Introduction of a new robotic technique for MRI-guided transrectal prostate biopsy: safety and accuracy aspects

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Chapter 1

General introduction
General introduction

Prostate cancer is the most common non-cutaneous cancer in the world. In America the estimated percentage of deaths due to prostate cancer in 2010 is 11% of all cancer deaths\(^1\). With 2421 deaths due to prostate cancer in 2008 this percentage is the same in the Netherlands\(^2\). In order to determine optimal treatment for each patient, it is necessary to determine the cancer characteristics. In this regard, prostate specific antigen (PSA), the results of digital rectal examination and histopathological prostatic biopsy findings (Gleason score) are important aspects. Biopsies are needed to determine aggressiveness and biological activity (Gleason score) of prostate cancer which is an important determinant in patient management. The introduction of PSA screening programs has led to a large increase in the number of men undergoing transrectal ultrasound (TRUS)-guided biopsy of the prostate to determine the presence of prostate cancer\(^3\). However, major shortcoming of TRUS-guided prostate biopsy is the low detection rate of prostate cancer in men with elevated PSA and over detection of insignificant cancer. Studies of 8 to 12-core extended schemes report cancer detection rates around 10% to 17% after the first negative biopsy session\(^4,5\). The detection rate of magnetic resonance image (MRI)-guided biopsies after two or more negative TRUS-guided biopsy sessions is 59%\(^6\). The latter demonstrated the potential role of MRI-guided biopsies in patients with negative TRUS-guided biopsy sessions and elevated PSA. Nevertheless, this procedure is unpleasant for the patient and time-consuming for the radiologist since needle guide positioning towards a cancer suspicious region is a precise work. For these reasons an in-house pneumatically actuated MR-compatible robot was developed where needle guide direction can be controlled inside the controller room. Consequently, the patient remains inside the scanner bore.

Before introducing this new technique into the clinic thorough research of the accuracy and patient safety was required. Chapter 2 describes the accuracy and safety aspects of the pneumatically actuated MR-compatible robotic technique in a phantom study. In this study we try to
find an answer to the following research question: *Is the new transrectal robotic technique accurate and safe enough to perform prostate biopsies in patients?*

This study was partially carried out during an internship in the second year of the master and was finished during the last year of the master. The accuracy experiments and the failure mode effect analysis (FMEA) were performed during an internship in the second year of the master. Experiments regarding radio frequency (RF) heating and the effect of the angle of the needle with respect to the static magnetic field on the artifact size were performed during the last year of the master.

After concluding that the robotic technique can be used safely in patients the accuracy was investigated *in vivo*. Chapter 3 describes the results of this study and a comparison with the existing manual technique was made. This in order to answer the following research question: *What is the accuracy of the new robotic technique used for transrectal prostate biopsies in comparison to the existing manual technique?*

In this chapter a method was introduced to quantify target displacement during the biopsy procedure for identification and quantification of needle placement error. This, to provide recommendations to optimize the biopsy procedure in the future.

Chapter 4 provides a summary and conclusions are drawn from the results in chapter 2 and 3. Also recommendations and improvements for further research are summarized in this chapter.
References


Chapter 2

The accuracy and safety aspects of a novel robotic technique for needle guide positioning to perform transrectal prostate biopsies.
The accuracy and safety aspects of a novel robotic technique for needle guide positioning to perform transrectal prostate biopsies

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Introduction

The recent symbiosis between robotics and medical science has made a rapid development, particularly in imaging and interventions. Different imaging modalities provide feedback to interventional devices which are crucial in precise positioning tasks such as needle insertion, biopsy interventions and catheter placement\(^1\). In the detection of prostate cancer, the most frequently diagnosed form of noncutaneous cancer in men\(^2\), this fusion may help to improve detection rate. The detection rate for TRUS-guided biopsies is low\(^3\). Despite the low detection rate and high false-negative biopsy rate, transrectal ultrasound (TRUS)-guided biopsy is still the standard procedure\(^4\).

Magnetic resonance imaging can be used as a diagnostic tool to detect, localize and stage prostate cancer\(^5\). The detection rate is improved in patients with elevated prostate specific antigen (PSA) and repetitive negative TRUS-guided biopsies using MRI-guided prostate biopsies\(^6-9\).

MR imaging has the reputation of being expensive. This seems to be conceivable when comparing an MRI-guided biopsy session with a conventional TRUS-guided biopsy session in the detection of prostate cancer. Nevertheless, it should be noted that the detection rate of prostate cancer in patients after the first negative TRUS-guided biopsy session is 22% and 14% for the third biopsy session. Generally, multiple TRUS-guided biopsy sessions are needed. The detection rate of MRI-guided biopsies after two or greater negative TRUS-guided biopsy session is 59%\(^10\). The latter demonstrated the potential of MRI-guided biopsies.
In literature, both manually and mechanically actuated experimental MR compatible biopsy devices are described\(^{11-17}\). Most of these devices have a needle entrance pathway (transgluteal and transperineal) where local anesthesia is needed, which is more invasive in comparison with the clinically most commonly used transrectal pathway, where no anesthesia is needed. Furthermore, the transperineal pathway has a longer trajectory to the prostate with more critical structures compared to the transrectal pathway. So far, the only commercially available transrectal MRI-guided prostate biopsy device is a manually adjustable standard for needle guide positioning\(^{18-20}\). This device cannot be controlled from distance, as opposed to the experimental devices that are mechanically actuated from outside the magnet room. A needle guide filled with gadolinium-doped water was inserted in the rectum of the patient. Based on the acquired MR images the needle guide was manually positioned in the direction of the region of interest. This procedure is unpleasant for the patient, operator-dependent, and time-consuming. For these reasons an in-house MR-compatible robot was developed with which the needle guide direction can be controlled outside the magnet room with real-time MRI guidance. Consequently, the patient does not need to be moved in and out of the magnet bore during needle guide repositioning. It is therefore conceivable that this robotic technique may improve procedure time, enhance patient comfort and improve needle guide positioning.

To our knowledge, this is the first pneumatically actuated and magnetic field compatible manipulator for needle guide positioning under real-time MRI-guidance, to perform transrectal prostate biopsies. The purpose of our phantom study was therefore to assess the accuracy and safety of the new transrectal MR compatible manipulator for guidance of prostate biopsies.
Materials and methods

System

The system consists of the manipulator and its controller unit. The controller unit includes a computer, motion control elements and electro-pneumatic and electronic interfaces which are located outside the MR cage of Faraday. Plastic tubes connect the manipulator to the control unit (Figure 1).

The entire manipulator consists of plastic to achieve magnetic field compatibility, for assuring patient safety and prevention of any signal artifacts. The manipulator was designed to interact with the patient within any standard clinical closed-bore MRI system. In this study a closed-bore 3 Tesla (gradient strength: 40mT/m) system was used (Magnetom Trio, Siemens Medical Solutions, Erlangen, Germany) with the body coil of the system as the radiofrequency transmit coil, and a spine and body-array coil for MR signal reception. Phase maps of a localizer image sequence (sagittal, coronal and axial gradient echo images with an echo time of 10 ms) of a volunteer were made with and without the manipulator in correct position to ascertain that the MR compatible manipulator did not disturb the homogeneity of the magnetic field. None of the images in this study were corrected for distortions.
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Figure 1: The robot shown from the side (left panel) and front (right panel). Most important parts are marked, with (1) needle guide, (2) safety mechanism with the suction cup, (3) pneumatic motors, (4) tubings to the motors, (5) ground plate for installation on the MR table, (6) angulation rail to move the needle guide in the sagittal plane, (7) angulation rail to move the needle guide in the coronal plane and the (8) tapping mechanism to introduce the needle guide.

Compressed air used in the pneumatic motors was generated in the controller unit and was transmitted through the plastic tubings (Figure 1). Valves located in the controller unit generate pressure waves to set the motors in motion. The graphical user interface (GUI) for motion control was connected to the controller unit. By selecting the desired motion control button in the GUI the corresponding valve was opened and thereby generating a pressure wave to the corresponding motor, resulting in movement of the needle guide in the desired position/direction. No electricity was required inside the MR magnet room.

The needle guide can be manipulated with five degrees of freedom (DOF), which allows positioning of the end-effector in the desired position. The angle of the needle guide with the main magnetic field could range from 30 to 55° in the sagittal plane and plus or minus 26° in the coronal plane.
To assure patient safety and meet standard safety requirements for the use in a medical environment, the needle guide has a mechanical safety mechanism consisting of a suction cup (Figure 1). When the force from the end-effector applied to the patients rectal wall reaches a primary set value this suction cup will automatically release, preventing the end-effector from harming the patient. The suction cup consists of a seal, underpressure generated in the suction cup results in fixation of the needle guide to the manipulator.

**Patient safety**

In a multidisciplinary group consisting of radiologists and (medical) physicists, a Failure Mode and Effect Analysis (FMEA) was performed. An FMEA is a systematic method to identify and prevent product and process problems before they can occur\(^{21,22}\). In this study an FMEA was performed to identify possible risks and hazards due the procedure or the manipulator itself, therefore ensuring that safety requirements are met.

To assure patient safety, the mechanical safety mechanism was tested using a force dynamometer (Correx, Haag-Streit, 0-2000 gram, Bern, Switzerland). In a previous study of the mechanical properties of the human gastrointestinal tract it was found that a force of 60 N/cm\(^2\) can cause irregularities of the serosa and internal muscular layer of the human small bowel, whereas the mucosa, submucosa and external muscular layer remained intact\(^{23}\). The force needed to release the suction cup was determined at three different positions and directions on the needle guide (A, B, and C; Figure 2). Measurements of this force were repeated 10 times.
Figure 2: Needle guide with the gadolinium-doped water reservoir (Invivo, Schwerin, Germany) to make the needle guide visible on MR images and the work channel (for needle insertion) are shown. The arrows A, B and C represent the direction of the forces applied on the needle guide during the safety experiments.

Depending on size and material, heating of metal wire or needle can occur due to deposited radio frequency (RF) power of the MR pulse sequence\textsuperscript{24}. To assure patient safety in future experiments possible heating of the needle tip in the agar gel was studied with temperature mapping of the agar gel immediately after excessive RF power deposition. Temperature maps of the agar gel were made based on the difference in chemical shift of water with temperature, reflected in a phase shift of the water signal of an MR image between two experiments. After an initial gradient echo image ([repetition time (ms) TR / echo time (ms) TE / flip angle (degrees) FA = 100/20/25], bandwidth 260Hz/pixel resolution 1.56 x 1.56 x 5.0 mm, acquisition time 13 s) as a reference phase map, a multiple spin echo sequence with a continuous power of 148 W for 104 seconds was applied to a 1 kg agar phantom to heat the sample ([TR/TE = 8000/107], bandwidth 465 Hz/pixel). After heating with RF, the temperature map was constructed with the phase map difference of a second gradient echo image and the reference phase map.
Accuracy measurements

To evaluate the ability of sampling with the manipulator, a phantom made of agar was used. Small plastic beads located in the agar represented targets. All beads were imbedded in the agar at the same depth (3 cm) and distance (2 – 3 cm) between them. The beads were 2 mm in diameter.

Figure 3: Flow chart of the biopsy procedure showing the different steps during the biopsy procedure.

A schematic representation of the steps taken to perform a biopsy is illustrated in the flow chart in Figure 3. After the manipulator was connected to the controller unit the phantom and manipulator were placed and secured on the table of the MR system (Step 1). A body-array surface coil was used for MR signal reception (Figure 4).
Figure 4: Measurement set up with the biopsy gun (1) the needle was inserted in the phantom (4) trough the needle guide (3). A body-array surface coil was used for MR signal reception (2). Plastic tubings connect the manipulator to the control room (5).

Once the manipulator and phantom were fixed within the MR system a T1-weighted 3D volumetric gradient echo sequence was used to acquire an image set (Step 2) ([TR/TE/FA = 6.5/2.5/10], resolution 0.72 x 0.72 x 0.72 mm, readout gradient direction H >> F, readout gradient strength= 6.5 mT/m, acquisition time 2 minutes and 20 seconds). The acquired 3D volume was used to select the target (Step 3) and as a reference to navigate on during positioning of the needle guide with real-time MR imaging. After this initial target selection, a software package (Interactive front end (IFE); work in-progress package; Siemens, Erlangen, Germany) was used to orient and direct the needle guide in the desired direction (Step 4). The IFE software provides both 2-D and 3-D display of real-time images. Manipulation of images and relevant controls can be performed in a single screen to simplify user interaction\textsuperscript{25,26}. This software package uses a trufi sequence (Siemens, Erlangen, Germany) which supports interactive changes of imaging parameters during real-time imaging, such as image position/orientation. The sequence is especially designed to assist MRI-guided interventional procedures which require interactive slice positioning for path planning and real-time monitoring of the acquired images. The sequence has the following parameters
(TR/TE/FA=732/1.9/70, resolution 1.65 x 1.65 x 5.0 mm, readout gradient strength= 15.4 mT/m, 3 slices in different planes (sagittal, coronal, transverse plane), refresh rate = 2.2 s).

After correct positioning of the needle guide (Step 5) according to the performing physician, the patient table with the manipulator and phantom was moved out of the magnet bore (Step 6), and the biopsy was taken manually (Step 7) with a standard biopsy gun (titanium 18-gauge, fully automatic, core-needle, double-shot biopsy gun with needle length of 170 mm and tissue core sampling length of 17 mm (Invivo, Schwerin, Germany)). The setup was returned to its original position in the magnet (Step 8). Again a 3D volumetric gradient echo (TR/TE/FA=4.6/2.0/10, resolution 0.72 x 0.72 x 0.72 mm, readout gradient direction H >> F, readout gradient strength= 25.5 mT/m, acquisition time 2 minutes and 20 seconds) image was acquired with the needle inserted in the phantom (Step 9) to evaluate the accuracy of sampling the target.

The time needed for every step in the biopsy procedure was measured in order to evaluate the time needed for the procedure.

The angle of the titanium needle with the static field (B0) of the MR scanner was of influence on the artifact size of the needle. To determine the influence of the angle on the size of the artifact, different insertion angles relative to the static field were made, and the same 3D image sequence used to determine the accuracy was utilized to measure the artifact size.

**Data evaluation**

To determine the accuracy for needle positioning the in-plane error was determined because the out of plane error is less critical in the biopsy procedure due to the core sampling length of 17 mm of the biopsy needle. The in-plane error is defined as the distance between the center of the target and the center of the biopsy needle in the plane perpendicular to the needle. Therefore, the tip of the needle was injected approximately 10 mm beyond the target for hypothetical sampling of the target.
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in the center of the 17 mm biopsy sampling core. In other words: we inserted the needle deep enough to be sure the tip of the needle was beyond the target. The in-plane error, which was the distance between the center of the target and center of the needle, was calculated using the following formula.

\[ \text{error} = \sqrt{(x_{\text{needle}} - x_{\text{target}})^2 + (y_{\text{needle}} - y_{\text{target}})^2 + (z_{\text{needle}} - z_{\text{target}})^2} \]

The x, y, z coordinates in the patient coordinate system were acquired from an image slice perpendicular to the needle guide, where both target and biopsy needle were visible (Figure 5). The image slices perpendicular to the needle guide were reconstructed from the original 3D-images. For this reason the coordinate system of the original image was still valid and therefore, the distance needed to be calculated from all three dimensions. With the commercially available viewing program Dynacad (Invivo, Schwerin, Germany) the three-dimensional coordinate positions of the center of the needle and target were provided from the reconstructed 3D MR images.

**Figure 5:** In the left panel an image of the phantom is show where both needle and target are visible. The image slice was perpendicular to the needle. The white double arrow represents the in-plane error. From this image it can be seen that the needle artifact was bigger than the real needle diameter (white circle). The influence of the angle with the static field of the MR scanner on the needle artifact is shown in the right panel.
A 3D image set with isotropic voxels was chosen to be sure that the measured distance in every direction will have the same error due to the voxel size and to minimize this error in the reconstructed images, where voxels are not square anymore due to the angulation.

Results

System

In total 19 biopsies in phantoms were performed. No technical problems occurred during the procedure and all predefined targets could be reached. No artifacts from the manipulator were seen on the MR images. Phase maps in all orientations with and without the manipulator in place did not show any differences (data not shown), illustrating that the manipulator did not interfere with the magnetic field homogeneity in any way. The simple interface for manipulation, 5 DOF and fast manipulation speed of the end effector made it effortless to reach a target. Therefore most of the manipulation time was spent on fine-tuning of the final needle guide position, even when two predefined targets were far apart.

Patient safety

The FMEA risk analysis showed minor items for improvement. Most important failure modes observed were incorrect installation of the manipulator on the MR table and incorrect slice selection through the needle guide. Therefore, small technical adaptations were performed such as improved connection of the tubings on the MR table to prevent damage. Also the instructions for correct image slice selection were improved. Most important recommendation in this risk analysis was to test the mechanical safety mechanism.
The mean (± standard deviation) force required before the safety mechanism was activated during positioning of the needle guide was 5.5 ± 0.3 N, 8.1 ± 0.3 N, 15.1 ± 0.9 N for position and direction A (needle guide tip), B and C respectively (Figure 2). If we assume 20 N as the maximum force that can be applied on the needle guide (the mechanical safety tests show that this is in the direction of arrow C) before the safety mechanism will be activated, which includes a safety margin of 4.9 N, we can estimate the minimal contact surface needed to refrain from damaging the rectal wall. Taking 60 N/cm² as the maximum allowed force per surface on the patient in order to prevent bowel wall damage, the minimal contact surface between the needle guide and rectal wall of 0.3 cm² is allowed. Regarding these results, the flexibility of the rectal wall and the estimated surface of the tip of the needle guide (1.8 cm²) we can conclude that the forces applied on the rectal wall by the manipulator cannot cause harm to the patient.

The 1kg agar phantom did heat up a few degrees due to the applied continuous power of 148W for 104 seconds with the high-power multiple spin echo pulse sequence. Temperature mapping showed an inhomogeneous increase in temperature of the agar phantom, with more heat deposited at the bottom of the phantom than near the top. However, from the temperature map after RF heating (Figure 6) it can be seen that there is no local heating around the needle tip in this phantom setup.
Figure 6: Temperature map of a 1 kg agar phantom (left panel) after applying a continuous power of 148 W for 104 seconds to a 1 kg phantom. The temperature map showed an inhomogeneous increase in temperature of the agar phantom. However, no local heating of the needle tip was seen. The colors indicate the relative temperature increase. Blue indicates an increase of 0.0 – 1.0 °C, cyan of 1.0 – 2.0 °C, yellow 2.0 – 2.5 °C and red 2.5 – 3.0 °C with respect to the reference image made before applying a continuous power of 148 W for 104 seconds. An anatomical image of the set up is shown in the right panel.

Accuracy measurements

The installation of the manipulator on the MR table and the connection to the controller unit was accomplished within 10 minutes (Step 1; Figure 3). The mean time needed for manipulation to place the needle guide in the desired position (Step 4) was 5 minutes (range 3 – 8 minutes). Total procedure time to perform a biopsy was less than 30 minutes for each sample (Steps 1–10). To perform an additional biopsy (Steps 4 – 9) 11 minutes extra to total procedure time was needed on average.

For needle placement the mean in-plane error was 3.0 mm (range 0 – 5.6 mm; Figure 7). In 3 out of 19 measurements there was an exact hit of the needle and target. As a result the plastic bead
moved with the needle in the agar phantom and was seen on the needle tip. In the other 16 biopsies the needle missed the target or bounced off on the plastic beads.

An additional difficulty in assessing the accuracy of the procedure was the dependency of the apparent size of the needle in relation to the insertion angle of the needle with respect to the static magnetic field of the MR scanner. The size of the void in the images at the position of the needle increases with the angle between the needle and the static magnetic field (Figure 5).

![Histogram of needle placement error](image)

**Figure 7:** Histogram of needle placement error (n=19), which is defined as the in-plane distance between the center of the target and the center of the needle. In three cases a direct hit of the target (error = 0 mm) resulted in movement of the plastic bead along with the needle tip in the agar phantom. In one case the bead probably bounced off the needle resulting in an error of 1.6 mm (half the diameter of the needle plus half the diameter of the target).

**Discussion**

Our MR-compatible transrectal prostate biopsy manipulator demonstrated promising results with respect to the precision of needle positioning and short manipulation time. Furthermore, the manipulator prevented the need of moving the phantom in and out of the scanner bore for manipulation and imaging of the needle guide. This will be an enormous advantage when performing the biopsy procedure with the manipulator in patients.
Safety

Regarding the mechanical safety mechanism tests, we can conclude that the manipulator cannot harm the patient. However, it should be noted that the utilized 20 N/cm² as a measure for rectal wall damage are ex vivo laboratory results for damage in the small intestine. Therefore, extra safety margins were taken into account for the calculations.

Local heating of the needle tip was not seen, in this experimental setup, after applying a continuous power of 148 W for 104 seconds to a 1 kg phantom. In patients in the 3T MR system the amount of RF power that is allowed to be deposited in the body is the SAR limit of 4W/kg averaged over a period of 6 minutes (this is only 9% of the RF power deposited in the phantom). According to these results it is safe to perform in vivo accuracy studies in the future without causing heating damage with the currently used needles to the patient. Nevertheless, care should be taken into account when performing in vivo studies since these results are obtained from one experiment with a particular setup. In our experiment we neither investigated the influence of the surrounding medium of the needle, nor differences in length, angle and position of the needle with respect to the static magnetic field.

Accuracy measurements

We found a mean in-plane error of 3.0 mm (range 0 – 5.6 mm) which is comparable to other devices used for prostate biopsies. Preliminary results of Fischer et al. showed that their transperineal robot successfully punctured five out of five 10 mm targets. The transperineal robot described by Muntener et al. is able to perform biopsies with a median error of 2.02 mm (range 0.86 – 3.18 mm). These results suggested that these devices, including our manipulator, are able to puncture most clinically relevant tumors as 80% of the tumors with a volume of less than 0.5 ml (diameter = 1.0 cm) are unlikely to be important during the life of a patient.
The mean total procedure time was less than 30 minutes which is comparable with the time Muntener et al. describe in their study (30 – 35 minutes). When comparing with the MR-compatible biopsy device (Invivo, Schwerin, Germany) used in clinical practice, the procedure time found in this phantom study was shorter. However, it should be noted that it is difficult to compare phantom studies with patient studies since more precautions are taken when performing a biopsy on a patient. Our results with respect to the procedure time are promising, taking into account that the learning curve for using the manipulator is expected to optimize the procedure times even further. Most procedure time was spent in installation and removal of the manipulator and phantom from the MR table.

The interface for manipulation of the needle guide is user-friendly and does not need a lot of experience from the practitioner. This interface in combination with the IFE software, for interactive changes of imaging parameters during real-time MR imaging, brings manipulation and orientation of the needle guide more together. Manipulation under real-time imaging enables monitoring of progress for the performing physician during intervention.

The pneumatic robot Fischer et al. describe also makes use of real-time imaging during needle guide positioning. However, the perineum is used as the entrance pathway which needs local anesthesia to ease patient discomfort and has a longer distance to the prostate (which may result in a larger biopsy error) when compared to our manipulator using the transrectal entrance pathway.

Limitations and further improvements

By calculating the accuracy as the distance between the coordinates of the centre of the needle and the centre of the target rather than the edge of the needle and target, an error is introduced when the needle touches the target. The target is a plastic bead which can be displaced in the gel by a direct hit of the needle resulting in an error of 1.6mm (half the diameter of the needle (1mm) plus
half the diameter of the target (0.6 mm)). This may have occurred in one needle (error 1.5 – 2 mm) (Figure 7).

The cannula of the needle guide is a fragment wider than the biopsy needle. This may result in an error in needle positioning due to the angle of insertion. This error increases with insertion depth.

The asymmetrical shape of the needle tip and tissue inhomogeneties may result in deflection of the needle.30,31 Bosch et al. use a tapping technique to minimize tissue deformation.17 Although deflection of the needle contributes to the measured error we did not investigate this aspect of needle placement error since this is beyond the scope of this study.

During manipulation under real-time imaging the practitioner has to manually adjust the image slice direction within the IFE software to see whether the needle guide points in the correct direction. However, it should be noted that manipulation time was only 5 minutes and probably will become shorter taking into account that the learning curve for using the manipulator is expected to optimize the procedure time even further.

During manipulation of the pneumatically driven needle guide some delay was seen resulting in overshoots of the needle guide towards the target. This delay was caused by the near-real-time imaging sequence (refresh rate 2.2 s) and by the fact that the pneumatic motors not directly stop moving after release of the motion button in the GUI.

The apparent size of the needle changes with the insertion angle and can be up to four times the actual needle size (5.3 mm). Although this is not of influence on positioning the needle guide with the manipulator (needle is not present yet), it could introduce a systematic bias in the calculated sampling error. The error was calculated from the center of the needle position to the center of the plastic bead. This may result in an error when the exact location of the needle within the signal void in the image is not known.
In this study we did not investigate the required insertion depth of the needle. It is expected that the insertion depth will not be a problem since the sampling length of the biopsy needle is 17 mm. However, the insertion depth should be taken into account in future patient studies.

The range of the new manipulator was comparable with the device used in clinical practice, which can range from 30 – 65° in the sagittal plane and plus or minus 20° in the coronal plane. It is therefore conceivable that the new manipulator can cover the whole prostate. However, apical lesion may become a problem since the range of the manipulator in the sagittal plane is 30 - 50° which is 15° less compared to the range of the manual device (30 - 65°). In a planning study for brachytherapy performed by van Gellekom et al. they showed that it is feasible to cover the entire prostate with the divergent single needle method\textsuperscript{32}. They found that the limited space in the scanner bore and internal patient anatomy were the major limitations for possible needle trajectories. Using the transrectal pathway may overcome these limitations when compared with the transperineal pathway.

The applied sequences have not been tested on patients since we optimized the sequences to obtain the best image contrast in the agar phantom. Before starting patients studies these sequences have to be optimized to obtain the best image contrast in patients and minimize needle artifacts.

In conclusion we can state that the new MR compatible manipulator is safe enough to do the first feasibility tests. It showed a high accuracy and short total procedure time, demonstrating great potential to improve the transrectal prostate biopsy procedure. The next step therefore is to establish the clinical feasibility of the system.
References


Accuracy and safety aspects of a novel robotic technique: a phantom study


Chapter 3

Accuracy of a robotic and manual technique for transrectal MRI-guided prostate biopsies
Accuracy of a robotic and manual technique for transrectal MRI-guided prostate biopsies

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Introduction

The detection rate of prostate cancer in men with elevated prostate specific antigen (PSA) after the first negative transrectal ultrasound (TRUS)-guided biopsy session is poor. Studies of 8 to 12-core extended schemes reported cancer detection rates around 17% after the first negative TRUS-guided biopsy session\(^1,2\). The detection rate of magnetic resonance image (MRI)-guided biopsies after two or more negative TRUS-guided biopsy sessions is 59%\(^3\). The latter demonstrated the potential role of MRI-guided biopsies in men with repeated negative TRUS-guided biopsy session and rising PSA. Nevertheless, this procedure is unpleasant for the patient and time-consuming for the radiologist since needle guide positioning towards a cancer suspicious region is a precise work. For these reasons an in-house pneumatically actuated MR-compatible robot was developed where needle guide direction can be controlled inside the controller room\(^4\). Consequently, the patient remains inside the scanner bore. It is thought that this will improve procedure time, enhance patient comfort and improve needle guide positioning.

In a phantom study the new robotic technique demonstrated a short manipulation time of 5 minutes (range 3 – 8 minutes) and a high accuracy of 3.0 mm (range 0 – 5.6 mm)\(^4\). In a feasibility study transrectal prostate biopsies were performed within 10 patients using the new robotic technique (Figure 1). The median duration time between moving the needle guide from target to target was 2.5 minutes (range 1 – 5 minutes) (unpublished data).
Eighty percent of the tumors with a volume larger than 0.5 cm$^3$ (diameter = 1.0 cm) are likely to be clinical significant during the life of a patient. It is therefore desirable to have a biopsy technique that has a biopsy error which is less than 5 mm. Needle positioning, with either the robotic or manual technique, is influenced by different factors. Besides needle guide positioning towards the lesion, motion of the patient and prostate, as well as tissue deformation have effect on the accuracy. All these factors have effect on final needle position in the prostate. Consequently, the needle does not always reach the targeted region. To optimize the biopsy procedure it is necessary to identify and quantify the cause of the biopsy error. To our knowledge this is the first study which describes the accuracy of a new robotic technique in comparison to the existing manual technique used in clinical practice. Thus, the purpose of this study was to determine the accuracy of the new robotic technique used for transrectal prostate biopsies in comparison to the existing manual technique.

**Figure 1:** In the left panel the robot is shown with (1) needle guide, (2) safety mechanism with the suction cup, (3) tapping mechanism to introduce the needle guide, (4) pneumatic motor, (5) tubings to the motors, (6) ground plate for installation on the MR table, (7) angulation rail to move the needle guide in the coronal plane. In the right panel the patient set up was shown. The patient was positioned in prone position in the MR system. After the needle guide was inserted rectally it was attached to the robot.
Materials and methods

Patients

This study was approved by the ethics review board of the Radboud University Nijmegen Medical Centre and written informed consent was obtained from all patients who were biopsied with the robotic technique. From February to September 2010, 13 consecutive patients with a PSA between 7 and 28 ng/mL, prostate volume between 44 and 100 cm$^3$ and at least one negative TRUS-guided biopsy session were referred from the Department of Urology for MRI-guided biopsies. Prior to the MRI-guided biopsy, patients received a 3T (Magnetom TRIO, Siemens, Germany) multiparametric MRI examination of the prostate for identification of possible cancer suspicious regions (CSRs). Axial T2-weighted (T2-w) images, axial diffusion weighted images (DWI) and dynamic contrast-enhanced (DCE)-MR images were obtained using 15 ml gadopentetate dimeglumine$^{3,9}$.

Analysis of the MR images was performed with an in-house developed analytical software workstation. Calculated DCE-MRI parameters were projected as color overlays over anatomical images. Also apparent diffusion coefficients (ADC) maps can be displayed on the same screen. CSRs were determined in consensus by 2 readers with at least 6 year of experience in prostate MR images$^{10}$.

MRI guided biopsy

MRI-guided biopsies were performed within 12 weeks after initial diagnostic MR imaging. Antibiotic prophylaxis was given 3 times with 500 mg ciprofloxacin orally. A schematic representation of the steps taken to perform a biopsy is illustrated in the flow chart (Figure 2).
A needle guide filled with gadolinium doped water was inserted in the rectum of the patient. Subsequently, the needle guide was mounted to the robot or the device used for the manual biopsy technique (Step 1). The MR imaging protocol (Step 2) for target selection and to navigate on during the biopsy procedure is shown in Table 1.

<table>
<thead>
<tr>
<th>Sequence</th>
<th>TR/TE/FA</th>
<th>Resolution (mm)</th>
<th>Acquisition time (minutes)</th>
</tr>
</thead>
<tbody>
<tr>
<td>T2-w turbo spin echo</td>
<td>3620/104/120</td>
<td>0.8 x 0.8 x 4.0</td>
<td>3:26</td>
</tr>
<tr>
<td>DWI b-values, 0, 100, 500 and 800</td>
<td>2000/67</td>
<td>1.8 x 1.8 x 4.0</td>
<td>2:06</td>
</tr>
<tr>
<td>s/mm²</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T2-w 3D volumetric gradient echo*</td>
<td>4.5/2.2/43</td>
<td>1.0 x 1.0 x 1.0</td>
<td>2:20</td>
</tr>
<tr>
<td>T2-w 3D volumetric spin echo</td>
<td>1000/102/100</td>
<td>1.0 x 1.0 x 1.0</td>
<td>2:36</td>
</tr>
</tbody>
</table>

Table 1: Imaging protocol with sequence specifications. The T2-w turbo spin echo and DWI were used for target selection and to navigate on during the biopsy session. Volumetric images were utilized to identify anatomical landmarks used to quantify target displacement.

* first 2 procedures using the robotic technique

Targets were selected (Step 3) on these images based on the targets found in the previously made multiparametric detection images. Manipulation of the needle guide was done using either the
Accuracy of a robotic and manual technique: a patient study

robotic or manual technique (Step 5). After correct alignment of the needle guide the depth of the target was measured on a transversal TRUFI image (true-FISP, in which FISP stands for fast imaging with steady precession) to determine the insertion depth of the needle. The patient was retrieved from the scanner bore to insert the biopsy needle manually (titanium 18-gauge, fully automatic, core-needle, double-shot biopsy gun with needle length of 175 or 200 mm and tissue core sampling length of 17 mm (Invivo, Schwerin, Germany).

Again, a T2-w 3D volumetric gradient echo (first two procedures with the robotic technique) or a T2-w 3D volumetric spin echo image (all other patients) was acquired with the needle inserted (Step 7). When the needle was in the correct position according to the radiologist, another target could be targeted (Steps 3 – 8) or the patient was removed from the MR table (Step 9).

Needle guide positioning using the robotic technique

With a simple graphical user interface the direction of the needle guide can be adjusted by clicking on the corresponding arrow for that direction. A software package (Interactive front end (IFE); Siemens, Erlangen, Germany) was used to orient and direct the needle guide in the desired direction (Step 5) under real-time image guidance. The IFE software provides both 2-D and 3-D display of real-time images. Manipulation of images and relevant controls can be performed in a single screen to simplify user interaction. The software was designed to assist MRI-guided interventional procedures which require interactive slice positioning for path planning and real-time monitoring of the acquired images11,12. This software package uses a TRUFI sequence which supports interactive changes of imaging parameters during real-time imaging, such as image position and orientation. The sequence has the following parameters (TR/TE/FA=894/2.3/60, resolution 1.6 x 1.6 x 5.0 mm, readout gradient strength= 7.53 mT/m, 3 slices in different planes (sagittal, coronal, transverse plane), 0.9 s/slice).
Needle guide positioning using the manual technique

Transversal and sagittal TRUFI images (TR/TE, 4.48/2.24; resolution 1.1 x 1.1 x 3.0 mm) through the needle guide were acquired to determine needle guide direction. Then the radiologist had to manually adjust the biopsy device to point the needle guide towards the target. Consequently the patient had to be withdrawn from the scanner bore. To confirm that the needle guide was in correct position sagittal and transversal TRUFI images were acquired through the needle guide again. These actions were repeated until the needle guide was in the correct position.\(^\text{13}\)

Accuracy

Motion and deformation of the prostate may occur during the biopsy procedure. This will have an effect on the position of the target. Since targeting of the CSR in both methods was done on the images acquired in Step 2, which do not take deformation and motion into account, it is important to distinguish between targeting and biopsy error. These errors are defined in the following sections.

Targeting error \((\varepsilon)\):

The targeting error is defined as the normal distance from needle to the original target location. This error does not take tissue deformation and patient motion into consideration (Figure 3). This error is a measure for needle guide positioning towards the intended target.

Biopsy error \((\delta)\):

The biopsy error is defined as the normal distance from needle to the transformed target location. The coordinates of the transformed target are corrected for tissue deformation as well as patient and prostate motion. The transformed target coordinates were calculated by adding the mean displacement in each direction \((x, y, z)\) to the original target coordinates. In order to do this it is necessary to determine target displacement.
Target displacement ($\phi$):

Target displacement is defined as the distance between the original and transformed target locations. The 3D volumetric images made before (Step 2) and after (Step 7) needle insertion were used to determine target displacement. In these images identical anatomical landmarks around the target were manually selected with the aid of an open source fusion package\textsuperscript{14}. Calcification, verumontanum and the urethra were used as anatomical landmarks. Coordinates of these anatomical landmarks ($\geq 5$) were used to create a 3D vector field where the arrows represent the direction and distance of displacement of the anatomical landmarks (Figure 4). The mean vector of this vector field is a quantitative measure for target displacement since anatomical landmarks around the target were selected.

![Diagram of needle insertion](image)

**Figure 3:** Representation of the needle inside the prostate illustrating targeting error ($\varepsilon$), target displacement ($\phi$) and biopsy error ($\delta$). The targeting error, defined as the normal distance from needle to the original target coordinate ($T$), is shown. Target displacement, defined as the distance between original target ($T$) and transformed target ($T'$), is represented by $\phi$. Furthermore, the biopsy error ($\delta$) is shown which is defined as the normal distance between transformed target ($T'$) and needle.
To calculate the targeting and biopsy error the needle trajectory should be determined. This was done by fitting a line through multiple points (≥8) within the needle artifact. These points were obtained from the 3D volumetric MR images obtained in Step 7. Line fitting was done by orthogonal linear regression in 3D-space using principal components analysis. To evaluate whether the target was within the 17 mm sampling core of the biopsy needle the distance from the tip of the needle to the original and transformed target position on the needle was calculated. Target coordinates were obtained from the T2-w and DW images acquired in Step 2.

**Figure 4:** 3D vector field where the blue arrows represent the direction and displacement of the anatomical landmarks. The red arrow is the mean vector representing target displacement. Furthermore, the needle trajectory (black line), targeting error ($\varepsilon$), original target ($T$), biopsy error ($\delta$) and transformed target ($T'$) are shown.
Direction of target displacement

Both the needle trajectory and target displacement can be described as vectors. It is therefore possible to calculated the angle between needle trajectory and target displacement direction. This was done in order to see whether the target moved along the needle trajectory or in a random direction.

To determine the influence of needle insertion location in the prostate on target displacement distinction was made between insertion in the basis, middle and apex of the prostate (Figure 5). For these locations the mean target displacement was calculated.

Figure 5: Sagittal anatomical TRUFI image of the pelvis. The prostate is located in the middle of the image. The prostate can be divided in the apex (A), mid prostate (M) and basis (B).

Time

Total procedure time and manipulation time were recorded for both the robotic and manual techniques.
Statistical analysis

Two-tailed independent t-tests were performed to determine whether there were significant differences between the robotic and manual techniques for targeting error, biopsy error, target displacement, procedure and manipulation time. The same analyses was performed to calculate significant differences between the location of needle insertion in the prostate and target displacement. Significant differences were considered at p<0.05. Statistical analysis were performed with SPSS, version 16.0.01 (Chicago, Illinois).

Results

In total, 13 patients with 32 needle positions were analyzed. Table 2 describes the patient characteristics for both the robotic and manual techniques.

<table>
<thead>
<tr>
<th>Patient characteristics</th>
<th>Robotic</th>
<th>Manual</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>8</td>
<td>5</td>
</tr>
<tr>
<td>Number of needle placements</td>
<td>19</td>
<td>13</td>
</tr>
<tr>
<td>Mean needle positions per patient</td>
<td>2.4 (range 1 – 3)</td>
<td>2.6 (range 1 – 4)</td>
</tr>
<tr>
<td>Mean PSA (ng/ml)</td>
<td>15 (range 8 – 28)</td>
<td>14 (range 7 – 19)</td>
</tr>
<tr>
<td>Mean prostate volume (cc)</td>
<td>67 ( range 44 – 98)</td>
<td>72 (range 49 – 100)</td>
</tr>
<tr>
<td>Number of repeated negative</td>
<td>2 (range 1 – 4)</td>
<td>2 (range 1 – 4)</td>
</tr>
</tbody>
</table>

Table 2: Patient characteristics for both the robotic and manual techniques.

Accuracy

The mean targeting error for both the robotic and manual techniques was almost similar (Figure 6).

The mean biopsy error was less with the manual technique compared to the robotic technique. Target displacement was larger with the robotic technique. None of these differences were significant different.
Accuracy of a robotic and manual technique: a patient study

Figure 6: Histogram showing the mean targeting error, biopsy error and target displacement for both the robotic and manual techniques. The error bars represent the standard deviation.

When using the robotic technique, the insertion depth was not correct in 5 out of 19 needle positions. As a consequence the original target location was not in the 17 mm sampling core. When looking at the transformed target location, 4 out of 19 needle positions were not correct. For the manual technique 4 out of 13 needle positions were not correct for the original target location, and 3 out of 13 for the transformed target location.

Direction of target displacement

The mean angle between needle trajectory and target displacement direction for the robotic and manual techniques was 36.7° (range 4.0 – 82.2°) and 37.6° (range 7.7 – 73.3°), respectively. Thus, all target displacements were within the insertion direction of the needle.

Most target displacement was seen when the needle was inserted in the apex (mean 7.8 mm; range 2.8 – 13.7 mm) and basis (mean 6.3 mm; range 4.2 – 8.0 mm) when compared to the mid
prostate (mean 5.7 mm; range 2.0 – 9.3 mm). There was no significant difference between the location of needle insertion and target displacement.

**Time**

The mean time to perform a biopsy procedure using the robotic technique was 76 minutes (range 60 – 100 minutes) and 61 minutes (range 52 – 64 minutes) with the manual technique. The total procedure time includes the extra time that is needed to acquire the 3D volumetric images. This is at least 5 minutes extra procedure time. The mean manipulation time to move from target to target was 6 minutes (range 3 – 11 minutes) with the robotic technique and 8 minutes (range 5 – 11 minutes) with the manual technique.

The differences in manipulation time and procedure time between both techniques were not significant.

**Discussion**

Both the robotic and manual techniques demonstrated comparable results regarding targeting error and target displacement. The biopsy error was larger when using the robotic technique, however not significant. The robotic technique prevented the need of moving the patient in and out of the scanner bore for manipulation and imaging of the needle guide.

Most of the target displacement found in our study was in the direction of the needle trajectory. Furthermore, the results suggested that the location of needle insertion in the prostate is of influence on target displacement. Most target displacement was seen when the needle was inserted in the apex and basis. However, these differences were not significant.

Several robots for transperineal seed delivery in brachytherapy have been described in literature\textsuperscript{15-18}. Our robotic and manual techniques demonstrated a larger targeting error (mean 5.7
mm; range 0.11 – 11.3 mm). Muntener et al. found a targeting error of 2.02 mm (range 0.86 – 3.18 mm) with their robot in a canine model\textsuperscript{17}. The targeting error for a transrectal biopsy device described by Susil et al. was 1.8 mm (range 0.4 – 4.0 mm) in three patients\textsuperscript{19}. Xu et al. found a targeting error of 2.2 mm (range 0.5 – 5.7 mm) with the same device in five patients\textsuperscript{20}. In this study, they report a biopsy error of 5.1 mm (range 1.6 – 11.0 mm) and target displacement was 5.4 mm (range 1.6 – 11.1 mm). Although the targeting error was less compared to our results, the biopsy error and target displacement are in concordance with our results.

**Limitations and further improvement**

The anatomical landmarks chosen in the MR images acquired in Step 2 and Step 7 to determine target displacement, were selected manually. This may have introduced an additional error since it is difficult to select exactly the same position. Automatic registration would be an alternative to diminish this error. However, automatic (elastic) registration is difficult and also introduces errors\textsuperscript{16}. Furthermore, the images that need to be registrated are different in the area of the target. This because the needle is causing an artifact in the area where best registration is needed.

The biopsy procedures with the robotic and manual techniques were not performed by the same radiologist. To overcome the limitation of inter-variability, the performing physician of each procedure performed the biopsy session in consensus with the PhD student who attended all sessions.

In the first MRI-guided prostate biopsy procedures using the robotic technique we utilized a gradient echo sequence to determine needle trajectory and target displacement. In the first patient we found an acceptable needle artifact size, varying from 3.5 to 4.5 mm. In the second patient the angle of the needle with the static magnetic field was bigger. As a result the artifact size of the needle increased drastically to 8.5 mm. Therefore, we decided to use a 3D spin echo sequence which was less influenced by distortions of the magnetic field. Needle artifact size now varied from 3.8 to 4.7 mm. However, image contrast was less and acquisition time was increased from 2:20 to 2:36.
minutes. Both 3D volumetric image sequences had isotropic voxels to be sure that the measured distance in every direction will have the same error due to the voxel size.

The quantitative method described to determine target displacement cannot discriminate between patient motion, prostate motion and tissue deformation. However, the mean angle between the needle trajectory and target displacement trajectory was 36.7° (range 4.0 – 82.2°) and 37.6° (range 7.7 – 73.33°) for the robotic and manual techniques. Thus the main target displacement was in the direction of the needle insertion. Suggesting that most of the target displacement was caused by needle insertion.

The TRUFI images used for needle guide positioning with both the robotic and manual techniques used relatively thick MR images of 3 and 5 mm, respectively. This may have influenced the targeting error since it is not certain whether the centre of the needle guide was shown in the conformation scan used for targeting of the needle guide. The needle guide itself was 10 mm in diameter. Slice thickness reduction may help to reduce targeting error. However, targeting error with the manual technique (which uses a smaller slice thickness) was not better.

During the biopsy procedure displacement of the target was seen. This effected the biopsy error. Image registration during the biopsy procedure may attribute to reduce the biopsy error since targeting was done on the static images made before manipulation of the needle guide\textsuperscript{21}. Nevertheless, image registration is often a time consuming process. Furthermore, our results suggested that movement of the target is meanly caused by needle insertion. Thus, image registration during the biopsy procedure would not correct for prostate motion due to needle insertion. Deformation models of the prostate to predict tissue deformation due to needle insertion may help to overcome this problem\textsuperscript{22}. An alternative is to reduce target displacement. Different techniques for needle insertion have been investigated, such as rotating needles and a tapping device\textsuperscript{23-26}.
Although the length of the sampling core of the biopsy needle was 17 mm it was observed that the target was not always within the sampling core for both the original and transformed target. Real time imaging during needle insertion may help to overcome this problem\textsuperscript{18}.

During manipulation under real-time imaging the practitioner has to manually adjust the image slice direction within the IFE software to see whether the needle guide points in the correct direction. Automatic needle tracking during manipulation of the needle guide to automatically adjust image slice direction may help to improve manipulation time. However, it should be noted that the mean manipulation time was only 6 minutes.

With this robotic technique the practitioner has to manually adjust needle guide direction. Manipulation time may be improved when manipulation of the needle guide is performed by the robotic technique. Thus, the practitioner allocates the target and the needle guide is positioned in the correct position automatically.

The robot was designed to perform transrectal prostate biopsies. However, it is conceivable that (focal) treatment of prostate cancer will be possible in the future with the aid of robotics and MR imaging. Emerging treatment types such as focal cryosurgery\textsuperscript{27}, and laser ablation\textsuperscript{28} are now under investigation. These therapies need accurate needle placement. Major advantages of treatment in the MR scanner are the ability of soft tissue imaging and monitoring the therapy. In example, temperature mapping of the tissue during the intervention is possible\textsuperscript{29}.

Although the results of this new robotic technique were comparable to the manual technique, we demonstrated the potential role of a novel robotic technique for transrectal prostate biopsies. Furthermore, this study provided a better insight in displacement of the target during a biopsy procedure, which help to increase the accuracy of transrectal prostate biopsies.
References


Chapter 4

Summary and conclusions
Summary and conclusions

In the phantom study in chapter 2, we demonstrated that the new MR compatible manipulator can be used safely for patient care. The risk analyses met patient safety requirements and no RF induced local heating around the needle tip was observed. It showed a high accuracy of 3.0 mm (range 0 – 5.6 mm). The manipulation time to place the needle guide in the desired position was 5 minutes (range 3 – 8 minutes) and the total procedure time was (30 minutes). Furthermore, the dependency of the apparent size of the needle in relation to the insertion angle of the needle with respect to the static magnetic field of the MR scanner was investigated. The size of the void in the images at the position of the needle increases with the angle between the needle and the static magnetic field.

Chapter 3 describes the accuracy of the new robotic technique in patients. It was found that the accuracy of the robotic and manual techniques was less compared to the results obtained in the phantom study. The mean time needed to move from target to target was 6 minutes (range 3 – 11 minutes) with the robotic technique. This is comparable with the results obtained in the phantom study.

Both the robotic and manual techniques demonstrated comparable results regarding targeting error and target displacement. The biopsy error was larger when using the robotic technique. The robotic technique prevented the need of moving the patient in and out of the scanner bore for manipulation and imaging of the needle guide.

Most of the target displacement found in this study was in the direction of the needle trajectory. Suggesting that most target displacement was caused by needle insertion. Furthermore, the results suggested that the location of needle insertion in the prostate is of influence on target displacement. Most target displacement was seen when the needle was inserted in the apex and basis of the prostate. However, these differences were not significant.
Although the results of this new robotic technique were comparable to the manual technique we demonstrated the potential role of a novel robotic technique for transrectal prostate biopsies. Furthermore, this study provided a better insight in what is happening with the target during a biopsy procedure.

Further research and recommendations

In this study we observed that the biopsy error for both the MRI-guided transrectal prostate biopsy techniques leaves room for improvement. Some recommendations that may help to improve the biopsy error are listed below:

1. Slice thickness reduction of the TRUFI images, used for targeting the needle guide, may help to reduce biopsy error since the targeting error can be reduced.

2. Image registration during the biopsy procedure may attribute to reduce the biopsy error by visualizing target displacement. In this study targeting was done on the static images made before manipulation of the needle guide. Thus the practitioner does not know whether the target moved during the procedure.

3. Our results suggested that movement of the target is meanly caused by needle insertion. Deformation models of the prostate to predict tissue deformation due to needle insertion may help in needle trajectory planning. This can reduce biopsy error.

4. An alternative is to reduce target displacement by using other techniques for needle insertion, such as rotating needles and a tapping device.

Not only the biopsy error help to improve the biopsy procedure. Also other options are worth investigating.

1. Real-time imaging during needle insertion may help to overcome the problem that the target is not always in the sampling core of the biopsy needle.
2. Automatic needle guide tracking during manipulation of the needle guide to automatically adjust image slice direction may help to improve manipulation time.

3. Manipulation time may be improved when manipulation of the needle guide is performed by the robotic technique automatically. Thus, the practitioner allocates the target and the needle guide is positioned in the correct position automatically.

The symbiosis between robotics and MR imaging will play an important role in the treatment of prostate cancer in the future. New developments in scanning protocols, such as temperature mapping, provide major advantages in treatment of prostate cancer, and deserve to be investigated in clinical practice.
Dankwoord

Als eerste wil graag mijn directe begeleiders Jurgen Fütterer en Sarthak Misra bedanken voor de intensive begeleiding tijdens mijn afstudeer traject. Zij hebben mij laten ervaren hoe het is om wetenschappelijk onderzoek te doen. Daarnaast wil ik de commissie leden bedanken. In het bijzonder Paul van Katwijk voor de proces begeleiding en de gezellige vrijdagen.

Omdat een technisch geneeskundige zich thuis voelt in een omgeving van mensen met verschillende disciplines wil ik graag de klinisch fysici van de afdeling radiologie bedanken voor de kritische vragen. Van de imaging groep wil ik in het bijzonder HenkJan Huisman en Pieter Vos bedanken. Tom Scheenen wil ik graag bedanken voor het helpen ontwerpen van de nodige MR sequenties. Van de MRI planning wil ik in het bijzonder Marijke Hogenkamp bedanken voor het inplannen van patiënten met de robot.

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