Evaluation of Inter-session 3D-TRUS to 3D-TRUS Image Registration for Repeat Prostate Biopsies

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Abstract. To ensure accurate targeting and repeatability, 3D TRUS-guided biopsies require registration to determine coordinate transformations to (1) incorporate pre-procedure biopsy plans and (2) compensate for *inter-session* prostate motion and deformation between repeat biopsy sessions. We evaluated prostate surface- and image-based 3D-to-3D TRUS registration by measuring the TRE of manually marked, corresponding, intrinsic fiducials in the whole gland and peripheral zone, and also evaluated the error anisotropy. The image-based rigid and non-rigid methods yielded the best results with mean TREs of 2.26 mm and 1.96 mm, respectively. These results compare favorably with a clinical need for an error of less than 2.5 mm.

Keywords: surface-based registration, image-based registration, accuracy, prostate, repeat biopsy, inter-session, 3D TRUS, peripheral zone.

1 Introduction

Current diagnostic tests for prostate cancer (PCa) include prostate-specific antigen (PSA) tests and digital rectal exams (DRE), but two-dimensional (2D) transrectal ultrasound (TRUS) guided biopsy (Bx) is the clinical standard for definitive diagnosis. 2D TRUS guidance, however, is not without limitations. A 2D view restricts the anatomic information available to the physician for the accurate characterization of tumor location, which is vital for targeting and needle guidance. PCa is particularly difficult to target with 2D TRUS-guided Bx since this cancer tends to be small and multifocal. Furthermore, up to 80% of the cancer can be located in the prostate's peripheral zone (PZ) [1], an area subject to deformation due to ultrasound transducer pressure during the exam (Fig. 1). These difficulties contribute to false negative rates as high as 34% [2], and the detection rate of cancer on the necessary repeat Bx ranges between 10% and 25% [3]. In order to reduce the need for repeat Bxs, and provide better planning for required repeat Bxs, improved techniques are necessary to accurately identify tumor locations and record biopsy cores so as to avoid negative areas and target precancerous lesions. Techniques for obtaining an accurate 3D record of Bx locations and providing guidance of repeated Bxs to specific locations are of

profound importance to the timely diagnosis of prostate cancer, and lead to high impact on patient care and quality of life.

A three-dimensional (3D) TRUS-guided prostate biopsy system has been developed in our laboratory, using a mechanically stabilized and tracked end-firing probe that provides a 3D view of the anatomy and records the 3D location of each Bx core (Fig. 1(c)) [4]. In order to accurately transform the 3D locations of Bx cores taken during a previous session into the coordinate space of the current session, 3D-TRUS to 3D-TRUS image registration needs to be performed. The transformation given by this registration will compensate for differences in prostate position and deformation between sessions, which can be substantial due to the time between biopsy sessions, and may be due to differences in patient positioning, edema and swelling due to needle insertion, and bladder and/or rectum filling.

In this study, we evaluate the accuracy of four algorithms for 3D-TRUS to 3D-TRUS registration of prostate images taken during different biopsy sessions. We evaluate rigid and non-rigid variations of both surface-based and image-based registration algorithms. We determine a mean target registration error (TRE) for each algorithm and provide an analysis of the spatial anisotropy in the TRE. Furthermore, since the PZ of the prostate is of particular clinical interest, and we hypothesize that this region may undergo characteristically different (from the remainder of the gland) deformations due to its proximity to the ultrasound transducer, we perform a separate accuracy analysis on this region. Our primary success criterion is a clinically desired TRE of 2.5 mm or less, with a non-dominant fiducial localization error (FLE) [5].

Previous related work focuses on *intra-session* registration of 3D-TRUS to 3D-TRUS [5, 6], and 3D-TRUS to magnetic resonance (MR) [7] prostate images, and accuracies as high as 1.50 mm have been reported. However, to the best of our knowledge, an evaluation of 3D-TRUS to 3D-TRUS *inter-session* registration, with its attendant challenges as described above, has not been previously conducted for image-guided prostate biopsies.

Fig. 1. Axial view of prostate with PZ highlighted in black (a) without deformation and (b) with deformation caused by transducer probe pressure. (c) Mechanically assisted 3D-TRUS biopsy system with real-time tracking and recording of the 3D position of the biopsy needle.

2 Materials and Methods

2.1 Materials

3D TRUS prostate images were obtained from 10 different patients who had undergone two prostate imaging sessions one week apart. The physician inserts the

transducer probe into the patient's rectum and rotates it (by rolling it about the probe axis) to acquire 180 2D images in 1 degree increments. The 2D US images from the US machine are digitized using a frame grabber and reconstructed into a 3D image. Acquisition of the 3D image requires approximately 10 seconds and the reconstruction occurs as the images are acquired, allowing the physician to view the 3D image as it is being acquired. The first set of scans was acquired using a HDI-3500 ultrasound machine and second was acquired using a HDI-5000. The same transducer probe (Philips C9-5) was used with both machines, but calibrated differently. From each patient, 2 images from the two different procedures were selected to be the source (I_S) and target images (I_T). The image dimensions were $448 \times 448 \times 350$ (voxel size of $0.19 \times 0.19 \times 0.19 \text{ mm}^3$). The selection of images for this study was based on our ability to localize in 3D a set of corresponding intrinsic fiducials (small calcifications) in the image pairs for use in computing the TRE. In all 10 image pairs, we found a total of 92 fiducial pairs, of which 18 were located in the PZ. It is important to note that the fiducials in our study are used only to evaluate the registration methods, and are not used as inputs to the registration algorithms.

2.2 Surface-Based Registration

For surface-based registration, we first segmented the images semi-automatically using a dynamically deformable contour model [8]. We then rigidly registered the surfaces using the iterative closest point (ICP) algorithm [9], where both surfaces are represented by point clouds. In order to align the surfaces, a rigid transformation T is required that maps each point in the source image of patient i , (I_S^i), to its corresponding point in the target image of patient i , (I_T^i). The algorithm proceeds by (1) establishing correspondence between closest point pairs, and (2) by estimating the transformation required to align the corresponding points. Steps (1) and (2) are iterated until a convergence criterion (RMS of the sum of squares of the closest point distances) of 0.01 mm is met [9].

Following rigid registration, we performed a non-rigid registration using a thin-plate spline (TPS) [10]. Parametric correspondence between surfaces I_S^i and I_T^i was established by radially projecting equal-angle rays from the centroid of the rigidly aligned surfaces, and corresponding the point pair lying on each ray. This approach to correspondence establishment is justified due to the approximately spherical shape of the prostate. A 3D TPS is defined in the 3D image space and aligns the corresponding points. The TPS is applied to I_S^i in order to register it to I_T^i .

2.3 Image-Based Registration

We adopt the block matching approach proposed by Ourselin et al. for rigid registration [11]. The registration consists of the following four steps: (1) dividing the source image into rectangular block regions; (2) for each block in I_S^i , finding the block in a local neighborhood within I_T^i having the optimal value of a chosen image-to-image metric; (3) constructing a vector field mapping each I_S^i block to its best matching I_T^i

block; and (4) performing a least trimmed squares optimization to regularize the vector fields [12] in order to determine the transformation mapping I_S^i to I_T^i . Steps (1) through (4) are iterated, with a progressively smaller block size, in order to provide a coarse-to-fine registration of the images. The chosen image-to-image metric is mutual information [13], due primarily to the effects of directionally-dependent shadowing artifacts present in 3D TRUS images. We used the implementation provided by MedINRIA (INRIA, Asclepios Research Team, 2009) that adopts a multi-resolution approach. Results were achieved using a multi-resolution image pyramid where the finest and coarsest image resolutions used were tuned empirically to $32 \times 32 \times 32$ and $16 \times 16 \times 16$, respectively. The block size, N , is initialized to $N = \min\left(\frac{X}{8}, \frac{Y}{8}, \frac{Z}{8}\right)$, where X , Y and Z are the 3D image dimensions and the initial search area, Ω , is equal to $2N$ [14]. The parameters are halved when refining the scale and the process stops when the block size is $N = 4$.

For image-based non-rigid registration, the moving image deformation is defined using a regular 3D grid of B-spline control points. We used a limited-memory Broyden Fletcher Goldfarb Shannon optimizer [15], and mutual information [13] as the image-to-image metric. We used the implementation provided by the 3D-SLICER software (Surgical Planning Lab, Harvard Medical School, Boston, USA), which permits the tuning of the following parameters: the number of optimization iterations (we set this parameter to 50), the number of elements along each side of the grid of B-spline control points (10), the number of histogram bins (20) and randomly-sampled voxels (100,000) to use in computing the mutual information metric, and the maximum allowed deformation of the B-spline grid control points (1).

2.4 TRE

We measured the TRE as the overall misalignment of manually marked, corresponding, intrinsic fiducials in I_S^i and I_T^i . The TRE is defined, for the j th corresponding fiducial in patient i , as the Euclidean distance between the transformed fiducial $\tilde{f}_S^{ij} = T(f_S^{ij})$ from I_S^i and the corresponding fiducial f_T^{ij} in I_T^i , written as $TRE^{ij} = \|\mathbf{v}^{ij}\|_2$, where $\mathbf{v}^{ij} = (f_T^{ij} - \tilde{f}_S^{ij})$. The mean TRE for patient i is denoted as $TRE^i = \sqrt{\sum_j (TRE^{ij})^2 / N_i}$, where N_i is the number of fiducials identified in I_S^i . The overall mean TRE is denoted as $TRE = \sqrt{\sum_i \sum_j (TRE^{ij})^2 / N}$, where N is the total number of fiducial pairs used in the calculation. In this study, there were 92 fiducial pairs in total, of which 18 were within the PZ of the prostates.

2.5 Error Anisotropy

We performed a 3D principal component analysis (PCA) of the 3D point set $\Delta = \{f_{Tx}^{ij} - \tilde{f}_{Sx}^{ij}, f_{Ty}^{ij} - \tilde{f}_{Sy}^{ij}, f_{Tz}^{ij} - \tilde{f}_{Sz}^{ij}\}, \forall i, \forall j\}$ in order to evaluate the directional

anisotropy of the TRE. Using MATLAB (The Mathworks Inc., Natick, MA), we computed the PCA by finding the eigenvectors ($\mathbf{e}_i$) and eigenvalues (λ_i) of the covariance matrix of Δ . This was done for both the whole gland (WG) and PZ. The 95% standard error ellipsoid volumes were defined with their semi-principal axes parallel to the eigenvectors, with lengths $a_i = \sqrt{\lambda_i \times \chi_{\alpha,v}^2}$, ($i = 1, 2, 3$ and $\chi_{\alpha,v} \approx 2.80$), where $\chi_{\alpha,v}^2$ is the probability distribution evaluated for 95% confidence ($\alpha = 0.05$) and 3 degrees of freedom ($v = 3$) [16].

Fig. 2. WG (black) and PZ (white) frequency distributions of (a) pre-registered distances between all 92 fiducial pairs, (b) rigid surface-based TRE_{ij}^{ij} , (c) non-rigid surface-based TRE_{ij}^{ij} , (d) rigid image-based TRE_{ij}^{ij} , (e) non-rigid image-based TRE_{ij}^{ij}

3 Results

3.1 TRE

Our pre-registration mean misalignment was ~ 7.45 mm, ranging from 0.28-18.0 mm. The frequency distributions of the WG and PZ TREs are shown in Figure 2 and the TRE results are summarized in Table 1. The two-tailed paired t-test results shown in Table 2 indicate that surface- and image-based rigid registration TREs were statistically significantly different with $p = 4.29 \times 10^{-6}$. The surface- and image-based non-rigid TREs were also significantly different, with $p = 1.60 \times 10^{-9}$.

Table 1. Whole gland (WG) and peripheral zone (PZ) mean TRE results for surface-based (SB) and image-based (IB) registration

Registration	WG		PZ	
	SB	IB	SB	IB
Pre-registration mean TRE (mm)	7.36 ± 4.17		5.23 ± 3.29	
Rigid mean TRE (mm)	3.20 ± 1.46	2.26 ± 0.98	3.45 ± 1.21	2.30 ± 0.90
Non-rigid mean TRE(mm)	3.29 ± 1.50	1.96 ± 0.85	3.62 ± 1.12	2.11 ± 0.91

Table 2. t-test results for surface-based (SB), image-based (IB), rigid (R), and non-rigid (NR) registration

	SB vs. IB	SB vs. IB	SB	IB
	R	NR	R vs. NR	R vs. NR
WG p-value	4.29×10^{-6}	1.6×10^{-9}	0.05	1.38×10^{-7}
PZ p-value	1.88×10^{-4}	6.21×10^{-6}	0.12	0.07

3.2 Error Anisotropy

Figure 3 shows the 95% confidence ellipsoids for the PCA performed on the directional components of the WG and PZ TREs for the non-rigid registration methods. The WG pre-registered ellipsoid volume (EV) is 4.46 cm^3 while the post-registration EVs range from 0.12 cm^3 to 0.41 cm^3 . The EVs for surface-based rigid and non-rigid TRE were greater than the image-based EVs by an average of 0.27 cm^3 .

The PZ pre-registered EV is 1.58 cm^3 while the post-registration volumes range from 0.14 cm^3 to 0.37 cm^3 . The EVs for surface-based rigid and non-rigid TRE were greater than the EVs for image-based TRE by an average of 0.22 cm^3 . Table 3 shows the ratios of the eigenvalues for each registration approach as well as for the unregistered case, to illustrate any anisotropy in the error.

Fig. 3. Error ellipsoids for WG and PZ: (a) WG pre-registered data, (b) WG surface-based non-rigid registration, (c) WG image-based non-rigid registration, (d) PZ pre-registered data, (e) PZ surface-based non-rigid registration, and (f) PZ image-based non-rigid registration

Table 3. Ratios of 95% TRE confidence ellipsoid eigenvalues

Registration Method	WG			PZ		
	λ_1 / λ_2	λ_2 / λ_3	λ_1 / λ_3	λ_1 / λ_2	λ_2 / λ_3	λ_1 / λ_3
Unregistered	1.16	1.37	1.43	1.24	1.72	1.95
Surface-based rigid	1.51	1.36	1.42	2.08	1.6	1.6
Surface-based non-rigid	1.76	1.86	2.02	2.58	2.75	3.13
Image-based rigid	1.16	1.37	1.43	1.24	1.72	1.95
Image-based non-rigid	1.51	1.36	1.42	2.08	1.6	1.6

4 Discussion

Using 3D image registration to correct for prostate motion and deformation that occurs between Bx procedures is vital to accurate Bx planning and needle guidance. The desired TRE is 2.5 mm since the smallest tumor considered clinically significant has a radius of ~ 5 mm (for a 0.5cm^3 spherical tumor) [17]. Since the TRE (RMSE) provides an estimate of the standard deviation of the normal distribution of biopsy targets given by a registration algorithm, a TRE of 2.5 mm gives a confidence interval with 95.4% of the registered targets within the clinically significant 5 mm radius.

The non-rigid image-based method yielded the lowest WG and PZ TRE values of 1.96 mm and 2.11 mm, respectively. Figures 2(d) and (e) show that the image-based method outperformed the surface-based method by illustrating the right-skewed distribution of the TRE values (for both WG and PZ), with $\sim 65\%$ of the values below the respective means. In a previous evaluation of image registration methods in the *intra-session* context, the non-rigid image-based TRE for images taken 6 minutes apart was

1.50 mm [5]. This shows that after a time gap of 1 week, the same image-based registration algorithm, tuned as in [5], is able to achieve comparable results.

The t-test results in Table 2 reveal statistically significant differences in all cases except when comparing surface-based rigid and non-rigid registration values. We speculate that this could be due to the variability introduced by segmentation (± 1.31 mm) [5]. The FLE [18] was 0.21 mm [5], and thus was not dominant.

Figure 3 shows the anisotropy in the TRE where both WG and PZ pre-registered fiducial misalignments are predominantly in the z-direction, which is along the transducer probe axis where we might expect misalignments due to probe pressure. The surface-based errors are predominantly anisotropic in x and y, which may be the result of inconsistent segmentation due to poor image contrast at the prostate boundaries parallel to the ultrasound beam. Table 3 indicates increased error anisotropy in the PZ, in comparison to the WG. This may be due to deformation that characteristically pushes the central region of the PZ upward in response to probe pressure, while the lateral "lobes" of the PZ bulge downward and laterally. The post-registration 3D EVs are dramatically reduced (by a factor of 10–37 for WG, and 4.27–11.29 for PZ) as compared with the pre-registered EVs.

Our results demonstrate that in the *inter-session* scenario with 1 week between sessions, the tested surface-based and image-based 3D TRUS image registration techniques yield clinically sufficient accuracy, with image-based registration giving the lowest error. Furthermore, due to the segmentation step required for surface-based registration, the two methods are comparable in execution time on a contemporary single-core workstation (90–105 s). The image-based method is preferred since it is more accurate, does not require segmentation and can potentially be automated.

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