CHAPTER 9

English Summary & Discussion
The aim of the research described in this thesis was to investigate methods to improve the accuracy of CT-guided needle placement both in lung and liver and to find factors affecting the size of the ablation zone with liver tumor ablation.

In Chapter 2, the complication rates of CT-guided core biopsy and fine needle aspiration (FNA) of lung nodules were investigated in a meta-analysis as a baseline. In total, over 8,000 biopsy procedures and almost 5,000 FNA procedures were included. The pooled overall complication rates were 38.8% and 24.0% and major complication rates were 5.7% and 4.4%, respectively. Overall complication rate was higher for core biopsy compared to FNA (p<0.001). For core biopsy, no significant risk factors were identified. For FNA, larger needle diameter was a risk factor for overall complications (Chapter 2, figure 4). Note that higher gauge needles have a smaller diameter than lower gauge needles. The odds ratio of complications for very small diameter needles (≥22-gauge) was as low as 0.30, compared to larger diameter needles (p<0.001). For major complications, increased traversed lung parenchyma and smaller lesion size were risk factors.

The use of smaller biopsy needles results in a smaller biopsy sample and potentially a lower diagnostic yield, especially when additional genomic testing is required for mutation analysis to optimize treatment. Some results regarding the use of smaller needles for mutation analysis are promising: Solomon et al. have demonstrated that biopsy with 18- to 20-gauge core needle yielded sufficient material in 16 of the 18 cases, with similar mutation assay results to that of the surgical specimens obtained after biopsy [1]. However, Lian et al. have demonstrated in a study with 250 cases that the use of smaller core biopsy needles (19-20 gauge) resulted in a lower positive epidermal growth factor receptor (EGFR) detection rate compared to larger needles (16-18 gauge, 24% vs. 45.5%, p=0.006) [2]. Additionally, Schneider et al. have found that core needle biopsy (18-22 gauge) resulted in a higher number of samples sufficient for molecular testing than FNA specimens (22-25 gauge, 67% vs. 46%, p=0.007) [3]. Therefore, the best way to reduce complications, while maintaining a high diagnostic accuracy, is to minimize lung parenchyma damage in other ways. The number of biopsy needle repositionings required to reach the lung nodule was generally not reported in the included studies of the meta-analysis and therefore it cannot be judged whether this is a risk factor. However, the fact that larger needle size and increased traversed lung parenchyma (both increasing tissue damage) were identified as risk factors, suggests that minimizing the number of biopsy needle repositioning attempts will reduce complications. This can be achieved by accurate first-hit targeting, eliminating the need for needle repositioning.
To be able to assist the operator with accurate percutaneous needle placement, the needle placement system (NPS) was developed in cooperation with DEMCON [4]. It consists of a robotic arm that mounts on a rail parallel to the CT table and can be manually positioned on top of the entry point on the skin. After locking the system, it automatically orients a needle guide towards the target. Subsequently, the needle can be inserted by the operator to the specified depth. The system was developed to be used for CT-guided liver tumor ablation and also has great potential for CT-guided lung biopsy. Clinical implementation of the NPS is more straightforward for microwave ablation of liver tumors, compared to lung biopsy. This is because CT-guided liver tumor ablation is performed under general anesthesia, eliminating the need for respiratory compensation. Additionally, liver MWA is associated with a lower complication rate, making it a safer procedure to perform initial validation of a new system [5, 6]. The current issue with liver tumor MWA is incomplete ablation. Complete coverage of the tumor and safety margin is dependent on accurate MWA antenna placement and on the creation of a consistent reliable ablation zone. Robotic guided antenna placement has the potential to resolve the first cause of incomplete ablation.

To test the NPS in a pre-clinical setting, an anthropomorphic liver phantom model was developed to simulate CT-guided liver ablation, mimicking clinical practice. In Chapter 3, MWA antenna placement with the NPS was compared to freehand antenna placement, using this phantom. Two experts and two novices had to target twelve 1-mm balls, suspended in gelatin, with different depth and angulation. Angulation category refers to whether targets were within the same axial plane (in-plane) or in a different plane (out-of-plane) as the entry-point at the skin surface. The goal was to get within 5 mm of the targets. The phantom proved to function well. The median number of antenna repositionings was 1 for the freehand group, ranging from 0 to 4. With the use of the NPS, this was reduced to 0, with a range of 0 to 2 (p<0.001). Overall, the accuracy was 2.2 mm for the NPS group, compared to 4.5 mm for the freehand group (p<0.001). Robotic needle guidance resulted in 70% fewer antenna repositionings, with an increase in overall accuracy of more than 50 per cent.

Over the years, numerous systems have been developed to facilitate accurate needle placement. FDA approved devices, comparable to the NPS include the MAXIO (Perfint Healthcare, Chennai, India), a large floor-mounted 5-DOF robotic device with a reported accuracy of 6.5 mm [7]; the CAS-One (CAScination, Bern, Switzerland), a table-mounted navigation system that utilizes visual fiducials requiring a direct line-of-sight, with a reported accuracy of 4.9 mm [8]; and the 5-DOF iSYS1 (iSYS Medizintechnik, Kitzbühel,
Austria), which is most similar to the NPS using CT fiducials and has a reported accuracy of 2.3 mm [9]. In phantom studies, none of these devices have demonstrated accuracy superior to the NPS used in our study (2.2 mm).

In the freehand group, the accuracy was hardly influenced by target depth; the positioning error was more strongly correlated with the angulation category. From table 1 (Chapter 3) it is clear that the out-of-plane procedures resulted in a higher error for freehand positioning and that the accuracy of NPS antenna placement was independent of in-plane or out-of-plane needle insertion. This is because the system does not rely on two-dimensional images as feedback and, thus, is not hindered when out-of-plane insertions are required. With freehand needle orientation, an out-of-plane target requires the operator to angle the needle in two planes, resulting in a combined error that is usually larger. Some phantom studies specifically focused on the use of navigation systems for out-of-plane procedures. For example, Moncharmont et al. investigated the performance of novices in CT-guided punctures using a navigation system specifically for out-of-plane needle positioning [10]. With a single attempt, the operators achieved a median error of 3.7 mm using the navigation system. With freehand CT-guidance this was 15 mm (p<0.001). In our study, these errors were less. This is likely because although the operators received feedback from the navigation system, the actual needle orientation was still performed by hand. The authors did not investigate the use of the system for in-plane targets. Meiser et al. demonstrated that improvements with needle guidance were more significant for out-of-plane targets [11]. However, these were all performed under ultrasound guidance, so they cannot be directly compared with CT-guided procedures.

Finally, it was interesting to find that for our study no differences between experts and novices could be demonstrated in the freehand group. In the NPS group, they performed equally well, so both experts and novices made significant improvements under robotic guidance.

To validate the NPS for CT-guided liver tumor MWA in clinical practice, a randomized controlled trial was designed. The primary endpoint was the number of antenna repositionings that was required to reach an adequate position. Chapter 4 describes the results of the 47 tumors that have been included. Twenty-one were included in the freehand group and 26 in the NPS group, of which five were later excluded because they could not be finished with the NPS. Three could not be finished because of technical problems with the NPS and two because of antenna deflection. The technical issues are expected to be resolved in a next version of the device. The MWA antenna initially used
was very flexible and rather blunt, which led to deflection when the needle was entering
the liver capsule which was not encountered in the phantom study. Despite this
unanticipated needle deflection, the MWA antenna did not require additional
repositioning to reach an adequate position in any of the included NPS procedures. In
contrast, during the freehand procedures, the median number of repositionings was 1,
ranging from 0 to 7 (p<0.001). The overall total number of antenna manipulations to
reach an adequate initial position was 21 and 54 for the NPS and freehand group,
respectively. Based on these numbers, one might expect to be able to reduce
complications under robotic guidance. This RCT was not designed and thus not powered
to detect a difference in complication rate. In both study arms, one complication
occurred.

Although the error in Euclidian distance was smaller for the NPS (NPS: 9.6 mm,
freehand: 13.8 mm, p=0.018), the lateral error did not significantly improve for
procedures overall (NPS: 6.6 mm, freehand: 8.2 mm, p=0.204). However, similar to the
phantom study, after stratification by angulation category it was clear where robotic
guidance is outperforming freehand needle repositioning. Figure 4a of Chapter 4 shows
how the median number of needle repositionings in the freehand group increased from
one to three in the different angulation categories, while this number remained zero in
all categories for the NPS group. Additionally, the lateral error of the out-of-plane
procedures was 5.9 mm and 10.1 mm (p=0.007) for NPS and freehand procedures,
respectively.

Despite the relatively large number of (experimental) robotic systems, there are only a
few randomized patient studies that assess their functionality in real clinical
environments. Only two other randomized patient studies were identified that compare
the performance of robotic systems with freehand CT-guided needle placement. In 2005,
the AcuBot was tested for CT-guided RFA of liver tumors in a randomized study with
only 14 patients and unclear methodology [12]. It reduced the number of needle
manipulations from 3.7 to 1, but no accuracy was reported. To this date, the device is
not on the market. In an RCT of 100 patients, Anzidei et al. evaluated the functioning of
the ROBIO-EX for percutaneous lung biopsy [13]. The ROBIO-EX is made by the same
manufacturer (Perfint Healthcare) as the MAXIO mentioned earlier and has a similar
design. They required more needle repositioning (2.7 adjustments) and achieved a
higher accuracy (3.6 mm) than we did. However, results in lung biopsy cannot be
directly compared to MWA antenna placement in the liver, as lung parenchyma does
not cause needle deflection to the same extent as (diseased) liver tissue. Additionally,
biopsy needles are generally stiffer and sharper than (non-metallic) MWA antennas, resulting in straighter needle tracts. It would be interesting to know how the ROBIO-EX would perform in MWA antenna placement for liver tumor ablation. This has been done in a small study with 11 patients, but no accuracy was reported [14]. In another, non-randomized clinical study Engstrand et al. analyzed the accuracy and procedural safety of the CAS-One for CT-guided percutaneous MWA of liver tumors [15]. In 28 tumors they reported a lateral accuracy of 4.0 mm, although no comparison with freehand positioning was made.

In conclusion, previously published non-randomized studies are generally positive regarding the use of robotic devices in CT-guided procedures, but interpretation of their results is often questionable, because of their quality and/or study size. With the more substantial RCT presented in Chapter 4, we have shown that robotic devices truly are of added value for CT-guided liver MWA. However, at the moment this value is proven to be most prominent for the more difficult, out-of-plane procedures. Thus, for superficial in-plane tumors it may not always be advantageous to use needle guiding systems.

In 2021, the results of the MAVERRIC trial are expected [16]. This multicenter trial started in 2015 and recruitment is performed at the Karolinska Institutet, Sweden, at the University Hospital Bern, Switzerland, and at the University Medical Center Groningen, the Netherlands. Patients with colorectal liver metastases treated with robotic CT-guided microwave ablation are included. In most patients, MWA antenna placement is performed with the CAS-One and in some patients from the University Medical Center Groningen with the NPS. Currently, the enrolment of one-hundred patients is almost complete. The primary outcome is the 3-year survival rate. This will be compared to patients that received open or laparoscopic resection of liver metastases identified in the Swedish liver registry database. This large database offers the opportunity to perform a matched pair analysis of resected patients to the included patients treated by percutaneous ablation in the MAVERRIC study. Although MAVERRIC is a non-randomized study, the results will be of major importance because it is a multicenter, prospective study with survival as its primary endpoint. If MWA proves to be non-inferior to surgery, there will be higher level evidence that robotic guided MWA antenna placement is a good alternative to surgery.

In order to use robotic guidance effectively for lung biopsy, the next step was to deal with respiratory motion. In Chapter 5, a system utilizing a Kinect camera to track respiratory motion was presented and tested. This system was able to accurately track
the surface motion of the skin to provide biofeedback of the level of inspiration in the form of a circle moving up and down on a screen (Chapter 5, figure 4). Eight healthy volunteers were positioned on a vacuum mattress in a simulated CT environment and asked to return to a similar level of breath-hold, repeatedly. This was performed with and without biofeedback and validated with spirometry. The median difference from initial breath-hold improved on average from 147.6 mL to just 27.7 mL (p<0.001), with biofeedback. This translates to lung nodule movement of well below half a mm, potentially elimination targeting errors, caused by respiratory motion.

Arguably, some patients could be less capable of understanding the biofeedback and patients with pulmonary disease could have more difficulty to maintain breath-hold compared to the healthy young volunteers. However, the breath-hold procedure can be easily practiced, without acquiring additional CT scans. The radiologist will see the biofeedback, too, and can confirm to the patient if the breath-hold is within limits. If so, the radiologist starts with biopsy preparations. After disinfection of the skin, injection of local anesthetics and making a small incision, the biopsy needle can be angled towards the lesion, using freehand (or NPS) guidance and inserted to a limited depth. Subsequently, the breath-hold instructions can be repeated and the radiologist can verify if the patient performs the breath-hold correctly. If so, the biopsy needle can be advanced towards the lesion. If not, the patient can repeat the effort until the breath-hold is within limits, without acquisition of additional CT scans. When a patient is unable to maintain any breath-hold at all, the system will still be of added value. After initial CT acquisition and system calibration, the patient can be instructed to breathe shallow breathes “around” the level where the CT is acquired at, in order to minimize errors caused by respiratory motion. It will most likely not be as accurate as absolute breath-hold, but it will still be an improvement, compared to no feedback at all.

In 2018, Silverstein and Snyder performed a comparative analysis of respiratory motion tracking (without feedback) using the Kinect V2 and compared it to two commercially available tracking systems (Varian’s RPM system and Anzai belt) [17]. They concluded that the Kinect V2 has a respiratory motion tracking accuracy similar to that of the other systems. Although this may sound promising, the other tracking systems have proven to be inadequate for image-guided procedures; logically, the Kinect would be inadequate, too. However, the main difference in tracking technique between their study and ours, is that we selected the entire surface of the skin to be tracked with the Kinect (Chapter 5, figure 3), where Silverstein and Snyder selected just nine points/pixels, thereby eliminating more than 99% of the pixel depth information. This is
also the reason they require a filter to remove noise from the data, demonstrating that it is not just about using the correct device, but also about designing the software correctly. On theoretical grounds, the design presented in Chapter 5 is superior to any of the available tracking systems, because it utilizes the entire surface of skin that moves with respiration, instead of a few points or the circumference of the thorax.

Another method to deal with respiratory movement is to adjust the needle direction, during insertion. This can be achieved by needle steering. Often, biopsy needles are bevel-tipped and have a natural tendency to deflect because of the forces exerted on their asymmetric tip. By rotating the needle after initial insertion, but before reaching target depth, the direction of deflection can be actively controlled, thereby steering the needle. In Chapter 6, a novel CT-compatible robotic setup for steering a bevel-tipped flexible needle is presented. It consists of a needle insertion device (NID) that is attached to a remote-center-of-motion robot arm and allows for automatic needle rotation and insertion (Chapter 6, figure 2). The robot arm orients the NID and thus the needle towards the target. After initial automatic insertion, the direction of the needle can be verified using CT and if needed, the NID automatically rotates the needle thereby steering it to compensate for errors. Additionally, an electromagnetic tracking system is used with a sensor in the tip of the needle, to be able to track the needle tip’s position in real-time, during insertion. CT is used to update the position of the target and needle-tip accurately, four times during insertion. In static phantom experiments, five spheres at a depth of 56-100 mm were targeted with this system, resulting in a mean targeting error of 1.78 ± 0.70 mm. More recently, the NID was mounted on a 6 degrees-of-freedom robotic arm in order to target a moving phantom and ex-vivo liver [18]. Mean errors of 1.2 ± 0.8 mm and 2.5 ± 0.7 mm were achieved, respectively, thus demonstrating the system was able to compensate for a moving target. Unfortunately, the authors used ultrasound as a real-time imaging modality, making it unsuited for lung biopsy procedures.

Despite the positive results of these needle steering studies, there are several disadvantages of automatic needle steering that make clinical implementation on short term difficult. The amount of needle deflection cannot be predicted exactly, therefore, the position of the target and the needle need to be updated to the NID several times during insertion. Ultrasound is less suitable for lung biopsy and ablation of liver tumor in cirrhotic livers, and additional CT acquisitions make needle insertion a cumbersome time-consuming iterative process, resulting in a higher patient radiation dose. Another issue with needle insertion with the NID is the lack of force feedback through the needle.
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to the operator. With freehand insertion, the operator can feel the resistance of the tissue which has several advantages. It can be used to verify the needle’s position, for example when the pleura or the liver capsule is punctured, so the operator knows exactly how deep the needle is inserted. It also functions as a safety measure: when a rib is hit by accident the operator can stop further insertion. Finally, for these experiments a 24-gauge needle was used. Generally, biopsy and FNA needles are not that thin (16-22 gauge) and thus less flexible for needle steering. Ablation antennas are even thicker (13-15 gauge) and more rigid, making needle steering probably not suitable.

In chapters 7 and 8, a different challenge with liver tumor ablation was investigated. Complete coverage of the entire tumor and a surrounding safety margin is not only dependent on accurate MWA antenna placement. Equally important is the creation of an ablation zone that is consistent, regarding size and shape. These and other largely unknown variables are essential to prevent the most devastating outcome of thermoablation, namely incomplete ablation. Manufacturers’ provided protocols are often based on experiments in non-perfused, ex-vivo porcine or bovine livers. As a baseline, in Chapter 7 all preclinical and clinical data regarding the performance of most FDA approved MWA devices was summarized, in a systematic review. In total, 34 studies were included and described, 14 of which reported sufficient data that could contribute to an analysis of the ratio of ablation zone volume to the applied energy, R(AZ:E). The general conclusion was that the results of animal liver ablation algorithms are not reliable predictors of the size of the ablation zone in relation to the amount of energy applied. More clinical research is needed to verify the effects of different tumor types and underlying liver parenchyma on R(AZ:E).

Chapter 8 describes the effort to find tumor and/or liver characteristics that might help to optimize ablation zone protocols. The purpose was to find the relation between the amount of applied energy and the resulting ablation zone volume. Retrospectively, 90 liver tumor ablation procedures were analyzed, based on one RFA and two MWA devices (MWA_A and MWA_B). For each procedure, the ablation zone volume and the amount of applied energy were determined to calculate the energy deposition ratio R(AZ:E). Subsequently, R(AZ:E) was compared between HCCs and CRLMs. For RFA, no differences were found (RHCC = 0.22, RCRLM = 0.15; p=0.110), but for MWA, R(AZ:E) was significantly higher for HCC compared to CRLM for both devices (MWA_A: RHCC = 0.81, RCRLM = 0.43; p=0.001), MWA_B: RHCC = 0.67, RCRLM = 0.43, p=0.040). This indicates that relatively less energy is required to achieve a certain ablation zone volume in HCC. Whether it is because of differences in tumor or underlying liver parenchyma
characteristics is not entirely sure. The HCC’s were all in patients with cirrhotic liver, whereas the metastatic colorectal liver tumors are generally present in non-cirrhotic liver parenchyma. This interesting result has not been published before. Remarkably, a study by Amabile et al. with a different MWA device resulted in conflicting results.[19] The authors speculate that the HCCs resulted in larger ablation zones because of a reduction of water content in the cirrhotic tissue, resulting in a lower absorption of microwave energy. This may be true and it might have contributed to the difference they found. On the other hand, cirrhotic livers are generally believed to be less perfused, thus resulting in a lower heat-sink from the microvasculature of the parenchyma [20, 21]. Amabile et al. only included single cycle procedures. In our study, ablation of liver tumors was generally achieved by creating multiple overlapping smaller ablation zones. Furthermore, the findings are all device specific. We found different $R_{HCC}$ values for the two microwave devices we investigated and Amabile et al. used yet another MWA device. Although the MWA devices operate on the same basic principles, they all utilize different techniques to try and produce consistent, spherical ablation zones. Due to the complexity of the underlying mechanisms of microwave ablation, regarding to electrical properties (relative permittivity and electrical conductivity) and thermal properties (thermal conductivity, specific heat capacity, density and nominal blood perfusion rate) it is hard to tell exactly why Amabile et al. found difference in outcome, compared to our study.

Percutaneous liver tumor ablation has more and more replaced the role of surgery over the last decade because several studies found that MWA is at least as effective as surgical resection [22, 23]. In order to continue this trend towards the less invasive approach, it is critical that validation of current and new ablation devices is performed in perfused and diseased liver, while keeping in mind that findings cannot be blindly translated between different MWA devices. This way ablation protocols can be personalized towards the individual patient, in an effort to eliminate the risk of incomplete ablations.

**Future developments and perspective**

*Dealing with needle deflection*

In Chapters 3 and 4 we have demonstrated that robotic needle guidance can result in very accurate percutaneous needle placement. However, the limiting factor with regard to accuracy was needle deflection. In fact, in some clinical cases MWA antenna placement could not even be finished under robotic guidance, because of extreme antenna deflection. In Chapter 6, a system is presented that could potentially deal with this deflection by steering bevel-tipped MWA antennas. But as mentioned there are
disadvantages to this method that prevent it to be clinically implemented in the near future. Thus, the easiest way to deal with needle deflection is to limit the extent that the antennae can deflect, by using stiffer needles and by limiting steeper entry angles into the liver.

Due to a global recall by the manufacturer of the MWA antennas initially used in the clinical trial, a different MWA device with other antennas was used for the remainder of the study (last 13 procedures, 8 of which robotic guided). The new antenna proved to be sharper and stiffer. As a consequence, none of the last 13 procedures suffered from antenna deflection to the extent that the first 34 procedures did and the lateral accuracy for the NPS group improved from 7.4 mm to 4.8 mm (p=0.007). Unfortunately, the study was not designed to compare these two types of antenna. In a new study it would be interesting to compare the effect of antenna type and the effect of coaxial antenna insertion; the antenna that was used in the last procedures was suited to be used in combination with a coaxial needle. The coaxial needle can initially be inserted with a solid metal sharp stylet inside, resulting in a very stiff coaxial/stylet combination that can puncture the liver capsule. Subsequently, the stylet can be removed and replaced with the MWA antenna that is then inserted to the target depth. This research can be performed as a cadaver or phantom study, where the setup must be such that the (substitute) skin and liver capsule are representative of clinical practice and have to be punctured under various angles. If such a study does indeed prove that stiffer coaxial/stylet combinations are capable to penetrate into the liver at steeper angles with high accuracy, there is evidence that subsequent studies with robotic guided liver MWA have to be performed with stiffer needles.

The downside of using coaxial needles for CT-guided lung biopsy is that the coaxial needle is larger in diameter, compared to just using a biopsy needle. From Chapter 2 we learned that an increase in needle diameter may lead to a higher complication rate. Therefore, it is promising that in 2018, Zhang et al. showed in a retrospective study of 485 patients, that the use of coaxial needles increased diagnostic accuracy, while reducing the change of a pneumothorax [24]. So, despite the increased complication risk of the larger needle size of coaxial needles, it seems to prevent air leakage. This is probably because the coaxial needle allows for a single puncture in the pleura, even when several biopsy specimens are acquired, which in turn reduces tissue damage.

To conclude, robotic guided liver ablation and lung biopsy will probably both benefit from using a stiff coaxial needle/stylet combination. So, it is critical that future clinical
studies that analyze robotic guided needle placement take this into account in order to be able to profit optimally from the accuracy provided by robotic devices.

**Respiratory tracking in clinical practice**

In order to track the level of respiration combined with visual biofeedback the Kinect has shown great potential to facilitate consistent level of breath-hold in healthy volunteers. Unfortunately, (support for) the Kinect camera (V1 and V2) has been discontinued by Microsoft since 2018 [25]. However, Intel recently introduced RealSense Depth Cameras [26]. These low-cost devices are available as individual cameras or as modules to be integrated in other (robotic) devices. Additionally, Siemens recently introduced FAST 3D Camera which is based around a Kinect camera, as an add-on to some of their CT systems [27]. The 3D Camera is integrated in the ceiling of the CT scanner’s room and helps to automatically align the patient. These developments show that depth cameras can be integrated in clinical work-flow, either from the ceiling as a separate camera, or integrated into a robotic device.

The next step will be to test the Kinect, or one of the more recently introduced depth cameras, in clinical practice, for application with CT-guided lung biopsies. The clinical feasibility of such a system can be demonstrated in a pilot study. By initially selecting only patients with easily delineable lung nodules, the consecutive CT scans of the procedures can be used to accurately track the (lack of) movement of the lung nodules between the different scans. These can subsequently be compared with a benchmark of retrospectively analyzed CT-guided biopsy procedures that match those in the pilot study, with respect to patient size and nodule location. This will show whether patients will indeed be capable of interpreting the biofeedback adequately and if their level of breath-hold will be more consistent.

The final hurdle to be solved is to combine both systems: CT-guided lung biopsy with robotic guidance and respiratory tracking. Technically, there will be two additional difficulties. First, use of regular surgical drapes will prevent accurate tracking of the skin. Either surgical drapes with a larger opening can be used, so a larger part of the disinfected skin is visible to the camera or flexible surgical drapes with adhesive backing are an option. These conform to the contours of the patient, allowing for tracking of these kind of drapes. Secondly, the robotic arm will cover part of the thorax, blocking some of the respiratory surface resulting in inadequate respiratory level tracking. This can be solved with software adaptations to the current script. Respiratory motion is relatively slow and limited: the skin moves only a few millimeters up and down per breathing cycle. Using a simple threshold, this can easily be distinguished from the
relatively large and abrupt changes in pixel distance caused by positioning the robot or by the radiologist’s arm, for that matter. By removing the data from these pixels, during real-time acquisition and from the depth image acquired when the initial level of breath-hold was set, any movement in the camera’s field of view other than respiratory movement will be ignored. Implementation of these small adaptations should be relatively straightforward.

This thesis has provided technical developments, validation (phantom and clinical) and ideas for improvements to be able to validate the combination of robotic guided needle placement with respiratory level tracking in clinical practice in the near future. Although the focus of this thesis was on the use of robotics for MWA antenna placement to treat liver tumors and for lung biopsy, the results presented here can be relevant in a broader context. Rapidly evolving genome therapy has enabled patient specific precision oncology; not only for lung or liver cancer, but for other areas, as well [28]. Despite developments in liquid biopsy, where a blood sample is used to analyze cell free DNA from plasma in cancer patients, tissue context of the specific lesion has proven to be a critical factor [29, 30]. This means that obtaining a tissue sample from suspected lesions will be of increased importance to be able to facilitate personalized treatment. Robotic guidance will increase the accuracy of percutaneous biopsy needle placement and thus has the potential to help with diagnosis and specific treatment of hard-to-reach lesions for all kinds of tumors.
References
