Published in final edited form as:

J Magn Reson Imaging. 2015 July ; 42(1): 63–71. doi:10.1002/jmri.24770.

3T MR Guided in bore transperineal prostate biopsy: A Comparison of robotic and manual needle-guidance templates

Gaurie Tilak, BS, Kemal Tuncali, MD, Sang-Eun Song, PhD, Junichi Tokuda, PhD, Olutayo Olubiyi, MD, Fiona Fennessy, MD, Andriy Fedorov, PhD, Tobias Penzkofer, MD, Clare Tempany, MD, and Nobuhiko Hata, PhD

Department of Radiology, Brigham and Women's Hospital

Abstract

Purpose—To demonstrate the utility of a robotic needle-guidance template device as compared to a manual template for in-bore 3T transperineal MR-guided prostate biopsy.

Materials and Methods—This two-arm mixed retrospective-prospective study included 99 cases of targeted transperineal prostate biopsies. The biopsy needles were aimed at suspicious foci noted on multiparametric 3T MRI using manual template (historical control) as compared with a robotic template. The following data was obtained: the accuracy of average and closest needle placement to the focus, histologic yield, percentage of cancer volume in positive core samples, complication rate, and time to complete the procedure.

Results—56 cases were performed using the manual template, and 43 cases were performed using the robotic template. The mean accuracy of the best needle placement attempt was higher in the robotic group (2.39 mm) than the manual group (3.71 mm, $p < 0.027$). The mean core procedure time was shorter in the robotic (90.82min) than the manual group (100.63min, $p < 0.030$). Percentage of cancer volume in positive core samples was higher in robotic group ($p < 0.001$). Cancer yields and complication rates were not statistically different between the two sub-groups ($p = 0.557$ and $p = 0.172$ respectively).

Conclusion—The robotic needle-guidance template helps accurate placement of biopsy needles in MRI-guided core biopsy of prostate cancer.

Keywords

MRI-guidance; prostate cancer; transperineal biopsy; robotic device

Introduction

Prostate cancer is the most common malignancy in men and the second leading cause of cancer deaths in the United States (1). Magnetic resonance imaging (MRI)-guided biopsy was originally proposed as an alternative to transrectal ultrasound (TRUS) guided biopsy after repeated negative outcomes in diagnosis despite rising Prostate-Specific Antigen (PSA)

values (2–4). Current multi-parametric MRI provides much improved prostate imaging with a markedly increased ability to define suspicious areas and detect, characterize, and stage prostate cancer. It is superior to TRUS in visualizing suspicious foci and can both target and guide biopsy needles to the foci allowing superior image targeted biopsies (5). Previous studies have found that in-bore MRI-guided biopsy results in a tumor detection rate of 51–59% (2,6) compared to an estimated yield of 15–32% using TRUS alone (7–9). In men with at least one prior negative TRUS biopsy and suspected cancer, the rate of diagnosis from in-bore MRI-guided biopsy can be as high as 70% (10).

Robotic devices have been introduced to overcome some of the access challenges to in-bore MRI-guided biopsies and to improve needle placement accuracy with a goal of better diagnostic yield (11,12). A number of MRI compatible robotic devices have been developed and applied clinically aiming to improve transrectal and transgluteal biopsies under MRI guidance (13–15). Schouten et al. reported a robotic device that was able to achieve accuracy of 5.7 mm in transrectal prostate biopsies in 8 subjects (13,16). Another transrectal device developed in (17) and clinically evaluated in 24 subjects (18) reported targeting accuracy of 2.5 mm. Robotic biopsy can also be performed transgluteally as presented by Zangos et al. reporting the results of 19 subjects (19). Robotics devices for transperineal approach has not been used clinically in MRI-guided biopsies; their reports are limited to phantom or animal studies (20–23). A recent review article in (24) stated concern that the clinical usefulness of MRI compatible robotic devices remains to be seen in MRI-guided biopsies of prostate.

The objective of this study, therefore, is to report the utility of a robotic needle-guidance template for in-bore 3T transperineal MR guided prostate biopsy through a two-arm mixed retrospective-prospective study with relatively large subject population (25). This paper also serves as the original report of a robotic device for MRI-guided transperineal biopsy.

Materials and methods

Patients

This mixed retrospective-prospective cohort study was approved by the ethics review board of our institution and written informed consent was obtained from all patients who enrolled. The study complied with the Health Insurance Portability and Accountability Act. All eligible patients had an abnormal PSA and had at least one MR suspicious lesion on 3T multi-parametric MRI. Exclusion criteria were contraindications to MRI (cardiac pacemakers, brain aneurysm clips or significant claustrophobia) and cardiac disease with risk of silent ischemia.

96 consecutive patients were enrolled between December 2009 and October 2013 and underwent a total of 99 procedures. Three patients underwent second biopsies in the study due to negative outcome in the first biopsy session despite presence of suspicious foci in MRI and rising abnormal PSA, making the total number of procedures 99 out of 96 subjects. Patients were assigned to manual or robotic procedure based on the date of their enrollment in the protocol. The patients who underwent biopsies between December 2009 and

September 2012 were assigned to the manual template cohort, and between September 2012 and October 2013 were assigned to the robotic cohort.

The robotic needle-guidance template we tested was developed elsewhere (26) to help operators to place biopsy needles accurately while keeping the patient fixed in position inside MRI scanner. More recently, a detailed clinical analysis of all cases without distinction between manual and robotic approach has been published elsewhere with specific attention to pathological outcome including Gleason scores and clinical impacts (27). This paper is an extension of these prior arts (25–27) to measure the utility of robots in MRI-guided interventions.

Pre-Biopsy planning—Three radiologists identified suspicious targets by reviewing pre-procedural MRI obtained in a 3-tesla (T) MRI (GE Signa HDx 3.0T MR scanner, GE Medical Systems, Milwaukee, WI). The protocol of consenting on which targets to be aimed in the biopsies are outlined in (27). The pre-procedural imaging protocol included T1-weighted (T1W), T2W, diffusion weighted imaging (DWI), and dynamic contrast enhanced (DCE) sequences with the patient in the supine position, as reported in (28). In particular, the T2W images were acquired using a 2D fast recovery fast spin echo (FRFSE) sequence with the following parameters: repetition time (TR) 2700–4600 ms, echo time (TE) 85–107 ms, field of view = 160 x 160 mm, matrix 384×224, slice thickness 3 mm, pixel spacing 0 mm, and later registered to intra-procedural images for planning.

Biopsy procedure—All biopsy procedures were conducted in a 3T wide-bore MRI scanner (MAGNETOM Verio 3T, Siemens AG, Erlangen, Germany). The procedural setup in the scanner was identical to that reported in (25). Patients were positioned feet-first in the supine position in the scanner. The template, either manual or robotic, was attached on a custom-made tabletop placed on the gantry table of the scanner and registered to the MRI coordinate system using a Z-frame (25) attached to the templates imaged by an axial volume interpolated gradient echo images (TR/TE = 12/2.02; acquisition matrix = 256 x 256; flip angle = 45°; field of view = 160 x 160 mm; slice thickness = 2mm). Figure 1 illustrates the patient setup as well as both templates in position. In a biopsy session, the targets in pre-procedural images were re-identified in intra-procedural T2W images obtained using a combination of Body Matrix Coil (anteriorly placed) and Spine Matrix Coil (posteriorly located) elements (Siemens Medical Systems, Erlangen, Germany). Specifically, this intra-procedural T2W images were taken by turbo spin echo (TSE) sequence (TR/TE 3000–5250/100 ms, field of view = 160 x 160 mm, matrix 320×224, slice thickness 3 mm, pixel spacing 0.4 mm). The image registration of the pre-procedural and this intra-procedural T2W image was performed to further facilitate this re-identification of the suspicious targets (29). Complications documented in the patients' medical record up to the time of hospital discharge were collected.

Manual approach—The detailed description of the manual approach is described in (25). The manual approach used a manual needle guidance template consisting of a grid of holes 1.3mm in diameter spaced 5mm apart. For each core sample collection, the clinician used planning and navigation software, 3D Slicer (www.slicer.org), to plan which guide hole to use for biopsy needle insertion and how deep to insert the needle. The clinician inserted an

18-gauge MRI compatible needle (15cm or 17.5cm long) through the hole and took a confirmation image using axial 2D multislice Turbo Spin Echo images (TR/TE = 2700 ms/106 ms; acquisition matrix = 280×280 ; flip angle = 48; field of view = 200×200 mm²; slice thickness = 3 mm; receiver bandwidth = 252 Hz/pixel; imaging time: approx. 1 min). If the needle was too far from the target, the clinician removed the needle partially or entirely and reinserted. Confirmation images were taken after each insertion. When the clinician felt the needle was acceptably close to the target, a core sample was taken.

Robotic approach—The detailed description of the robotic approach in in-bore transperineal biopsy is described in (26) as well as in Figure 1 and Figure 2. The robotic needle-guidance template (Figure 3) is a motorized template with an ability to set the needle insertion hole with a control resolution of 0.001 mm (26). 3D Slicer software was modified from the one used for the manual approach in (25) to issue motion control command to the robotic needle-guidance template, to align the needle insertion hole to transperineal needle placement trajectory. An axial T2 weighted MR image was taken after the needle was aligned to the target to confirm the accurate placement of the needle to the planned trajectory. If further adjustment was needed, the 3D Slicer software was used to guide the robot in adjusting needle position. The axial T2 weighted MR image was also taken after each adjustment. When the clinician felt the needle artifact was acceptably close to the target in the needle confirmation image, a core sample was taken.

Accuracy—MR images from procedures were maintained on a workstation in Digital Imaging and Communications in Medicine (DICOM) standard format for further analysis. Cases were not used if a needle artifact could not be identified in the image series. A log file containing target coordinates, initial needle hole position for the initial insertion attempt, as well as adjusted needle hole position for succeeding sampling attempt for the same target was kept for every procedure. Adjusted needle hole in manual procedures were often neighboring needle hole from the initial one, whilst adjusted needle insertion positions in robotic procedures were mostly within few millimeter from the initial locations. Finer needle placement adjustments were possible with the robotic needle-guidance template.

Images were reviewed to identify the in-plane distance between the target location and needle tip position. Target location was acquired from the procedure log files. Multi-planar reconstruction view in the DICOM PACS workstation (aycan OsiriX pro, Rochester, NY) was used to identify the needle artifact in each image. The right-left and anterior-posterior coordinates of tip of the needle artifact were recorded. These coordinates and the coordinates of the target were used to find the distance between the two points.

The average distance from the target over all attempts was measured, as well as the best attempt for each target. The accuracy of needle placement was at its best when we found the distance from the target to a needle tip to be minimal. This accuracy from the “best attempt” was collected because the clinician often made multiple adjustments to the needle hole before taking a sample so the closest distance to the target represents the point where sampling actually occurred.

Histopathologic outcomes—Biopsy cores were fixed in formalin and processed according to standard clinical procedure for prostate biopsy. Number of cores collected from each target were recorded. All biopsy core pathology reports were reviewed, when prostate adenocarcinoma was diagnosed. All cores with Gleason score 6 and higher was counted in as a positive cancer. This diagnostic record for each core is hereafter referred to as “diagnosis per core.” If one of the cores from the subject is cancer positive, the diagnosis for the subject was recorded as such. This diagnostic record for each subject is hereafter referred as “diagnosis per subject”. In case a subject has a positive diagnosis in any cores, average percentage of cancer volume per core was recorded for each subject. We hereafter refer this average percentage as “fractional positive tissue rate.”

Procedure time

We compared the procedure time between robotic and manual approach. Two kinds of procedure time were recorded for this comparison. First, “core” procedure time was defined as the time between the registration image scan and the final image scan; as determined from the image header information stored in the images in DICOM standard format. The second was “whole” procedure time that was retrieved from the logbook in the operating rooms. In general, “whole” procedure time was measured between patients entering the MRI scanner room and leaving the scanner room. Induction of anesthesia, placement of the patients in the stir-ups, placement of MRI, preparation of perineum sites, “core” procedure, and ending of anesthesia are all included in the “whole” procedure time.

Statistical analysis

All outcome parameter distributions were tested for normality using skewness/kurtosis test for normality and histograms. Log-transformation was applied to outcome parameters which exhibited significant skewness, and the transformed parameter distributions were confirmed for normality via skewness/kurtosis test. In this study, the skewness was found in accuracy measurements and procedure time. All statistical analysis on accuracy measurements hereafter involved the log-transformed values. All numbers reported hereafter for accuracy and procedure time are log-transformed values, which were transformed backward after skewness of data distribution was corrected by log transform to accommodate statistical analysis using F-test and t-test described below.

Similarity of variances was confirmed using F-test for difference in variance, and a two-sample t-test with unequal variance was employed for the pair that has significantly different variance. Two-sample t-tests were applied to compare each measurement item in manual and robotic procedures. In addition, we conducted adjusted analyses for each outcome measure using a multiple regression model method, adjusting for age, PSA, and volume of prostate. We adjusted for age and PSA to ensure that the patient populations studied were equivalent on basic characteristics.

All tests were conducted in Stata version 11 at an alpha level of 0.05, and only two-sided p-values were reported.

Results

Patients

Of 99 procedures performed. 56 procedures performed between December 2009 and October 2013 used the manual template. 43 procedures between September 2012 and October 2013 were performed using the robotic needle-guidance template. 6 of the manual procedures were performed after September 2012 and originally planned for robotic procedures, but converted to manual procedures, at least a day before the date of procedure, due to malfunction of optical motion limiter(s) of the robot or slippage of screw drive.

The mean age of the patients was 66.01 (± 6.81) years (range: 48–81 years), median prostate-specific antigen level of 8.50 ng/mL (range: 0.02 –86.70 ng/mL) and median prostatic volume of 42.75 cc (range: 10.3 – 177.0 cc). Characteristics of the patients in the manual and robotic groups were not statically different ($p = 0.11$). Patient characteristics are summarized in Table 1.

Accuracy

Data for image based accuracy analysis was available for 88 cases (47 manual, 41 robotic) (Table 2). Log-transformation of average distance and best distance from the target was compared between the two approaches. The difference in their log of average distance from all needle placement attempts was not statistically significant ($p < 0.20$) even after adjusting for the confounders ($p < 0.30$), at a statistical study power of 17%. However, there was significant statistical difference in their log of accuracy when only the best attempts of needle placement were included; robotic approach 0.87 (± 0.97) had statistically higher accuracy than manual approach 1.31 (± 0.86) by $p < 0.027$. This difference remained significant even after adjusting for the confounders ($p < 0.032$) at a statistical study power of 61%. Figure 4 illustrates this phenomenon with a representative case for the manual and robotic groups. The initial attempt in each case was approximately the same distance away from the target. However, the second and third attempts with the robot came progressively closer to the target while subsequent attempts with the manual template remained the same distance away.

Time

The mean core procedure time for the manual group was 100.63 (± 26.24) and robotic group was 90.82 (± 15.93) minutes. The whole procedure time was 151.29 (± 37.88) minutes for manual group and 141.67 (± 19.47) for the robotic group. Only the individual biopsy sampling time was statistically significantly shorter in the robotic approach ($p = 0.030$) with a statistical study power of 62%; the overall entire procedure time was not statistically different between the robotic and the manual groups ($p = 0.40$) with a statistical study power of 36.84%.

Pathology results

The histopathologic outcomes are summarized in Table 3. Robotic approach prompted collection of more cores per target than manual approach does, confirming the trend in Figure 4. In reviewing the record of diagnosis per subject, positive cancer was confirmed in

30 of 56 cases in the manual group (53.57%) and 25 of 43 cases in the robotic group (58.13%). This diagnosis per subject were not statistically different between manual and robotic groups. In studying the diagnosis per core, 147 of the 541 cores (32.16%) taken from patients in the manual group were cancer positive, and 137 of the 310 cores (44.19%) taken from the robotic group was cancer. A the statistical analysis showed that the robotic approach had more chance to provide positive cancer core than manual approach does ($p=0.018$). Fractional positive tissue rate also showed a significant difference ($p<0.001$) between the manual and robotic group showing robotic approach has more chance to provide higher fractional positive tissue rate than manual approach does. This trend remained significant after adjusting for the potential confounder (volume of prostate PSA and age, $p<0.011$).

Complications

Nine cases, or 16.07 % of manual cases, had asymptomatic hematoma in peri-prostatic area visible in intra-procedural MRI, whereas 13 cases, or 30.23% of robotic cases, had similar hematoma visible in MRIs. All hematoma resolved without further intervention in all cases. Five cases, or 8.92% of the manual cases, experienced hematuria, while one case, or 2.32% of the robotic cases, had hematuria in the robotic case. There was no significant difference among the 2 groups in any of the complications. Specifically, the rates of peri-prostatic hematoma had p value of 0.092 and post-operative hematuria had p value of 0.172 in the statistical comparisons with a statistical study power of 62%.

Discussion

In this study, we demonstrated the utility of a robotic needle-guidance template device as compared to a manual template for in-bore 3T transperineal MR-guided prostate biopsy. Our study, which involved 96 patients and 99 cases, has shown that a robotic needle-guidance template resulted in better targeting accuracy, more positive tissue from the cancer core, and reduced core procedure time when compared with the manual approach. Rates of “diagnosis per subject” were similar between the two groups. Differences in complication rates between the robotic and the manual group were not statistically significant.

Our study is in accordance with previous work on MRI-guided robotics for prostate biopsy. Previous work on robotic biopsy devices has shown average targeting accuracy to range between 2.5 mm and 5.7 mm (13,17,18). Our mean targeting error in log transformed value of 5.57 mm falls within this range. One of the benefits of using MRI guidance is that the clinician can employ intraoperative images not only to see the target, but also to adjust the needle position. For this reason, the needle placement accuracy test in our study included both measurements from all needle placements to a target, as well as the best attempt, where needle placement was closest to the target. Often the best attempt was achieved after multiple needle insertion attempts and image-based assessment of the accuracy of needle placements. We found that accuracy improved in subsequent needle placement attempts with the robot to a greater extent than it did with the manual template (3.86 mm with the robot vs. 2.80 mm with manual placement in log transformed values). This indicates that the robot is better able to help the clinician fine tune the needle position. The manual template,

on the other hand, consists of a grid of holes that are 5 mm apart, and this does not allow for the same level of precision in adjustment. Despite these findings, even the manual template had an average accuracy rate of 5.76 mm, which is within the range reported in the literature.

The robotic approach took as long as the manual approach by core procedure time measure, but allowed for and prompted more core sample collections from target sites. It is presumed that when using the robot, physicians had enhanced opportunities to fine tune the access to the targeted sampling sites through automated, more precise targeting enabled by the robot.

We compared the pathology results from both groups to see if this gain in accuracy was reflected in the rate of diagnosis or the profile of cores taken. The diagnostic rate per subject from the robotic procedure was 59.52%, which is on the high end of published values for MRI-guided biopsy, ranging from 51% to 59% in the literature (2,6). This is comparable to the published yield of 54% from a transrectal robotic device designed by Yakar et al. using another form of robotic biopsy but with fewer subjects (15). The rate of diagnosis in the manual group per subject was also within this range, at 53.57%. In comparing our results with MRI-targeted and ultrasound guided biopsies, the diagnostic rate was lower than 62.9% reported in (30) and 69.7% in (31), but higher than 54.4% reported in (32). The literature (30,32) reported that the detection rates depend on the level of suspicion of the prostate on MRI; a more fair comparison among biopsy approaches, including the robotic approach, requires case-matched comparison using the suspicion level in subjects' MRIs.

Practice varies among institutions in terms of the number of targeting sites aimed at and the number of core samples collected per core. In (32), an average of 5.8 cores per patient were collected, aiming at 2.6 targets. Similarly, an MRI-guided transrectal approach collected 5.22 cores (33) from an unknown number of sampling sites. Again, there is a paucity of literature and studies available to compare the impact of a variety of MRI-guided approaches on diagnostic efficiency without matching of biopsy strategy across such studies.

We further analyzed the fractional positive tissue rate to determine if the improvement in accuracy changed the profile of the cores taken. Previous studies have shown that the volume of cancer found in the biopsy sample is useful in predicting the outcome of therapy (34,35). Our pathology results indicate that biopsy sampling with the robot results in cores with a higher fractional positive tissue rate than the manual template results. The procedure time was also comparable in both groups.

In a related study of transperineal MRI-guided biopsy in a closed bore scanner, the average time for needle placements, defined as time between the first needle placement and the final needle placement, was 67.8 min on average (36). Our study, however, included additional procedure time by starting the measurement from the time of template or robot registration and T2W imaging for target planning. These two steps precede actual needle placements. Inclusion of registration and target planning was necessary to measure the improvement in software and the level of automation and digitization with the robotic approach. We found that the more inclusive procedure time revealed a difference in the manual and robotic approach by observing an average of 100.63 minutes in the manual approach and an average

of 90.82 minutes in the robotic approach. It is therefore presumed that the time for the registration and target planning ranged from 23 to 33 minutes, subtracting time for needle placements.

Our study was a mixed retrospective-prospective cohort study (37,38). The criteria for this emerging study design, primarily seen in epidemiology, include (a) the retrospective arm must be similar to the prospective arm in demographics, methods, and other prevailing conditions, and (b) the two arms must remain comparable throughout the entire study period. To fulfill the similarity condition of this study design, our retrospective controls, or “manual” group, were selected based on the same inclusion criteria that were used for the prospective “robotic” cohort. Specifically, all study patients are aged 48–81 years, with no significant difference between mean ages of the control and intervention groups, at $p=0.134$ (Table 1). Limiting patient inclusion to only those managed by a single physician in the same facility for a similar indication (biopsy) further rendered these two patient populations similar and very comparable. Finally, other intrinsic patient parameters, such as prostate gland volume and serum PSA levels, were confirmed to have no significant difference between the two groups, at $p=0.384$ and 0.841 , respectively. Therefore, based on age, sex, diagnosis, procedure, indication for the procedure, managing surgeon, facility used, prostate gland volume, and serum PSA levels, all of the patients are quite similar.

As M. Roberts and S. Ilardi noted in their book (38), the mixed retrospective-prospective design has a positive effect on studies and their outcomes. First, the design allows for inclusion of a larger cohort, hence higher statistical study power, while maintaining “randomization in time.” This randomization was possible because the patients naturally fell into the corresponding arms based on their period of presentation to the hospital for care. Second, a mixed retrospective-prospective design can allow for less observer-induced bias on operating physicians by circumventing the need to randomize patients in the prospective group. Randomizing the prospective arm would limit control over this “Hawthorne effect” on the group. Finally, the data reviewed retrospectively in this study was very detailed, containing specific information on all relevant parameters of the patients, procedural method and outcomes, rendering the data quality very comparable to that of the data acquired prospectively. Therefore, by using high-quality, retrospective data in this mixed retrospective-prospective design, we were able to maximize the advantages of a prospective study and simultaneously minimize the limitations of a retrospective study.

A notable limitation of our study is small sample size which consequently limited the overall statistical power of the study. For instance, based on the demonstrated difference between accuracy of the two surgical methods employed in this study, this study has a moderate (60%) statistical power of identifying this difference, leading us to conclude that the robotic approach produces higher needle placement accuracy in best placement attempts and lower core procedure times, excluding time for patient preparation.

In conclusion, this study presents a quantitative comparative analysis of the accuracy of an MRI-guided prostate biopsy robot. Further studies with larger samples may allow us to conduct a more thorough quantitative analysis of all of our investigative variables. The robot

was found to be more accurate than a manual template. This design could further be adapted for use in focal transperineal radiotherapy or cryoablation, in which accuracy is essential.

Acknowledgments

Grant Support

This work was supported in part by the National Institutes of Health under Award Number P41EB015898, R01CA138586, R01CA111288, P41RR019703, U01CA151261, and U54EB005149. TP received funding from RWTH Aachen University Hospital. NH is a member of the Board of Directors of AZE Technology and has an equity interest in the company. AZE Technology develops and sells imaging technology and software. NH's interests were reviewed and are managed by the Brigham and Women's Hospital and Partners HealthCare in accordance with their conflict of interest policies.

The authors thank Angela Kanan-Roddy and Janice Fairhurst for their dedication and excellent patient care.

References

1. Siegel R, Naishadham D, Jemal A. Cancer statistics, 2012. CA: a cancer journal for clinicians. 2012; 62(1):10–29. [PubMed: 22237781]
2. Hambrock T, Somford DM, Hoeks C, et al. Magnetic resonance imaging guided prostate biopsy in men with repeat negative biopsies and increased prostate specific antigen. The Journal of urology. 2010; 183(2):520–528. [PubMed: 20006859]
3. Hoeks C, Schouten MG, Bomers JG, et al. Three-Tesla Magnetic Resonance–Guided Prostate Biopsy in Men With Increased Prostate-Specific Antigen and Repeated, Negative, Random, Systematic, Transrectal Ultrasound Biopsies: Detection of Clinically Significant Prostate Cancers. European urology. 2012; 62(5):902–909. [PubMed: 22325447]
4. Roethke M, Anastasiadis A, Lichy M, et al. MRI-guided prostate biopsy detects clinically significant cancer: analysis of a cohort of 100 patients after previous negative TRUS biopsy. World journal of urology. 2012; 30(2):213–218. [PubMed: 21512807]
5. Jung AJ, Westphalen AC. Imaging Prostate Cancer. Radiologic Clinics of North America. 2012; 50(6):1043–1059. [PubMed: 23122037]
6. Beyersdorff D, Winkel A, Hamm B, Lenk S, Loening SA, Taupitz M. MR Imaging–guided Prostate Biopsy with a Closed MR Unit at 1.5 T: Initial Results. Radiology. 2005; 234(2):576–581. [PubMed: 15616117]
7. Lujan M, Paez A, Santonja C, Pascual T, Fernandez I, Berenguer A. Prostate cancer detection and tumor characteristics in men with multiple biopsy sessions. Prostate Cancer and prostatic diseases. 2004; 7(3):238–242. [PubMed: 15289810]
8. Pallwein L, Mitterberger M, Pelzer A, et al. Ultrasound of prostate cancer: recent advances. European radiology. 2008; 18(4):707–715. [PubMed: 17938936]
9. Sartor AO, Hricak H, Wheeler TM, et al. Evaluating localized prostate cancer and identifying candidates for focal therapy. Urology. 2008; 72(6):S12–S24. [PubMed: 19095124]
10. Moore CM, Robertson NL, Arsanious N, et al. Image-guided prostate biopsy using magnetic resonance imaging–derived targets: a systematic review. European urology. 2013; 63(1):125–140. [PubMed: 22743165]
11. Elhawary, H.; Zivanovic, A.; Rea, M., et al. Medical Image Computing and Computer-Assisted Intervention–MICCAI 2006. Springer; 2006. The feasibility of MR-image guided prostate biopsy using piezoceramic motors inside or near to the magnet isocentre; p. 519–526.
12. Fütterer JJ, Barentsz JO. MRI-guided and robotic-assisted prostate biopsy. Current opinion in urology. 2012; 22(4):316–319. [PubMed: 22617059]
13. Schouten MG, Bomers JG, Yakar D, et al. Evaluation of a robotic technique for transrectal MRI-guided prostate biopsies. European radiology. 2012; 22(2):476–483. [PubMed: 21956697]
14. Xu, H.; Lasso, A.; Vikal, S., et al. Medical Image Computing and Computer-Assisted Intervention–MICCAI 2010. Springer; 2010. MRI-guided robotic prostate biopsy: a clinical accuracy validation; p. 383–391.

15. Yakar D, Schouten MG, Bosboom DG, Barentsz JO, Scheenen TW, Fütterer JJ. Feasibility of a pneumatically actuated MR-compatible robot for transrectal prostate biopsy guidance. *Radiology*. 2011; 260(1):241–247. [PubMed: 21406625]
16. Schouten MG, Ansems J, Renema WKJ, Bosboom D, Scheenen TW, Fütterer JJ. The accuracy and safety aspects of a novel robotic needle guide manipulator to perform transrectal prostate biopsies. *Medical physics*. 2010; 37:4744. [PubMed: 20964192]
17. Krieger A, Song S-E, Bongjoon Cho N, et al. Development and evaluation of an actuated MRI-compatible robotic system for MRI-guided prostate intervention. 2011
18. Xu H, Lasso A, Guion P, et al. Accuracy analysis in MRI-guided robotic prostate biopsy. *International journal of computer assisted radiology and surgery*. 2013:1–8.
19. Zangos S, Melzer A, Eichler K, et al. MR-compatible assistance system for biopsy in a high-field-strength system: initial results in patients with suspicious prostate lesions. *Radiology*. 2011; 259(3):903–910. [PubMed: 21364080]
20. Fischer GS, Iordachita I, Csoma C, et al. MRI-compatible pneumatic robot for transperineal prostate needle placement. *Mechatronics, IEEE/ASME Transactions on*. 2008; 13(3):295–305.
21. Muntener M, Patriciu A, Petrisor D, et al. Transperineal Prostate Intervention: Robot for Fully Automated MR Imaging—System Description and Proof of Principle in a Canine Model. *Radiology*. 2008; 247(2):543–549. [PubMed: 18430882]
22. Seifabadi R, Song S-E, Krieger A, et al. Robotic system for MRI-guided prostate biopsy: feasibility of teleoperated needle insertion and ex vivo phantom study. *International journal of computer assisted radiology and surgery*. 2012; 7(2):181–190. [PubMed: 21698389]
23. Plante, J-Sb; Tadakuma, K.; DeVita, LM., et al. An MRI-Compatible Needle Manipulator Concept Based on Elastically Averaged Dielectric Elastomer Actuators for Prostate Cancer Treatment: An Accuracy and MR-Compatibility Evaluation in Phantoms. *Transactions of the ASME-W-Journal of Medical Devices*. 2009; 3(3):031005.
24. Sridhar AN, Hughes-Hallett A, Mayer EK, et al. Image-guided robotic interventions for prostate cancer. *Nature reviews Urology*. 2013; 10(8):452–462.
25. Tokuda J, Tuncali K, Iordachita I, et al. In-bore setup and software for 3T MRI-guided transperineal prostate biopsy. *Physics in medicine and biology*. 2012; 57(18):5823–5840. [PubMed: 22951350]
26. Song SE, Tokuda J, Tuncali K, Tempny CM, Zhang E, Hata N. Development and preliminary evaluation of a motorized needle guide template for MRI-guided targeted prostate biopsy. *IEEE transactions on bio-medical engineering*. 2013; 60(11):3019–3027. [PubMed: 23335658]
27. Anonymous. *****. ***** 2014;*****(*).*****_*****.
28. Hegde JV, Mulkern RV, Panych LP, et al. Multiparametric MRI of prostate cancer: an update on state-of-the-art techniques and their performance in detecting and localizing prostate cancer. *Journal of magnetic resonance imaging : JMRI*. 2013; 37(5):1035–1054. [PubMed: 23606141]
29. Fedorov A, Tuncali K, Fennessy FM, et al. Image registration for targeted MRI-guided transperineal prostate biopsy. *Journal of magnetic resonance imaging : JMRI*. 2012; 36(4):987–992. [PubMed: 22645031]
30. Rastinehad AR, Turkbey B, Salami SS, et al. Improving Detection of Clinically Significant Prostate Cancer: Magnetic Resonance Imaging/Transrectal Ultrasound Fusion Guided Prostate Biopsy. *The Journal of urology*. 2013
31. Pokorny MR, de Rooij M, Duncan E, et al. Prospective study of diagnostic accuracy comparing prostate cancer detection by transrectal ultrasound-guided biopsy versus magnetic resonance (MR) imaging with subsequent MR-guided biopsy in men without previous prostate biopsies. *European urology*. 2014; 66(1):22–29. [PubMed: 24666839]
32. Pinto PA, Chung PH, Rastinehad AR, et al. Magnetic resonance imaging/ultrasound fusion guided prostate biopsy improves cancer detection following transrectal ultrasound biopsy and correlates with multiparametric magnetic resonance imaging. *The Journal of urology*. 2011; 186(4):1281–1285. [PubMed: 21849184]
33. Anastasiadis AG, Lichy MP, Nagele U, et al. MRI-guided biopsy of the prostate increases diagnostic performance in men with elevated or increasing PSA levels after previous negative

- TRUS biopsies. *European urology*. 2006; 50(4):738–748. discussion 748–739. [PubMed: 16630688]
34. Vance SM, Stenmark MH, Blas K, Halverson S, Hamstra DA, Feng FY. Percentage of Cancer Volume in Biopsy Cores Is Prognostic for Prostate Cancer Death and Overall Survival in Patients Treated With Dose-Escalated External Beam Radiotherapy. *International Journal of Radiation Oncology* Biology* Physics*. 2012; 83(3):940–946.
35. Linson PW, Lee AK, Doytchinova T, et al. Percentage of core lengths involved with prostate cancer: does it add to the percentage of positive prostate biopsies in predicting postoperative prostate-specific antigen outcome for men with intermediate-risk prostate cancer? *Urology*. 2002; 59(5):704–708. [PubMed: 11992844]
36. Penzkofer T. Transperineal in-bore 3T MRI-guided prostate biopsy: A prospective clinical observational study. *Radiology*. 2014 (in print).
37. Li W, Han J, Hu FB, Curhan GC, Qureshi AA. Psoriasis and risk of type 2 diabetes among women and men in the United States: a population-based cohort study. *The Journal of investigative dermatology*. 2012; 132(2):291–298. [PubMed: 21993559]
38. Roberts M, Ilardi SS. *Handbook of Research Methods in Clinical Psychology*. 2005

Figure 1.

Apparatus setting in in-bore MRI-guided transperineal prostate biopsy. Stirrups (1) are placed on a patient board (2) placed on the table. The robotic needle-guidance template (3) is screwed on to the patient board after patient is placed on the patient board and preparation at perineum site is performed. An abdominal surface coil (4) is over the patient pelvis and the robotic template.

Figure 2. Comparison of manual template (A) and robotic needle-guidance template (B). Both templates are positioned at the patient's perineum and attached to the tables with screws.

Figure 3. Robotic needle-guidance template. The two crossing bars move independent of each other by ultrasonic motors placed in the rear of the device. The bars localize a needle insertion hole at their intersections. The rectangular frame encasing the bars is placed against the perineum.

Figure 4. Magnified views of prostate gland using axial T2-weighted turbo spin-echo MR image. White star indicates target and white circles represent needle positioning attempts, number 1 through 3 chronologically. (A) In manual procedure, subsequent needle positioning attempts do not get closer to the target. Distance from the target is 3.9 mm, 4.0 mm, and 4.00 mm respectively. (B) In robotic procedure, needle positioning attempts get progressively closer to the target. Attempts are 3.1 mm, 1.9 mm and 1.0 mm away from the target.

Table 1

Patient characteristics

		All	Manual	Robotic
Number of patients		99	56	43
Age (y)	Mean($\pm$ SD)	66.01($\pm$ 6.81)	66.91($\pm$ 6.50)	64.84($\pm$ 7.09)
	Range	48.00–81.00	50.00–81.00	48.00–78.00
PSA (ng/mL)	Median	8.50	8.55	8.40
	Range	0.02–86.70	1.69–48.78	0.02–86.70
Prostatic volume (cc) *	Median	42.75	47.85	38.00
	Range	10.30–177.00	11.0–177.00	10.30–107.65

* Data is reported for 83 patients – 49 manual, 34 robotic

Table 2

Procedure time and accuracies

	All	Manual	Robotic	p-value	Adjusted p-value
Average distance (mm) *	Median	5.76	5.39		
	Range	1.48–26.78	1.94–26.27		
Average distance [Log $\pm$ SD] (mm)	Mean	6.05 [1.80 $\pm$ 0.55]	5.42 [1.69 $\pm$ 0.48]	0.20	0.30
	($\pm$ SD)	(3.42, 9.68)	(3.35, 8.76)	Power = 17%	
Best distance (mm) *	Median	3.86	2.80		
	Range	0.07–24.18	0.07–23.68		
Best distance [Log $\pm$ SD] (mm)	Mean	3.71 [1.31 $\pm$ 0.86]	2.39 [0.87 $\pm$ 0.97]	0.027	0.032
	($\pm$ SD)	(1.19, 7.77)	(0.90, 6.30)	Power = 61%	
Whole Procedure time(minutes)	Mean($\pm$ SD)	151.29($\pm$ 37.88)	141.67($\pm$ 19.47)	0.14	0.40
				Power = 36.84%	
Core Procedure time (minutes) **	Mean($\pm$ SD)	100.63($\pm$ 26.24)	90.82($\pm$ 15.93)	0.030	0.323
				Power = 62%	

* Data is reported for 88 patients – 47 manual, 41 robotic

** Data is reported for 98 patients – 55 manual, 43 robotic

Table 3

Histopathology

	Total	Manual	Robotic	p-value	Adjusted p-value
Per patient diagnosis (positive cases/total cases)	55 /99	30/56	25/43		
Ratio (%)	55.55	53.57	58.13	0.557	0.367
Number of cores per target, Mean (SD)	1.88 (1.12)	1.63(0.88)	2.19 (1.31)	0.014	0.012
Per core diagnosis (positive cores/total cores collected)	311/851	174/541	137/310		
Ratio (%)	36.54	32.16	44.19	0.627	0.018
Fractional positive tissue rate, mean (SD)	0.35 (0.26)	0.26 (0.24)	0.42 (0.25)	0.001	0.011