided diagnostic and therapeutic procedures in a prospective, single-center study. [25] The precision of needle placement was higher in the intervention group than the control group, but no statistically significant differences were found for the outcome measures patient radiation exposure, interventional time and complication rate. [25] However, a few factors in the study design have increased the risk of bias and should be considered during evaluation of these findings. First, the results of the prospective, navigated procedures were compared to historical controls instead of contemporaneous controls. Secondly, three radiologists conducted the procedures, which means that inter- and intra-operator variability may have affected the results. Furthermore, the number of therapeutic procedures was higher for the navigated group than the control group (respectively 33/55 patients, 67%, and 46/101 patients, 46%), which also shows from the number of needle placement per procedure, respectively 1.6 and 1.0 per procedure. Finally, the device was used during biopsy procedures and microwave ablation and irreversible electroporation procedures in a large range of different target organs, which were not specified. However, the outcome measures may be related to the type of organ.

Evaluating the benefits and disadvantages of these type of devices according to the outcomes of the above mentioned studies: all authors report that the use of robotic assistance is promising. The strengths of these devices include the simple workflow, the potential to reduce patient and physician radiation exposure and the fact that no disposable consumables are required to use the system, which reduces the cost per use. The set-up effort for both the ROBIO EX and MAXIO devices is limited, which facilitates the process of mounting and registering the device to the acquired imaging datasets. For example, in [17] the robotic assistance of ROBIO EX caused the procedural time of CT-guided biopsies of lung lesions to decrease. This is quite remarkable, as the biopsies were performed by a physician with 8 years of experience and the fact that the procedural time for biopsies performed in the thoracic region is often already lower than for other anatomical areas and furthermore. This is very promising, but only if the set-up time was incorporated in the procedural time. Otherwise, the additional effort to set-up the device before use may outweigh the potential reduction in needle placement time. [25]

The most important limitation that was identified for these devices is that the path planning is based on a static CT-scan; therefore, approaches using breath-holds [17, 25] or end-expiratory apnea [14, 25, 26] were currently used in respectively conscious and generally anesthetized patients to improve the needle placement accuracy in case of target organ movement under influence of the respiration. The majority of patients remain conscious during image-guided procedures. Especially for this patient group, this could be a significant drawback as the reproducibility of breath-holds on patients is limited. [27]

Passive needle guidance

Navigation and tracking systems

The feedback of the real-time position and orientation of an instrument is provided in relation to anatomical imaging. To accomplish this, the coordinate systems of the instrument, patient anatomy and medical imaging dataset need to be registered; often optical or electromagnetic (EM) tracking devices are used to do so. [3]

An example of a navigation system based on electromagnetic tracking is the IMACTIS® device (Imactis, Grenoble, France). The system is intended for a broad range of CT-guided percutaneous procedures, including drainage, biopsy, ablations and other punctions. A magnetic field generator is positioned near the needle entry site and an electromagnetic sensor is embedded in the needle holder. The system enables the physician to track and evaluate the needle trajectory by visualizing the (real-time) needle trajectory on static CT-images. [11, 28]

Moncharmont et al. (2015) have also investigated the performance of the IMACTIS robotic assistance during CT-guided procedures in a prospective, randomized, comparative study in phantoms. They found that the navigation system enabled operators to decrease the path planning and needle positioning time. It also enabled them to position the needle tip more closely to the target on their first attempt. The authors have conducted a study in a very large operator population consisting of 54 subjects. However, the test set-up was rather different from the clinical practice. First of all, the needle positioning was performed on a simple phantom consisting of pre-pierced PVC plates. Only double-oblique punctures, that require needle angulation in both mediolateral and craniocaudal directions and that represent complex punctures, were simulated. Second, no perprocedural CT-imaging was available, so only the accuracy of the initial placement could be evaluated. Lastly, the majority of the included operators were inexperienced; including mostly diagnostic radiologists, radiology

residents and even radiology technicians. It is questionable whether the results can be translated to a more experienced operator group.

The performance of the IMACTIS device was also evaluated in a multi-center prospective randomized controlled trial (ClinicalTrials.gov Identifier: NCT01896219) including 500 patients. The trial was conducted to evaluate the clinical benefit of this device by comparing the safety, efficiency and performance to the conventional freehand method. [11] Unfortunately, the results of this study are not published yet.

Evaluating this type of systems based on these preliminary findings, one of the major advantages of a tracking and navigation system is that they enable the physician to evaluate the feasibility of different trajectories and entry points in real-time. However, as electromagnetic tracking is used, the device cannot be used in patients with non-EM-compatible devices or implanted material, such as pacemakers and implantable cardioverter defibrillators, due to potential interference. The same is true for patients with implanted ferromagnetic materials, as these materials may distort the electromagnetic field and therefore potentially decrease the accuracy of the navigation. [11, 29] Furthermore, to use the IMACTIS device, few consumables for single use are required, including the needle holder and a sterile drape to cover the EM-receiver that is connected to the needle holder. [11] Similar to other devices, the provided guidance is based on the assumption that the needle is rigid and the needle follows a straight path towards the target lesion. As the EM sensor is located in the needle holder, any deflection of the needle will negatively influence the needle positioning accuracy. Also, the device cannot track and therefore account for respiration-induced motion, which causes the need to adopt a breath-hold approach during certain procedures in order to increase the accuracy of needle placement.

Table 1 : Summary of included studies evaluating the performance of robotic assistance or navigation technology during diagnostic or therapeutic image-guided percutaneous interventions

Study	*Device*	*Study type and number of subjects*	*Procedure and anatomy*
Ben-David (2018)	XACT	Non-randomized, uncontrolled preclinical animal study with 8 animals (45 needle placements)	Biopsy (simulated) in lung, liver, kidney and retroperitoneum
Abdullah (2013)	ROBIO EX	Non-randomized, uncontrolled clinical study with 11 patients (17 navigated needle placements)	Radiofrequency ablation of hepatic lesions
Anzidei (2014)	ROBIO EX	Prospective, randomized controlled clinical trial with 100 patients (50 navigated and 50 freehand needle placements)	Biopsy of lung lesions
Abdullah (2014)	MAXIO	Non-randomized, uncontrolled clinical study with 20 patients (40 needle placements)	Radiofrequency and microwave ablation of hepatic lesions
Smakic (2018)	MAXIO	Prospective non-randomized clinical study with retrospective controls with 156 patients (89 navigated and 101 freehand needle placements)	Biopsy, microwave ablation, irreversible electroporation in a broad spectrum of organs (not specified)
Moncharmont (2015)	IMACTIS	Randomized, comparative phantom study with 2 targets (54 navigated and 54 freehand needle placements	Punctures in a PVC phantom
Durand (2017)	IMACTIS	Prospective, randomized, controlled clinical trial with 120 patients (60 navigated and 60 freehand needle placements)	Biopsy, infiltration, drainage, sympathicolysis, and thermal ablation therapy in lung, liver, adrenal gland and bone.
Wallach (2014)	Atlas and CasOne	Non-randomized, comparative phantom study with 5 targets (25 navigated freehand, 50 navigated with an aiming device)	Puncture in an anthropomorphic 3D model of the liver (anatomy, vascular structures and lesions)
Moser (2013)	LNS	Randomized, comparative phantom study with 60 targets (30 navigated and 30 control needle placements)	Injections in an anthropomorphic plastic model of lumbar spine
Moser (2013)	LNS	Prospective randomized clinical trial with 29 patients (29 navigated, 29 control needle placements)	Epidural and perineural lumbar injections in the lumbar spine region
Gruber-Rouh (2015)	LNS	Prospective, randomized, comparative clinical study with 58 (29 navigated, 29 control needle placements)	Biopsy of lung, lymph node, liver, adrenal gland and bone lesions, drainage of fluid in abdominal or thoracic cavity

Table 2: Procedural time

Device [ref]	*Time (minutes)*	*Comments*
XACT [19]	nav: 30 – 45 min	Procedural time included set-up time.
ROBIO EX [17]	nav 20.1 ± 11.3 min vs. control 31.4 ± 10.2 min ($p < 0.05$)	Time: included planning, but specific definition was not provided.
MAXIO [25]	nav: 20.6 ± 11.4 min vs. control: 22.1 ± 9.4 min ($p > 0.05$) Subgroup analysis of out-of-plane needle insertion: nav: 17.4 min ± 10.9 min vs. control: 33.3 ± 7.2 min ($p< 0.05$)	Procedural time: time between acquisition of first CT-scan and confirmation of adequate needle tip position.
IMACTIS [28]	nav: 01:16 min (IQR: 00:50 - 01:58 min) vs. control: 03:34 min (IQR: 03:01 - 04:24 min)	Procedural time: includes both path planning (required position and orientation of needle) and needle insertion itself.
Atlas and CasOne [13]	nav: 02:29 min ± 01:06 min vs. nav+ad/adc: 05:02 min ± 02:39 min vs. nav+ad/pdc: 02:14 min ± 00:57 min	Total procedural time: no exact definition is provided, assumed: time between start positioning aiming device (if applicable) or time start needle positioning and time needle positioned adequately.
LNS [12]	Phantoms: nav: 05:04 + 03:15 vs. control: 09:18 ± 03:50 ($p < 0.05$) Clinical: nav: 06:54 + 01:22 vs. control: 09:00 ± 03:40 ($p < 0.05$)	Procedural time: time between first planning CT acquisition and control CT-scan showing adequate needle tip placement.
LNS [16]	nav: 12:37 min vs. control: 15:22 min ($p < 0.05$)	Procedural time: manually added average time between first insertion (of the interventional needle) and intervention ended.

Table 3: Target positioning error

Device [ref]	*Target positioning error (mm)*	*Comments*
XACT [19]	nav: 1.8 mm ± 1.4 mm	
ROBIO EX [17]	x-direction: nav: 2.3 ± 1.1 mm vs. control: 3.0 ± 1.3 mm y-direction:nav: 2.5 ± 1.5 mm vs. control: 2.1 ± 1.6 mm (p = 0.05)	
MAXIO [25]	nav: 1.2 ± 1.6 mm vs. control 2.6 ± 1.1 mm (p < 0.05)	Target positioning error: difference between planned and achieved needle tip position.
IMACTIS [28]	nav: 3.7 mm (IQR 2 - 6.7 mm) vs. control: 15 mm (IQR 10 - 20 mm) (p < 0.05)	Accuracy determined at first needle placement attempt.
Atlas and CasOne [13]	nav: 4.9 ± 1.7 mm vs. nav + aiming device and active depth control: 4.6 ± 1.3 mm vs. nav + aiming device and passive depth control: 4.6 ± 1.2 mm	Target positioning error: 3D distance between needle tip and target.
LNS [12]	nav: 2.0 ± 1.2 mm vs. control: 3.0 ± 1.7 mm (p < 0.05)	Target positioning error: 3D difference between planned and achieved needle tip position.

Table 4: Patient radiation exposure

Device [ref]	*DLP due to CT-fluoroscopy [mGy·cm]*	*DLP total procedure [mGy·cm]*	*Comments*
ROBIO EX [26]	nav: 383 ± 180 mGy·cm	nav: 956 ± 400 mGy·cm vs. control: 1703 mGy·cm	Total procedural DLP contains both CTF as CT-scans.
ROBIO EX [17]	-	nav 324 ± 115 mGy·cm vs. control 541 ± 447 mGy·cm (p < 0.05)	DLP: unclear whether only procedure, or also planning and control.
MAXIO [14]	nav 352 ± 228 mGy·cm vs. control 501 ± 367 mGy·cm (p > 0.05)	nav. 1382 ± 536 mGy·cm vs. control 1611 ± 708 mGy·cm (p > 0.05)	DLP: subdivided in CTF-induced dose and total procedural dose. Historical control group was used to compare radiation doses to.
MAXIO [25]	nav: 140 ± 111mGy·cm vs. control: 103 ± 72 mGy·cm (p > 0.05)	-	DLP procedure: unclear whether only interventional CT-scans, or also planning and control scans included in reported DLP values.
LNS [16]	nav 43 mGy·cm (range: 10 - 125 mGy·cm) vs. control 60 mGy·cm (range: 25 - 176 mGy·cm) (p < 0.05)	nav 402 mGy·cm (range: 15 - 176 mGy·cm) vs. control 457 mGy·cm (range: 10 - 125 mGy·cm)	Total procedural DLP: unclear whether only CTscan, or also CTF.

Table 5: Clinical outcomes

Device [ref]	*Success*	*Complications*	*Comments*
XACT [19]	43/45 (2x: needle advancement not possible)	2% (pneumothorax 1/43 total cases, of which 13 were lung procedures)	
ROBIO EX [26]	Technical success: 10/11 patients (1 no confirmation on CE-CT due to renal impairment)	none	
ROBIO EX [17]	nav 92%, control 94%, p = 0.05	nav 10% vs. control 11% (p = 0.05)	Success: defined as diagnostic biopsy.
MAXIO [14]	Success: 19/20, 1 case of residual disease	none	Success: undefined when needle placement was successful.
MAXIO [25]	-	nav 7% vs. control 11% (p > 0.05)	
IMACTIS [28]	nav: 41%, control: 0%	-	Success defined as: needle tip adequately positioned at target lesion at first needle placement attempt.
LNS [12]	Success rate: nav 100%, control 100%	nav 0% vs. control 0%	
LNS [16]	-	nav: bleeding in 2 patients vs. control: 6 pneumothorax, 2 bleeding	

Discussion

An overview has been created by identifying research on previously existing and newly developed devices intended for use within the field of image-guided percutaneous procedures. Several factors may influence the extent to which these type of devices are adopted within the clinical practice.

The clinical feasibility and applicability of these devices depend on multiple factors, including but not limited to: (i) the intended interventional aim, distinguishing diagnosis and therapy, (ii) the intended anatomical target region, and (iii) the intended setting, for instance the type of hospital, discerning university medical centers, peripheral teaching hospitals and peripheral hospitals. These factors strongly influence the requirements that the new technology should meet, but they are not frequently discussed within the available literature. Additionally, research conducted to assess the performance of needle guidance technology often focuses on one of the many facets of image-guided procedures, especially for the evaluation of the benefit that these systems provide.

Many performance assessments have focused on whether needle guidance technology increased the tool positioning accuracy, as a common hypothesis is that improves the procedural success rate and outcome. [12-14, 17, 25, 28] Yet, for only a selected range of procedures a needle positioning accuracy between 1 – 5 mm is necessary to achieve procedural success. Examples include therapeutic percutaneous procedures, such as irreversible electroporation (IRE) and thermal-based ablation therapy. During IRE, multiple electrodes need to be positioned parallel to each other to ensure adequate tissue conductivity and therefore technical success. The achieved needle angulation should not deviate more than 10 degrees from each other, as this may cause reversible electroporation and unsuccessful therapy. [30, 31] During thermal-based ablation therapy accurate needle tip positioning is also important. The complexity of needle insertion increases especially for larger tumors, when multiple radiofrequency electrodes or microwave antennas are used to achieve a larger ablation zone covering both the lesion and an additional safety margin. Increasing the positioning accuracy may help to decrease the rate of inadequate ablation of the safety margin, a known risk factor for ablation site recurrence, but also to preserve the surrounding tissues as much as possible.

On the other hand, in most diagnostic procedures the only accuracy requirement is that the needle tip is positioned within the target. Therefore, the needle placement error should be lower than at least half of the lesion size. A prospective analysis of 1000 procedures found most lesions were between 20 – 50 mm in size, with a total range of 1 – 21 cm. [32] A needle placement error of 5 mm would therefore be sufficient in the vast majority of cases, which is achieved by most of the described devices in preclinical [12, 28] and clinical settings [17, 25].

Thus, even though robot-assistance or navigation technology may improve tool positioning accuracy, this does not necessarily provide added value to daily clinical practice and is dependent on the procedural aim. In the case of diagnostic procedures, the target positioning error should be considered as a requirement in order to be able to even perform at the same level as the conventional freehand approach. In the author's opinion, the current needle positioning accuracy is not the main clinical problem. On contrary, in the case of therapeutic interventions such as IRE and thermal ablation, decreasing the target positioning error may lead to better procedural outcomes. Here, the use of needle guidance technology seems promising and may improve patient care.

In the extension of the previous argument, the intended type of user and hospital are also important in the evaluation of the potential performance of these technologies and the added value they provide within daily clinical practice. The complexity of cases presenting at a large university medical center is usually higher than for smaller, peripheral hospitals. This is reflected in physician experience, the number of cases per year, the diversity of procedural types and the amount of conducted research. Especially for complex cases, the use of needle guidance technology may aid in improvements of the procedural outcome. Therefore, the window of opportunity within the daily practice of a peripheral center is expected to be much narrower, but this should be evaluated critically based on clinical data of a broad range of procedures and anatomical targets areas.

The extent to which these devices are adopted within daily practice is also dependent on the evidence showing that the introduction of needle guidance technology would solve current clinical problems. In the author's opinion, the amount of high-quality evidence is low, which can be attributed to several factors. Most of the research is performed either on phantoms or in a clinical setting without comparing the results to those achieved with the conventional freehand approach, which leaves the true added value of needle positioning technology unclear. Also, the research scope is often limited, meaning that commonly a single procedure, anatomical target or performance measure are investigated. Lastly, a large variety exists in the methods adopted to assess the performance, which limits the extent to which the studies can be compared to each other and to clinical data.

Another reason that may prevent widespread adoption of these technologies is the fact that the assumptions that were done during device development may not be applicable within clinical practice. A common assumption is that the needle follows a straight path within the body and that the target and surrounding tissues remain at the same position throughout the whole procedure. Therefore, needle deflection, patient motion, respiration and the needle insertion itself may cause needle targeting errors. Incorporating a method to encompass or minimize these effects could optimize the clinical applicability and feasibility of needle guidance technology.

Furthermore, the influence of the device on the current workflow in terms of procedural time, efficiency, learning curve and ease of use should not be underestimated as they are an important factor in the overall applicability and feasibility of these devices. During the evaluation of performance, it is often described that systems that are time consuming in terms of usage, e.g. due to pre- or

intraprocedural data import of processing are less feasible to adopt within daily clinical practice. [14] Disadvantages of novel needle guidance systems, such as additional set-up times, slow down or may even prevent the process of adopting and implementing these techniques within clinical practice, [12] as the added value does not outweigh the disadvantages.

To conclude, the amount of high-quality evidence regarding the merits and disadvantages is limited. Creating quality improvement guidelines for evaluating and reporting the performance could improve the extent to which the performance of new devices can be compared to those achieved during current clinical practice and to the performance of other devices. Furthermore, clinical data should be acquired over a broad spectrum of procedures, anatomical targets and performance measures to act as a benchmark to adequately assess the benefits and drawbacks of adopting these kind of technologies within daily clinical practice. Lastly, the incorporating a method to encompass or minimize the unwanted effects of target motion on needle positioning accuracy could optimize the added value that needle guidance technology is able to provide within daily clinical practice.

Chapter 3 – Quantification of the efficacy of percutaneous CT-guided interventions

Introduction

The efficacy of CT-guided interventions has often been assessed in published studies. However, often these reports focus on a single diagnostic or therapeutic procedure, an anatomical target region or specific outcome measures. To adequately evaluate the added value of needle guidance devices, a broad overview should be available to compare the results achieved in the daily clinical practice with those achieved with robotic assistance.

However, a clear overview, aiming to quantify the procedural efficacy of diagnostic and therapeutic CT-guided interventions performed in a wide range anatomical targets, is lacking to the best of the author's knowledge. This hinders the ability of both the end-users and product developers to adequately evaluate the claims regarding needle guidance technology, to assess the current procedural efficacy, and thus to identify the potential merits and disadvantages of adopting these technologies within current clinical practice. The aim of this study was therefore to create more insight in the current clinical practice at a large peripheral medical center in the Netherlands. The procedural efficacy was assessed by evaluating procedural time, number of needle manipulations, patient radiation dose and procedural outcomes of CT-guided interventions.

Methods

Study design

A single-center, prospective, observational study was conducted at the Meander Medical Center in Amersfoort, the Netherlands. The study protocol was evaluated and approved by the Institutional Review Board. The study population was selected from the group of patients scheduled for CT-guided interventions in the four-month period between April 2018 and July 2018. Patients were scheduled to undergo a percutaneous intervention based on clinical relevance; either for diagnostic purposes to obtain tissue samples for histopathological analysis of suspected malignancies by means of needle biopsy, or for therapeutic purposes such as drainage, ablation or placement of iodine

seeds. All procedures took place in a dedicated interventional CT suite at the radiology department of the Meander Medical Center.

Study population

Adult patients (≥ 18 years) who were scheduled for a CT-guided percutaneous intervention were informed about the study prior to the procedure. Written informed consent was obtained of each of the participating patients. According to the CIRSE guidelines on percutaneous needle biopsy, contra-indications for CT-guided interventions, and therefore inclusion in this study, included lack of a safe access route, uncorrected coagulopathy and patient refusal. [33] The patient's coagulation status was assessed prior to the procedure according to interventional radiology guidelines. [34]

CT-guided intervention protocol

All image acquisitions were performed using a 64-slice CT-scanner (Siemens SOMATOM Definition AS, Siemens Healthcare, Erlangen, Germany). Prior to the start of the procedure, one of the CT technicians prepared the CT-imaging protocols from the control room, which was adjacent to the dedicated interventional CT suite, while the patient was received in the CT room and was assisted to position themselves on the CT-table by the other CT technician. Patients were positioned in a prone, supine or lateral recumbent position depending on the location of the target lesion as determined on pre-interventional imaging studies.

Patients remained conscious and unsedated in most procedures. Patients scheduled for ablations were sedated to increase patient comfort during the procedure and provide adequate pain management. Patients were also sedated during drainage procedures in case it was expected that surrounding tissues were severely inflamed and puncture would expose the patient to excessive pain.

A spiral CT-scan was acquired of the anatomic region of interest and relevant surrounding tissues to plan the needle path. The scan range was limited where possible to reduce patient exposure to radiation. In some cases, intravenous contrast was administered to enhance the visualization of the target or surrounding anatomy. The dataset was then displayed on the workstation positioned in the CT control room to enable the physician to identify the lesion and the needle target position. The needle entry point was chosen such that the planned needle trajectory did not traverse any critical or impenetrable structures. The slice position of the chosen entry point was retrieved from the DICOM data.

The CT technician subsequently moved the CT-table with the patient to the planned slice position, and in case an out-of-plane needle path was planned, the gantry was angulated. A laser line was projected from the CT gantry to indicate the slice position. A radiopaque marker, such as a grid, a line marker or a hypodermic needle, was placed onto the patient's skin at the indicated laser line. The needle entry point on the skin, located at the intersection of the CT gantry laser line with one of the radiopaque markers, was then indicated with a black permanent marker and the radiopaque markers were removed. The skin was disinfected using chlorhexidine and the area around the needle entry position was covered with sterile drapes.

A local anaesthetic was then administered in and around the planned needle trajectory and a small incision was made at the needle entry site. Subsequently, a coaxial needle was inserted in a stepwise manner: the necessitated needle position and orientation were estimated based on the path planning, and the needle was advanced using the CT gantry laser light to keep the needle within the axial plane. To reduce exposure to radiation while remaining present in the CT-room during fluoroscopic imaging, the radiologist wore a protective lead apron and thyroid collar and either stood beside the gantry or increased their distance with respect to the gantry when images were made. Three axial fluoroscopic CT slices were acquired using a foot pedal and were displayed on an in-room monitor to visualize the new position of the needle tip with respect to the predefined target. This process of estimation, advancing the needle and imaging was iterated until the tip of the introducer needle was located within the target lesion. The inner stylet was then removed from the introducer needle and replaced by the interventional needle to carry out the intervention. The interventional needle was removed, together with the introducer needle, once the procedure was finished. If it was deemed necessary by the radiologist, a (spiral or fluoroscopic) control CT-scan was acquired immediately after the procedure to rule out adverse events.

Standard post-procedural care consisted of a two to four hour monitoring period after the completion of the procedure, during which patients were observed, the pain was evaluated and vital signs were checked. After lung biopsies, imaging control was performed by acquiring a control chest radiograph two hours after the procedure to rule out pneumothorax or haemorrhage. In case of biopsies, the tissue samples were fixed in formalin for histopathological analysis.

Data acquisition

Subjects enrolled in the study received the regular treatment according to the hospital guidelines. All data were acquired by one of the investigators through either retrospective analysis of the medical records of the patients or perprocedural observations.

Baseline patient, lesion and needle insertion characteristics

Baseline patient characteristics, including patient age and gender, were denoted prior to the start of the procedure. Additional clinical information included target organ and organ system, and the type of intervention, subdivided in (i) biopsy, (ii) drainage, (iii) ablation and (iv) placement of iodine seeds. Other data relevant to the procedure was also assessed: the lesion size, the distance between the needle tip and the skin entry point and the angulation of the needle with respect to the vertical image axis. The lesion size was measured in mm on the path planning CT-scan for both the long and short axis. The needle insertion depth and angle were determined on the (fluoroscopic) CT image showing the needle tip located within the target, as shown in Figure 2.

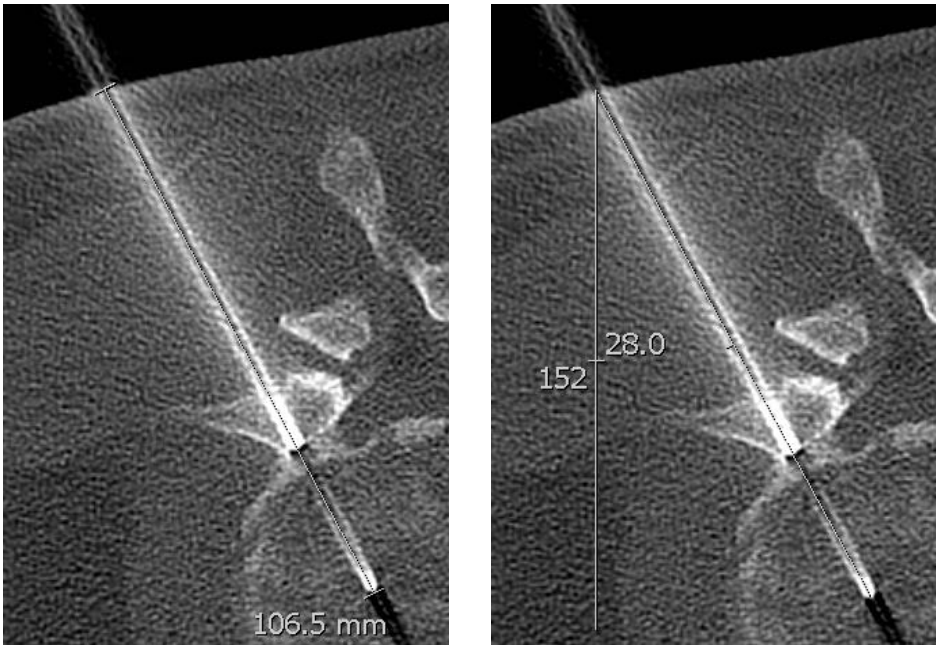

Figure 2. Method of measuring the needle insertion depth (left image) and angulation with respect to the vertical image axis (right image). Needle insertion depth was defined as the distance between the skin entry point and the needle tip (in mm). The angulation was determined as the angle between the needle path and the vertical image axis.

The number of times the needle was manipulated, defined as either advancing the needle or correcting the angle of the needle and subsequently acquiring a control (fluoroscopic) CT-scan, was determined by clinical observations. The number of needle manipulations was counted for: (i) the insertion of the hypodermic needle to administer the local anesthesia, (ii) the insertion of the coaxial needle, counting until the needle tip of the interventional needle, such as a biopsy needle, was located at the target lesion for the first time, (iii) the repetitions of the intervention, e.g. to acquire additional biopsies after the first tissue specimen was obtained.

Procedural time

The time (in minutes:seconds) was recorded by means of a stopwatch, denoting the times of the start and end of each of the predetermined phases on a dedicated reporting form. The procedure was subdivided into the following phases: (i) *preparation*: the time between the previous patient leaving and the participating patient arriving in the interventional CT room, (ii) *patient preparation*: the time between arrival of the patient in the interventional CT room and the first (spiral) CT-scan, (iii) *path planning*: the time between the first (spiral) CT-scan, marking the needle entry point on the patient's skin and the first (hypodermic) needle insertion to administer the local anesthetic, (iv) *needle targeting and positioning*: the time between the first (hypodermic) needle insertion and the time that the needle tip was positioned at the target lesion, such that the (first) intervention could take place, (v) *intervention*: the time the positioning of the needle tip at the target lesion and the completion of the intervention, defined as retraction of both the introducer and interventional needle and (vi) *completion of the procedure*: the time between retraction of the needle and the departure of the patient from the interventional CT room. The procedural time was calculated by summing the durations of the phases *path planning, needle targeting and positioning* and *intervention*.

Patient radiation exposure

The patient radiation exposure was evaluated for both the spiral and fluoroscopic CT-scans by means of the dose-length product (DLP, in mGy·cm), which was retrieved from the patient protocol that was automatically generated by the software of the CT-scanner. Additionally, the number of times fluoroscopic CT-scans were acquired during the procedure was documented.

Clinical outcome measures

Additional to the primary outcome measures procedural time, number of needle manipulations and patient radiation exposure, the procedural success rate and complication rate were determined as measures for clinical outcome. A non-diagnostic biopsy was defined as an insufficient amount of material to perform histopathological analysis and achieve a diagnosis based on the specimen. Complications were defined according to the guideline for classification as provided by the Cardiovascular and Interventional Radiological Society of Europe and the Society of Interventional Radiology. [33, 35]

Statistical analysis

IBM SPSS Statistics software version 23.0 for Windows (IBM Corporation, Armonk, NY, USA) was used for the data analysis. The Shapiro-Wilk test was used to test the assumption of a normal distribution of the data. Normally distributed data were represented using mean ± standard deviation, whereas median (range: minimum value – maximum value) was used to display non-normally distributed data. A p-value ≤ 0.05 was considered statistically significant.

Results

A total of 64 image-guided interventions were observed. The data from one ablation procedure were excluded as ultrasound was used as imaging modality instead of CT. The 63 CT-procedures were carried out by eight radiologists and four radiology residents from our radiology department. The less experienced radiologists and the residents performed the procedures under supervision of, or together with, a more experienced radiologist. The radiologists have performed a total of 43 procedures, with a median of six procedures per physician (range: 1 – 19). The radiology residents have carried out a total of 20 procedures under supervision, each resident performing a median of three procedures (range: 1 – 13).

Baseline patient, lesion and needle insertion characteristics

The most prevalently performed procedure was biopsy, accounting for a total of 54 interventions (86%) within the studied patient group, followed by drainage (n = 6), ablation (n = 2) and placement of iodine seeds (n = 1). The most commonly targeted lesions were respectively lung (n = 24), skeletal (n = 14) and peritoneal lesions (n = 7). Table 6 summarizes the baseline patient characteristics.

Table 6: Baseline patient and procedural characteristics	
Age (years)	66 (36 – 84)
Gender	*n* = 63 (100%)
Male	35 (56%)
Female	28 (44%)
Intervention type	
Biopsy	54 (86%)
Drainage	6 (10%)
Ablation	2 (4%)
Placement of iodine seeds	1 (2%)
Target organ of intervention	
Adrenal gland	3 (5%)
Bone	14 (22%)
Fluid in the abdominal cavity	6 (10%)
Kidney	2 (3%)
Liver	1 (2%)
Lung	24 (38%)
Lymph node	6 (10%)
Peritoneum	7 (11%)

Data are presented as median (range) or as total number *n* (percentage of total %).

Table 7: Baseline lesion and needle insertion characteristics

	Lesion size, long axis [mm]	*Lesion size, short axis [mm]*	*Needle insertion depth [mm]*	*Needle angulation [°]*	*Nr. of needle manipulations*
Biopsy					
Thorax (*n = 24)*	31 (6 – 75)	23 (5 – 53)	79 (52 – 113)	29 (1 – 115)	8 (5 – 15)
Abdomen (*n* = 25)	28 (11 – 55)	23 (10 – 48)	112 (63 – 165)	19 (2 – 78)	10 (6 – 25)
Bone (*n* = 14)	28 (10 – 44)	18 (7 – 43)	85 (46 – 117)	28 (8 – 67)	12 (4 – 25)
Total (*n* = 55) *	31 (6 – 75)	22 (5 – 53)	89 (46 – 165)	26 (1 – 115)	9 (4 – 25)
Drainage (*n* = 6)	59 (32 – 105)	35 (16 – 93)	108 (45 – 125)	30 (6 – 78)	8 (6 – 30)
Ablation (*n* = 2)	25 (18 – 32)	17 (15 – 19)	82 (65 – 99)	54 (49 – 59)	17 (9 – 24)
Total	32 (6 – 105)	22 (5 – 93)	89 (45 – 165)	28 (1 – 115)	9 (4 – 30)

Data are presented as median (minimum value – maximum value). * The single procedure of placement of an iodine seed took place in the lung and was listed under biopsies.

The target size of the total group was 32 mm (range: 6 mm – 105 mm) x 22 mm (range: 5 mm – 93 mm). The needle was inserted 89 mm (range: 45 mm – 165 mm) deep, measured as the skin entry point and the tip of the needle that was located in the target lesion, with a median angulation of the needle with respect to the vertical image axis of 28° (range: 1° – 115°). The baseline lesion characteristics, including lesion size, needle insertion depth, needle angulation and number of needle manipulations, are shown in Table 7.

Procedural time

For the total patient group, the time between the patient entering and leaving the CT-room was 40:15 min (range: 23:50 min – 162:51 min). Figure 3 presents the duration of the phases *patient preparation*, *path planning*, *needle positioning* (subdivided in the time required to administer the local anesthesia and positioning of the interventional needle), *the intervention* and *completion of the procedure*, for the different procedures. The time between the patient entering and leaving the CT-room was lowest for the biopsy procedures and highest for the ablation procedures (median times: biopsy – 39:34 min; drainage – 55:52 min; ablation: 140:22). The time spend on patient preparation was longer for the ablation procedures as the patients were sedated. Additionally, the duration of the intervention itself was higher than of a biopsy or drainage. Lastly, in one of the two cases the initial RFA electrode placement was performed under ultrasound guidance, but subsequent CT control imaging showed an incorrect placement. When the RFA antenna was repositioned, it became apparent that antenna did not function properly, causing the need to replace the antenna again. These factors increased the time spend on path planning and needle positioning to 80:48 minutes, while this was 21:03 minutes for the other ablation procedure.

Figure 4 shows the duration of the procedural phases for the biopsies of the different anatomical targets. The data showed that the total CT-room time was highest for biopsies in lesions of the adrenal gland, bone and abdominal lymph nodes and lowest for the lung biopsies. This is also reflected in the procedural duration, the time between the first CT-scan and the retraction of the needle (adrenal gland – 34:10 min; bone – 28:54 min; lymph node – 29:24 min; lung – 19:02 min). The time required for path planning ranged between 7:26 min and 8:31 min, but larger differences between the anatomical targets were found for the time required to position the interventional needle (adrenal gland – 8:03 min; bone – 9:56 min; lymph node – 6:33 min; lung – 4:34 min).

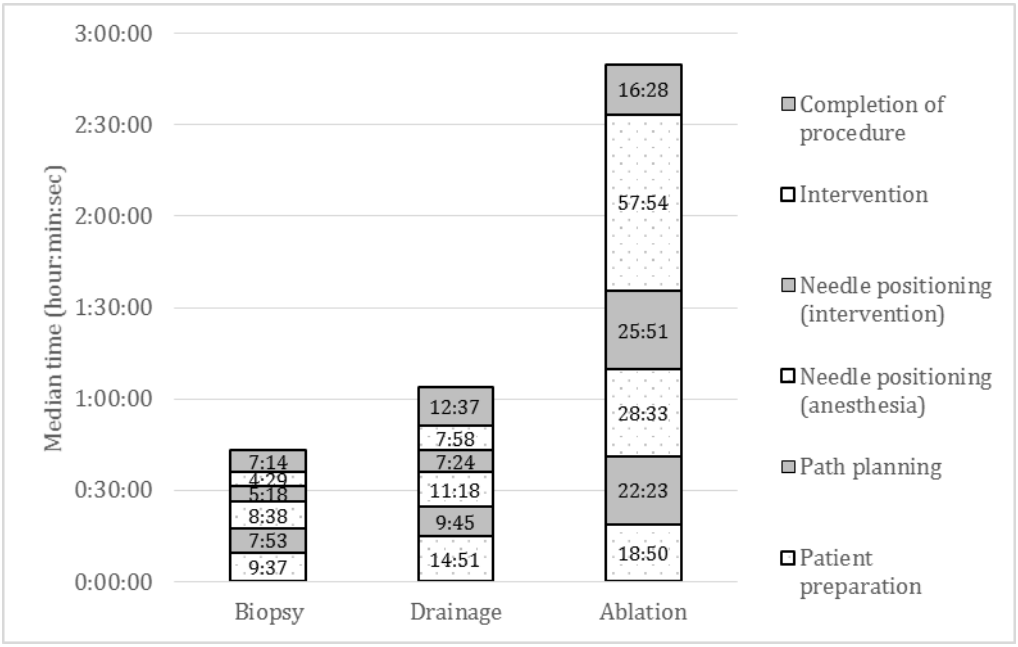

Figure 3. The median times of the phases *patient preparation, path planning, needle positioning* (subdivided in the time administering the local anesthesia and positioning of the interventional needle), *the intervention* and *completion of the procedure*, are presented for the biopsy, drainage and ablation procedures.

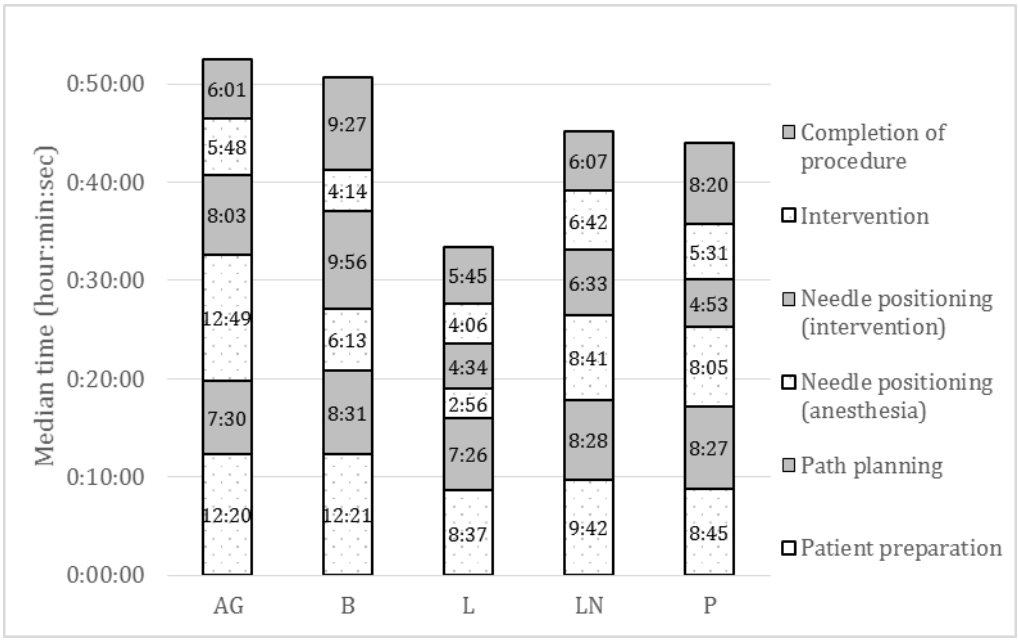

Figure 4. The median time of the phases *patient preparation*, *path planning*, *needle positioning* (subdivided in the time administering the local anesthesia and positioning of the interventional needle), *the intervention* and *completion of the procedure*, are presented for the biopsy procedures within different anatomical target regions; adrenal gland (AG), bone (B), lung (L), lymph node (LN) and peritoneum (P).

The preparation time was also measured. The duration of this phase was not displayed in Figure 3 and Figure 4, but the time between the previous patient leaving the CT-room and the next patient entering was 15:20 min (range: 00:30 – 75:32 min). Several factors contributed to this time. In seven cases, the patient preparation was incorrect, including no placement of a peripheral catheter or determination of the INR (5x), no patient transfer available (1x) or inadequate preparation by the CT-technicians (1x). Furthermore, the radiologist was not present at the start of the procedure in seven cases, because they were double scheduled, were not aware who was doing the procedure or were too inexperienced.

Patient radiation exposure

The median dose-length product (DLP) of the fluoroscopic control CT-scans was 101 mGy·cm (range: 23 – 856 mGy·cm). Subgroup analysis of the three types of procedures showed that the perprocedural DLP was highest for the ablation procedures with a mean perprocedural DLP of 574 mGy·cm (range: 291 – 856 mGy·cm), which accounted for 33% of the total procedural DLP. Figure 5 shows box-plots of the DLP of the fluoroscopic scans for the ablation, biopsy and drainage procedures, as well as the subgroups based on the anatomical target of the biopsy.

The median number of CTF control acquisitions was also highest for the ablation procedures, with a median of 51 (range: 36 – 66). For the biopsy and drainage procedures, the number of CTF control acquisitions was 21 (range: 7 – 61) and 16 (range: 9 – 57) and the DLP due to fluoroscopic CT-scans was 101 mGy·cm (range: 23 – 329 mGy·cm) and 85 mGy·cm (48 – 307 mGy·cm) respectively, accounting for 31% and 15% of the total DLP of the procedures.

In eight out of sixty three procedures (13%), contrast-enhanced spiral CT-scans were acquired to increase the lesion conspicuity with respect to the surrounding tissue, respectively in three cases of hepatic and renal target lesions, in three cases during a drainage procedure and an additional two case for during a biopsy procedure where the lesion that were located in close proximity to blood vessels.

The physician radiation exposure was not measured in this study and the hand dose was not evaluated. However, it should be noted that in eight cases the physician acquired a control scan while securing the needle with his or her hand.

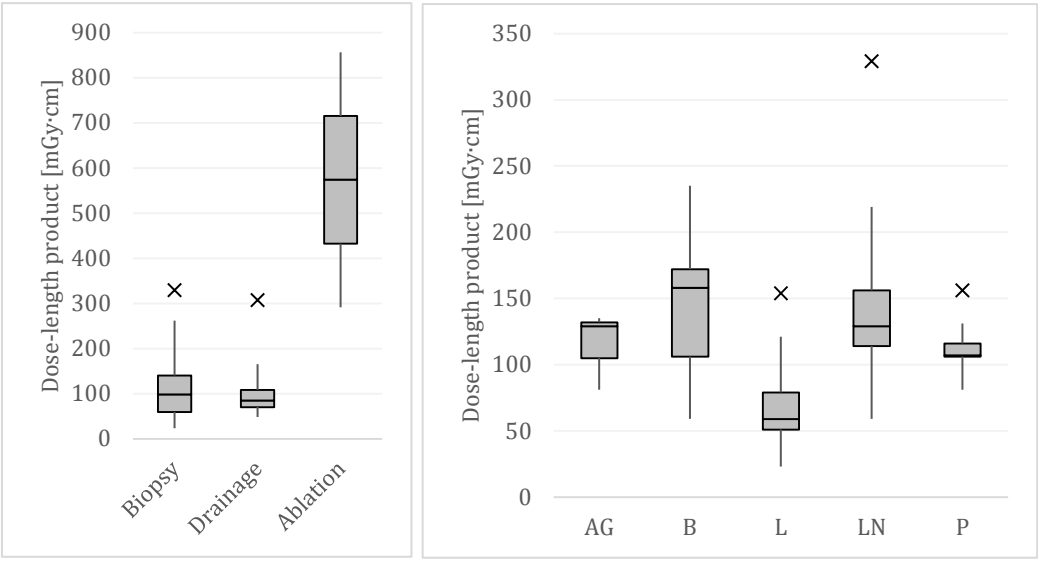

Figure 5. Left: the box-plots displaying the dose-length products (DLP) attributed to the fluoroscopic control CT-scans for the three types of procedures; biopsy, drainage and ablation. The single procedure of placement of an iodine seed was listed under biopsies. Right: the box-plots displaying the dose-length products (DLP) attributed to the fluoroscopic control CT-scans during biopsies within different anatomical target regions; adrenal gland (AG), bone (B), lung (L), lymph node (LN) and peritoneum (P). Outliers (value > 1.5 IQR) are denoted by ×.

Clinical outcome measures

Procedural success was achieved in 54 out of 63 different procedures (86%). The biopsy procedure was successful in 47 out of 54 patients (87%). Per procedure, a median number of 2 samples (range: 1 – 6 samples) were obtained. Histopathological analysis of these samples showed a primary or secondary malignant lesion in 43 patients and a benign lesion nature, confirmed by lesion regression in follow-up imaging, in four patients (7%). In one case (2%) the procedural success could not be evaluated because the biopsy sample was obtained for a clinical study and the results of the histopathological analysis were therefore not denoted in the patient records. In six patients, the procedure was not successful (11%). The biopsy sample contained an insufficient amount of tissue and histopathological analysis did not yield a diagnosis in five cases (lung: 3x; lymph node: 2x). In the last case, procedural success was not achieved as the peritoneal lesion could not be discerned from the surrounding tissue due to extensive scattering artifacts caused by a total hip prosthesis and no biopsy sample was obtained. The success rates for thoracic, abdominal and musculoskeletal biopsies were respectively 83%, 92% and 100%.

One out of the six drainage procedures (17%) was not successful. This patient presented with a prevertebral abscess that was hard to discern from the surrounding tissue despite acquiring a contrast-enhanced CT-scan. Although the tip of the coaxial needle was located within the fluid collection during multiple attempts but the fluid could not be aspirated or drained.

The technical success of an ablation procedure was assessed on a spiral CT-scan acquired immediately after completion of the intervention. In both cases, the radiologist that performed the procedure determined whether the ablation zone encompassed the target lesion. Technical success seemed to be achieved in both cases, leading to a technical success rate of 100%. However, the technique efficacy, which is demonstrated after imaging follow-up, was lower. In one case, the three-month control (contrast-enhanced) CT-scan showed a lesion at the cranial side of the ablation zone that was suspected to be residual unablated tumor, following the definition of the Cardiovascular and Interventional Radiological Society of Europe [36], and required further therapy. In the other case, the observed intervention was a re-ablation procedure. The control (contrast-enhanced) CT-scan acquired two months after the procedure showed a new hypodense lesion within the same hepatic segment, suspected for either local tumor progression or new foci of disease within the same organ.

No major complications have occurred. Minor complications occurred in 17 out of 63 patients (27%), all cases underwent a biopsy procedure. The highest complication rate was found in the thoracic procedure subgroup. In 13 out of 24 thoracic biopsies a pneumothorax occurred (54%), with focal haematoma (n = 2, 8%) and subcutaneous emphysema (n = 1, 4%). In two cases, focal haematoma was induced (n = 2, 18%), causing haemoptoe (n = 1, 4%). In the nonthoracic biopsy subgroup, two non-clinically significant haematoma occurred, respectively after biopsies of a vertebral body and lymph node.

Discussion

Currently, image-guided percutaneous approaches are regularly used during diagnostic and therapeutic interventional radiologic procedures. [1-4] The disadvantages of the iterative nature of the conventional manual approach are often highlighted in research regarding image-guided procedures and needle guidance technologies. However, the evidence base that these systems provide added value within the daily clinical practice remains limited and the rationale to implement these technologies should be further investigated based on clinical data. Therefore, the main objective of this research was to

evaluate the efficacy of percutaneous CT-guided procedures performed at a large peripheral medical center in the Netherlands, which was done by assessing the needle insertion characteristics, the procedural time, the patient radiation dose and clinical outcome of CT-guided diagnostic and therapeutic procedures.

Procedural time

Efficiency, and therefore procedural time, is an important factor during the evaluation of the efficacy of CT-guided procedures due to the close relation to the procedural costs. The influence of clinically using needle guidance technology on the total procedural time should therefore be evaluated critically by weighing the advantages and drawbacks of introducing the technology. The rationale to do so should follow from clinical data. This is why the procedural time, and the contribution of the several phases to the total time, was studied in detail.

The CT-room time and the procedural time, including the phases that have contributed to this time, were evaluated in subgroups based on the procedural type and on the anatomical targets during the procedures. As expected, the duration of the procedure, and of the contributing procedural phases, was highest for the ablation procedures, as expected, which can be attributed to the longer preparation and interventional time. However, in one of the two cases, a technical failure of the ablation system occurred, causing the procedural time to increase disproportionally with respect to the normal situation. The procedural efficiency as presented for the ablation procedures may therefore be underestimated based on these data.

Regarding the biopsy procedures; it was hypothesized that the total procedural time would depend on the anatomical target. More specifically, the time required to plan the path and position the interventional needle was expected to increase with procedural complexity, for example biopsies of small and deeply located lesions or those in close proximity to critical and impenetrable structures. [9, 10] The data of the current study shows that could be the case, as a high variation was found in the total procedural times. The duration was highest for biopsies in lesions of the adrenal gland, bone and abdominal lymph nodes and lowest for the lung biopsies, which also shows in the procedural time (adrenal gland – 34:10 min; bone – 28:54 min; lymph node – 29:24 min; lung – 19:02 min).

The time required for path planning ranged between 7:26 min and 8:31 min for the different anatomical targets. Larger differences in the duration of the path planning phase for each of the anatomical targets were assumed, depending on the procedural

complexity and proximity of the lesion to impenetrable or vulnerable structures, but the range was narrow. This may be explained by the fact that the path planning time only included the time the radiologist spends on planning the path during the procedure. However, most of the physicians assess previous image acquisitions of the patient prior to the start of the intervention, which reduces the duration of the path planning phase during the procedure. Therefore, the time spend during the procedure may not adequately reflect the complexity of the case. Furthermore, the relation between the time required to plan the procedure and the anatomical target may also have been obscured by the definition of this phase. The end point was defined as the first insertion of a needle. The time required to perform the preparatory steps, such as creating the sterile field, was therefore also included, which clouds the complexity-induced difference across the different anatomical regions and procedures.

On the other hand, larger differences were found for the time required to position the interventional needle (adrenal gland – 8:03 min; bone – 9:56 min; lymph node – 6:33 min; lung – 4:34 min). Lesion depth probably played an important factor. Of the abdominal lesions, the adrenal gland and lymph node lesions were located the deepest, with respectively median skin-to-target depths of 131 mm and 127 mm. Additionally, lesion size also may have further increased the procedural complexity, and therefore time; the abdominal lymph nodes had a median lesion size, measured along the long axis, of 21 mm compared to 31 mm of the total biopsy cohort.

The longer needle positioning time during bone biopsies may have been caused by several factors; first, the size of the anatomical window was often much smaller than the lesion size, especially during percutaneous transpedicular vertebral biopsy. The width of the pedicles was measured on the CT acquisitions and was often around 7 – 8 mm wide. Small deviations of the planned needle orientation would therefore have a relatively large effect, compared to the other biopsy procedures. Additionally, small deviations of the planned needle path are harder to correct when the needle is already partially drilled within the bone compared to soft tissue lesions, which may cause radiologists to position the needle more carefully before entering the bone. A factor that would not be influenced by the use of needle positioning technology is the following: an electric needle drill is used to obtain a bone biopsy. The time per manual needle manipulation is shorter in soft tissue than the drill-approach required to biopsy bone as the latter involves attaching the drill to the needle, drilling and subsequently detaching the drill before control CT examination can take place. [37]

When comparing the procedural times to other research performed within this field, the results of this study were often within the same order of magnitude as those presented by others, or a slightly slower. For the total spectrum of biopsy targets, we found a median procedural time of 26:18 min, which is comparable to the results of Gruber-Rouh et al. (2017). [38] They also evaluated biopsy procedures within a broad spectrum of targets, including thoracic, abdominal and skeletal lesions, and presented the time between the first planning and last control CT acquisitions was 25:15 min (range: 17:03 – 43:00 min). [38] Rathmann et al. (2015) used another definition; they defined the interventional time as the time between the first needle insertion to administer the local anesthesia and the moment the needle tip was positioned at the target. Across a broad spectrum of anatomical target regions, they found the interventional duration was 14 minutes for experienced radiologists and 15 minutes for inexperienced radiologists (performed < 50 procedures in total). [39] According to this definition, the interventional time at our center was a bit slower, with a median of 18:25 minutes across the biopsy subgroup.

For the thoracic biopsies, the procedural time of 19:02 min at our center was within the range of times described by other research. The time at our center was a bit longer than the time described by Kim et al. (2011) during thoracic biopsies of 17:16 min, measured from the first CT acquisition to retraction of the interventional needle. [40] On the other hand, Prosch et al (2012) performed biopsies in a median 31 minutes (range: 10 – 74 min). [41]

For the bone biopsies, the duration was bit longer. In our study, a median time of 20:23 min was required to perform these procedural steps during the bone biopsies. Lee, Ng and Griffith (2013) have reported their experience with using a drill system for CT-guided percutaneous bone biopsy and found that the mean time between the first needle insertion and needle withdrawal was 10.5 minutes (range 6 – 20 minutes). [37] A different distribution of the locations of the bone lesions could have explained this difference, but in both studies the predominant target locations were the vertebral body and pelvis, with similar contributions to the total patient group.

The use of needle guidance technology would be expected to alter the time required to position the interventional needle. For drainage and ablation procedures, positioning the interventional needle accounted for respectively 12 and 15% of the time the patient was present in the interventional CT room. For the biopsy procedures, this phase accounted for 12% (median, range: 11 – 20% depending on target anatomy). This seems like a substantial proportion of the procedure.

However, the absolute time spend on positioning the interventional needle during biopsies ranged between 4:34 min for thoracic lesions to at most 8:03 min for adrenal gland lesions. For drainage and ablations procedures this was respectively 7:24 min and 25:51 min (but in 1 out of 2 ablation cases a technical failure of RFA antenna occurred, so it should be expected that this is an outlier and that the median time approximates 6:11 min, which was the needle positioning time during the other ablation procedure).

Even when the assumption is made that the needle positioning time is shortened by the use of needle guidance technology, the saved time will be at most 11 – 20% (the range of the percentage that time spend on needle positioning contributed to the patient CT-room time). Additionally, the use of new device also takes time, e.g. to set-up the hardware, computational time of the software or acquiring an extra CT-scan, which reduces the time savings. Thus, when the added value of implementing needle guidance technology within the clinical workflow is assessed solely based on procedural time and the potential to decrease this, the feasibility of implementing needle guidance technology within the current setting is limited in the opinion of the author.

Patient radiation exposure

One of the major advantages of needle guidance technology is the potential to reduce radiation exposure. [39] Decreasing the number of needle positioning iterations would lead to less control CT-scans and therefore patient radiation dose.

The patient radiation dose was expected to be highest for the ablation procedures, which was also the case. The median number of CTF control acquisitions (ablation: 51, biopsy: 21, drainage: 16) was highest for the ablations, which was also reflected in the median DLP attributed to the control scans during the different procedures (ablation: 574 mGy·cm, biopsy: 98 mGy·cm, drainage: 85 mGy·cm).

Leng et al. (2011) investigated the radiation dose levels for a broad spectrum of CT-guided procedures, including 42 cryoablations, 329 biopsies and 103 drainages. Their results contrast our findings on the ablation procedures, with lower DLP values caused by CTF control scans for these interventions, but only slightly higher radiation exposure during biopsies and drainages (cryoablation: 132 ± 244 mGy·cm, biopsy: 110 ± 111 mGy·cm, drainage: 108 ± 125 mGy·cm).

The radiation dose associated with CTF control image acquisitions was reported to be lower by Gruber-Rouh (2015) than at our center (thorax: 15 vs. 59 mGy·cm; abdomen: 35 vs. 116 mGy·cm; bone: 38 vs. 158 mGy·cm). [38] However, their findings

may be systematically lower than other reported values; for example, at our center the DLP for bone biopsies was 158 mGy·cm, which is lower than findings of Lee (DLP bone biopsy: 164 ± 35 mGy·cm) and Greffier (DLP vertebral biopsy: 198 mGy·cm, range: 157 – 286 mGy·cm, as calculated by dividing the reported estimated effective dose (mSv) by the described abdomino-pelvic-specific conversion coefficient). [37, 42]

The use of needle guidance technology would be expected to decrease the number of image acquisitions to check the position of the needle tip during the procedure. It is often hypothesized that this will lead to decreased patient radiation dose. Decreasing the number of control scans can be achieved quite easily; at out center, currently between 16 and 51 image acquisitions are made during the needle placement phase depending on the procedural type. The fluoroscopic CT-scans accounted for 15 – 33% of the total procedural DLP, which includes the planning, needle positioning and control CT-scans, which implies there is also room for improvement in the patient radiation dose. However, the extent to which the reduction in radiation dose is clinically significant is questionable.

Additionally, it should be noted that it would be unfeasible if the use of needle guidance technology is associated with increasing the radiation dose. Examples include, but are not limited to, the need to acquire an additional helical CT-scan during the workflow, to increase the field of view of an acquired CT-scan or, in case the device is imaged together with the patient, the presence of highly attenuating materials within the device, which would cause the CT-scanner to automatically compensate for the higher attenuation by increasing the tube current and hereby the patient radiation dose. However, also in this case, the extent to which the increase in radiation dose is clinically significant is questionable and deserves further attention.

Physician radiation exposure

The use of needle guidance technology could not only influence the patient radiation exposure, but also the physician dose. This could decrease the physician radiation dose, even potentially to zero if the physician would leave the CT-room during image acquisition. Especially for complex cases this may be valuable; it is shown in [39] that the physician radiation dose increases significantly with increase procedural complexity. However, they also evaluated the effective dose to which radiologists were exposed per procedure. The mean whole body dose, measured with thermoluminescent dosimeters positioned above the protective lead aprons and thyroid collars, was 33 ± 32 μSv for difficult procedures and 23 ± 31 μSv for very difficult procedures. Therefore,

assuming the most unfeasible case and no protective clothing, one procedure would result in a whole body dose of 97 μSv in 95% of the cases. Following the European Direction 2013/59/Euratom, the annual dose limit for exposed workers is 20 mSv. To stay below this limit, the number of procedures one physician could perform is 206 per year. [43] As the total number of CT-guided procedures performed at this center during a year is about 300 – 350 at maximum, assuming a mean number of 6 procedures a week, it's unlikely that one physician would reach the dose limit. Additionally, the whole body dose per procedure is lower than reported, as the radiologists do wear protective lead clothing. The relevance of the potential reduction of physician radiation dose seems to be low. On the other hand, radiation exposure should be as low as reasonably achievable (ALARA), which may justify further research to investigate the extent to which the potential reductions in radiation dose can be achieved.

Clinical outcome measures

For the success rate of biopsies, the Society of Interventional Radiology has suggested quality improvement thresholds; respectively 75% for thoracic and other biopsy sites and 70% for musculoskeletal percutaneous needle biopsies. [35] The success rates of biopsies at our center, respectively 83%, 92% and 100% for thoracic, abdominal and musculoskeletal biopsies, are well above these suggested thresholds for quality improvement.

Regarding thoracic biopsy procedures, Heck, Blom and Berstad (2006) and Kim et al. (2011) presented that in respectively 88% and 89% of thoracic biopsies a tissue sample was obtained that was adequate for histopathological analysis. [9, 40] Gupta et al. found that the mean reported success rate was 89% (77 – 96). [35] These success rates are a bit higher than those achieved at our center. The reported rates for minor complications such as pneumothorax and chest tube placement were respectively 12 – 45% and 2 – 15%, with suggested quality improvement thresholds of 45% and 20%. [35] The percentage of patients in whom an iatrogenic pneumothorax was induced was 54% at our center, which is above the suggested threshold. However, the clinical relevance of this complication should be taken into account; in most cases, the monitoring period and length of hospitalization were not increased and no interventions were required. Additionally, all cases of pneumothorax were included in the registration of minor complications, instead of only the symptomatic pneumothoraces or pneumothoraces showing a rim larger than 2 cm on conventional postprocedural X-ray. [44]

For biopsies of musculoskeletal lesions, reported diagnostic rates range between 78 – 98%. [45-48] The review of Gupta (2010) showed that the mean reported success rate for musculoskeletal biopsy sites was 82% (range: 76 – 93%), which is in close accordance to the other studies found. [35] The median success rates of biopsies at our center are within the same order of magnitude as the results as presented by others. The reported complication range for musculoskeletal biopsies was 0 – 1.6% [37, 46, 47]. In [35] only the rate of major complications is mentioned, so our results cannot be adequately compared to these threshold, but the two cases of a minor complications occurring in the non-thoracic biopsy subgroups were both non-clinically significant.
The clinical outcome after thoracic biopsy can be improved most according to the current data. A side note is that current success rate is already well above the set threshold for quality improvement and the current method of pneumothorax registration may have increased the complication rate compared to other research.

The role that needle guidance technology could play within this process depends on the causes of procedural failure and the type of complication. As the needle tip was visibly located within the target lesion on CT control imaging in the majority of the biopsy cases, it can be assumed that improving the accuracy needle targeting would not necessarily improve the clinical outcome. However, reducing the number of needle manipulations would be beneficial in the case of lung biopsies as the rate of pneumothorax increases with each time the pleura is passed or manipulation with the needle. Additionally, when a pneumothorax is induced during the procedure, this causes the lung to collapse partially, which complicates (further) biopsies and the procedure may end prematurely. The occurrence of perprocedural pneumothorax could be related to the fact that the cause for obtaining an insufficient amount of material to enable histopathological analysis. When only this performance measure is evaluated, the adoption of needle guidance technology may be feasible, provided that a method to account for perprocedural (respiration-induced) target motion is incorporated within the trajectory planning and guidance workflow.

Limitations

The current study has some limitations that are worth mentioning. First of all, the interventional type was not distributed equally as the number of biopsies was much higher than the other procedures. Also, the lungs were the most prevalent target anatomy. This is an accurate reflection of the clinical practice at our center and is caused by the consecutive patient inclusion strategy. However, the large differences in

the available data per procedures and anatomical area may have compromised the adequacy of comparisons between different procedural types and target regions. It is recommended to obtain additional data of patients undergoing the drainage and ablation procedures in order to increase the strength of evidence and the conclusions based on these data. Furthermore, the follow-up time should be increased for the ablation procedures in order to evaluate the procedural success adequately. No definitive conclusions were drawn for ablation and drainage procedures as the data for these procedural types were limited in this study. For drainages, there seems to be little room for improvement based on each of the individual performance measures. During ablation therapy, the target positioning error is directly linked to the adequacy of the ablation zone and procedural success. Methods to improve the needle positioning accuracy seem to be promising and should be investigated further, especially focusing on the long-term procedural success.

The second limitation concerns the method of the registration of minor complications. During this process, all occurring pneumothoraces were included. However, the clinical relevance of asymptomatic pneumothorax is questionable. Therefore, it is recommended to register whether the pneumothorax was symptomatic, with the patient displaying symptoms of chest pain, mild, moderate or severe dyspnea, tachycardia and/or hypotension. Another metric that could be used is whether the rim of the pneumothorax as visible on conventional X-ray exceeds 2 cm or not. [44] Furthermore, it is recommended to investigate simple methods to reduce the pneumothorax rate, for instance by adopting rapid needle-out patient-rollover or needle track sealing techniques. [49, 50]

Lastly, it is important to note that radiologists performed procedures within different anatomical regions, depending on their level of experience and specialization. For instance, of the in total twenty four procedures during which a lung lesion was targeted, thirteen cases were performed by specialized thoracic radiologists and eleven by radiology residents under supervision (46%). In comparison, respectively only four out of fourteen bone punctures (29%) and one out of six biopsies (17%) of abdominally located lymph nodes were performed by residents. This indicates that the comparison of the different anatomical target areas may be biased due to inter-operator variability and the difference in experience. Furthermore, the presence of a resident often induced a more training–based setting, during which the supervising radiologist explained the procedural steps and the considerations that should be taken into account. This may have influenced the primary and secondary outcome parameters.

Conclusion

Based on the evaluation of the performance of biopsy procedures, taking the procedural time and the relevance of potential decreased patient and physician radiation exposure, and clinical outcome measures into account, the extent to which needle guidance technologies provide additional value within the daily practice of a large peripheral medical center seems to be limited. The clinical applicability and feasibility are higher for therapeutic and complex diagnostic cases, and would increase further when a method to manage perprocedural motion, such as respiration-induced displacement of thoracic and abdominal lesions, would be incorporated.

Chapter 4 – concept of design for (respiratory) motion compensation within the workflow of robotic assisted image–guided percutaneous interventions

Introduction

Image–guided interventions are increasingly adopted within medical practice, with percutaneous approaches arising as alternative options to open diagnostic or therapeutic procedures. [1-4] Although the procedural complexity is dependent on several factors, as described earlier, the non–static nature of the human body plays an important role.

The three main factors causing movements of the lesion or surrounding anatomy are; (i) respiration–induced motion of both the target lesion and the surrounding tissues [5, 21, 22] or poor patient compliance to or inability to follow respiratory instructions, (ii) voluntary and involuntary patient movements or inability to cooperate, including but not limited to motions under influence of pain and stress [20], and lastly, (iii) deformation or displacement of the target lesion or organ system caused by the pressure exerted by the needle during insertion [23, 24].

As actual real–time imaging is lacking during CT– and CT–fluoroscopy guided procedures, [12, 20, 51] the deformations and displacements of the target lesion or surrounding tissues that may occur between different image acquisitions remain unnoticed until another scan is made. These deformations and displacements need to be accounted for during the procedure as they cause needle positioning inaccuracy [20, 24], which may require repositioning or reinserting of the needle, hereby increasing the number of iterations of the needle positioning process. [3, 5, 12, 52]

The use of needle guidance technology has the potential to improve the accuracy of percutaneous needle positioning, by decreasing both the positioning error and the number of needle placement iterations, especially for complex cases. However, the trajectory guidance provided by most needle guidance systems is based on the assumption that the target lesion does not deform or displace. Therefore, intraprocedural motions of the patient or the target lesion are not taken into consideration during path planning and needle insertion and could cause needle targeting errors. The optimal method to deal with these challenges has yet to be found.

Incorporating a method to encompass or minimize the effect of respiration-induced perprocedural target motion on needle insertion efficacy would optimize the clinical applicability and feasibility of these type of systems. This could unlock the potential of these systems to improve the efficacy of image-guided percutaneous procedures. The objective was to explore the available options and propose a concept technology to achieve this, focusing on clinically applicability and feasibility.

Methods

The design process was started by analyzing the problem of perprocedural motion from several perspectives. First, a literature search was performed to create insight in the order of the magnitude of respiration-induced organ motions. Parallel to this process, multiple procedures were attended to elucidate the clinical challenge that respiration-induced motion presents, after which the observations were discussed with the radiologists performing the procedures at our center.

User and system requirements for the new technology were defined. In order to do so, use cases were described on the clinical observations and discussions. A stakeholder analysis was then performed, taking the following stakeholders into account: (i) patients, (ii) hospital, including the departments of radiology, medical physics, central sterilization, finance and the hospital board, (iii) insurance companies and (iv) DEMCON, including the departments for production, assembly, maintenance, quality, sales, finance and the project manager(s) and mechatronic system engineers. For each of the stakeholders, their respective requirements and wishes for the future technology were evaluated. Based on these results, the user and system requirements were defined and a scoring list was created to assess the clinical applicability and feasibility of concept technologies.

Results

The results of the literature search, the clinical observations and discussions with radiologists were described in the sections 'respiration-induced organ motion' and 'current approaches for motion encompassing and compensation'.

Respiration-induced organ motion

Tissues located within and surrounding the thoracic and abdominal cavity move under influence of the respiration [53]; the extent to which this occurs is, amongst others,

dependent on the anatomical location and the relations with other tissues (e.g. boundaries or other geometric constraints), and tissue type of the organ.

For intrathoracic lesions, Mageras et al. (2004) measured the motion of lung tumors on respiration-correlated CT-scans and found that the movement in the superior-inferior direction was largest: in seven out of twelve patients (58%), the lung lesion displaced more than 10 mm under influence of the respiration, and for one patient the lesion moved up to 25 mm. [54]

The extent of motion depends on the anatomical location of the lesion; the displacement of lesions located in the lower lung lobes was larger than for those located in the middle and upper lung lobes. [27, 54, 55] Median displacements of 9.2 mm and 3.3 mm were described in [54] for lesions located in the lower and upper lung regions respectively, which is comparable to the mean motion amplitudes for respectively 12.3 ± 8.1 mm and 3.1 ± 1.2 mm as described in [55].

The magnitude respiration-induced motion of abdominal structures, such as the liver, kidneys and diaphragm is often above 10 mm [56] and varies between 10 and 25 mm for shallow breathing patients. [27] For deep breathing modes, the mean reported liver motion ranges between 37 and 55 mm, whereas for the diaphragm displacements between 35 and 101 mm in the superior-inferior direction have been measured. [27]

Current strategies for motion management

After attending several procedures, it became clear that three different strategies were adopted in case target displacement occurred during a conventional, freehand percutaneous procedure.

The first group of physicians did not use motion encompassing or compensation strategies in their daily practice at all. In their experience, the amount of target displacement is relatively small. When the two other strategies were used, the physicians did account for the respiration-induced target motion.

During the second approach, the physicians inspected the movements of the patient's thoracoabdominal abdominal surface while the patient was quietly breathing. They advanced the needle and acquired the perprocedural CT (fluoroscopy) scans at the same respiratory phase, often towards the end of the expiration, hereby minimizing the effect of respiration-induced target displacement.

The third approach closely resembled the second approach, but instructions were used to temporarily stop the respiration. The radiologist monitored the patient's thoracoabdominal surface and instructed the patient to hold their breath at a certain

level. Subsequently, the target anatomy was scanned, the radiologist assessed the acquired images on the current location of the target lesion and the safety of needle placement, and the patient could continue breathing. This process was repeated with the same or different breath-holds levels until the target lesion was located within the axial scanning plane and the needle could be inserted safely.

Although these approaches have the potential to reduce the influence of respiration-induced target motion, the magnitude of lesion displacement is often still large enough to increase procedural complexity, reduce the efficacy or even induce needle targeting errors, even for quietly breathing patients. Additionally, the reproducibility of breath-holds is low, with some studies even showing that the location of the target lesion is more reproducible when the patient continues to breathe in 'quiet respiration mode' than when the patient is instructed to hold their breath during a specified respiratory phase.

Respiration-induced motion not only poses a challenge for the freehand approach. The trajectory guidance provided by several (prototypes) of needle guidance technology is based on the assumption that the target lesion does not deform or displace. Similar to the freehand method, this could lead to needle positioning errors.

Most commonly, the extent of intraprocedural motion is minimized as much as possible. Gross patient movement is limited by wrapping an immobilizer around the patient [14, 26] or by means of a vacuum mattress [17]. Respiratory motion can be minimized by adopting breath-hold techniques, [25] or, in case patients are generally anesthetized, by inducing temporary apnea during the CT acquisitions and needle placement. For instance, in [14] and [26] the respiration was suspended in the end expiration phase by disconnecting the endotracheal tube from the mechanical ventilator during the path planning and needle insertion. After the needle tip was located at the target lesion and the ablation was started, the ventilator settings were adapted to a high tidal frequency and increased oxygen level to further minimize target motion. Inducing end-expiratory apnea in generally anesthetized patients is an approach that is often adopted to minimize the breathing motion and therefore target displacement.

Although it is considered common practice that patients undergo ablation under sedation or general anesthesia to increase perprocedural patient comfort, the protocol for patients undergoing ablation therapy is dependent on the experience of the radiology and anesthesiology departments. Some centers choose to only sedate the patient. This means that the patient's consciousness is reduced, but the patient

continues to breathe spontaneously. Furthermore, other procedures such as biopsies, placement of iodine seeds and drainages are often performed using only local anesthesia. As inducing general anesthesia is associated with drawbacks, including increased complication risk, procedural time and the need for additional staff, another option to decrease perprocedural motion in daily clinical practice was sought for.

Design process

The most important findings of clinical observations and description of the current clinical practice were described in the previous section. The full description of the current clinical practice and use cases can be found in Appendix 1 and Appendix 2 respectively. The results of the stakeholder analysis can found in Appendix 3. The results of each step of the design process were thoroughly discussed within a team consisting of (technical) physicians and engineers, each with different specializations.

User requirements

The user requirements for the new concept technology to deal with the challenge of respiration-induced target motion were based on the results of the design process. The main user requirement was: 'the technology should facilitate adequate needle positioning in a non-static environment, consisting of the target lesion and surrounding tissues'. Additional important requirements to achieve clinical applicability and feasibility were: the use of the technology (i) increases the performance of the needle guidance device, in terms of accuracy, efficacy and safety, and (ii) is associated with a low impact on the current, freehand workflow, in terms of usability, effort to set up and use the device, but is also tolerable for patients in terms of required cooperation and compliance to instructions.

Suggested method for motion management

Each part of this proposal is described below, together with the choices and considerations that were made during the process. In short, it is proposed to use gating as motion management strategy, such that the path planning and needle insertion both take place within the end-expiratory phase of the patient's respiration. The aim is to minimize the effect of respiration-induced lesion motion on needle targeting accuracy. To do so, a 3D depth camera will be used to track the respiratory (surrogate) signal and to create a personalized guiding breathing wave. The physician uses this feedback to perform the path planning and needle positioning within the gating window, whereas

the patient may improve the regularity, and therefore motion, of the respiration. The various principles behind this method, and the considerations on the choices made, are explained in the following sections.

Minimization of the effects of respiration-induced motion

Respiratory gating is a method to reduce the effects of breathing-induced motion on imaging, or in this case, needle targeting accuracy. It is suggested to let the path planning and needle insertion phase take place when the respiration of the patient is at the same level and position of the respiratory cycle. The hypothesis is that minimizing the effect of respiration-induced motion on the trajectory planning and guidance is sufficient to ensure the required needle targeting accuracy and procedural success. It is assumed that the locations of the target lesion and the surrounding tissues are very similar when the respiratory level and phase are equal. It is important to note that both respiratory parameters should be equal due to the hysteresis effect; even though (a surrogate signal for) the respiratory level appears to be equal, the position of the target lesion is different depending on whether the subject is currently within the exhale-to-inhale or inhale-to-exhale part of the breathing cycle. [57, 58]

The choice for a specific window within the respiratory signal was based on other research. Vedam, Keall, Kini and Mohan (2001) have investigated the parameters for respiratory gating during radiotherapy and recommended using the flection points of the breathing curve from end-expiration to start-inspiration or end-inspiration to start-expiration, which represent the minimal and maximal expiration levels respectively. [59] Their explanation is that at these positions within the breathing cycle, the respiration-induced target motion is minimal. This makes sense, as the direction of the motion inverses at these times, which causes the lesion velocity to approach zero.

They add that, compared to other time windows, the magnitude of the lesion motion is minimal during expiration. [59] The findings of [54] also indicate that the extent of target motion is least between mid- and end-expiration. Blackall et al. (2006) provide an interesting explanation for this observation; they reasoned that as quiet expiration is passive, the variation in the shape the lungs, diaphragm and upper abdominal organs assume is lower than during the (active) inspiration, during which a thoracic, abdominal or mixed respiratory mode can used. [57] Next to the low variability of motion during expiration, the duration of this phase is also often longer than the inspiration. [60] The end-expiratory phase therefore seems to be most feasible time for the gating window.

Several methods of respiratory gating exist. In [61], multiple gating schemes were compared. Two types of information can be used to perform the gating: (i) time and (ii) amplitude. Furthermore, the width of the gates can be: (i) equal, i.e. the width of all time gates is 400 ms, or (ii) variable, i.e. the gate width is 20% of the total signal, so if the total amplitudes of two respiratory cycles are respectively 10 and 20 mm, then the gate widths will be 2 and 4 mm respectively. When the breathing motion is regular, the performance for all four combinations would be more or less equal. [61] During normal respiration, variations in amplitude, period and regularity of the respiration occur over time, and the gating approach should account for these changes such that the lesion displacement is minimized. As the increase and decrease of the lung volume cause the displacement of other tissues over time, the time-based gating methods are deemed to be unfeasible. As the breathing amplitude is closely related to the position of the lesion, an amplitude-based, equal width gating approach is proposed. The gates should be equal in width instead of variable, as the range of locations that the lesion may be positioned within the gate should be fixed. It was explored how these techniques could be implemented within the workflow, and assess the preliminary feasibility. The results of this are stated in Appendix 6.

Reducing the variability of respiratory motion

Additional decreasing the effect of respiration on needle targeting accuracy, an effort is made to minimize the inter-cycle variations in amplitude, phase and periodicity of the breathing motion and their effect on trajectory planning and needle guidance. During the procedure, respiratory biofeedback will be provided to both the patient and the physician. The aim of providing the feedback to the patient is to improve the regularity of the breathing motion [62] by facilitating cooperation. This is an alternative to the more complex methods of immobilizing the lesion itself or compensating for the target motion in real-time.

Research assessing the impact of using respiratory biofeedback for breathing motion management has shown that not only the the regularity of breathing motion improves [63, 64] and the reproducibility of breath-holds [65] and lesion position [62] increases, but also that the correlation between the respiratory motions of surrogates and the target lesion increases [66], compared to free breathing only.

Venkat et al (2008) evaluated the effect of providing audiovisual biofeedback on variations in respiratory amplitude and frequency, comparing the results to those achieve during a free breathing situation. They found that the variability in amplitude

and frequency were decreased to respectively 50% and 70% compared to a free breathing situation. [63] The results as described in [65] further increase the level of evidence by showing that the variation in the level of breath-hold significantly reduces when visual biofeedback is provided to volunteers. Lee et al. (2017) studied the influence of audiovisual biofeedback on the reproducibility of breath-holds performed by patients presenting with lung lesions. [62] In their study, the feedback was also provided to patients by displaying the current 'breathing position' in a personalized guiding breathing wave. This enabled patients to monitor the level of respiration and hold their breath at the indicated level. Providing audiovisual guidance during breath-hold improved the reproducibility of the central target position reduced from 8.8 to 4.2 mm and from 6.3 to 3.0 mm in respectively the superior-inferior and anterior-posterior directions. [62] Additionally, the correlation between the respiratory motion patterns of internal and external surrogates and the lesion increases. [66] The external motion of the abdominal surface was measured with a 1D abdominal marker, similar to the previous study. The motion patterns of the diaphragm, which acted as internal surrogate signal, and the lesion were measured on cine-MR images. When audiovisual biofeedback was provided to help increase the reproducibility of the respiration, the correlation between the surrogate and lesion improved 11 – 13% compared to a free breathing situation.

Regarding the type of feedback; visual feedback seems to be more effective than audio feedback. Although both methods increase the regularity of the motion, providing audio-only feedback tended to increase the breathing amplitude, and therefore target motion, which is an unwanted effect. [64] It is recommended to provide a combined form of audiovisual feedback, as the reproducibility of the respiration increased more compared to approaches where a single form of feedback was provided.

Workflow

Similar to the workflows as proposed in [62] and [63], a personalized guiding wave will be created to provide the audiovisual feedback. In these studies, the respiratory signal was acquired by tracking a 1D marker positioned on the abdominal surface of the patient with a real-time position management system during ten respiratory cycles. We propose to use a depth camera, for instance Microsoft Kinect (Microsoft, Redmond, WA, USA), to track the motion of the thoracoabdominal surface of the patient. The camera should be fixed to the table in order to move together with the patient when they are moved into and out from the gantry. For a table-mounted needle positioning system, it

would be most feasible to incorporate the depth camera in the system as otherwise the view between the camera and the patient surface would be partially obstructed by the system itself.

During the preparation phase, the patient is positioned onto the CT-table. The distance between the camera and the patient surface will be measured during approximately 10 – 15 respiratory cycles. The change in depth can be used to calculate the change in volume by computing the point-to-point 3D distance and counting the voxels. The mean displacement of the surface over time represents the respiratory surrogate signal. By averaging the cycles, a mean respiratory guiding wave is created.

Depending on the type of procedure the patient will undergo, the type of anesthesia and the need for sedation are determined. For conscious patients undergoing the procedure under local anesthesia, the patient is instructed to follow the respiratory guiding wave that is visualized on a screen together with the current position within the respiratory cycle. The same feedback is also provided to the physician. This enables them to check the respiratory level of the patient and assess the feasibility of the timing of needle positioning during the breathing cycle in a quantitative manner. It also helps them prepare the needle placement itself by anticipating the correct time window.

A planning CT-scan is acquired during the end-expiration phase (breath-hold or free breathing, depending on whether the patient is conscious and if they tolerate a breath-hold). The normal steps are then taken to prepare the device before needle insertion. When the needle guide is aligned to the planned path, the needle insertion can take place during gate window indicated on the screen. For patients who can perform breath-holds, a one-hit insertion may be performed. A step-wise approach should be used for patients under sedation, who cannot actively control their respiration as they are unconscious, as the end-expiratory window will be shorter than during a breath-hold. After initial insertion, the needle should be released from the needle holder to enable free motion together with the displacing internal organs. When the current respiratory cycle approaches the gating window, the physician prepares the needle insertion and advances the needle further at end-expiration, repeating the process until the needle is inserted at the required depth.

Discussion

Perprocedural respiration-induced motion of the target lesion and surrounding tissues increases the complexity and inefficiency of image-guided percutaneous procedures and can increase needle targeting errors. Currently, the use of needle positioning

technology often does completely match the clinical requirements, as perprocedural motions are often not accounted for. The objective was therefore to explore potential concept technologies that could aid in minimizing the effect of respiration-induced perprocedural target motion on needle insertion efficacy.

A gated approach, during which biofeedback is provided to both the patient and the physician, was proposed. The gating approach will minimize the effect of motion on path planning and needle insertion, whereas the biofeedback will contribute to reducing the variability in respiratory level, frequency and regularity. By these approaches, the adoption of more technically complex solutions to track or compensate for respiratory motion in real-time is avoided, which increases the clinical applicability and feasibility.

The surface tracking is a relatively simple method that closely resembles the method radiologists currently employ to assess the respiratory phase. As no external markers are required to use the technology, there is no need to sterilize additional components. Furthermore, the data can be acquired with a high frame rate (up to 40 Hz) and the surface information provides a better view on the respiration-induced motion than a 1D measurement, such as with an optical marker positioned on the abdomen of the patient.

Drawbacks of the surface tracking approach include the following. First, the applicability for patients positioned in a lateral decubitus position is unknown. [65] It is expected that the accuracy of respiratory tracking will be lower, as the size of the surface is lower, and the extent to which patients are able to lay still may also be limited. Also, to increase the duration of the needle targeting window, patients may be asked to hold their breath. The provided feedback helps them to follow the instructions, therefore, the instructions are assumed not to increase the cognitive load for the patient to such levels that the instructions cannot be followed. [64, 65] However, in case patients present with (lung related) co-morbidities, the extent to which they tolerate breath-holds may be limited. In this case, the breathing guidance will still improve the regularity of the breathing-motion.

Second, the approach is based on the assumption that the correlation between the surrogate signal and respiration-induced (target) motion is high; the target location is not checked in real-time using (imaging) feedback. However, dissimilarities between the motion patterns measured with a surrogate signal and the actual lesion motion may occur in the direction, period and phase. [66] Larger phase shifts were found when an external surrogate signals was used compared to an internal surrogate. Further

research regarding methods to track the internal abdominal anatomy, such as a 1D US probe, should be performed.

Lastly, the suggested workflow decreases the influence of respiration-induced motion on needle targeting errors, patient movement and needle insertion may still cause (significant) needle positioning inaccuracy. Further research should be performed in order to investigate how to compensate for target displacement induced by needle insertion. Although the evidence is limited, a few studies have shown and quantified the deformation and displacement of the target lesion and the surrounding tissues caused by needle insertion. [19, 23, 24] The magnitude of this motion is dependent on the type, and as hypothesized in [23], the sharpness of the used needle. The distance of target movement ranged between 5.3 ± 2.1 mm and 9.1 ± 4.5 mm for ablation needles with widths between 13 and 17 Gauge, inserted in a range of thoracic, abdominal and musculoskeletal tissues. [23] The findings of [19] are similar, with a total intraprocedural target movement of 5 ± 3.3 mm, with hepatic lesions moving on average 6.4 ± 3.9 mm. The insertion-induced motion was in the same order of magnitude in the directions parallel and perpendicular to the direction of the needle trajectory (broad target spectrum: 3.8 ± 2.5 mm vs. 2.9 ± 2.7 mm, liver: 4.4 ± 2.9 mm vs. 4.3 ± 3.2). Although these displacements are of a smaller order of magnitude than those induced by the breathing motion, their effect on the total procedural accuracy should be evaluated in future studies.

To conclude, an approach was presented to reduce the both the variability and the magnitude of respiration-induced lesion motion. Based on the results of other studies, the extent to which this will be the case seems promising, but further research is warranted to investigate these hypotheses.

Chapter 5 – General discussion and conclusion

The overall objective, as described in Chapter 1, was to assess the clinical applicability and feasibility of needle guidance technology within the daily clinical practice of the radiology department of a large, non-academic hospital located in the Netherlands.

The research has started by creating an overview of preclinical and clinical studies evaluating the performance of robotic assistance or navigation technology intended for use during diagnostic or therapeutic CT-guided percutaneous interventions. The underlying aim was to formulate hypotheses on why widespread adoption of these techniques has not taken place yet, even though the preliminary results and performance of these techniques are often promising. In the author's experience, two important factors play a role in this.

First of all, there seems to be a limited amount of high-quality evidence showing the added value within current clinical practice. The disadvantages of the iterative nature of the conventional manual approach are emphasized in research regarding image-guided procedures, but a quantification of these drawbacks and the extent to which these can be improved by needle guidance technologies is lacking. This research has contributed to the knowledge base by evaluating the efficacy of the freehand approach for a broad spectrum of procedures and anatomical targets as performed within a large peripheral center. Based on these results, the relevance of the potential improvements associated with adopting needle guidance technology seems to be limited. The current time required to position the interventional needle, which is the process that needle guidance technology would affect, currently takes up 11 – 20% of the CT-room time. However, the relevance of these time savings quickly disappears when the duration of patient transitions and the time that use of an additional device would cost, i.e. to set up the hardware, the computational time of the software or the need to acquire an extra CT-scan, are taken into account. Regarding the radiation dose; a common claim is that the use of needle guidance technology would decrease the number of image acquisitions, which seems to be very likely based on our results. On the other hand, the claim that this lead to reduced patient radiation dose is achievable as the CT-scans accounted for 15 – 33% of the total procedural DLP, but only if the use of the technology is not associated with increases of radiation dose, for example by the need to acquire an additional helical CT-scan to perform the patient-to-image registration, to

increase the field of view of an acquired CT-scan or, in case the device is imaged together with the patient, the presence of highly attenuating materials within the device, which would cause the CT-scanner to automatically compensate for the higher attenuation by increasing the tube current and hereby the patient radiation dose. When the clinical outcome measures are evaluated, there is some room for improvement in the complication rate, but other, less complex options could be more feasible. However, the high accuracy that is provided by needle guidance technology could improve the procedural success. Therefore, the clinical applicability and feasibility seems to be higher for complex cases, including biopsies of lesions that are small, located deep within the body or need to be approached through a narrow anatomical window, and for ablation therapy. It is expected that the added value of needle guidance technology increases further when a method to manage perprocedural motion, such as respiration-induced displacement of thoracic and abdominal lesions, would be incorporated. (*Chapter 3)*

The second factor that plays an important role in the (lack of) adoption of these techniques is that an adequate method to account for the needle tip positioning errors induced by perprocedural lesion displacements is often lacking, which reduces the feasibility of several (prototypes of) needle guidance devices. An explorative study was performed on the technologies available to account for respiration-induced lesion motion. A gated approach, during which biofeedback is provided to both the patient and the physician, was proposed. The end-expiratory gating will minimize the effect of motion on path planning and needle insertion, whereas the biofeedback will contribute to reducing the variability in respiratory level, frequency and regularity. By these approaches, the adoption of more technically complex solutions to track or compensate for respiratory motion in real-time is avoided, which increases the clinical applicability and feasibility. The data acquired with a 3D depth camera, that measures the distance between the camera and the external surface of the patient in real-time, is used to calculate a respiratory guiding wave. The guiding wave is displayed together with the current breathing state, which acts as audiovisual biofeedback. The method of acquiring the respiratory surrogate signal is a relatively simple method that enables a workflow that closely resembles the current clinical practice. However, the applicability of this technique for patients positioned in a lateral decubitus position is unknown. Furthermore, the approach is based on the assumption that the correlation between the surrogate signal and respiration-induced (target) motion is high, but the actual target location is not checked in real-time. Dissimilarities between the motion patterns

measured with a surrogate signal and the actual lesion motion may occur in the direction, period and phase. The use of an internal surrogate signal may decrease the extent to which these phase shifts occur and is recommended to investigate in further studies. Lastly, the suggested workflow decreases the influence of respiration-induced motion on needle targeting errors, patient movement and needle insertion may still cause needle positioning inaccuracy. The proposed approach seems to be promising, but some important drawsbacks were identified, that should be investigated further. (*Chapter 4*)

In conclusion, the key output of this research is two-sided. A contribution was made to the evidence base of the clinical applicability and feasibility of needle guidance technology by evaluating the efficacy of the freehand approach for a broad spectrum of procedures and anatomical targets as performed within a large peripheral center. Furthermore, a method based on gating and biofeedback was proposed to account for the needle tip positioning errors caused by breathing-induced lesion displacements.

Future research should focus on the creation of guidelines to improve the quality of method of performance evaluating and reporting of needle guidance technology. As described previously, additional clinical data should be obtained from other medical centers and for complex procedures. Creating more insight in the procedural complexity by assessing the extent to which procedures are mentally challenging would increase the knowledge base further. For the motion management method, the performance of different methods to acquire a respiratory surrogate signal should be evaluated and compared to each other.

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Appendix 1 – Description of current clinical practice

This section contains a description of the freehand approach, as performed by interventional radiologists at the Meander Medical Center.

Preparation

The procedure takes place in a dedicated (interventional) CT-imaging suite at the radiology department. Adjacent to this room is the control room, from which the CT technician operates the scanner. The interventional radiologist examines the anatomic region of interest on previous imaging studies. One of the CT technicians prepares the sterile set containing the tool and instruments required during the intervention, such as the sterile drapes and gloves, skin disinfectant and the needle. The other CT technician receives the patient in the CT room. Patients position themselves on the CT-table and may be assisted by one of the CT technicians in case this is necessary. The radiologist then performs the time-out procedure with the other members of the team: he or she provides the patient with information on the planned treatment (method, complication risk, etc.), answers any remaining questions and checks that the procedure is not contraindicated for the patient. After the radiologist has obtained informed consent, the patients are positioned in a prone, supine or lateral recumbent position, depending on the target anatomy. In principle, patients position themselves on the CT-table, but they may be assisted by one of the CT technicians.

Path planning

A baseline, spiral CT-scan is acquired of the anatomic region of interest. Instead, a contrast-enhanced CT-scan can also be made for medical reasons (e.g. to increase lesion conspicuity or to visualize vascular structures in the vicinity of the target lesion). The radiologist identifies the lesion and determines the needle target position. The needle entry point is chosen such that the planned needle trajectory does not traverse any critical or impenetrable structures. The method of retrieving the needle entry point depends on the preferences of the physician but frequently used methods are: (i) determine the anatomical region of interest on previous imaging studies, place a radiopaque grid or markers on the patient's skin, perform the baseline CT and determine the needle entry point on the imaging study or (ii) performing the baseline CT, determine the anatomical region of interest, place radiopaque grid, radiopaque stickers or a hypodermic needle, use CT fluoroscopy to visualize the marker and the lesion, determine the needle entry point on the imaging study. The entry point (as

determined on the scans) is retrieved by translating the CT-table to the selected slice position, such that the CT gantry laser line that intersects the radiopaque marker. The entry point is then indicated on the patient's skin with a marker and the radiopaque grid or stickers are removed. The patient's skin is disinfected with chlorhexidine and a sterile work field is created.

Needle targeting and positioning

A local anaesthetic is administered in and around the planned needle entry point and the trajectory to reduce the per- and postprocedural pain. A small incision is often made at the needle entry site to reduce the extent of needle deflection at the skin. The physician translates the 2D planned trajectory from the CT-scan to the 3D patient anatomy, estimates the necessitated needle position and orientation and advances the needle accordingly. In case an in-plane approach is adopted, the CT gantry laser light is often used to keep the needle within the axial plane. Three axial (fluoroscopic) CT slices are acquired to visualize the position of the needle tip with respect to the predefined target. The process of estimation, advancing the needle and imaging is iterated until the distance between the needle tip and the target is sufficiently minimized, as visualized on control (fluoroscopic) CT-imaging. The intervention is then carried out and the needle is retracted at the end of the procedure. A final control CT-scan is sometimes acquired to rule out adverse events, such as haemorrhage or pneumothorax.

Appendix 2 – Use cases

Biopsy of a pulmonary lesion

The intervention was a CT-guided biopsy of a lung carcinoma situated in the upper lobe of the right lung. The lesion size was 14 x 14 mm (long axis x short axis). The needle traversed 90 mm inside the patient towards the lesion and was angulated 6 degrees measurement from the vertical axis. An in-plane approach was adopted during the intervention.

The preparation phase was performed according to the description of the freehand approach. The patient remained conscious and unsedated during the procedure. The patient was lying in a prone position on the CT-table, with the head towards the imager bore. The path was then planned according to the method described before. The use of contrast-enhancement was not necessary as the lesion could be clearly distinguished from the surrounding lung parenchyma. It was decided to target the lesion using a dorsal approach, as the needle trajectory inside the lung could be minimized this way. Ideally, the needle would traverse only the skin, subcutaneous tissue, the muscles of the back and subsequently the lung lesion. The duration of this was 14 – 15 minutes (time retrieved retrospectively from DICOM timestamps, measuring the time between the first spiral CT-scan and the first needle insertion). Due to the retrospective nature of the analysis, the exact time spend on preparation and path planning could not be retrieved.

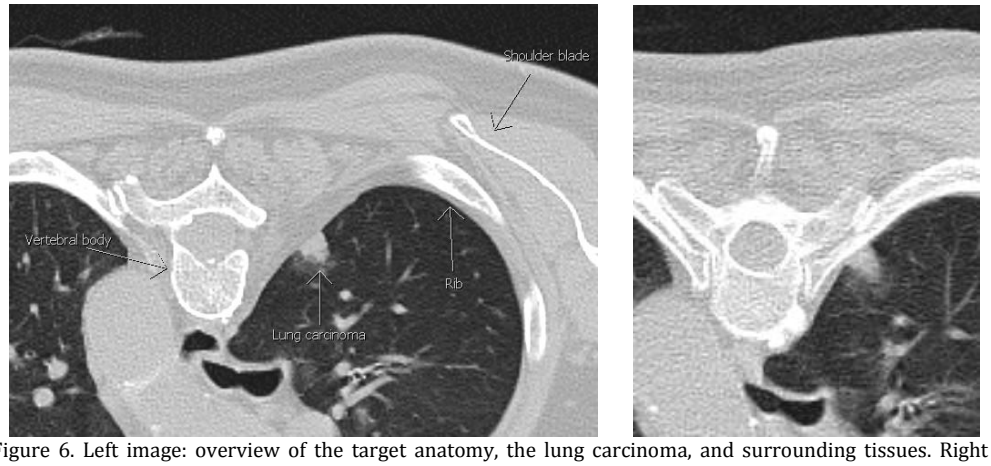

Figure 6. Left image: overview of the target anatomy, the lung carcinoma, and surrounding tissues. Right image: tumor displaced such that the ribs and vertebrae interpose the planned needle trajectory

The process of estimation, advancing the needle and imaging was iterated a total of 19 times, from which 2 times with the hypodermic needle to administer the local anaesthetic, until the tip of the needle was located at the target lesion for the first time. During the needle positioning, the tumor displaced multiple times under influence of the patient's respiration, as seen in Figure 6. The physician first tried to compensate for the motion by observing the respiration and advancing the needle during the end expiratory phase, but failed. Subsequently, the physician provided the patient with respiratory instructions, which after a few tries, enabled the physician to position the tip of the needle inside the lesion. To minimize the risk on pneumothorax, the tip of the guide needle remained extrathoracal during the needle targeting; only the biopsy needle entered the thoracic cavity once the guide needle was positioned such that advancement of the biopsy needle would result in adequate positioning of the needle tip. The duration of the needle targeting and positioning phase was ± 9 minutes. The dose-length product (DLP) of the fluoroscopy CT-scans was 75.5 mGy·cm (a total of 69 CT slices), whereas the DLP of the whole procedure was 300 mGy·cm (1 spiral CT with a total of 81 CT slices, accounting for 220.6 mGy·cm).

Use case – radiofrequency ablation of a renal carcinoma

The intervention was a CT-guided radiofrequency ablation of a carcinoma of the left kidney, located centrally in the parenchyma of the lower renal pole. The lesion size was 9 x 7 mm (long axis x short axis). The needle traversed 94 mm inside the patient towards the lesion and was angulated 27 degrees measured from the vertical axis. The approach adopted during the intervention was in-plane, but the needle deviated slightly from the axial plane, rendering the needle trajectory just out-of-plane.

The procedure was performed under sedation to reduce the patient discomfort during the procedure by reducing the patient's consciousness. The patient's spontaneous respiration is maintained or lightly lowered in frequency (as most sedative agents can cause respiratory depression). The patient was positioned into a right lateral recumbent position, as seen in the left image of Figure 7. The duration of this phase is not available due to retrospective analysis of the data.

To increase the conspicuity of the renal carcinoma on CT-imaging, a contrast-enhanced CT-scan was performed during path planning. CT-scans were acquired during the phases for arterial, venous and late venous enhancement. The safest needle trajectory could be achieved by using a dorsal targeting approach (needle entry point at the patient's back), as the needle would ideally traverse only the skin, subcutaneous

tissue and the muscles of the back. However, as the colon was positioned in close vicinity to the planned needle trajectory, the patient was repositioned to a (near) prone position, after which the risk of unintentional needle placement into adjacent critical structures decreased. The duration of this was ± 21 minutes (time retrieved retrospectively from DICOM timestamps, measuring the time between the first spiral CT-scan and the first needle insertion). This is an overestimation of the real time spend on path planning, as during this phase the physician also tried to fuse the CT-imaging with real-time ultrasound but failed.

The process of estimation, advancing the needle and imaging was iterated a total of 19 times and took place within ± 7 minutes. The dose-length product (DLP) of the fluoroscopy CT-scans was 139.9 mGy·cm, whereas the DLP of the whole procedure was 489 mGy·cm (1 spiral CT: 63 slices, 116.9 mGy·cm, 1 spiral CT: 38 slices, 67 mGy·cm and 3 CT's for the arterial, venous and late venous phases for the contrast-enhanced CT).

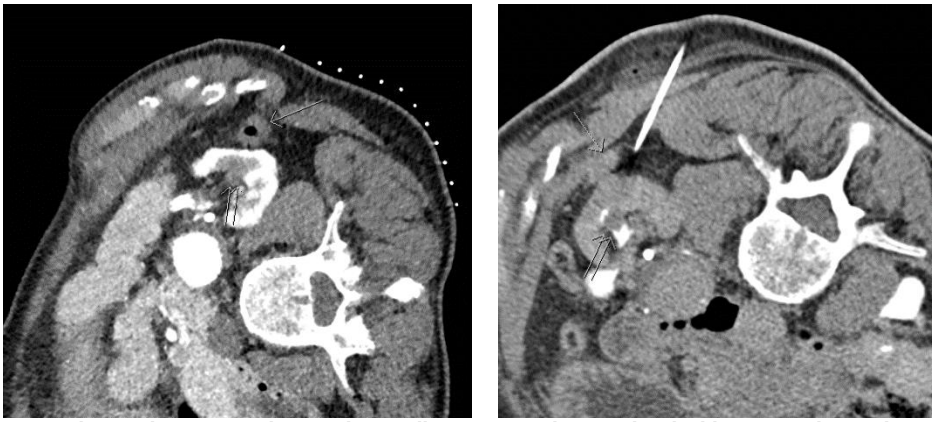

Figure 7. The single arrow indicates the small intestine, whereas the double arrow shows the renal carcinoma. Left image: first positioning of the patient in a right lateral recumbent position. Right image: after repositioning the patient in a (near) prone position.

Appendix 3– Stakeholder analysis

Requirements and wishes of the stakeholders, used in preparation for user requirements

1. Patients

- Impact on workflow
    - Procedural time (total procedure): ≤ current practice
    - Interventional time (CT-guided intervention): ≤ current practice
- Comfort/burden/load
    - Physical load, burden or the extent to which the use of the device causes physical discomfort, e.g. pain, the need to carry out additional invasive (restricted) activities such as punctures, incisions, administering of contrast agent, radiation exposure, etc.
    - Mental load, burden or the extent to which the use of the device causes mental discomfort, e.g. when the patient needs to cooperate or to comply with instructions; the looks of the device (does it look trustworthy, etc.)
- Effectivity
    - High accuracy and precision to increase chance on procedural success (e.g. biopsy from target tissue, complete ablation, etc.)

2. Hospital

- Hospital board
    - Safety and number of complications
    - Efficiency and effectivity
    - PR

- Department: medical physics
    - Usability: comfort/burden/load
        - Physical load, burden or the extent to which the use of the device causes discomfort
        - Mental load, burden or the extent to which the use of the device causes discomfort. Initial effort: complexity of technique/learning curve. Iterative effort: complexity of maintenance, resolving technical errors.

- Management
    - Influence on current workflow; number of procedures per day, number of employees, storage, time for training of staff

- Department: central sterilization
    - Components to be sterilized after each procedure; total amount, size, presence of grooves and ridges complicating sterilization.

- Department of radiology: radiologists
    - Impact on workflow and efficiency
        - Procedural time (total procedure): ≤ current practice
        - Interventional time (CT-guided intervention): ≤ current practice
        - No assistance from other staff required during procedure
        - Device does not get in the way/block the access to the patient/requires to be moved in and out of the sterile field, etc.
    - Effectivity
        - High accuracy and precision to increase chance on procedural success (e.g. biopsy from target tissue, complete ablation, etc.)
    - Comfort/burden/load
        - Physical load, burden or the extent to which the use of the device causes discomfort; e.g. ergonomics, requirement to hold certain positions for prolonged periods, etc.
        - Mental load, burden or the extent to which the use of the device causes discomfort. Initial effort: complexity of technique/learning curve. Iterative effort: complexity of technique (few vs. many procedural steps), e.g. 3D visualization skills, 'translation' of navigation instructions to real-time needle advancement and compensation for motion, etc.
    - Safety
        - Physician-controlled incision, needle insertion and needle advancement

- Department: finance
    - Initial costs: device cost price
    - Iterative costs: requirement to make/sterilize components that are used during the procedure, potential extra staff, training of current staff, requirement to use certain type of accessories (e.g. specific needles, etc.)

- Department of radiology: CT technicians
    - Impact on workflow and efficiency
        - Device does not get in the way/block the access to the patient/requires to be moved in and out of the sterile field, etc.
        - No assistance from other staff required during procedure
        - Device should been easy to (keep) clean and the amount of loose components should be minimized.
    - Comfort/burden/load
        - Physical load, burden or the extent to which the use of the device causes discomfort; e.g. set-up effort, ergonomics, requirement to hold certain positions for prolonged periods, etc.
        - Mental load, burden or the extent to which the use of the device causes discomfort. Initial effort: complexity of technique/learning curve in setting up the device. Iterative effort: complexity of technique (few vs. many procedural steps), e.g. image fusion, image registration, calibration etc.

<u>3. Insurance companies</u>
- Equal or lower procedural costs
- Efficiency and effectiveness

<u>4. DEMCON</u>
- Sales, support and finance
    - Development: time and costs to design and create the technology and produce the device.
    - Cost price of the system
    - Iterative costs, e.g. requirement to produce sterile components for single use, etc.
- Production/assembly/maintenance
    - Complexity and diversity of production, maintenance and repair of devices
    - Required accuracy and precision
- Quality
    - Safety; required accuracy and precision, number of complications
    - CE marking
- Project management
    - Time management: time allocated to project
    - Qualified staff
    - Workflow NPS+motion compensation doesn't require much adaptions from NPS workflow

Appendix 4 – Scoring list

- Impact on current workflow
    - Changes with respect to current workflow
        - Single vs. multiple operators required (other personnel required to use device?)
            - E.g. induction of general anaesthesia for HFJV, (in)compatibility with other commercially available/currently used instruments or devices (CT-scanner)
        - Tasks the user(s) should perform (especially tasks after creating sterile work field)
    - Influence on procedural time and efficiency
        - Procedural time ≤ current procedural time.
        - Preparation and set-up time
            - E.g. device: learning time of a potential respiratory model. Patient: learning time (e.g. breath hold using visual feedback).
    - Learning curve (initial effort: time to get used to the system)
        - Staff: training time, physical/mental load
    - Usability: ease of use/complexity of handling the device (iterative effort)
        - Staff: physical and/or mental load
        - Need for additional soft- or hardware

- Performance
    - Accuracy and precision
        - Number of needle manipulations << current number of needle manipulations
    - Procedural success rate ≥ current success rate
    - Ability to compensate for non-static target environment (target lesion and surroundings)
    - Operator-dependency

- Safety and risk
    - Complication rate
    - Physician- versus device controlled needle advancement
    - Staff exposure to ionizing radiation ≤ current exposure

Patient burden/load

- Required patient cooperation or compliance to instructions
    - E.g. mental: understand instructions or physical: consistently hold breath for multiple iterations
- Additional invasive (restricted) activities
    - E.g. punctures, incisions, administering of contrast agent, additional radiation exposure, etc.
- Other (mental or physical) load for the patient

- Potential of the (new) business case(s)
    - Marketability → indication range and procedural uniformity (applicability for different patient populations)
    - Strength of business case; e.g. consumables.
    - Aesthetics; the extent to which the device is appealing to potential users (gut feeling)

- Costs
    - Development (time & costs)
        - Design, research and validation
        - Production of device, e.g. complexity and diversity of production
        - Reparation and maintenance
    - Initial costs: cost price of the system
    - Iterative costs: requirement to make/sterilize components.

Appendix 5 – User requirements

The following user requirements were defined:

Number	Requirement	Comments
UR001	*Effectiveness*: the procedural success rate should be equal to, or higher than the rate achieved during current clinical practice.	Freehand procedure was unsuccessful in 9/63 cases (14%) e.g. due to tissue samples inadequate for histopathological analysis.
UR002	*Efficiency*: the procedural time shall be equal to, or lower than current clinical practice.	The complexity of setting up the device (CT technicians), handling the device (radiologists), following the instructions (radiologists, patients) and overall impact on current workflow. Median CT-room time was 40:15 min (range: 23:50 – 162:51 min) for all procedures, 25:20 (range: 23:50 – 56:19) for lung biopsies
UR003	*Efficiency*: the number of needle manipulations should be (significantly) lower than during current clinical practice.	Median (range) # needle manipulations is 9 (4 – 30) for the total dataset, and 8 (5 – 15) for lung biopsies.
UR004	The use of the system should not expose the patient to additional physical discomfort and/or invasive (restricted) activities.	For example, due to the need to hold an uncomfortable position for prolonged periods and exposure to additional activities such as punctures, incisions, administering of contrast agent, radiation exposure, etc. In 17/63 a minor complication occurred; pneumothorax, haematoma, subcutaneous emphysema and/or haemoptoe
UR005	The use of the system should not expose the staff to additional exposure to ionizing radiation.	Median (range) dose-length-product was 101 mGy·cm (23 – 856 mGy·cm) for the CTF scans for the total group, for the biopsies, the median DLP was 101 mGy·cm (23 – 329 mGy·cm). The perprocedural DLP accounted for 15 – 33% of the total procedural DLP.

UR006	The use of the system should not expose the patient to additional mental discomfort.	Patients should be able to cooperate or to comply with instructions provided by the user/physician.
UR007	The system should be CT compatible.	Additionally, in the most optimal case, the workflow, software and hardware (e.g. required accessories such as the system to mount the NPS to the CT-table) are equal for different types of CT-scanners and manufacturers.
UR008	*Efficiency*: the user/physician should be able to operate the device by themselves without assistance.	Both before and after a sterile environment has been created. No assistance from other staff should be required during procedure, as this would disrupt the workflow and decrease the clinical applicability of the device.
UR009	The system should enable manual, automatic and/or autonomous needle insertion.	To be decided; during manual insertion the physician receives haptic feedback, which suits the current procedure better, but automatic insertion could provide advantages of reduced physician radiation dose and improved accuracy.
UR010	The system should facilitate operator-independent needle-positioning.	Operators should be able to use the system and achieve the same results, independent on their level of experience.
UR011	The system should enable needle positioning in non-static environments (target lesion and surrounding tissues).	Device must compensate for movement of the target tissue and the surrounding environment during needle path planning and guidance.
UR012	*Accuracy*: the user should be able to position the needle tip with a maximal error of 5 mm with respect to the indicted target lesion.	Current accuracy requirement is <5 mm, with a design goal of <2 mm. Based on the median lesion sizes, this should be sufficient to perform adequate biopsies in >94% of the lesions (only 4/63 lesions had a short axis lesion size < 10 mm). Median needle insertion depth was 89 mm (45 – 165 mm). The depth range for the accuracy requirement should be 135 mm (sufficient for 62/63 cases)

Appendix 6 – Respiratory surrogate signal

Introduction

Respiration-induced motion of thoracic and abdominal organs can cause needle targeting inaccuracy during image-guided percutaneous procedures as the trajectory is planned based on a static imaging dataset.

The motion of a lesion or the host organ is often difficult or infeasible to track in real-time during the procedure. An indirect approach of motion tracking is therefore often adopted. Several methods exist to acquiring a surrogate signal of the respiration, from scalar to higher dimensional signals. Scalar surrogate data includes those acquired by respiratory bellows, a spirometer or the displacements of optical markers or electromagnetic transponders positioned on the thorax or abdomen of the patient, whereas multidimensional data could be acquired from surface scanning techniques or 3D imaging. [58] Independent from the approach that is employed to acquire the surrogate respiratory trace, a method is needed extract the information from the signal that is relevant to the gating window and the time during which the trajectory planning and needle insertion can take place.

In this chapter, we propose such a method. The aim was to explore the approaches that can be adopted to provide visual feedback regarding the current patient breathing motion to the physician during image-guided procedures, and assess their feasibility.

Methods

Materials

For all processing, calculation and visualizing steps, Matlab R2015b (academic use, MATLAB version 8.6.0.267246. Natick, Massachusetts: The Mathworks Inc, 2015) has been used. The author was not involved in the acquisition of the motion data; the data had previously been acquired by measuring the displacements of an electromagnetic transponder inside a moving phantom over time in the superior-inferior and anterior-posterior direction. The displacements were measured in millimeter and were provided in two arrays, together with an array that contained measurements of the time in seconds.

Peak and trough detection (retrospective)

The respiratory surrogate signal was indicated as **X**, the array contained a total number of samples *n*. The difference between the values of the displacement amplitudes of the current index *i* and the following index *i*+1 was calculated for every index i by performing an array-based subtraction: [**X**(2) - **X**(1) **X**(3) - **X**(2) ... **X**(n) - **X**(n-1)]. The resulting array was considered as the approximate derivative **dX**.

The property that the derivative passes through zero at inflection points was used to determine the location of the peaks and troughs. At the location of a peak, the sign will change from positive to negative, and in the case of a trough the other way around. To determine the sign of the approximate derivative, the elements of the array were divided (in an element-wise manner) by their absolute value: **dX** /|**dX**|. Positive values will become the + 1, whereas negative values will become -1. The difference between each index *i* and the following index *i*+1 was calculated for the resulting array by means of array-based subtraction. An inflection point is located at the positions where the sign changes. The subtraction will result in zero in case of two sequential indices with the same value, but will result in -2 and 2 at the positions of respectively peaks and troughs. The indices of the negative and positive nonzero entries of the resulting array are the locations of the candidate peaks and troughs respectively.

To get rid of 'false positive' peaks and troughs, it was evaluated whether the distance between the candidate locations was higher than the threshold set for the minimal duration of one respiratory cycle. Candidate locations that did not fulfill this requirement were removed from the peak and trough data. The thresholds for the minimal and maximal duration of one cycle were set to 3 and 7.5 seconds, assuming that the normal breathing frequency ranges between 8 and 20 cycles per minute.

Peak and trough detection (prospective)

The latter method can be made real-time by determining the peak in a prospective manner. Again, the approximate derivative **dX** is calculated and the property that the derivative passes through zero at inflection points was used. When a peak or trough is approached, the value of the approximate derivative will decrease to zero. Upcoming peaks or troughs can be found by thresholding the data, for example by a value of zero ± 5% of the total value range of the derivative, depending on whether the peaks or troughs need to be detected.

Respiratory gating

Using the peak and trough data, the durations of the respiratory cycles were calculated. To extract the end-expiratory phases, time-based, fixed gating was be used. Defining the start and end of one respiratory cycle as the positions of two sequential troughs, the gate representing the end-expiratory phase was assumed to account for the last 20% of the duration of an average cycle and the first 5% of the following cycle.

The gates can also be defined based on the motion amplitude. In this case, a fixed width gate was used in order to make sure that the position range remains equal for each of the gates, as this is a crucial premise to minimizing the effect of lesion motion on needle targeting. Two approaches can be used to implement this. The first approach is based on the 95% confidence interval of the amplitudes of respiratory troughs; the width of the interval will act as width of the amplitude gate. A second approach that may be adopted is that the gate starts end when the current becomes below and above a threshold. Taking into account the accuracy requirement, it is proposed to set the threshold at the level of the mean amplitude of the troughs + 2.5 mm.

Results

Figure 8 shows the displacement motion over time. The average duration of one respiratory cycle was 2.93 seconds ± 0.06. The order of magnitude of the standard deviation is about 2% of the signal. The time-based, variable width gate has lead to an amplitude range of 1.5 ± 0.4 mm and an average gate width of 0.6 seconds. A visualization is provided in Figure 9. The amplitude range for the amplitude-based, fixed width gates was on average 2.5 ± 0.4 mm, with an average duration of the gates of 1.9 seconds. The results are displayed in Figure 10. Lastly, the average amplitudes of the peaks and troughs are visualized together with the 95% confidence intervals are provided in Figure 11.

Discussion

Although the performance of fixed gate widths has been shown be less than variable gate widths, the accuracy range is within the predefined requirements. However, a trade-off was made between the extent to which the motion was minimized and the duration of the gate. The latter should be long enough to enable fixing the needle within

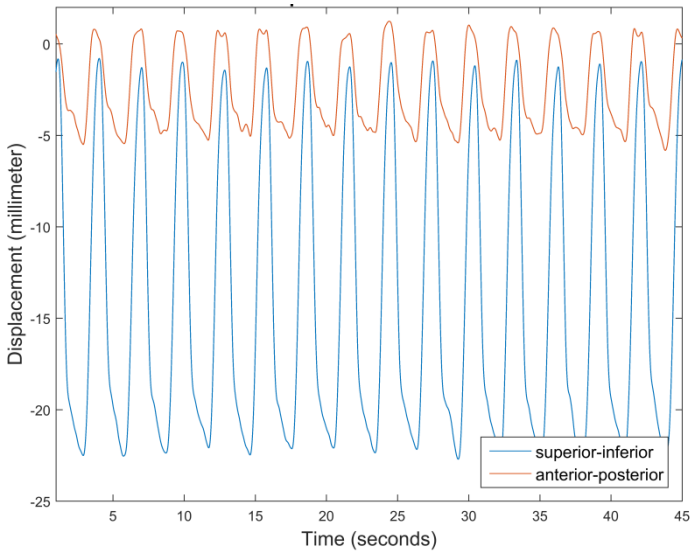

Figure 8. The displacements in the superior-inferior direction (blue line) and anterior-posterior direction (orange line) displayed over time.

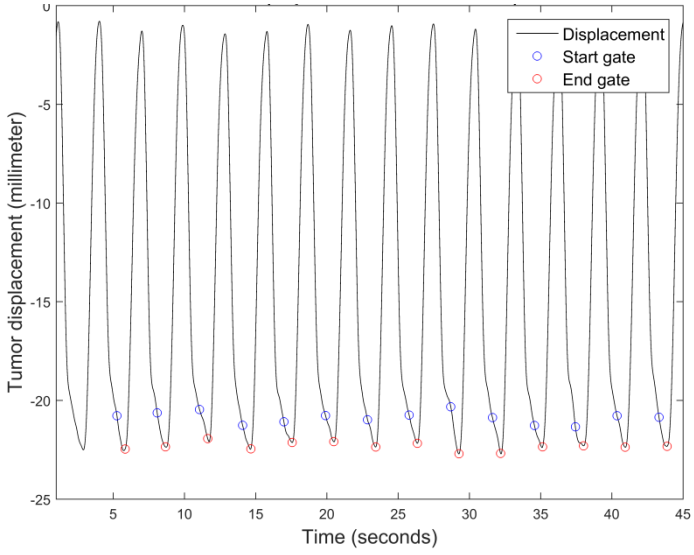

Figure 9. The displacements in the superior-inferior direction (black line) are displayed over time, together with the start and end positions of the time-based, fixed gating.

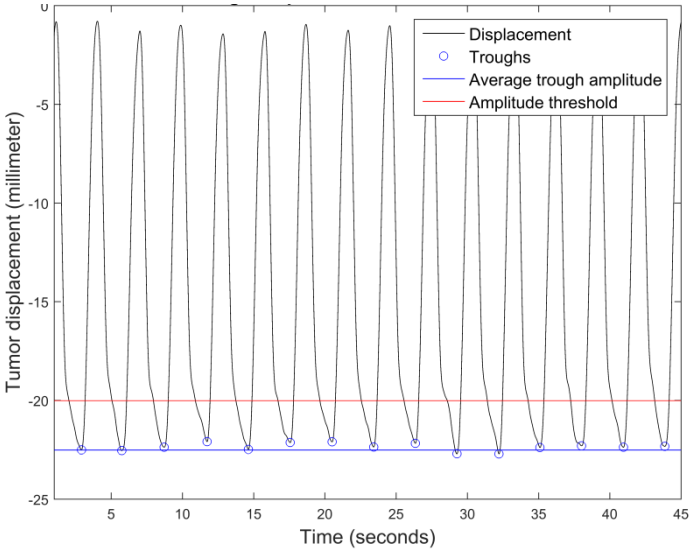

Figure 10. The displacements in the superior-inferior direction (black line) are displayed over time, together with the start and end positions of the amplitude-based, fixed gating.

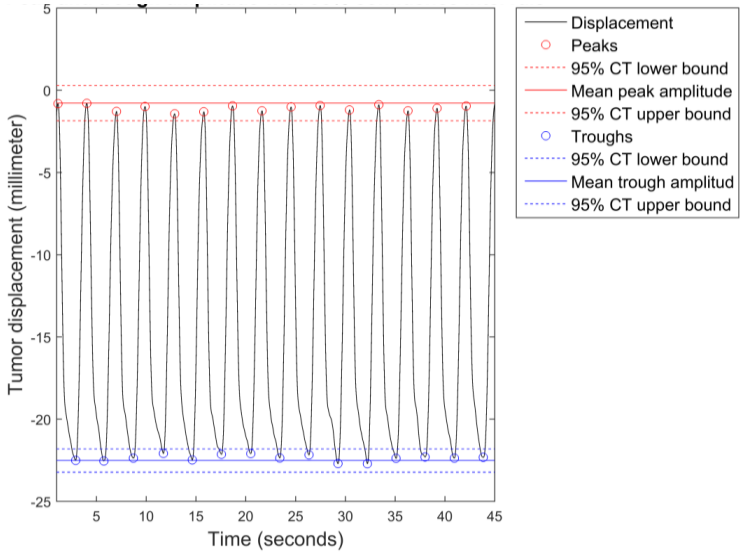

Figure 11. The displacements in the superior-inferior direction (black line) are displayed over time, together with the 95% confidence intervals of the amplitudes of the peaks and troughs.

the needle clip, inserting the needle and releasing, in case of unconscious patients. For conscious, the duration of the gate can be increasing by asking the patient to hold their breath, which would facilitate a single-insertion needle placement.

Overall, it seems that adopting a gating technique, next to the implementation of a biofeedback system, is promising to reduce the effect of respiration-induced motion during percutaneous procedures.