Image Registration Accuracy of a 3-Dimensional Transrectal Ultrasound–Guided Prostate Biopsy System

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Objective. For a follow-up prostate biopsy procedure, it is useful to know the previous biopsy locations in anatomic relation to the current transrectal ultrasound (TRUS) scan. The goal of this study was to validate the performance of a 3-dimensional TRUS-guided prostate biopsy system that can accurately relocate previous biopsy sites.

Methods. To correlate biopsy locations from a sequence of visits by a patient, the prostate surface data obtained from a previous visit needs to be registered to the follow-up visits. Two interpolation methods, thin-plate spline (TPS) and elastic warping (EW), were tested for registration of the TRUS prostate image to follow-up scans. We validated our biopsy system using a custom-built phantom. Beads were embedded inside the phantom and were located in each TRUS scan. We recorded the locations of the beads before and after pressures were applied to the phantom and then compared them with computer-estimated positions to measure performance.

Results. In our experiments, before system processing, the mean target registration error (TRE) ± SD was 6.4 ± 4.5 mm (range, 3–13 mm). After registration and TPS interpolation, the TRE was 5.0 ± 1.03 mm (range, 2–8 mm). After registration and EW interpolation, the TRE was 2.7 ± 0.99 mm (range, 1–4 mm). Elastic warping was significantly better than the TPS in most cases (P < .0011). For clinical applications, EW can be implemented on a graphics processing unit with an execution time of less than 2.5 seconds.

Conclusions. Elastic warping interpolation yields more accurate results than the TPS for registration of TRUS prostate images. Experimental results indicate potential for clinical application of this method. Key words: elastic warping interpolation; phantom validation; prostate cancer; surface-based registration; thin-plate spline interpolation; 3-dimensional transrectal ultrasound.

Prostate cancer (PCa) is the most common noncutaneous human malignancy and the second most lethal tumor among American men. In 2008, an estimated 186,320 men will have a diagnosis of PCa; 28,660 of them will die of this disease in the United States. In general, a biopsy is recommended when the patient shows elevated prostate-specific antigen (PSA) levels, a possible indicator of underlying malignancy. Transrectal ultrasound (TRUS)–guided biopsy is used to remove tissue from the prostate gland for pathologic classification. One of the most perplexing aspects is that patients with PCa who have similar PSA levels, clinical stages, and histopathologic features in their biopsy...
tissue can have markedly different clinical outcomes. Although localized PCa can become lethal in some patients, most men die with PCa rather than of it. Autopsy studies have confirmed histologically apparent PCa in the prostate glands of approximately 42% of men older than 50 years who died of other causes. Nevertheless, the 5-year survival rate for American men with a diagnosis of PCa was nearly 100% based on patients with a diagnosis between 1996 and 2002 and followed through 2003. Therefore, early detection and treatment play important roles in the clinical management of this disease.

Currently, there are 2 important clinical challenges: (1) diagnosis of clinically threatening cancer and (2) selection of a suitable treatment regimen. Prostate biopsies are subjected to serious sampling errors. The success of prostate biopsies largely depends on the size and location of the tumor rather than the clinical importance of the disease. There have been efforts to find optimal locations for prostate biopsies, but the selection does not guarantee that malignancy will be detected in the first session. If the initial biopsy results are negative, a second biopsy is usually recommended when PSA levels remain elevated. Studies have shown that up to 10% of cases with initial negative biopsy results may produce positive results during a subsequent biopsy. For a subsequent biopsy, it is useful to know the previous biopsy locations so that the physician may plan the current procedure by revisiting or avoiding some locations.

Because of the relatively long latency of PCa, a considerable proportion of men with localized PCa are subject to overdiagnosis and receive unnecessary therapy with attendant morbidity, coupled with substantial cost escalations from detection of minor tumors via aggressive screening. Because most cases of PCa currently diagnosed by prostate biopsies have an intermediate Gleason score, with either good or poor clinical outcomes, some of these patients may be treated with focal therapy as opposed to more aggressive treatments, eg, surgery and radiation. Patients with disease localized to one side of the prostate can be treated with focal therapy, thereby eliminating the usual side effects associated with surgery and radiation. The success of focal therapy largely depends on the screening procedure (brachytherapy and template-guided saturation biopsy) and the ability to focus treatment in relation to specific locations within the prostate. Therefore, it is necessary to accurately relocate initial biopsy locations (those having malignancies) during focal treatment.

However, it is very difficult for a physician to relocate the initial biopsy locations obtained across the TRUS images during a subsequent biopsy or therapy session. Although template-guided transperineal biopsy procedures may provide some degree of relocation accuracy, currently there is no mechanism to accurately relocate biopsy locations performed transrectally. This is partly due to use of a live 2-dimensional TRUS image, whereas a 3-dimensional (3D) TRUS image of the gland may provide anatomic features that are more easily discerned. Furthermore, the gland tends to move or deform because of external physical disturbances, discomfort introduced by the procedure, changes due to cancer progression, therapy, or intrinsic peristalsis. The quality of the image also depends on the type and particular settings of the machine. It is, therefore, necessary to find the correspondence between TRUS images so that the previous biopsy sites can be identified on an ultrasound scan during subsequent visits. Hence, there is a clinical need for a 3D TRUS-guided prostate biopsy system in which initial biopsy locations can be accurately relocated during follow-up visits.

A 3D TRUS-guided biopsy scheme was initially demonstrated. It uses a mechanical tracker having 4 degrees of freedom. An integral personal computer–based workstation can register biopsy locations in 3D space and accurately relocate them in follow-up visits. In this study, we evaluate the accuracy and utility of 2 image interpolation methods in this 3D TRUS-guided prostate biopsy system using tissue phantoms.

Materials and Methods

System Overview

The 3D TRUS-guided biopsy system is partitioned into the following subsystems: image acquisition, prostate segmentation, target planning, tracking, and reporting. Three-dimensional image registration completed as a part of target planning is a surface-based registration technique.
This aligns the segmented surface of the current 3D prostate gland with that computed from the previous visit so that previous biopsy sites can be interpolated onto the current 3D TRUS volume. Only surface information is used in 3D TRUS image segmentation because ultrasound image quality is poor in certain regions within the prostate and makes intensity-based registration methods impractical.

Both semiautomated and fully automated image segmentation techniques are available in this system. Figure 1 shows the process flow for the selection of biopsy sites based on a previous biopsy report. Figure 2 illustrates the essential components of the surface-based registration technique adapted into our system. Figure 3 shows a sample graphical user interface design to load a previous biopsy plan onto the current ultrasound scan. Once a patient’s previous visit is selected, the corresponding previously segmented prostate surface is registered to the currently segmented surface. After this, the previous biopsy sites are interpolated on the current volume based on the correspondence established through registration.

Two interpolation techniques are implemented. One is based on a thin-plate spline (TPS) method, whereas the other is based on elastic warping (EW). The TPS method uses the concept of minimizing the “bending” energy of a thin sheet of metal. In 3D cases, given 2-point sets $P$ and $Q$, each has $n$ points. Each point $(p_i, i = 1 \ldots n)$ in $P$ corresponds to 1 point $(q_i, i = 1 \ldots n)$ in $Q$. Thin-plate spline interpolation is described by $3(n + 4)$ parameters, which include 12 global affine motion parameters and $3n$ coefficients for correspondences of the $n$ control points (Equation 1):

$$f(x, y, z) = [a_1, a_2, a_3, a_4] + \sum_{i=1}^{n} w_i [u_{i1}, \ldots, u_{in}]^T.$$

The definition of $U_{ij}$ ($i = 1 \ldots n, j = 1 \ldots n$) is

$$U_{ij} = \sqrt{(x_{p_i} - x_{q_j})^2 + (y_{p_i} - y_{q_j})^2 + (z_{p_i} - z_{q_j})^2}.$$

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**Figure 1.** Process flow diagram for the mapping of biopsy sites from a previous patient visit onto the current visit.

**Figure 2.** Surface-based registration flow chart.

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These parameters are computed by solving the linear system. Elastic warping uses modeling of elastic sheets, which are warped by an external force applied to points \((x, y, z)\) in data set D1, so that they are deformed to the coordinates of their corresponding points \((f^u(x, y, z), f^v(x, y, z), f^w(x, y, z))\) in data set D2. Given a set of \(n\) corresponding points, EW interpolation is used to find the solution of function \((U, V, W)\) to the equations describing the deformation of an elastic sheet:

\[
\mu \Delta \vec{U}(X) + (\lambda + \mu) \nabla (\nabla \cdot \vec{U}(X)) + q(X)(f(X) - \vec{U}(X)) = 0 ,
\]

Where \(\vec{U}(X) = [U \ V \ W]^T\), \(X = (x, y, z)\), and \(q(X) = q(x, y, z)\) is unity when there is a correspondence and 0 otherwise. Equation 3 is discretized, and the resulting linear system is solved iteratively.

### Evaluation Protocol

We used 5 custom-built tissue phantoms to evaluate the accuracy of the 3D TRUS-guided biopsy scheme. A typical tissue phantom design is illustrated in Figure 4. Spherical beads comprising 2-mm stainless steel balls are planted inside each tissue phantom at random locations to emulate several targeted biopsy sites and can be identified on ultrasound scans. As shown in Figure 5, the ultrasound signal was locally distorted by the presence of the beads; the beads, however, were identifiable, and the segmentation method was unaffected. The evaluation procedure is as follows:

1. A 3D TRUS image scan of tissue phantom is acquired.
2. The spherical beads in the ultrasound scan are identified. The centers of spherical beads are saved and designated as \(P\). Then, either the semi-automated segmentation process or the fully automated segmentation process is performed, and the segmented prostate volume is obtained and designated as a floating 3D image (labeled \(A\)).
3. Next, mechanical pressure is applied in an arbitrary direction on the tissue phantom. This mimics anatomic deformations (shape and size variations) or movement of the prostate. The aforementioned steps are repeated to obtain 3D TRUS images, with the spherical beads centers designated \(Q\). The deformed tissue phantom surface is segmented and designated as a target 3D image (labeled \(B\)).

4. The floating 3D image, \(A\), is registered to the target 3D image, \(B\), and then a nonrigid deformation between the 2 images is obtained. Now the 3D image, \(A\), is aligned to the target 3D image, \(B\). Therefore, the set of points, \(P\), inside the floating 3D image, \(A\), is accordingly deformed and registered as points \(P'\) inside the target 3D image, \(B\).

5. The target registration error (TRE) is defined as the mean euclidean distance \((D)\) between corresponding locations of the ground truth and the computer estimation. Before registration, the TRE is computed between \(P\) and \(Q\). After registration, the TRE is computed between \(P'\) and \(Q\), as illustrated in Figure 6. The TRE is used to assess the accuracy of the registration technique.

6. The above protocol is repeated several times, and the TRE is computed. The mean and SD of the TRE are calculated to determine whether the system meets the required performance standards for clinical applications.

7. The above steps are repeated the same number of times for the 2 interpolation techniques, TPS and EW, respectively. The mean and SD of the TREs are calculated and compared.

Target registration error metrics are calculated from the measurements obtained using the following equations. For each set of experiments, the euclidean distance between \(P\) and \(Q\) is computed using Equation 4, where \(N\) is the total number of beads in the phantom. The mean \((\overline{D})\) and SD \((\sigma)\) from all of the experiments were computed using Equations 5 and 6, respectively, as follows:

\[
D_i = \|Q_i - P_i\|, \quad i = 1, \ldots, N
\]

\[
\overline{D} = \mu = \frac{\sum_{i=1}^{N} D_i}{N}
\]

\[
\sigma = \sqrt{\frac{1}{N} \sum_{i=1}^{N} (D_i - \overline{D})^2}
\]
Results

Five custom-built tissue phantoms having 3 to 5 beads randomly located within each phantom were used to evaluate the accuracy of the system. For each tissue phantom, 10 to 15 TRUS scans were obtained using the Falcon 2101 ultrasound machine with a type 8667 transducer (5–10 MHz; BK Medical, Herlev, Denmark). The first scan was performed without any pressure. Remaining scans were performed with varying mechanical pressure applied in an arbitrary direction on the tissue phantom. All scans were segmented, and then the segmented surfaces from the same phantom were registered with a corresponding deformed phantom in pairs. Figure 7 shows an example of overlapped surfaces before and after registration as well as the locations of the beads (both computer estimated and ground truth).

Altogether, the evaluation procedure was repeated 100 times for each phantom, and then the TREs for each trial were recorded both before and after registration. The same procedure was performed for both the TPS interpolation and EW methods. Table 1 lists the TRE (both mean and SD) for all phantom trials. The results for the TPS and EW are shown side by side for comparison. Before system processing, the TRE was 6.4 ± 4.5 mm (range, 3–13 mm). After registration and TPS interpolation, the TRE was 5.0 ± 1.03 mm (range, 2–8 mm). After registration and EW interpolation, the TRE was 2.7 ± 0.99 mm (range, 1–4 mm). Figure 8 illustrates the TREs for trials on phantom 4. In most cases, EW outperformed the TPS method (2-tailed t test, \( P < .0011 \)).

Discussion

We have presented a 3D prostate biopsy system that can be used to map previous biopsy sites onto a current ultrasound scan. This is very important during a prostate biopsy procedure because the urologist may want to either avoid or rebiopsy previous sites.

A custom-built phantom was used to simulate the prostate deformation between 2 scans. Because the identification from the second scan can serve as the ground truth, it can be used to measure the performance of the registration system. In our experiments, 2 interpolation methods were implemented, and the results were compared. Elastic warping outperformed the TPS method in most cases. Both the TPS and EW are approximations of prostate tissue property. However, the TPS is used to solve a given finite number of equations, more suitable to a collection of scattered points marking distinct surface features, whereas EW tends to preserve the shape and relative position of given point sets because of its smoothness. Because the structure of the segmented surface is fairly consistent on a case-by-case basis, EW is more appropriate for our system. The EW approach is also more robust compared with the TPS because the solution...
Clinical application of either method will depend on computing time. For a 15-minute biopsy session, for example, it is desirable to have a registration procedure done in 20 seconds. The current central processing unit time for the registration procedure on an Intel Core 2 processor (Intel Corporation, Santa Clara, CA) with a 2.66-GHz clock speed is 150 seconds; this is unacceptable in clinical practice. When the registration algorithm was implemented on a graphics processing unit (an 8800 GT video board running at 640 MHz and accessing 512 MB of onboard RAM; NVIDIA Corporation, Santa Clara, CA), the running time was reduced to 12 seconds. For the interpolation procedure, the TPS method can be performed onboard the central processing unit in 0.3 second, whereas the EW method requires 15 seconds. However, after EW migrated to a graphics processing unit implementation, its total time was reduced to 2.5 seconds. This meets the clinical requirement.
In addition to the errors introduced by the interpolation methods, there are other sources of error contributing to the overall TRE. A bead identification error is introduced by the operator while locating the beads in the phantom scan; this is due to poor ultrasound scan image quality and the software tool used. Table 2 lists the experimental results for the bead identification error. Three operators were requested to identify the beads inside 6 phantom scans, respectively. The locations were recorded and compared. The overall bead identification error was 0.8682 ± 0.2377 mm.

Segmentation error is also important because the segmented prostate volume is always different from the actual phantom volume. For example, in our experiments, the customized phantom has a designed volume of 44 cm³, whereas the average segmented volume is 36.77 cm³: a segmentation error of 8.07%. Also, the error due to surface registration adds to the TRE. Image calibration and acquisition errors can also contribute to errors in the TRE.

Table 1. Comparison of TREs Before and After System Processing (Registration and Interpolation)

<table>
<thead>
<tr>
<th>TRE, mm</th>
<th>Preprocessing</th>
<th>Postprocessing</th>
</tr>
</thead>
<tbody>
<tr>
<td>D</td>
<td>μ 6.396</td>
<td>5.060</td>
</tr>
<tr>
<td></td>
<td>σ 4.500</td>
<td>1.630</td>
</tr>
<tr>
<td>D_{max}</td>
<td>μ 6.915</td>
<td>6.220</td>
</tr>
<tr>
<td></td>
<td>σ 4.626</td>
<td>1.840</td>
</tr>
<tr>
<td>D_{min}</td>
<td>μ 5.880</td>
<td>3.787</td>
</tr>
<tr>
<td></td>
<td>σ 4.390</td>
<td>1.960</td>
</tr>
</tbody>
</table>

Target registration errors from 2 interpolation methods (TPS and EW) are also listed; EW gave better results.

Table 2. Bead Identification Error for 6 Phantom Trials

<table>
<thead>
<tr>
<th>Trial</th>
<th>Maximal, mm</th>
<th>Minimal, mm</th>
<th>Average, mm</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1.3265</td>
<td>0.2500</td>
<td>0.7112</td>
</tr>
<tr>
<td>2</td>
<td>1.6247</td>
<td>0.7586</td>
<td>1.007</td>
</tr>
<tr>
<td>3</td>
<td>1.2384</td>
<td>0.4223</td>
<td>0.7457</td>
</tr>
<tr>
<td>4</td>
<td>2.5616</td>
<td>0.2162</td>
<td>1.1802</td>
</tr>
<tr>
<td>5</td>
<td>2.1363</td>
<td>0.3063</td>
<td>0.8758</td>
</tr>
<tr>
<td>6</td>
<td>0.9619</td>
<td>0.2268</td>
<td>0.6886</td>
</tr>
</tbody>
</table>

Each trial had a different number of beads; the maximal, minimal, and average identification errors for each trial are listed.
There are other variabilities that may also introduce errors due to (1) probe or transducer settings, (2) the scanning method during the ultrasound scan or navigation, and (3) the changes in the morphologic shape due to medications and other factors. Issue 1 can be compensated by our hardware interfaces, whereas the other 2 issues related to the pressure of the probe or transducer on the prostate gland and the shape deformation can be mitigated by physician training and motion compensation procedures.

In conclusion, we have presented a 3D image registration system in which previous patient biopsy sites can be mapped onto a current ultrasound scan. Our system is based on a robust, surface-based registration algorithm. The transformation method to project biopsy sites after registration is fast and accurate. Two interpolation methods were implemented and compared, and has been shown that EW performs better than the TPS method. The registration system reported here is currently being integrated in our Artemis system, a US Food and Drug Administration 510(k)–approved 3D TRUS-guided prostate biopsy system developed by Eigen Inc (Grass Valley, CA). The phantom-based validation results have been published, and the product is now at hospital sites for clinical validation.

References