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LEARNING NONRIGID DEFORMATIONS FOR CONSTRAINED POINT-BASED REGISTRATION FOR IMAGE-GUIDED MR-TRUS PROSTATE INTERVENTION

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Abstract

This paper presents and validates a low-dimensional nonrigid registration method for fusing magnetic resonance imaging (MRI) and trans-rectal ultrasound (TRUS) in image-guided prostate biopsy. Prostate cancer is one of the most prevalent forms of cancer and the second leading cause of cancer-related death in men in the United States. Conventional clinical practice uses TRUS to guide prostate biopsies when there is a suspicion of cancer. Pre-procedural MRI information can reveal lesions and may be fused with intra-procedure TRUS imaging to provide patient-specific, localization of lesions for targeting. The state-of-the-art MRI-TRUS nonrigid image fusion process relies upon semi-automated segmentation of the prostate in both the MRI and TRUS images. In this paper, we develop a fast, automated nonrigid registration approach to MRI-TRUS fusion based on a statistical deformation model of intra-procedural deformations derived from a clinical sample.

Index Terms

nonrigid registration; statistical deformation model; robust point matching; image-guided intervention; prostate biopsy

1. INTRODUCTION

Nonrigid image registration of multi-modal images is a challenging task. Rather than attempting to deal with the highly nonlinear intensity relationships that contribute to image registration optimization difficulties, an alternative strategy to maximizing mutual information, for example, is to first segment corresponding anatomical structures in both images and then register these structures to each other. However, image segmentation is itself a challenging problem and segmentations are prone to error and high variability. In this paper, we present a solution to the problem of nonrigidly registering potentially inaccurate surfaces by learning a low-dimensional parameterization of deformations needed to model a specific task. We present results applying our approach to nonrigidly register prostate

surfaces segmented from magnetic resonance imaging (MRI) and trans-rectal ultrasound (TRUS) imaging for image-guided prostate biopsy localization.

Prostate cancer is one of the most commonly occurring forms of cancer and one of the major causes of cancer-related death in the U.S. It is estimated that over 450,000 men will be diagnosed with prostate cancer by the year 2015 [1]. Biopsy is the current clinical standard for diagnosing prostate cancer, and the standard procedure utilizes TRUS imaging for biopsy guidance. The current biopsy sampling technique takes 12 tissue cores, in a systematic, non-patient-specific plan, from different regions of the prostate. No other major malignancy is biopsied in an untargeted manner. Using this general approach to biopsy sampling has been likened to a game of chance with no more than 0.45% of an average-sized gland being biopsied [2]. Furthermore, TRUS cannot be reliably used for targeting suspicious lesions because of poor image quality and lack of contrast. However, cancerous lesions are more readily seen using other imaging modalities, such as MRI. Compared to TRUS, multi-parametric MRI (mpMRI) that combines T2-weighted imaging with functional sequences, *e.g.* diffusion-weighted MRI, spectroscopic MRI and dynamic contrast enhanced MRI, shows significantly better localization of suspicious lesions within the prostate [3]. However, performing biopsies under MRI guidance can be time consuming, expensive and impractical [2]. To avoid these problems, current practice aims to fuse pre-procedure mpMRI with intra-procedure TRUS imaging. Here, suspicious prostatic tissue is first identified via mpMRI and TRUS imaging is used to provide targeted image-guided navigation for biopsy. A rigid image fusion method between the MRI and TRUS is inadequate for accurate biopsy guidance due to prostate gland deformation caused by (i) variations in patient orientation, (ii) changes in bladder or rectal filling, (iii) and presence or absence of an endorectal MR coil, and (iv) deformation caused by handheld TRUS probes.

Nonrigid registration is therefore necessary to compensate for these deformations. Mitra *et al.* [4] proposed an intensity-based registration but validated it only on mid-gland MR-TRUS slices, while Sun *et al.* [5] proposed non-rigid MR-TRUS registration using local intensity descriptors. Previously proposed surface registration algorithms to align the segmented prostate surfaces from the MRI and TRUS images [6, 7] are highly operator dependent because they rely upon semi-automated segmentation methods, which are both time-consuming and prone to significant variability. Hu *et al.* [8] trained a patient-specific deformation model using simulated finite element mesh deformations generated from manual segmentation of the prostate and surrounding anatomy. Rather than rely upon a biomechanical model, we propose to build a statistical deformation model (SDM) of procedure-induced nonrigid deformations [9] from a training set of MRI-TRUS image-guided procedures derived from a population of clinical cases.

We perform a principal component analysis (PCA) of intra-subject nonrigid deformations between pre-procedure MRI and intra-procedure TRUS imaging. While PCA has difficulty modeling high-dimensional data, we aim to capture the gross, intra-subject deformations observed between MRI and TRUS image acquisitions with our SDM. We adapt a robust point matching (RPM) framework [10, 11] to perform PCA-based SDM registration of MRI and TRUS prostate surfaces. We emphasize the key advantages of this approach: (i) the SDM will constrain the deformation to be realistic based on the actual deformations

encountered during the TRUS procedure as observed from a large population of training data; and (ii) the SDM is a low-dimensional parameterization that allows for highly efficient computation that fits within the time constraints of TRUS-guided biopsy procedures (typically 15 minutes). Our results show that our approach robustly registers surfaces in the presence of inaccurate prostate segmentations to provide effective patient-specific, nonrigid image fusion.

2. METHODS

In this work, we model the prostate surface S as a discrete set of points $X \in S$ within a triangulated mesh. Denoting the reference point set as X and the transform point set as Y , the goal of RPM registration is to estimate the transformation $T : X \mapsto Y$. The RPM methodology [11] functions by alternately estimating surface point correspondences and estimating the transformation, where T^k is the estimate of T at iteration k . Section 2.1 discusses our method for training an SDM of procedure-induced deformation, and Section 2.2 then describes how we incorporate this SDM into the RPM framework to nonrigidly register MR and TRUS images.

2.1. Training the Deformation Model

From a clinical database of patients undergoing prostate biopsy, we randomly select $N = 30$ patients to train our SDM. For each patient, the dataset contains a pre-procedure T2-weighted MR image I_{MR} and intra-procedure TRUS image I_{TRUS} with estimated segmented prostate surfaces S_{MR} and S_{TRUS} . Both surfaces were generated using a semi-automated, clinical segmentation tool (Eigen, Grass Valley, CA). The SDM creation procedure, outlined in Figure 1, follows: (i) rigidly register each patient's S_{MR} and S_{TRUS} surface pair using standard RPM [11]; (ii) nonrigidly register each S_{MR} to an MR prostate template surface $S_{\text{MR}}^{\text{template}}$ with standard RPM using a free-form deformation (FFD) [12] with 10.0mm control point spacing; (iii) nonrigidly register each patient's MR and TRUS surface pair, aligned within common reference space, using RPM with 10.0mm FFD control point spacing to capture the deformation due to the procedure, denoting the estimated transformations $T_{\text{TRUS} \rightsquigarrow \text{MR}}$ ($i \rightsquigarrow j$ indicates nonrigid transformation from space i to j); and (iv) construct the SDM using a principal component analysis (PCA) of the deformations. For this procedure, the template MR prostate surface is a single subject's prostate surface (not included in the training set). To remove some of the bias introduced by using a single subject template in step (ii), we warp this surface by the inverse of the mean transformations of the MR training surfaces to the template, and then repeat step (ii) using the bias-corrected template as the reference surface.

The N transformations $T_{\text{TRUS} \rightsquigarrow \text{MR}}$ yield a training set of deformations, which are realizations of the distribution of deformations $\mathcal{D}$ between the pre-procedure MRI and intra-procedure TRUS imaging *as a result of the procedure*. We approximate the distribution of deformations $\mathcal{D}$ using PCA of the FFD transformation model [13], where the PCA estimates the eigenvectors of $\mathcal{D}$'s covariance matrix. The eigenvectors $\phi_1, \dots, \phi_J$ are the J principal modes of intra-patient deformation due to the procedure. Figure 2 illustrates some example deformations generated by our SDM.

2.2. Nonrigid Point-based SDM Registration

Given a previously unseen pre-procedure MRI and intra-procedure TRUS image pair for a new patient, we use the learned SDM to drive the nonrigid registration of the segmented prostate S_{TRUS} to the segmented pre-procedure prostate S_{MR} . We must first transform the images into the SDM's reference space as done in Section 2.1 by (i) rigidly registering S_{TRUS} to S_{MR} using linear RPM, denoting this transformation $T_{\text{TRUS} \rightarrow \text{MR}}$ ($i \rightarrow j$ indicates rigid transformation from space i to j), and (ii) nonrigidly registering S_{MR} to the reference template S_{MR} using standard RPM [11]. We transform the two surfaces into SDM space such that $S'_{\text{MR}} = S_{\text{MR}} \circ T_{\text{MR} \rightsquigarrow \text{MR}}$ and $S'_{\text{TRUS}} = S_{\text{TRUS}} \circ T_{\text{TRUS} \rightarrow \text{MR}} \circ T_{\text{MR} \rightsquigarrow \text{MR}}$, where $\circ$ is the transformation operator.

With the surfaces now transformed to the SDM reference space, our proposed method nonrigidly registers S'_{TRUS} to S'_{MR} by constraining the nonrigid RPM registration framework to deform according to the SDM. Rather than estimate a FFD deformation by optimizing the control point locations, the SDM's weights λ offer a low-dimensional parameterization of a dense FFD nonrigid transformation T_{SDM} . We estimate this transformation

$T_{\text{SDM}} = \sum_{j=1}^J \lambda_j \phi_j$, where ϕ_j are the eigenvectors of the training deformation covariance matrix and J is the number of degrees of freedom, by iteratively estimating the point correspondences and transformation within the RPM annealing framework described by Papademetris *et al.* [11]. Our proposed SDM RPM method minimizes the cost function at each iteration k

$$T_{\text{SDM}}^k = \underset{\lambda \in \Lambda}{\operatorname{argmin}} \sum_i w_i \|T_{\text{SDM}}(X_i) - V_i\|^2, \quad (1)$$

where $X_i \in S'_{\text{MR}}$ and V_i are the estimated point correspondences from points $Y_i \in S'_{\text{TRUS}}$ and w_i is the confidence of the correspondence determined by RPM estimate of point i 's "outlierness". We bound the SDM transformation to have weights within 3 standard deviations of the mean value, *i.e.* $|\lambda_j| \leq 3 \sqrt{\varepsilon_j}$ where ε_j is the eigenvalue corresponding to the j -th eigenvector.

3. RESULTS AND DISCUSSION

We tested the performance of our proposed registration method using MR-TRUS datasets from 9 patients not included in our SDM's training set. The segmented prostate surfaces S_{MR} and S_{TRUS} (median number of surface points was 601 for both surfaces) came from the same clinical prostate guidance system as our training data. For each patient, we first transformed each surface into SDM reference space to create surfaces S'_{MR} and S'_{TRUS} and then performed nonrigid surface registration using our SDM as described in Section 2.2. We repeated our nonrigid registration method using different numbers of modes of variation $J = 1, 2, 3, 4, 5, 10, 20, 30$. We compared our registration approach to standard affine, and nonrigid RPM methods.

Segmentation of TRUS images during the biopsy procedure will contain errors. The current clinical procedure performed by urologists at our institution involves manually selecting a small number of landmarks followed by automatic contour estimation [14]. These contours can “leak” in places of low contrast, which is common in TRUS. To test our method’s performance with respect to inaccurate segmentations, we synthetically perturbed S'_{TRUS} to simulate errors. For surface points $\mathbf{u}, \mathbf{v} \in S'_{\text{TRUS}}$, we select a random seed point $\mathbf{u}$ and moved the surface points along their surface normal to the new location $\mathbf{v}' = \mathbf{v} + \alpha \mathbf{n}_{\mathbf{v}} \exp \{-\|\mathbf{u} - \mathbf{v}\|^2 / 2\sigma^2\}$ where $\mathbf{n}_{\mathbf{v}}$ is the normal for point $\mathbf{v}$, α defines the perturbation magnitude and σ the smoothness of the perturbation. We generated perturbed surfaces with parameters $\alpha = \pm 7.5\text{mm}$ and large kernel widths $\sigma = 10.0, 15.0\text{mm}$ to mimic a smoothly varying segmentation error (36 total perturbed surfaces). Values of $\sigma < 10.0\text{mm}$ had little impact on registration performance as standard RPM is robust to acute perturbations. These perturbations are random and do not correspond to any observed features in the image data. We registered each patient’s S'_{MR} with these perturbed surfaces S^P_{TRUS} . Figure 3 shows an example registration to a perturbed surface using both standard nonrigid RPM and our proposed method.

With the assumption that the testing segmentations were correct, we evaluated algorithm registration performance by computing the Dice overlap of registered surface $S'_{\text{MR}} \circ T$, where T is the estimated transformation to S^P_{TRUS} , and the original S'_{TRUS} . Evaluating registration in this manner, we measured how much the perturbation adversely affected registration performance with respect to unperturbed data. Figure 4 shows the results using box and whisker plots. Our proposed method using $J = 20, 30$ eigenvectors performed significantly better than standard nonrigid RPM (paired t-test, $p = 0.05$). Our method was also less variable, having standard deviations of 4.50 and 4.54 for $J = 20$ and 30, respectively, compared to standard nonrigid RPM’s 5.46. Standard nonrigid RPM, with a FFD transformation model having 630 degrees of freedom, is too flexible and can accommodate noisy perturbations of the surface that would otherwise be physically implausible. On the other hand, using the low-dimensional SDM, with $J = 30$ degrees of freedom, to constrain the transformation adds robustness to the registration procedure because the surface is constrained to deform according to the learned model of intra-procedure deformations.

The registration algorithm running times (mean $\pm$ standard deviation, in seconds) were 11.8 ± 2.3 for standard nonrigid RPM, 10.3 ± 2.3 for SDM RPM 20, and 14.8 ± 2.5 for SDM RPM 30 on an Intel® Xeon® Processor X5690.

4. CONCLUSION

If the MR-TRUS prostate segmentations were perfect, then standard nonrigid RPM would be sufficient for surface registration; however, prostate segmentation is the subject of ongoing research and current state-of-the-art segmentations methods remain prone to errors and variability. Our proposed point-based surface registration method is robust to segmentation errors, and the low-dimensionality deformations captured by the SDM

effectively constrain the prostate registrations to mimic observed procedure-induced deformations. Because our training data originated from a clinical system that potentially contains segmentation errors, we anticipate that additional manual-correction of these segmentations and training on these corrected surfaces will further improve our algorithm's performance. Our use of Dice overlap to evaluate registration performance is likely not sufficient. In the future, we aim to quantify target registration error of expertly identified landmarks that are visible in both MR and TRUS images to get a better sense of target biopsy localization accuracy.

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Fig. 1.

Construction of a prostate statistical deformation model that captures the principal directions of prostate deformation between its pre-procedural and intra-procedural shapes in MRI and TRUS images, respectively.

Fig. 2.

Visualizing example nonrigid deformations of the prostate as a result of the TRUS biopsy procedure according to our statistical deformation model. The middle shape represents a patient's prostate deformed by the mean deformation, while $\pm\phi_1$ show deformations along the first principal mode (eigenvector) of deformation (ϕ_2 for the second mode). This model, learned from a population of actual deformations, captures gross variations in prostate deformation.

Fig. 3.

Example MR-TRUS prostate registration. (a) The patient's original TRUS prostate surface segmentation (blue) with an overlay of a synthetically perturbed version of the same surface (gray) that mimics segmentation errors. (b) The patient's MR prostate surface segmentation (orange) surface rigidly registered to the perturbed TRUS surface. Registration of the MR and TRUS surfaces using (c) standard nonrigid RPM and (d) our proposed statistical deformation model (SDM) RPM. The arrows highlight where the unconstrained RPM method incorrectly accommodates the perturbed surface, while the proposed SDM RPM method constrains the surface deformation in a more realistic manner.

Fig. 4.

Box and whisker plots showing MR-TRUS surface registration results evaluated by Dice overlap. These results represent registration of the 36 perturbed surfaces. We compared our proposed statistical deformation model (SDM) RPM with standard affine and nonrigid RPM point-based registration. SDM RPM J indicates using our proposed method with the first J modes of variation (eigenvectors). SDM RPM 20,30 performed significantly better than standard nonrigid RPM (paired t-test, $p = 0.05$).