Mechanically assisted 3D ultrasound guided prostate biopsy system

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There are currently limitations associated with the prostate biopsy procedure, which is the most commonly used method for a definitive diagnosis of prostate cancer. With the use of two-dimensional (2D) transrectal ultrasound (TRUS) for needle-guidance in this procedure, the physician has restricted anatomical reference points for guiding the needle to target sites. Further, any motion of the physician’s hand during the procedure may cause the prostate to move or deform to a prohibitive extent. These variations make it difficult to establish a consistent reference frame for guiding a needle. We have developed a 3D navigation system for prostate biopsy, which addresses these shortcomings. This system is composed of a 3D US imaging subsystem and a passive mechanical arm to minimize prostate motion. To validate our prototype, a series of experiments were performed on prostate phantoms. The 3D scan of the string phantom produced minimal geometric distortions, and the geometric error of the 3D imaging subsystem was 0.37 mm. The accuracy of 3D prostate segmentation was determined by comparing the known volume in a certified phantom to a reconstructed volume generated by our system and was shown to estimate the volume with less than 5% error. Biopsy needle guidance accuracy tests in agar prostate phantoms showed that the mean error was 2.1 mm and the 3D location of the biopsy core was recorded with a mean error of 1.8 mm. In this paper, we describe the mechanical design and validation of the prototype system using an in vitro prostate phantom. Preliminary results from an ongoing clinical trial show that prostate motion is small with an in-plane displacement of less than 1 mm during the biopsy procedure. © 2008 American Association of Physicists in Medicine. [DOI: 10.1118/1.3002415]

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I. INTRODUCTION

Digital rectal exams and prostate-specific antigen (PSA) blood tests are common screening tests for prostate cancer (PCa) in asymptomatic men. Combined with the public’s increased awareness of PCa and PSA testing, the proportion of men diagnosed with early stage prostate cancer has increased. When diagnosed at an early stage, the disease is treatable, and even at later stages, treatment can be effective. However, if a tumor has extended beyond the prostate, the risk of metastases increases significantly.

The definitive diagnosis of PCa requires histological assessment of tissue cores drawn from the prostate during a biopsy procedure. The physician uses a conventional 2D transrectal ultrasound (TRUS) probe to guide the needle into the prostate. Biopsies are commonly performed with an 18-gauge needle mounted on a spring-loaded biopsy “gun.” This gun is connected to an “end-firing” 2D TRUS probe, by a guide, which forces the needle to stay in the imaging plane so it is always visible in the US image. The TRUS probe is held by the physician and inserted into the patient’s rectum in order to image the prostate through the rectal wall (Fig. 1). Typically, an average of 10 biopsy cores are obtained in a single biopsy procedure. Each core is separately identified as to its location within the prostate so that the pathologist can report the extent and grade of cancer.

While the TRUS-guided prostate biopsy has become a commonly performed urological procedure, it is not without limitations. Many patients’ initial biopsy will be negative for PCa; however, because the sensitivity of the procedure is poor, PCa cannot be ruled out in these patients. Physicians...
procedures are still suboptimal. If an initial biopsy fails to detect cancer, how should a repeat biopsy be directed? Should the repeat biopsy be lesion directed, random, or based on the details of the patient’s anatomy? Since there are an appreciable number of men with false-negative biopsy who, in fact, harbor, curable PCa, the physician is faced with a difficult challenge. Sometimes these patients are imaged with other modalities and undergo a second or even a third biopsy, in which the physician tries to avoid the location of the first negative biopsy.

Various reports have shown that the detection rate of PCa for repeat biopsy procedures ranges from 10% to 25% (after initial biopsy results were shown to be negative). Because PCa is present in at least 1/10 to 1/4 of patients who have undergone an initial negative biopsy, current biopsy procedures are still suboptimal. If an initial biopsy fails to detect cancer, how should a repeat biopsy be directed? Should the repeat (and initial) biopsy be lesion directed, random, or based on the details of the patient’s anatomy (e.g., prostate regions, volume, shape)?

Another important challenge facing physicians is men diagnosed on biopsy to have premalignant lesions, i.e., high-grade prostatic intraepithelial neoplasia, and particularly atypical small acinar proliferation (ASAP). These are challenging to manage as there is a 40%–50% chance of finding cancer on repeat biopsy with ASAP. Since coexisting cancer might be present, especially with ASAP, where the pathologist finds only a small amount of histological “atypia” but not enough material to confidently diagnose cancer, these patients require a repeat biopsy soon after the first. In these situations, it is vital to rebiopsy the same area. Currently, 2D US provides only a vague location of the abnormal findings, and it is not possible to be certain that the same area has been sampled by the repeat biopsy.

Due to the increasing number of younger men with potentially early and curable PCa undergoing repeated prostate biopsy, it is important not to rebiopsy the same area if the original biopsy was negative, and it is particularly vital to rebiopsy the exact area if a possible abnormal area was detected on first biopsy as ASAP. Thus, the locations of the cores obtained in 3D from the prostate must be known accurately to help guide the physician during the repeat biopsy to help in correlating any imaging evidence of the disease, and to provide improved planning for any subsequent therapy.

As there is a clinical need for a prostate biopsy system allowing recording of the core locations and guiding tools to allow sampling of specific targets in 3D, special purpose TRUS biopsy systems have emerged in the marketplace. EnVisio Engineering Medical Technologies (St. Louis, MO) has developed a system, which uses a stationary endorectal ultrasound probe for biopsy. The Voluson prostate biopsy system (General Electric) is a 3D hand held US imaging system that allows for real-time imaging of the prostate. Several groups have reported using 3D prostate systems in both phantom and patient studies. Some of these studies have shown an improvement in the positional and the diagnostic accuracy of the procedure. However, there is still a group of patients with ultrasound occult cancers. As a result, the use of real-time 3D US probes suffers from the same problems as 2D probes.

MRI imaging using high resolution T2 weighted images, and MRI spectroscopy are promising methods that can improve the detection of prostate cancer. Several groups have proposed and developed a number of potential solutions that use CT or MRI for prostate biopsy. Fichtinger et al. integrated CT with a side-firing TRUS system to guide the needle to a preplanned target using a robotic arm. MRI has also been used to identify potential malignant tumors while a robotic device has been used to guide the biopsy needle. The DaVinci robot (Intuitive Surgical Inc., Sunnyvale, CA) has been used extensively for prostate surgery, and can also be adapted to guide a biopsy needle. However, these solutions require physicians to use CT, MRI, or specially modified biopsy systems, which are costly. As well, the workflow for each of the new designs differs significantly from current biopsy protocols, requiring physicians to retrain themselves. Furthermore, since there are more than one million biopsies performed each year, it would be beneficial to develop a biopsy system that utilizes ultrasound equipment currently in use for the procedure. Further, the use of 3D US coupled to a mechanical navigation system has the potential to provide a reproducible record and allow for image fusion with other imaging modalities such as MRI, assisting the physician in planning a repeat biopsy. This system can potentially eliminate most of the user variability of using con-
ventional nonfixed hand-held probes that render them unsuitable for precision biopsy, while preserving some of the user familiarity.

In this paper, we describe the development and testing of a mechanically assisted 3D TRUS prostate biopsy system, which addresses the limitations of current prostate biopsy procedures and also minimizes adoption cost and physician retraining. We also report briefly on the initial clinical use of this system for prostate biopsy.

II. SYSTEM DESIGN

Our 3D TRUS system is an integrated 3D workstation, mechanical guidance system, and software tools to record the core locations and guide the needle to its target. It allows real time tracking and recording of the 3D position and orientation of the biopsy needle as the physician manipulates the US transducer. The system uses: (1) passive mechanical components for guiding, tracking, and stabilizing the position of a commercially available end-firing transrectal US transducer, (2) software components for acquiring, storing, and reconstructing (in real time) a series of 2D US images into a 3D US image, and (3) software that displays a model of the 3D scene to guide and record the biopsy core locations in 3D.

II.A. Mechanical tracking system

The mechanical assembly consists of a passive four degree-of-freedom tracking device, an adaptable transducer cradle, and a hydraulic support (Fig. 2). The transducer cradle mechanically locks and fastens a commercially available end-firing TRUS transducer. The tracking device and transducer cradle are secured by the hydraulic support, which stabilizes the mechanical assembly while the physician performs a biopsy. When the TRUS probe is maneuvered, the software records the 3D position and orientation of the transducer tip via absolute encoders as described below.

The end-firing TRUS transducer (with the biopsy needle guide in place) is mounted to the mechanical tracking mechanism where the US probe is free to rotate and slide along its long axis (Fig. 3, wrist joint axis of rotation: J3). This allows the physician to insert the TRUS transducer through the patient’s rectum to view the prostate and to rotate it to acquire a 3D image. The tracking linkage contains angle-sensing encoders (Fig. 3) mounted to each joint to

![FIG. 2. Photograph of the tracking system to be used for 3D US guided prostate biopsy. The system is mounted at the base to a hydraulic actuated stabilizer while the linkage allows the TRUS transducer to be manually manipulated about a remote center of motion, to which the center of the probe tip is aligned. The spring loaded counterbalance was designed to fully support the weight of the system throughout its full range of motions about the RCM.](image)

![FIG. 3. A front perspective view of the mechanical tracker, which in turn is attached to a multijointed stabilizer at L1. The RCM is at the intersection of the primary, secondary, and tertiary axes. The encoders mounted at the pivot J1 is used to measure the relative angles between the two successive links L2 and L3. The encoder at pivot J2 measures the angle between L1 and L2. The differential gearing mechanism, which is coupled to the tracking linkage, decouples the two DoF provided by the cylindrical joint J3 supporting the shaft, which in turn is mounted to the transducer cradle. These two degrees of mobility represent the probe penetration and angular orientation about its longitudinal axis, respectively. Two additional encoders, mounted onto the wrist joint J3 are required to measure the angle and depth of penetration of the probe through the differential gear train.](image)
transmit the angle between the arms to the computer. This encoder arrangement allows for the continuous computation of the position of the transducer needle guide as the transducer is manipulated in the rectum.

The mechanical tracking device is a spherical linkage assembly that consists of three links and three hinged connections. The axis of each hinged connection converges to a common point to produce a remote center of motion (RCM). 27−29 The base link (Fig. 3, L1) defines the reference axis of the proposed coordinate system and is fixed to a multijointed stabilizer (Fig. 3, L1) that attaches to a cart. The angle between each hinged connection in the mechanism defines the size and shape of the operating envelope of the kinematics frame, which allows for two degrees of rotation (pitch and yaw) about the RCM.

The linkage assembly supports the TRUS transducer through the distant pinned connection (Fig. 3, wrist joint axis: J3) such that the long axis of the probe passes through its RCM. Therefore, the angular position of the axis of the probe relative to the base is determined by measuring the angle between two successive joint axes. Two encoders mounted at the pivots (shoulder joint axis: J1) and (elbow joint axis: J2) are used to measure the relative angles between the two successive linkages (Fig. 3, links: L1 and L2) and between the link L1 and stabilizer, respectively.

The probe is supported through the revolute axis by a sleeve and is allowed to pivot and slide freely along the axis of the revolute joint (Fig. 3, wrist joint axis: J3). This compound joint gives the tracking mechanism an additional two DoF where the probe penetration and relative rotation angle to the supporting frame are defined. As illustrated in Fig. 3, the differential gearing mechanism, which is coupled to the tracking mechanism, decouples the motion through the compound joint. These two degrees of mobility represent the probe penetration and angular orientation about its long axis (i.e., roll angle), respectively.

II.B. Forward kinematics equations of motion

The unit vector \( \hat{r} \) defines the 3D orientation of the TRUS tip in spherical coordinates relative to its fulcrum (O) (Fig. 4):

\[
\hat{r} = \begin{bmatrix} x \\ y \\ z \end{bmatrix} = \begin{bmatrix} \cos \theta \sin \phi \\ \sin \theta \sin \phi \\ \cos \phi \end{bmatrix}.
\]

In this description, the position of the probe tip \( \hat{r} = f(\phi, \theta) \) is specified by the angle \( \phi \), the angle along the axis of the probe makes with the z-axis, and the angle \( \theta \), which is the orientation of the TRUS transducer in the x-y plane. The relationship between the tracker coordinate system \( \hat{r} = f(\phi, \theta) \) and the reference frame defined by the encoders connected at each of the hinged connections is illustrated in Fig. 4. The tracker arm configuration measured by the encoders is defined by the spherical triangle (ABC), and is linked to the global reference frame by the spherical triangle (APC).

\[
\tan \frac{1}{2}(\theta + \alpha) = \cos \frac{1}{2}(\psi - \frac{\pi}{2}) \sec \frac{1}{2}(\psi + \frac{\pi}{2}) \cot \frac{1}{2} \xi, \quad (2a)
\]

\[
\tan \frac{1}{2}(\theta - \alpha) = \sin \frac{1}{2}(\psi - \frac{\pi}{2}) \csc \frac{1}{2}(\psi + \frac{\pi}{2}) \cot \frac{1}{2} \xi, \quad (2b)
\]

\[
\tan \frac{1}{2}(\theta) = \tan \frac{1}{2}(\psi) \sin(\theta + \alpha) \cos(\theta - \alpha). \quad (2c)
\]

This defines spherical coordinates of the vector \( \hat{r} = f(\phi, \theta) \) in terms of the geometric configuration of the linkage angles \( \psi \) and \( \xi \) (see Fig. 4).

Equations (3a) and (3b), which define the configuration of the linkage in terms of the angles measured by the encoders at the shoulder and elbow joints, respectively, were derived by solving the right spherical triangle (ABE): 28

\[
\tan \frac{1}{2} \psi = \cos \xi. \quad (3a)
\]
\[ \cot \left( \frac{1}{2} \psi \right) = \frac{1}{\sqrt{2}} \tan \gamma. \]  
(3b)

The position of each arm (AB and BC in Fig. 4) in the linkage was determined by measuring the spherical angles at each of the pinned couplings A and B, respectively. The encoder mounted at A measures the angle \( (\xi + \zeta) \) between \( L_1 \) and the \( x-z \) plane, and the encoder mounted at B measures the angle \( \gamma \) between the two arms (\( L_1 \) and \( L_2 \)). Equation (3b) is needed to decouple the values for \( (\xi) \) and \( (\gamma) \), required to solve Eqs. (2a)–(2c).

II.C. Software for acquiring and reconstructing 3D US images

Before the physician acquires a 3D image of the prostate, the tracking arm is locked into place to prevent the TRUS probe from changing its pitch, yaw, and depth of penetration while the probe is rotated. As the physician rotates the transducer manually about its long axis (Fig. 3, wrist joint axis: \( J_3 \)) to acquire a 3D scan composed of 200 images in 1 deg increments, the 2D US images from the US machine are digitized using a frame grabber and reconstructed into a 3D image.\(^{30}\) The last 20 images in the overlap region (from 180 deg to 200 deg and 0 deg to 20 deg of transducer rotation) are merged by averaging the duplicate images to remove any slight discontinuities that may arise from image lag\(^{31}\) or small patient motion. Our software has a graphical software interface to provide information to the physician on the proper rotational speed. The software interface provides a visual queue to indicate if the rotation was too rapid and the 2D US images were not acquired properly. Once the 3D TRUS image has been acquired, the software then displays the image in a cube view (Fig. 5).\(^{30}\)

A model of the prostate is then generated from the 3D image by a semiautomatic 3D segmentation algorithm developed in our laboratory and described in detail elsewhere.\(^ {31,32}\) The segmentation algorithm requires that the physician selects four points around the boundary of a 2D prostate cross section. The algorithm then segments the prostate by fitting a dynamic deformable contour to match the boundary of the prostate. The contour is then used in the adjacent slice as a template and deformed around the prostate boundary; the result is propagated through 180 deg and refined for each succeeding image slice.\(^ {32}\) After the software reconstructs the image and the model, the physician can slice through the 3D TRUS image to select target biopsy locations. If the procedure is a rebiopsy, then previous biopsy locations can be viewed for planning as shown in Fig. 6.

II.D. Software components for 3D tracking and recording

Once the 3D image scanning and biopsy plan are complete, the system displays a 3D needle guidance interface to facilitate the systematic targeting of each biopsy location. Throughout the biopsy procedure, the 3D location and orientation of the TRUS transducer is tracked and displayed in real time. Figure 7 shows the biopsy interface, which is composed of four windows: the 2D TRUS video stream, the 3D TRUS image, and two 3D model views. The 2D TRUS window (bottom left) displays the real-time 2D TRUS image.
streamed from the ultrasound machine. The 3D TRUS window (top left) contains the 3D TRUS image sliced in real time to correspond to the orientation and position of the TRUS probe. This correspondence allows the physician to compare the static 3D image with the real-time 2D image. Finally, the two 3D targeting windows show: (i) the coronal and perspective views of the 3D prostate model, (ii) the real-time position of the 2D TRUS image plane, and (iii) the expected path of the biopsy needle as defined by the biopsy guide.

The targeting windows are used to aid the physician in guiding the needle to each preplanned target. The targeting circle on the screen (Figs. 6 and 7) illustrates all accessible needle trajectories by rotating the US probe about its long axis. This shows the physician the shortest distance to each preplanned target.

### III. SYSTEM VALIDATION METHODS

We used an HDI 3500 US system and C9-5 (9–5 MHz) TRUS probe (Philips Medical Systems, Seattle, WA) in the

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**FIG. 6.** For rebiopsy, previous biopsy locations in a patient’s prostate can be viewed to plan which the physician can slice to view the previous biopsy locations. This image also allows the physician to compare the previously segmented prostate boundary (red/gray line) with the currently segmented boundary (green/white line) (bottom left). The coronal view of the patient’s prostate with the segmented boundary and the location of the previous biopsy cores as circles (top and bottom right). The 3D locations of the biopsy core are displayed within the 3D prostate models. The targeting ring in the bottom right window shows all the possible needle paths that intersect the selected target by rotating the TRUS about its long axis. The vertical white line through the targeting ring shows the orientation of the US imaging plane. The bladder (hypoechoic region anterior to the prostate boundary) and urethra is visible within the axial view (top left).

**FIG. 7.** The 3D biopsy system interface is composed of four windows: (top left) the 3D TRUS image dynamically sliced to match the real-time TRUS probe 3D orientation (bottom left), the live 2D TRUS video stream (right side), and the 3D location of the targets is displayed within the 3D prostate models. The targeting ring in the bottom right window shows all the possible needle paths that intersect the preplanned target by rotating the TRUS about its long axis. This allows the physician to maneuver the TRUS to the target (highlighted by the red/gray dot) in the shortest possible distance. The biopsy needle (arrow) is visible within the real-time 2D TRUS image. The bladder (hypoechoic region anterior to prostate) and calcifications within the prostate (arrow head) illustrate anatomical correspondence between the real-time and static 3D image.
following experiments. The resolution of the Philips scan head was determined experimentally by measuring the diameter of a wire (full width at half-maximum) within a preset focal zone 3 cm deep in a bath of distilled water and 7% glycerol by weight), giving a speed of sound of 1540 m/s at a temperature of 20 °C. The axial, lateral, and elevational resolution was 1.2, 1.4, and 2.5 mm respectively.

III.A. Geometric reconstruction

The accuracy of 3D geometric reconstruction of the TRUS image based on manual rotation of the transducer was verified using a string phantom, which was immersed in a bath of distilled water and 7% glycerol (by weight). The string phantom consists of four layers of orthogonally intersecting monofilament nylon string with a diameter of 0.10 mm, which are anchored to the sides of a brass frame of the following dimensions: 12.2 cm (length) by 12.2 cm (width) by 3.0 cm (height). The intersections of the strings and each of the layers are spaced 10 mm apart, and each layer is offset by 2.5 mm so that the upper layers of strings do not shadow the subsequent lower layers.

The tracking apparatus was positioned with the tip of the TRUS transducer placed below the surface of the glycerol solution. The transducer was then manually rotated 200 deg around its long axis (z-direction) to acquire a 3D US image of the string phantom. Using this 3D image, the spacing between the strings was measured in the three principal views \((x,y),(x,z),\) and \((y,z)\). The measurements for each plane were then repeated 15 times, and the mean, standard deviation, and the standard error for \(\Delta x, \Delta y, \Delta z\) were then determined.

III.B. 3D segmentation

A certified ultrasound calibration phantom, which is constructed of Zerdine®, (Computerized Imaging Reference Systems Inc., Norfolk, Virginia) was used to assess the accuracy of volumetric measurements. The phantom had an embedded 21.5 cm³ egg-shaped object 1 cm below the surface of the phantom simulating the location and size of a small-medium prostate.

To verify the 3D segmentation accuracy of our system, the reconstructed volume of the embedded egg-shaped object was compared to that of its known volume. A 3D TRUS image of the phantom was acquired and the semiautomated segmentation algorithm was then used to generate a 3D model of the embedded object. The volume of the segmented model was then compared to the certified volume of the object to quantify the volume measurement error of the 3D segmentation. The phantom was independently scanned 15 times and each object was semiautomatically segmented using the software described in Sec. II C to calculate mean and standard deviation values for the volume error. The volume error \(V_{\text{error}}(V, V^*)\) was defined as the percentage difference between the reconstructed volume \(V\) and the known volume of the scanned object \(V^*\):

\[
V_{\text{error}} = \frac{V - V^*}{V^*}.
\]

To determine the impact the semiautomated segmentation algorithm has on the volume error, the following volume metrics were used to compare the reconstructed volume to a manually segmented volume as a gold standard. The sensitivity \(S(V, V_{\text{man}})\) was used to determine the portion of the reconstructed volume \(V\) that intersects the manually segmented volume \(V_{\text{man}}\):

\[
S = \frac{V \cap V_{\text{man}}}{V_{\text{man}}}. \tag{5a}
\]

The difference \(D(V, V_{\text{man}})\) was used to measure the proportion of the segmented volumes that is not correctly overlapped:

\[
D = \frac{V \cup V_{\text{man}} - V \cap V_{\text{man}}}{V_{\text{man}}}. \tag{5b}
\]

III.C. Mock biopsy on prostate phantoms

Mock biopsy procedures were performed on an agar-based tissue-mimicking phantom to quantify the accuracy of the 3D TRUS system for biopsy guidance and recording the 3D location of the biopsy core. The agar phantom consisted of an agar-based prostate model embedded in surrounding background agar. The background and prostate model were constructed by adding 7% by mass of glycerol solution with agar powder to produce a speed of sound similar to that of human tissue (1540 m/s). The mold of the prostate model was generated from a segmented 3D image of a human prostate (volume=21.5 cm³). The background material contained cellulose (15% by weight) to create acoustic backscattering in US, making the surrounding region appear bright relative to the prostate. Tungsten powder (1% by weight) was added to the prostate model to increase the x-ray attenuation within the prostate, making it visible in the CT image. Finally, stainless steel ball bearings of 1 mm diam were placed in a geodesic configuration within the background material, surrounding the prostate model. These ball bearings served as fiducials for coordinate registration between the 3D TRUS and CT images.

Six independent mock biopsies were performed on five prostate phantoms for a total of 30 cores using the 3D TRUS biopsy system. To start the procedure, the tracking apparatus was positioned with the tip of the TRUS transducer contacting the surface of the agar phantom and aligned with the center of the prostate gland and immediately adjacent to its posterior aspect. A 3D TRUS image of the prostate was then acquired (and reconstructed) by manual 200 deg rotation of the TRUS probe about its long axis and was reconstructed in a Cartesian reference frame with isometric voxel dimensions (0.194 mm³). A semiautomated segmentation was then used to generate a 3D segmented model of the prostate. A traditional sextant biopsy plan was followed, with contralateral biopsy targets placed at the base, midgland, and apex of...
the prostate. A systematic biopsy of each target was performed and the location of each biopsy core was recorded within the 3D system (e.g., Fig. 7).

The agar phantom was imaged, postbiopsy, in an eXplore Locus Ultra Pre-Clinical CT scanner (GE Healthcare, London, ON), which is used for small animal microimaging. The high resolution CT image (isometric voxel dimensions of 0.15 mm³) served as the gold standard for the “true” location of each biopsy core. In the CT image, a biopsy core was evident as an air track left from the insertion of the 18-gauge needle into the agar phantom. The location of a biopsy core was extracted from a CT image by selecting multiple points along the center of the air track, from the base to the tip. A linear regression of the points was used to define the 3D trajectory of the needle and the location of the 19 mm biopsy core was defined relative to the tip of the air track. The centers of the 1 mm fiducial markers surrounding the prostate were manually selected from corresponding CT and 3D TRUS images to coregister the two coordinate systems.

III.C.1. Biopsy system errors

The 3D biopsy system was evaluated for its ability to: (a) guide a biopsy needle to a 3D target and (b) record the location of the biopsy core in 3D following the methods described by Cool et al. The process of directing a biopsy needle toward a target using the 3D TRUS system has human, machine, and tissue factors as all potential sources of error. The needle guidance error NGHE measured the mean complete error associated with a user guiding the biopsy needle to predefined targets. This error was quantified for all biopsy sites n as the perpendicular distance between the ith target location (ai) and the corresponding “true” biopsy core identified in the 3D CT image (biCT):

\[ \text{NGHE} = \frac{\sum_{i=1}^{n} D(a_i, b_i^{\text{CT}})}{n}, \]  

where \( D( ) \) is a function measuring the 3D minimum distance between a 3D target point \( a_i \) and a 3D biopsy core line segment, \( b_i^{\text{CT}} \). NGHE is comprised of two quantifiable errors: one related to human guidance error NGHE and the other related to the needle trajectory error NTE. Conceptually, NGHE represents the ability of the user to align the biopsy target within the center of the expected needle path of the biopsy system. NGHE was measured by comparing the 3D Euclidean distance between the biopsy targets \( a_i \) and the expected path of the biopsy needle \( p_i \) within the 2D TRUS image:

\[ \text{NGHE} = \frac{\sum_{i=1}^{n} |a_i - p_i|}{n}. \]  

It should be noted that the preplanned biopsy targets \( a_i \) were virtual targets, fixed within the 3D TRUS system tracking space, not within the real 3D world. Therefore, both the target \( a_i \) and the expected needle path \( p_i \) were within the same 3D tracking space and NGHE was only influenced by human errors and not by errors in the 3D system, such as positional tracking error, inaccurate system calibration, poor 3D TRUS image to world correspondence, etc.

Needle trajectory error NTE was calculated to determine how well the biopsy needle traveled along the expected biopsy needle path \( p_i \), defined by the TRUS manufacturer. NTE was measured within the 2D TRUS image plane and defined as the minimum distance between the actual needle trajectory \( b_i^{\text{TRUS}} \) and the expected needle trajectory \( p_i \):

\[ \text{NTE} = \frac{\sum_{i=1}^{n} D(p_i, b_i^{\text{TRUS}})}{n}. \]  

The accuracy of the biopsy system to record biopsy core locations in 3D [biopsy localization error (BLE)] was quantified using three metrics: \( \text{BLE}_{\text{min}}, \text{BLE}_{\text{center}}, \) and \( \text{BLE}^\theta \). \( \text{BLE}_{\text{min}} \) is defined as the minimum distance between the “true” biopsy core from CT, \( b_i^{\text{CT}} \), and the record 3D TRUS biopsy core, \( b_i^{\text{TRUS}} \):

\[ \text{BLE}_{\text{min}} = \frac{\sum_{i=1}^{n} |D(b_i^{\text{CT}}, b_i^{\text{TRUS}})|}{n}, \]  

where \( D(\cdot) \) measures the minimum distance between two 3D biopsy core line segments. \( \text{BLE}^\theta \) is the angle between the cores when projected on a plane perpendicular to \( \text{BLE}_{\text{min}} \):

\[ \text{BLE}^\theta = \frac{\sum_{i=1}^{n} \theta(b_i^{\text{CT}}, b_i^{\text{TRUS}})}{n}, \]  

where \( \theta(\mathbf{u}, \mathbf{v}) \) is the function that calculates the minimum angle between vectors \( \mathbf{u} \) and \( \mathbf{v} \). \( \text{BLE}_{\text{center}} \) is the center-to-center distance between corresponding biopsy cores:

\[ \text{BLE}_{\text{center}} = \frac{\sum_{i=1}^{n} |b_i^{\text{CT}}(0.5) - b_i^{\text{TRUS}}(0.5)|}{n}, \]  

where \( b(0.5) \) represents the center point of the 19 mm biopsy core \( b \).

III.D. Clinical evaluation

The 3D biopsy system was tested clinically on three patients to determine the extent of prostate motion and deformation and the system’s impact on workflow. All subjects provided written consent to the study protocol approved by the University of Western Ontario Standing Board on Human Ethics prior to imaging. The workflow of the current 2D standard procedure was maintained with the addition of a 10 sec 3D US scan at the start and end of the procedure. Anatomical landmarks such as the prostate boundary or calcifications within the patient’s prostate were used for qualitative comparison of the real-time 2D TRUS image with the 3D TRUS image to identify correspondence issues resulting from prostate deformation, patient motion, or tracking inaccuracy.

An in-plane quantitative assessment of prostate motion and deformation was evaluated by measuring the distance between calcifications found in the 2D slices of a 3D TRUS image, which is generated at the start of the procedure to the real-time 2D US images obtained at a later time. We defined
the in-plane displacement as the absolute distance between the true location of the landmark and its location within the initial 3D image.

IV. RESULTS

IV.A. Geometric reconstruction

A 3D TRUS image of the string phantom was successfully reconstructed without significant visible discontinuity or probe alignment artifacts. Table I shows the distances between the strings within the phantom measured in the three orthogonal views \{(x, y), (x, z), (y, z)\}. The distance measured in each plane overestimated the known manufactured interstring distance, with measured errors varying from 3.1% to 4.0% (Table I).

IV.B. 3D segmentation

Table II shows the results from the scan of the phantom and the segmentations of the 3D object. Multiple 3D TRUS images were successfully reconstructed from the certified industrial US phantom. The egg-prostate shaped object was segmented using both the semiautomatic segmentation algorithm with a mean volume error of 4.7%. Furthermore, the reconstructed prostate models overlapped with the gold standard volumes with a sensitivity 95.4%, and difference error of 7.5%.

<table>
<thead>
<tr>
<th>Table II. The volume of the segmented model was compared to the certified volume of the object to quantify the volume measurement error of the 3D segmentation. The volume error [Eq. (4a)] compares the difference between the reconstructed volume (V_R) and the known volume of the scanned object (V_s=21.5\ \text{cm}^3). The following volume metrics were used to compare the semiautomated segmented volume to a manually segmented. The sensitivity [Eq. (5a)] was used to determine the portion of the reconstructed volume (V_R) that intersects the manually segmented volume (V_m), and the difference [Eq. (5b)] measured the proportion of the segmented volumes that is not correctly overlapped.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Volume-based metrics</strong></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Mean (mm)</td>
</tr>
<tr>
<td>(</td>
</tr>
<tr>
<td>Error (%)</td>
</tr>
<tr>
<td>STD (mm)</td>
</tr>
<tr>
<td>(n)</td>
</tr>
</tbody>
</table>
| IV.C. Needle guidance

The quantitative results for 3D biopsy needle guidance and recording of biopsy cores are summarized in Table III. Navigation of the biopsy needle to each target had a mean NGE=2.13 ± 1.28 mm. A one-tailed \(t\)-test showed the needle-guidance error was statistically less than 5 mm (\(p < 0.001, B=0.2, n=29\)), which is the smallest tumor considered clinically significant. Figure 8 shows a plot of the NGE, which is decomposed into in- and out-of-plane errors. The needle deflection is primarily in-plane with little out-of-plane error. Human navigation error in directing the probe to the biopsy target NGHE had a mean error of 0.54 ± 0.41 mm. Trajectory error of the biopsy needle deviating from the expected needle path NTE was 2.08 ± 1.59 mm. Figure 9(a) shows a comparison of the 3D biopsy cores for an 18-gauge needle. The biopsy cores overlapped with each target (white spheres) showing that the needle was successfully guided to each biopsy target location. Figure 9(b) shows a qualitative comparison of the 3D biopsy cores recorded using the 3D TRUS system (black) with the gold standard cores (white). The biopsy cores were accurately localized to 1.51 ± 0.92 mm (BLE\(^{\text{min}}\)) and with a mean angulation difference of 6.68 ± 2.23 deg (BLE\(^{\text{avg}}\)). The center-to-center distance (BLE\(^{\text{center}}\)) between corresponding biopsy cores was larger then BLE\(^{\text{min}}\), at 3.87 ± 1.81 mm.

IV.D. Clinical evaluation

Figure 5 shows axial, sagittal, and coronal views of the 3D TRUS image of a patient’s prostate obtained during a biopsy procedure. There were no obvious discontinuities or artifacts within the 3D image, even in the coronal plane, which lies perpendicular to the axis of rotation for 3D scanning.

Figure 10 shows a sequence of images that were captured during a sextant biopsy at the start (top row), midpoint (third) biopsy (middle row), and at the end (bottom row) of the procedure. The 2D slice from the 3D static image (Fig. 10, left column) is shown with the prostate boundary in green. The corresponding 2D real-time video stream (Fig. 10, middle column) displays a dotted outline of the prostate boundary from the 3D image. The images in the right column show the real time 2D TRUS images after needle insertion (Fig. 10, white arrow). There is a strong correlation between the real-time 2D TRUS image (middle column) and
the original 3D image (left column) at each time point, suggesting that there were no major changes in prostate location and morphology during the biopsy procedure. Alignment between the initial 3D and real-time image was maintained throughout the entire procedure, even after six biopsies (bottom row). Similar anatomical landmarks (Fig. 10, calcifications) were visible in both the 3D and real-time 2D images, indicating a good correlation. The mean in-plane displacement of calcifications used as anatomical markers identified in images obtained from three patients within the prostate was 0.90 ± 0.97 mm (see Table IV). The measured in-plane displacements of calcifications as well as maintaining good correlation between the images in each row suggest that the prostate did not move or deform to a prohibitive extent.

Figure 11 shows a case where the patient had moved during the procedure. The 2D axial slice from the initial 3D image does not correlate well with the 2D TRUS image from the US machine. The prostate has moved from its original scanned position and the shape of the prostate boundary has also changed.

V. DISCUSSION

Volume calculations from the ultrasound phantoms were within 5% of the certified standard, and the shape-based metrics (sensitivity=95%, error=4.7%) show a high degree of overlap correspondence. Together with the string phantom results suggest that geometrical distortion due to manual ro-

### Table III. 3D biopsy system accuracy based on the biopsy core analysis described in Sec. III C. Needle guidance error, NGE [Eq. (6)], needle guidance human error, NGHE [Eq. (7)], and needle trajectory error, NTE [Eq. (8)], all evaluate biopsy targeting accuracy. The biopsy localization metrics: BLE\textsubscript{min}, BLE\textsubscript{center}, and BLE\textsuperscript{d} [see Eqs. (9)–(11)] indicate the errors in recording the 3D location of the biopsy cores, 95% CI represents the confidence interval of the mean. All of the values are reported as mean ± STD. The results from the experiment highlighted in bold are illustrated in Fig. 9.

<table>
<thead>
<tr>
<th>Experiment</th>
<th>NGE (mm)</th>
<th>NGHE (mm)</th>
<th>NTE (mm)</th>
<th>BLE\textsubscript{min} (mm)</th>
<th>BLE\textsubscript{center} (mm)</th>
<th>BLE\textsuperscript{d} (deg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>3.79 ± 0.86</td>
<td>0.37 ± 0.51</td>
<td>4.41 ± 0.27</td>
<td>1.93 ± 0.75</td>
<td>3.98 ± 1.45</td>
<td>5.65 ± 2.04</td>
</tr>
<tr>
<td>2</td>
<td>0.70 ± 0.32</td>
<td>0.27 ± 0.12</td>
<td>1.44 ± 0.46</td>
<td>1.08 ± 0.61</td>
<td>3.82 ± 2.52</td>
<td>5.61 ± 3.30</td>
</tr>
<tr>
<td>3</td>
<td>1.95 ± 0.39</td>
<td>0.19 ± 0.09</td>
<td>1.97 ± 0.59</td>
<td>2.39 ± 0.98</td>
<td>4.07 ± 1.22</td>
<td>7.76 ± 2.01</td>
</tr>
<tr>
<td>4</td>
<td>2.21 ± 1.39</td>
<td>0.99 ± 0.08</td>
<td>2.06 ± 1.94</td>
<td>1.20 ± 0.67</td>
<td>3.43 ± 3.17</td>
<td>6.46 ± 2.55</td>
</tr>
<tr>
<td>5</td>
<td>1.99 ± 0.77</td>
<td>0.90 ± 0.11</td>
<td>0.50 ± 0.51</td>
<td>0.97 ± 0.92</td>
<td>3.13 ± 2.00</td>
<td>7.93 ± 1.20</td>
</tr>
<tr>
<td>Mean</td>
<td>2.13 ± 1.28</td>
<td>0.54 ± 0.41</td>
<td>2.08 ± 1.59</td>
<td>1.51 ± 0.92</td>
<td>3.87 ± 1.81</td>
<td>6.68 ± 2.23</td>
</tr>
<tr>
<td>95% CI</td>
<td>(1.67, 259)</td>
<td>(0.39, 0.69)</td>
<td>(1.51, 2.65)</td>
<td>(1.18, 1.84)</td>
<td>(3.22, 4.52)</td>
<td>(5.88, 7.48)</td>
</tr>
</tbody>
</table>

\( ^{a} \)Statistically less than 5 mm using one-sided t-test (\( p < 0.001, B = 0.2, n = 29 \)).
tation of the transducer and semiautomatic segmentation algorithm were not significant.

The 3D system was able to accurately guide a biopsy needle in vitro to predefined targets with an average error of 2.1 mm. This error was primarily due to the large NTE as a result of needle deflection in our prostate phantom. In spite of this error, the targeting accuracy was within the 5 mm radius of the smallest tumors considered clinically significant (tumor radius less than 0.5 cm is considered insignificant). From the results of our ongoing patient study, we were able to guide the biopsy needle to predetermined targets and maintain proper correspondence of our real-time 2D and 3D images by minimizing prostate motion through a variety of mechanical and software mechanisms. By providing mechanical means to stabilize and support the US probe, constant pressure between the probe and rectal wall was maintained. The remote fulcrum (anus) further stabilized the pressure by minimizing motion between the RCM and probe tip. Further, constant pressure on the prostate was maintained with the probe tip by simply pivoting about the RCM. To complement this mechanical feature, we implemented a visual ring representation in the software interface where the axis of the needle intersects the depth of the preselected target (Fig. 5). This ring provides visual guidance in manipulating and orienting the probe to the target in the shortest distance possible, while minimizing motion of the probe and maintaining constant pressure on the prostate. The shortest path is the minimum yaw and pitch angle needed to align the needle guide to a predetermined target. This is accomplished by rolling the probe and changing the pitch angle to align the needle axis with the target. Although minimizing probe motion and its effects on the prostate would be preferred, it is also important that the physician avoids the urethra and nearby organs (bladder). This imposes restrictions on the entry points as it is necessary for the physician to be able to see sensitive areas so they can be avoided.

Patient motion on the biopsy table, which cannot be controlled (see Fig. 11) or prostate motion would result in the real-time 2D image not matching the 2D corresponding slice from the 3D TRUS image. This would provide a visual warning to the physician that the preselected targets are no longer valid, requiring the physician to perform another 3D scan. Prostate motion can be corrected by registering the planned and recorded biopsy locations in the 3D US image to the one after the prostate has moved. Although patient motion during
the procedure is infrequent, correction for patient motion errors is a focus of our future work.

VI. CONCLUSIONS

By adding 3D information to the prostate biopsy procedure, our system should improve the recording procedure as well as the physician’s ability to accurately guide the biopsy needle to selected targets identified using other imaging modalities. This would be beneficial in cases where the patient was diagnosed on biopsy to have ASAP and requires the physician to rebiopsy the same area. Using the 3D TRUS image, the physician was able to observe the patient’s prostate in views currently not possible in 2D procedures. Overall, our 3D system should result in prostate biopsy procedures that are stereotactic and more reproducible, which may lead to higher cancer detection rates and improve the yield on repeat biopsy.

Finally, integration of our system into the current prostate biopsy procedure requires minimal physician retraining as procedural workflow is maintained. By adhering to the imaging tools and protocols of current biopsy procedures, clinical integration of our 3D system should be cost effective.

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### Table IV

Mean in-plane displacement of anatomical landmarks identified in three patients participating in an ongoing clinical trial. The standard deviation (STD), maximum, and minimum displacement, and the number of landmarks ($n$) identified in the images are reported.

<table>
<thead>
<tr>
<th>Displacement (mm)</th>
<th></th>
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<tbody>
<tr>
<td>Mean</td>
<td>0.90</td>
</tr>
<tr>
<td>Maximum</td>
<td>4.60</td>
</tr>
<tr>
<td>Minimum</td>
<td>0.04</td>
</tr>
<tr>
<td>STD</td>
<td>0.97</td>
</tr>
<tr>
<td>$n$</td>
<td>21</td>
</tr>
</tbody>
</table>
project. JB was supported by a Canada Graduate Scholarship from the Natural Sciences and Engineering Research Council of Canada. AF holds a Canada Research Chair in Biomedical Engineering and acknowledges the funding from the Canada Research Chair Program.

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