Robotic Transrectal Ultrasound-Guided Prostate Biopsy

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Abstract—We present a robot-assisted approach for transrectal ultrasound (TRUS) guided prostate biopsy. The robot is a hands-free probe manipulator that moves the probe with the same 4 degrees-of-freedom (DoF) that are used manually. Software was developed for 3D imaging, biopsy planning, robot control, and navigation. Methods to minimize the deformation of the prostate caused by the probe at 3D imaging and needle targeting were developed to reduce biopsy targeting errors. We also present a prostate coordinate system (PCS). The PCS helps defining a systematic biopsy plan without the need for prostate segmentation.

Comprehensive tests were performed, including 2 bench tests, 1 imaging test, 2 in vitro targeting tests, and an IRB-approved clinical trial on 5 patients. Preclinical tests showed that image-based needle targeting can be accomplished with accuracy on the order of 1mm. Prostate biopsy can be accomplished with minimal TRUS pressure on the gland and submillimetric prostate deformations. All 5 clinical cases were successful with an average procedure time of 13 min and millimeter targeting accuracy.

Hands-free TRUS operation, transrectal TRUS guided prostate biopsy with minimal prostate deformations, and the PCS based biopsy plan are novel methods.

Robot-assisted prostate biopsy is safe and feasible. Accurate needle targeting has the potential to increase the detection of clinically significant prostate cancer.

Index Terms—Medical robot, prostate biopsy, ultrasound, TRUS, remote center of motion RCM

I. INTRODUCTION

PROSTATE cancer (PCa) is the most common non-cutaneous malignancy and the second leading cause of cancer related death among US men [1]. Nearly 1 of every 6 men will be diagnosed with the disease at some time in their lives [2]. The best current estimate of PCa aggressiveness is the Gleason score obtained from core needle biopsy [3]. The most common biopsy method is freehand transrectal ultrasound (TRUS) guided. Since ultrasound only rarely identifies PCa visually, systematic biopsy (SB) intends to sample the prostate evenly. But freehand biopsy is highly inconsistent, subjective, and results in uneven sampling [4-6], leaving large regions of the prostate unsampled, which can lead to under-sampling of clinically significant PCa, and implicitly under-staging of PCa diagnosis. In response, the current trend is directed towards a targeted biopsy (TB) approach guided by multiparametric Magnetic Resonance Imaging (mpMRI) [7]. TB has advantages over SB because it allows the biopsy needle to be guided to sampling areas based on imaging that shows cancer suspicious regions (CSR). TB methods include direct in-bore MRI targeting [8, 9] and methods that register (fuse) pre-acquired MRI to interventional ultrasound [10-13]: cognitive fusion [14] and device/software aided fusion [10-13]. Current fusion biopsy devices include [15]: Artemis (Eigen) [16], PercuNav (Philips) [17], UroNav (Invivo) [18], UroStation (Koelis) [19], and BK Ultrasound [20] systems.

With the fusion, few cores directed towards the CSRs are taken in addition to the 12-cores of SB. TB cores yield a higher cancer detection rate of clinically significant PCa than SB cores [7, 21]. But TB cores miss a large number of clinically significant PCa detected by SB [10-13], because mpMRI itself has 5%-15% false-negative clinically significant cancer detection rate [3]. A recent multicenter randomized trial [22] allowed men with normal mpMRI (PI-RADS≤2 [23]) to avoid biopsy and reported that TB alone may be preferable to the routine freehand SB. But the study does not tell how many men in whom biopsy was not performed might harbor clinically significant PCa [24]. TB alone is risky and SB plays an important role in prostate diagnosis [25]: 1) Fusion can only be offered to patients with mpMRI findings, yet 21% of biopsy patients have none (range 15%-30%, 3544 patients [10-12, 26]), SB on patients with no mpMRI findings found 42% of men to harbor PCa, of which 1/3 were clinically significant PCa [11]; 2) On equivocal mpMRI lesions (PI-RADS=3), TB alone misses 56% of Gleason 7–10 cancers [26]; 3) The MRI for TB adds $700-$1,500/case, and reliable mpMRI interpretation is limited [27]. The large majority of over 1 million prostate biopsies performed annually in the US [28] are SB. Therefore, SB plays an important role independently and together with TB [25].

Commonly, SB and TB are freehand procedures performed under transrectal ultrasound guidance with the TRUS probe manually operated by a urologist [4, 6] and a needle passed alongside the probe [3, 7]. To acquire ultrasound images, the TRUS probe must maintain contact with the rectal wall for the sonic waves to propagate, in turn pushing against the prostate. The TRUS probe is known to deform the gland, and the amount of pressure is typically variable throughout the

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procedure. Images at different regions of the prostate use different compression. If the deformed 2D images are rendered in 3D, the actual shape and volume of the gland are skewed. Further, if a biopsy plan (SB or TB) is made on the skewed images, the plan is geometrically inaccurate. Moreover, when the needle is inserted for biopsy, the probe deforms the prostate differently contributing to additional targeting errors. The errors can be significant, for example 2.35 to 10.1mm (mean of 6.11mm) [29]. Ideally, targeting errors for PCa biopsy should be <5mm [8] (clinically significant PCa lesion ≥0.5cm³ in volume [30]).

Biopsy planning and needle targeting errors are problematic for both SB and TB. At fusion TB, pre-acquired mpMRI is registered to the interventional TRUS images [31]. The registration is typically performed by aligning the shapes of the gland in ultrasound and MRI. This alignment is challenging due to shape differences caused by the dissimilar timing, patient positioning, imaging modalities, etc. [6, 10, 31]. Prostate deformations by the TRUS probe further magnify the registration problem. Several elastic registration algorithms have been developed to reduce errors [32], and improved the initial registration. However, handling prostate deformations at the time of each needle insertion for biopsy remains problematic [10].

Reducing prostate deformations at biopsy has been achieved on the transperineal needle path, for example with the TargetScan [33] device and Mona Lisa [34] robot. However, no current transrectal biopsy device can reliably minimize prostate deformations. Most devices freehand the probe [17-19, 35-37] and inherently deform the prostate unevenly. The only device that offers probe handling assistance is the Artemis device [16], which uses a mechanical encoded TRUS support arm. This arm helps to reduce deformations, but its manual operation leads to variability among urologists.

In this article, we report a robotic system that takes transrectal prostate biopsy one step further, with an actuated TRUS manipulation arm. Like no other, the robot enables the performance of hands-free, skill-independent prostate biopsy. The report includes the robotic system, the methods used to reduce prostate deformations (at 3D image scan and at biopsy), a novel method to define a SB plan, comprehensive pre-clinical test results, and the outcome of the first 5-patient clinical trial.

II. MATERIALS AND METHODS

A. Robotic System

The robot is a TRUS probe manipulator [38] that moves the probe with the same 4 degrees-of-freedom (DoF) that are used manually in transrectal procedures, closely replicating its movement by hand. As shown in Fig. 1, the TRUS probe can pivot in two directions (ξ₁ and ξ₂) about a fulcrum point (RCM) that is to be located at the anus, can be inserted or retracted (along axis ξ₃), and spun about its axis (ξ₄). The rotations about the fulcrum point are performed with a Remote Center of Motion (RCM) mechanism. The RCM is the most common mechanism used in medical robots [39, 40].

RCM is relatively small and uses belts to implement the virtual parallelogram [38, 41]. A preliminary version of the TRUS robot was reported [38] and used clinically for prostatectomy operations with ultrasound navigation assistance [42]. For biopsy, the robot was updated with a backlash-free cable transmission for the ξ₃ rotary axis and (previous used gears), and larger translational range along the ξ₃ axis. The robot was designed and analyzed in Creo (Parametric Technology Corporation, Needham, MA) and manufactured at our laboratory. Fig. 1 shows the latest version of the robot. The hardware limits of the joints are: θ₁ about ξ₁ (±86°), θ₂ about ξ₂ (−17° to 46°), θ₃ about ξ₃ (±98°), τ along ξ₃ (±49mm).

The robot is supported by a passive arm which mounts on the side of the procedure table. With special adapters the robot can support various probes. A 2D end-fire ultrasound probe (EUP-V53W, Hitachi Medical Corporation, Japan) was mounted in the robot and connected to a Hitachi HI VISION Preirus machine. As shown in Fig. 1, the probe is mounted so that axis ξ₃ is centered over the semi-spherical shaped point of the probe. The system diagram is shown in Fig. 2. The robot controller was built of a PC with Intel(R) Core(TM) i7 3.07-GHz CPU, 8GB RAM, NVIDIA GeForce GTX 970 GPU, Matrox Orion HD video capture board, MC8000 (PMDi, Victoria, BC, Canada) motion control board, 12V/4.25Ah UPS, and 24V power supplies.

Custom software was developed in Visual C++ (Microsoft,
Fig. 3. Software components; a) Robot control; b) Virtual reality for biopsy planning including real-time robot position, 3D ultrasound image, and biopsy plan; c) Navigation screen showing real-time ultrasound and green guide line showing the direction of the needle and insertion depth before firing the biopsy, so that after firing the core is centered at Target.

Seattle, WA) using commercial libraries comprising MFC [43], MCI [44], and MIL [45], and open-source libraries comprising Eigen [46], OpenCV [47], OpenMP [48], GDCM [49], VTK [50], and ITK [51]. Fig. 3 shows the graphic user interface (GUI) with three main components: robot control, virtual reality for biopsy planning, and navigation screen.

B. 3D Ultrasound Scan with Minimal Prostate Deformations

3D ultrasound is acquired from a 2D probe with a robotic scan. A one-time calibration process is required, to determine the transformation and scaling $T_{UV}$ (4x4 matrix) from the robot coordinate system $\Sigma_R$ to the image frame $\Sigma_U$ (Fig. 4). The calibration method was previously reported [52]. A calibration rig was made of a thin planar plastic sheet submersed in a water tank (Fig. 4a). In ultrasound this appears as a line, and was automatically detected using a RANSAC algorithm [53] at different poses of the probe set by the robot. The calibration matrix was then estimated by solving least-square problems [52]. The process was repeated at five depth settings of the ultrasound machine (50, 65, 85, 110, and 125mm), to have the proper calibration if the machine depth is changed.

3D ultrasound is acquired with a robotic rotary scan about $\xi_3$ axis. During the scan, images are acquired from the ultrasound machine over the video capture board. At the time of each image acquisition, the computer also records the current robot joint coordinates and calculates the position of the respective image frame in robot coordinates ($\Sigma_R$) through the calibration and forward kinematics. Overall, the raw data is a series of image-position pairs. A 3D volume image is then constructed from the raw data using a variation of Trobaugh’s method [54]. Rather than filling voxels with the mean of two pixels that are closest to the voxel regardless of distance (needed to fill all voxels in the case of a manual scan), we used only the pixels that are within a given distance (enabled by the uniform robotic scan). The distance was set to half of the acoustic beam width ($D$), which is determined at calibration. The speed of the rotary scan, $V_{\text{scan}}$, is calculated to fill the voxels that are farthest from $\xi_3$, at radius $R$, as:

$$V_{\text{scan}} = \frac{f \cdot D}{R} \text{ [rad/s]}$$  \hspace{1cm} (1)

where $f$ [fps] is the ultrasound frame rate (read on the machine display). Due to the rotary scan, pixels that are closer to the axis are denser, so the number of pixels that were averaged in each voxel was limited (i.e. 5). Practically, the speed of the scan is limited by the frame rate of the ultrasound machine (i.e. 15fps).

Experimentally, we found that the ultrasound array was not perfectly aligned with the shaft of the ultrasound probe and respectively with $\xi_3$. The rotary scan left blank voxels near the axis. To fill these, a small $\xi_3$ ($3^\circ$) motion normal to the image plane was performed before the pure rotary scan.

At the time of the scan, the end-fire probe is initially set to be near the central sagittal image of the gland and the current joint values of $\theta_1$ and $\theta_2$ are saved as a scan position ($\theta_1^1$ and $\theta_2^1$). The probe is then retracted (translation $\tau$ along $\xi_3$, typically under joystick control) until the quality of the image starts to deteriorate by losing contact, and is then slightly advanced to recover image quality. This insertion level sets the minimal pressure needed for imaging. The rotary scan is performed without changing the insertion depth. As such, the probe pressure over the gland is maintained to the minimum level throughout the scan since the axis of rotation coincides with the axis of the semi-spherical probe end and gel lubrication is used to reduce friction. The method enables 3D imaging with quasi-uniform, minimal prostate deformations. The method below will show that the minimal deformation can also be preserved at biopsy.

C. Needle Targeting with Minimal Prostate Deformations

For the accuracy of needle targeting according to and based on the acquired 3D image, it is essential that the gland maintains the same shape at biopsy. Therefore, the same level of prostate compression should be used as much as possible. The following 3 steps are used:

1) Optimizing the Probe Approach to Each Biopsy Site

The probe insertion level used at scanning is preserved ($\tau$ is locked). Still, infinitely many solutions for the joint angles $\theta_1$, $\theta_2$, and $\theta_3$ exist to approach the same target point. This is fortunate, because it leaves room to optimize the approach angles in order to minimize prostate deformations. As shown above, the rotation about the probe axis ($\xi_3$) preserves prostate deformations due to the semi-spherical probe point. As such, needle targeting should be performed as much as possible with $\xi_3$, and motions in the RCM axes $\xi_1$ and $\xi_2$, which are lateral.
to the probe, should be reduced.

If a biopsy target point is selected in the 3D ultrasound image, the robot should automatically orient the probe so that the needle-guide points towards the target. The volume image is in robot coordinates, therefore, the target point is already in robot coordinates. Robot’s inverse kinematics is required to determine the corresponding joint coordinates. Robot’s inverse kinematics were presented in publications [38, 55]. Here, we show the specific inverse kinematics that includes the needle and solves the joint angles $\theta_1, \theta_2$ for a given target point $\vec{p} \in \mathbb{R}^3$, insertion level $\tau$, and joint angle $\theta_3$.

As shown in Fig. 5, the needle-guide passes through a point $\vec{\delta} = (a_x, a_y, 0)^T$ (known from design and calibration [52]) and is parallel to $\xi_3$. For the target point $\vec{p}$ and chosen $\theta_3$, joint angles $\theta_1$ and $\theta_2$ have unique solutions, calculated with the second Paden-Kahan sub-problem approach, as follows.

The axes of the robot are:

$$
\begin{align*}
\xi_1 &= (\sin \phi, 0, -\cos \phi)^T \\
\xi_2 &= (0, 1, 0)^T \\
\xi_3 &= (0, 0, 1)^T
\end{align*}
$$

where $\phi = 60^\circ$ is a constant offset angle. The needle insertion depth $L$ required to place the needle point at the target $\vec{p}$ is:

$$L = L_e + L_p + \tau$$

where $L_e$ is a constant distance between the entry point of the needle guide and the RCM point in the direction of the axis $\xi_3$, and $L_p$ is a distance between the RCM point and the target point $\vec{p}$ in the direction of the axis $\xi_3$ such that:

$$L_p = \sqrt{\vec{p}^T \vec{p} - \vec{\delta}^T \vec{\delta}}$$

When the robot is in zero position as shown in Fig. 5a, the needle point $\vec{q}_1$ is given by:

$$\vec{q}_1 = (a_x, a_y, -L_p)^T$$

and when rotated by $\theta_3$ is:

$$\vec{d}_2 = e^{\xi_3 \theta_3} \vec{q}_1$$

where $\vec{d}_2$ is the cross-product matrix of $\xi_3$.

Then, $\theta_1$ and $\theta_2$ satisfy:

$$e^{\xi_1 \theta_1} e^{\xi_2 \theta_2} \vec{d}_2 = \vec{p}$$

where $\vec{d}_2$ are the cross-product matrices of $\xi_1$ and $\xi_2$, respectively. If $\vec{q}_3$ is a point such that:

$$\vec{q}_3 = e^{\xi_2 \phi} (\vec{d}_2 \times \vec{d}_2) = e^{-\xi_1 \theta_1} \vec{p}$$

then:

$$\vec{q}_3 = \vec{d}_2 + \gamma (\xi_1 \times \vec{d}_2)$$

where:

$$\gamma = \alpha \xi_1 + \beta \xi_2 + \gamma (\xi_1 \times \vec{d}_2)$$

Finally, $\theta_1$ and $\theta_2$ can be found by solving:

$$e^{\xi_2 \theta_2} \vec{d}_2 = \vec{q}_3$$

as:

$$\theta_2 = atan2 (\vec{d}_2^T \vec{q}_3, \vec{d}_2^T \vec{d}_2)$$

and

$$\theta_3 = \vec{d}_2^T \vec{q}_3$$

From the hardware joint limits of the robot, the range of $\theta_2$ is $-17.0^\circ \leq \theta_2 \leq 46.0^\circ$. Therefore, $\theta_1$ and $\theta_2$ are unique since $\vec{d}_3$ is unique ($\gamma < 0$).

For a given target $\vec{p}$ and $\theta_3$, a unique solution $\vec{d}_3$ that aligns the needle on target is calculated by solving the inverse kinematics ($J$) problem as shown above:

$$\left(\theta_1, \theta_2\right)^T = J(\vec{p}, \theta_3)$$

For example, the blue lines in Fig. 6 show $\theta_1$ and $\theta_2$ as a function of $\theta_3$ for a target $p = (10, 10, -100)^T$ and scan position $(\theta_1^0, \theta_2^0) = (0, 0)$. The optimal approach of the TRUS probe to a target is one that minimizes the movements of the $\theta_1$ and $\theta_2$ from their scan positions $\theta_1^0$ and $\theta_2^0$:

$$\theta_3^{opt} = \arg\min_{\theta_3} \left[(\theta_1 - \theta_1^0)^2 + (\theta_2 - \theta_2^0)^2\right]$$

For example, the red curve in Fig. 6 shows the sum of squared values for all $\theta_3$ angles, and the green line shows the optimal value.
A gradient descent algorithm was used to determine the minimum solution. Given the shapes of the curves, the global minimum was found by starting the minimization from each limit and the center of the $\theta_3$ range and retaining the lowest solution.

2) Optimizing the Order of the Biopsy Cores

Once the optimal approach angles are calculated for a set of $n$ biopsy points, the order of the biopsies can also be optimized to minimize the travel of the probe, a problem known as the travelling salesman problem (TSP). The TSP is to find the shortest route that starts from the initial scan position, visits each biopsy point once, and returns to the initial scan position $\mathbf{s}_0 = (\theta_1, \theta_2, 0)^T$. The optimal approach of biopsy point $i = 1, \ldots, n$ is $\mathbf{s}_i = (\theta_1, \theta_2, \theta_i)^T$. The squared distance between a pair of points is:

$$d(\mathbf{s}_i, \mathbf{s}_j) = (\mathbf{s}_i - \mathbf{s}_j)^T (\mathbf{s}_i - \mathbf{s}_j) \quad \text{for} \ i \neq j$$

(16)

The goal is to find an ordering $\pi$ that minimizes the total distance:

$$D = \sum_{i=0}^{n-1} d(\mathbf{s}_{\pi(i)}, \mathbf{s}_{\pi(i+1)}) + d(\mathbf{s}_{\pi(n)}, \mathbf{s}_{\pi(0)})$$

(17)

The solution of the TSP is found using a classic 2-step algorithm [56]. Fig. 7 shows an example of $n = 12$ biopsy points, represented in robot joint coordinates (Fig. 7a) and Cartesian space of the prostate (Fig. 7b).

3) Prostate Coordinate System (PCS) and Extended Sextant Biopsy Plan

The algorithms above calculate the optimal approach and order for a set of biopsy points. Symmectric or targeted biopsy points can be used, depending on the procedure and decision of the urologist. For systematic biopsy, we have also developed software tools to help the urologist formulate the plan, graphically, based on the acquired 3D ultrasound. The most common systematic biopsy plan is the extended sextant plan of 12-cores. The plan uses a Prostate Coordinate System (PCS) that we derived based on anatomic landmarks of the prostate [57]. The origin of the PCS is defined at the midpoint between the apex (A) and base (B) of the prostate. The direction of the PCS follows the anatomic Left-Posterior-Superior (LPS) system (same as in the Digital Imaging and Communications in Medicine (DICOM) standard). The S axis is aligned along the AB direction, and P is aligned within the sagittal plane.

Fig. 8a shows an example with the apex (A) and base (B) in a central sagittal view of the gland. In software, the A&B points are selected manually, and several steps allow their location to be quickly and successively refined: 1) Select A&B points in the original rotary slices (para-corporal); 2) Refine their locations in the current LP (axial) re-slices of the volume image and orient the P direction; 3) Refine the A and B in the current SL (coronal) re-slices; 4) Refine the A and B in the current PS (sagittal) re-slices. In the above, the PCS location is updated after each step.

The PCS facilitates the definition of the biopsy plan. A SB template is centered over the PCS and scaled with the AB distance. As such, defining the PCS allows to define the plan without the need for prostate segmentation. For the extended sextant plan, the 12 cores are initially placed by the software on the central coronal (SL plane) image of the gland and scaled according to the AB distance. The software then allows the physician to adjust the location of the cores as needed (Fig. 8b). Since prostate biopsies are normally performed more posteriorly, towards the peripheral zone (PZ) where the majority of PCa tumors are found (68% [58]), the program switches the view to central sagittal (PS), and displays a curve that can be pulled posteriorly below the urethra (Fig. 8c). The 12-cores are then projected in the P direction to the level of this curve to give the final 3D biopsy plan (Fig. 8d).
D. Robot Control and Navigation

The robot control component of the software is used to monitor and control the robot (Fig. 3c). A watchdog built on hardware and software removes the motor power should a faulty condition occur [38].

Fig. 3 shows an example of the navigation screen that shows a 3D virtual environment with the robot, probe, and real-time ultrasound image. The position of all components is updated in real-time. Furthermore, the navigation screen shows the biopsy plan, the current target number and name. The names of the cores follow the clinical system (Left-Right, Apex-Mid-Base, and Medial-Lateral), and are derived automatically based on the positions of the cores relative to the PCS.

The right side of the navigation screen (Fig. 3c) shows real time ultrasound images with an overlaid needle insertion guide. Most biopsy needles have a forward-fire sampling mechanism. The green guide marks how deep to insert the needle before firing the biopsy, so that when fired, the core is centered at the biopsy target. The depth line is located along the needle trajectory and offset from the target. The offset depends on the needle type, and is measured between the point of the loaded biopsy needle and the center of the magazine sample of the fired needle.

E. Clinical Procedure

The TRUS probe is cleaned and disinfected as usual, mounted in the robot, and covered with a condom as usual. The patient is positioned in the left lateral decubitus position and periprostatic local anesthesia are performed as usual. With the support arm unlocked, the TRUS probe mounted in the robot is placed transrectally and adjusted to show a central sagittal view of the prostate. The support arm is locked for the duration of the procedure. The minimal level of probe insertion is adjusted under joystick control as described in section B. A 3D rotary scan is then performed under software control as shown in section B. The PCS and biopsy plan are made by the urologist as shown in section C3. The software then optimizes the approach to each core (Sec C1) and core order (Sec C2). Sequentially, the robot moves automatically to each core position. The urologist inserts the needle through the needle-guide up to the depth overlaid onto the real time ultrasound (Fig. 3c), and samples the biopsy manually, as usual. Ultrasound images are acquired with the needle inserted at each site for confirmation. All data, including the ultrasound images and configurations, A-B points, PCS, targets, and confirmation images are saved automatically.

F. Experiments

Comprehensive experiments were carried out to validate the system. The validation experiments include two bench tests, an imaging test, two targeting tests, and five clinical trials on patients. Needle targeting accuracy and precision results were calculated as the average and standard deviation of the needle targeting errors, respectively.

1) Robot Joint Accuracy Test

An optical tracker (Polaris, NDI, Canada) was used to measure the 3D position of a reflective marker attached to the probe (~250mm from RCM point) as shown in Fig. 9. The tracker was setup according to [59] (1100mm away from the marker) to improve the accuracy of measurement (0.078mm).

One at a time, each joint of the robot was moved with an increment of 5° for \( \theta_1, \theta_2, \theta_3 \), and 5mm for \( \tau \) over the entire ranges of motion. According to [59], 500 position measurements of the marker were acquired and averaged at each static position.

For each axis, the measured increments between consecutive points were compared to the commanded increments. For the rotary axes, a plane was fitted to the respective point set using a least square technique. The point set was then projected onto the plane and a circle was fitted using a least square technique. Rotary axes increments were measured as the angles between the radials to each position, in plane. For the translational axis, a principal component analysis (PCA) was applied to the point set and the first principal axis was estimated. Translational axis increments were measured as the distances between consecutive points projected onto the first principal axis.

2) Robot Set Point Test

The experimental setup was similar to the previous tests, but the optical marker was fitted on a rod passed through the needle guide to simulate the needle point (~142mm from the RCM point, 55mm from the probe tip).

The axes were moved incrementally as follows: move \( \theta_1 \) from -45° to 45° with 5° increment (19 positions); For each, move \( \theta_2 \) from -15° to 40° with 5° increment (12 positions); For each, move \( \theta_3 \) from -90° to 90° with 30° increment (7 positions). The translation was fixed at \( \tau = 0 \) because its moving direction is parallel to the needle insertion axis. Each of the \( k = 19 \times 12 \times 7 = 1596 \) marker locations was measured with the tracker and formed the dataset \( \vec{g} \in \mathbb{R}^3 \). Each commanded joint position was passed through the forward kinematics of the robot to calculate the robot-space commanded dataset \( \vec{h} \in \mathbb{R}^3 \). The homogeneous transformation matrix \( F \in \mathbb{R}^{4 \times 4} \) between the tracker and robot coordinates was estimated with a rigid point cloud registration technique [60]. The virtual needle point positioning error \( e_v \) was evaluated as the average positioning error:

\[
e_v = \frac{1}{k} \sum_{i=1}^{k} \| F \cdot \vec{g}_i - \vec{h}_i \| \tag{18}
\]

3) 3D Imaging Geometric Accuracy Test

A 5-by-5 grid of strings (Ø0.4mm) spaced 10mm apart was built, submerged in a water tank, and imaged with a 3D rotary
scan (Fig. 10a). The 25 grid crossing points were selected in the 3D image and registered to a grid model (same spacing) using a Horn’s method [60]. Errors between the sets were calculated and averaged. The test was repeated 5 times for different depth settings of the ultrasound machine (50, 65, 85, 110, 125mm).

4) Grid Targeting Test

The grid described above was also targeted with the needle point to observe by inspection how close the needle point can target the crossings (Fig. 10b and Movie sequence). The stylet of an 18Ga needle (stylet diameter ~1mm) was inserted through the automatically oriented needle-guide and advanced to the indicated depth. No adjustments were made. Targeting errors were estimated visually to be ≤0.5mm if the point of the needle was on the crossing, ≤1.0mm if the error appeared smaller than the stylet diameter, and >1mm otherwise (Fig. 10c). The test was repeated 3 times for grid depths of 20, 40, and 60mm.

5) Prostate Mockup Targeting Test

A prostate mockup (M053, CIRS Inc., Norfolk, VA) was used (Fig. 11). The experiment followed the clinical procedure method of 12-core biopsy describe in section E above. The biopsy needle was an 18Ga, 20cm long, 22mm throw MC1820 (Bard Medical, Covington, GA). In addition, the prostate was also manually segmented, and a 3D prostate surface model was generated to quantify the magnitude of interventional prostate deformations, if present. A confirmation ultrasound image was saved at each needle insertion. A post-biopsy 3D rotary scan at the initial scan location (θ₁,θ₂) was also performed for initial/final prostate shape/location comparison.

In the analysis, the pre-acquired 3D prostate surface was intersected with the plane of the saved confirmation image to render the pre-acquired 2D prostate shape, as shown in Fig. 12a. This was then compared with the imaged prostate shape to determine the level of prostate displacement d_p (distance between centers, ĉ₁,ĉ₂) and deformation d_f. To measure deformations, the pre-acquired contour was translated with ĉ₂ = ĉ₁ to a common center. Deformations d_f were measured radially (φ = 15°) between the contours, as shown in Fig. 12b, and averaged for each confirmation image.

Needle insertion errors e_n were measured as distances between the imaged needle axis and the target point (shown later in Fig. 15a). Overall targeting errors e_t were calculated as the sum of the needle insertion error and the 2D displacements of the prostate d_p.

Finally, the 3D displacement and deformation of the prostate were measured between the pre- and post-biopsy ultrasound volumes. The displacement D_p was the distance between the centroids of the two surfaces. Then, the pre-biopsy surface was translated to align the centers, and the deformations were calculated as a mean D_f and maximum value D_f^max of the distances between the corresponding closest points of the surfaces, as shown later in Fig. 15b.

A final experiment was performed to visually observe the motion of the TRUS probe about the prostate and how the prostate deforms. The prostate mockup was made of a soft-boiled chicken egg, peeled shell, and placed on 4 vertical poles support. The support was made to gently hold the egg so that the egg could be easily unbalanced and pushed off, to see if biopsy can be performed on the egg without dropping it. A limitation of this experiment is that the egg mockup is unrealistic in many respects. We have derived it as a way to visualize the motion of the probe about the prostate, motion that is calculated by algorithms, and is difficult to observe with closed, more realistic mockups. The experimental setup is shown in a sequence of the attached movie.

6) Clinical Trial

An IRB-approved, Phase 0 clinical study was conducted to verify the safety and feasibility of robotic prostate biopsy. The study was carried out on five men with an elevated PSA level (≥4ng/ml) and/or abnormal DRE. For all the cases, extended sextant systematic prostate biopsies were performed based on the protocol described in section E. Fig. 13 shows the system setup for the clinical trial. Needle insertion errors e_n were calculated as described in Sec. F5. Needle targeting accuracy
and precision were calculated as the average respectively standard deviation of the errors, as usual. Partial and overall procedure times were also recorded.

III. RESULTS

1. Robot Joint Accuracy Test

The joint accuracies and precision of the robot are shown in TABLE I.

<table>
<thead>
<tr>
<th>Joint</th>
<th>Accuracy</th>
<th>Precision</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\theta_1$ [°]</td>
<td>0.112</td>
<td>0.079</td>
</tr>
<tr>
<td>$\theta_2$ [°]</td>
<td>0.021</td>
<td>0.028</td>
</tr>
<tr>
<td>$\theta_3$ [°]</td>
<td>0.040</td>
<td>0.033</td>
</tr>
<tr>
<td>$\tau$ [mm]</td>
<td>0.015</td>
<td>0.013</td>
</tr>
</tbody>
</table>

2. Robot Set Point Test

Fig. 14 shows an example of the set point test results ($\theta_3 = 0^\circ$). The virtual needle point positioning error $e_v$ was 0.56±0.30mm. The maximum error was 1.47mm.

3. 3D Imaging Geometric Accuracy Test

The accuracies and precisions of the 25 grid points with 5 different depth settings are presented in TABLE II.

<table>
<thead>
<tr>
<th>Depth Setting $d$ [mm]</th>
<th>Accuracy [mm]</th>
<th>Precision [mm]</th>
</tr>
</thead>
<tbody>
<tr>
<td>50</td>
<td>0.48</td>
<td>0.26</td>
</tr>
<tr>
<td>65</td>
<td>0.51</td>
<td>0.20</td>
</tr>
<tr>
<td>85</td>
<td>0.47</td>
<td>0.19</td>
</tr>
<tr>
<td>110</td>
<td>0.51</td>
<td>0.27</td>
</tr>
<tr>
<td>125</td>
<td>0.44</td>
<td>0.23</td>
</tr>
<tr>
<td>Total</td>
<td>0.48</td>
<td>0.23</td>
</tr>
</tbody>
</table>

4. Grid Targeting Test

A sequence of this experiment is shown in the attached movie. For the grid depth of 20mm, the number of experiments with targeting errors ≤0.5, ≤1.0, and >1.0mm were 18, 6, and 1 respectively. For the grid depth of 40mm, the corresponding number were 21, 3, and 1 respectively. For the grid depth of 60mm, the corresponding numbers were 20, 5, and 0. The two cases when the errors were >1.0mm appeared to be ≤1.5mm. One of these cases is shown in Fig.

5. Prostate Mockup Targeting Test

The results are presented in the TABLE III. Fig. 15 shows the needle insertion error and the 3D distance map of the prostate deformation. The 3D displacement $D_p$ and deformation $D_f$ of the prostate were 0.58 and 0.20mm, respectively. The maximum deformation distance $D_f^{\text{max}}$ was 0.89mm.

The biopsy on the egg experiment performed the 3D scan and positioned the probe for biopsy without pushing the egg off the support, as shown in the attached movie.
6. Clinical Trial

The robot allowed 3D imaging of the prostate, 3D size measurements, and volume estimation. The results are presented in TABLE IV.

<table>
<thead>
<tr>
<th>Patient</th>
<th>Prostate Size [mm]</th>
<th>Prostate Volume [cm³]</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Superior-Inferior</td>
<td>Anterior-Posterior</td>
</tr>
<tr>
<td>1</td>
<td>38.85</td>
<td>30.32</td>
</tr>
<tr>
<td>2</td>
<td>57.47</td>
<td>46.18</td>
</tr>
<tr>
<td>3</td>
<td>48.33</td>
<td>31.63</td>
</tr>
<tr>
<td>4</td>
<td>52.78</td>
<td>40.45</td>
</tr>
<tr>
<td>5</td>
<td>50.81</td>
<td>43.85</td>
</tr>
</tbody>
</table>

The robot also enabled hands-free TRUS operation for prostate biopsy and all 5 procedures were successful from the first attempt. The biopsy procedures took 13 min on average. Slight patient motion at the time of biopsy firing was occasionally observed. No remnant prostate shift was observed. There were no adverse effects due to the robotic system. Three of the five patients had malignant tumor with biopsy Gleason Scores of 3+3, 3+4, and 3+3. Numerical results are presented in TABLE V.

### TABLE V

<table>
<thead>
<tr>
<th>Clinical Trial Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>No of 3D scan ultrasound slices</td>
</tr>
<tr>
<td>Average time</td>
</tr>
<tr>
<td>3D image scan</td>
</tr>
<tr>
<td>PCS and biopsy plan</td>
</tr>
<tr>
<td>Biopsy sampling</td>
</tr>
<tr>
<td>Total procedure</td>
</tr>
<tr>
<td>Needle Targeting*</td>
</tr>
<tr>
<td>Accuracy</td>
</tr>
<tr>
<td>Precision</td>
</tr>
<tr>
<td>Cancer diagnosis</td>
</tr>
</tbody>
</table>

* Over 4 patients (we missed recording all confirmation images on a patient)

IV. DISCUSSION

Image registration is a commonly required step of clinical procedures that are guided by medical images [39, 61]. This step must normally be performed during the procedure and adds to the overall time. With the TRUS robot, and also with fusion biopsy devices [16, 18], intra-procedural registration is not required. Instead, a calibration is performed only once for a given probe [52]. The probe adapter was designed to mount it repeatedly at the same position when removed for cleaning and reinstalled, to preserve the calibration.

Bench positioning tests show that the robot itself can point a needle with submillimeter accuracy and precision (Sec. III 1.2). The geometric accuracy and precision of 3D imaging were submillimetric (Sec. III 3). Combined, image-guided targeting errors in a water tank (no deformations) were submillimetric in 97.3% of the tests and <1.5mm overall (Sec. III 4). Experiments on prostate mockups (Sec. III 5) showed that changes in the position and deformation of the prostate at the time of the initial scan and biopsy were submillimetric. Overall, needle targeting accuracy in a deformable model was 1.43mm. The biopsy on the egg experiment showed that the robot can operate the TRUS probe gently, with minimal pressure, as shown in the attached movie sequence.

Preserving small prostate deformations at the time of the 3D scan and biopsy was achieved by using primarily rotary motion about the axis of the probe and minimizing lateral motion. A similar approach may be intuitively made with the Artemis (Eigen) [16] system, which uses a passive support of the arm of the TRUS probe. Here, the optimal approach angles are derived mathematically.

In the experiments we observed that optimal solutions were uncommon, unintuitive, and not ergonomic to freehand. Fig. 16a shows the way that a physician would normally freehand the probe to a site. Instead, Fig. 16b shows the optimal approach to the same site, which is not ergonomic and difficult to freehand. Freehand biopsy is often suboptimal, because turning the probe upside down is not ergonomic. The attached movie shows that upside down TRUS operation is feasible with the robot.

We also present a coordinate system associated with the prostate (PCS), and a method to formulate a SB plan based on the PCS. Several prostate biopsy systems [20] use intraoperative methods to locate a system that is similar to the PCS, by manually positioning the probe centrally to the prostate. In our approach, the PCS is derived in the 3D image, possibly making it more reliable. The 2 methods were not compared in the present report.

The results of the clinical trial show that robot-assisted prostate biopsy was safe and feasible. Needle targeting accuracy was on the order of 1mm. Additional possible errors such as errors caused by patient motion should be further evaluated and minimized. No significant patient movement was observed during our limited initial trial, and no loss of ultrasound coupling was experienced. The development of a leg support to help the patient maintain the position and additional algorithms to correct for motion are in progress.

The TRUS robot and the Artemis device [16] are the only systems that manipulate the probe about a RCM fulcrum point. With the other systems that freehand the probe the fulcrum is floating. Thus far, we have not observed patient discomfort related to fixing the fulcrum. Performing biopsy with minimal probe pressure and motion could ease the discomfort and help the patient to hold still.

Clinically, our robot is for transrectal biopsy and the other approach is transperineal. Traditionally, transperineal biopsy was uncommon because requires higher anesthesia and an operating room setting, but offered the advantage of lower infection rates [62]. New transperineal approaches for SB and cognitive TB are emerging with less anesthesia and at the clinic [63]. Yet, the mainstream prostate biopsy is transrectal. Several methods reported herein, such as the PCS and TRUS imaging with reduced prostate deformations could apply as well to transperineal biopsy.
V. Conclusion

A robot for hands-free TRUS operation at prostate biopsy is presented. The robot can guide a biopsy needle on target regardless of human skills. The approach enables prostate biopsy with minimal pressure over the prostate and small prostate deformations, which can help to improve the accuracy of needle targeting according to the biopsy plan. We also present a PCS, and a way to formulate a SB plan based on the PCS, without segmenting the prostate. Hands-free TRUS operation, transrectal TRUS-guided prostate biopsy with minimal prostate deformations, and the PCS are novel approaches.

Extensive mockup experiments and a safety and feasibility clinical trial are reported. In preclinical experiments, the accuracy of image based needle targeting was on the order of 1mm. Clinically, targeting accuracy is substantially lower than the 5mm required to target clinically significant prostate cancer [8, 30]. The biopsy procedure took approximately 13min, and all cases were successfully completed, showing that the robotic approach is feasible. The approach can be used with SB and TB. Trials of clinical significance are needed to determine if more accurate biopsy targeting correlates with higher detection of clinically significant PCa.

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