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PROBABILISTIC NON-RIGID REGISTRATION OF PROSTATE IMAGES: MODELING AND QUANTIFYING UNCERTAINTY

Petter Risholm, Andriy Fedorov, Jennifer Pursley, Kemal Tuncali, Robert Cormack, and William M. Wells

Brigham and Women's Hospital, Harvard Medical School, Boston, USA

Abstract

Registration of pre- to intra-procedural prostate images needs to handle the large changes in position and shape of the prostate caused by varying rectal filling and patient positioning. We describe a probabilistic method for non-rigid registration of prostate images which can quantify the most probable deformation as well as the uncertainty of the estimated deformation. The method is based on a biomechanical Finite Element model which treats the prostate as an elastic material. We use a Markov Chain Monte Carlo sampler to draw deformation configurations from the posterior distribution. In practice, we simultaneously estimate the boundary conditions (surface displacements) and the internal deformations of our biomechanical model. The proposed method was validated on a clinical MRI dataset with registration results comparable to previously published methods, but with the added benefit of also providing uncertainty estimates which may be important to take into account during prostate biopsy and brachytherapy procedures.

Index Terms

prostate; registration; uncertainty; elastic

1. INTRODUCTION

Prostate cancer is the second leading cause of death from cancer in American men. Prostate Specific Antigen (PSA) is the biomarker most commonly used for detecting prostate cancer. Unfortunately, detection of cancer based on rising PSA levels has low specificity. Therefore, reliable diagnosis can only be done based on histological analysis of a prostate biopsy sample. Traditionally, sextant prostate cancer biopsy is performed under ultrasound (US) guidance. Recently, targeted approaches that use Magnetic Resonance Imaging (MRI) guided biopsy for improved sampling precision have been explored [1, 2]. One treatment option for prostate cancer patients is brachytherapy which utilizes radioactive seeds distributed over the prostate gland (PG) to kill cancer cells. A critical aspect in brachytherapy planning is how to achieve a highly accurate radiation delivery for localized prostate cancer while minimizing the radiation exposure of the neighboring critical areas (e.g., urethra and rectum). Planning of both biopsy and brachytherapy is performed using pre-procedural (diagnostic) MR images acquired using an endorectal coil, which enables superior contrast and spatial resolution. To simplify the procedure logistics, endorectal coils are usually avoided during intra-procedure imaging. Because of different rectal filling and patient positioning in pre- and intra-procedure imaging, there is significant change in shape and position of the PG [3]. With a registration algorithm we can deform the pre-procedural image to align with the intra-procedural anatomy and thereby increase the intra-procedure information content.

Several registration methods have successfully been applied to the registration of prostate images. Venugopal et al. [4] used a thin-plate spline method to estimate a deformation given homologous landmark points in the two prostate images. Intensity based methods aim at maximizing a similarity criterion based on comparing the image intensities. Mutual Information is a popular similarity criterion and has been reported to be effective for registering prostate images [5]. Bharatha et al. [6] used an elastic Finite Element (FE) model to align pre- with intra-procedural images of the prostate and showed a significant increase in overlap between the registered pre- and intra-procedural prostate compared to using a rigid transformation. Oguro et al. evaluated the use of B-spline registration with mutual information [7].

We proposed in [8, 9] a probabilistic non-rigid framework for registration of brain images which uses a Markov Chain Monte Carlo sampler to characterize the posterior distribution over deformations. In this work we adapt our probabilistic registration framework to registration of pre- and intra-procedural prostate images collected during an MR-guided prostate biopsy procedure. The method is not restricted to a specific imaging modality, but requires as input contours of the PG in both the pre- and intra-procedural images. It models the prostate tissue as an elastic material and jointly estimates the boundary conditions (surface deformations) and the volumetric deformations under the elastic constraint. The main contributions of the method is 1) that uncertainties in labeling of PG can be included in the estimation process and 2) that we characterize the full posterior distribution from which we can extract the most probable deformation as well as the registration uncertainty.

2. METHODS

2.1. Probabilistic Registration

Our aim is to align an image I_t of the prostate acquired before the procedure with an image I_r acquired during the procedure. We require a corresponding labelmap L_t of the pre-procedural image where the prostate is labeled in terms of the peripheral zone Ω^{pz} and central gland Ω^{cg} , and a labelmap L_r corresponding to I_r where only the prostate gland Ω^{pg} is labeled. Both in brachy- and radio-therapy, pre- and intra-procedural prostate images are routinely contoured to define treatment and critical areas. Thus, relying on contoured images does not change the clinical workflow to a large degree. We model the prostate as an elastic material and aim to match $\partial\Omega_t^{pg}$, the boundary of the prostate in the pre-procedural image, with $\partial\Omega_r^{pg}$. In contrast to Bharatha et al. [6] where they first estimate the boundary conditions followed by an estimation of the internal deformation based on an elastic model, we will jointly estimate the boundary conditions as well as the internal deformation under the elastic constraint.

From L_t we create a tetrahedral Finite Element (FE) mesh $\mathbf{m}$ which conforms to the area defined by Ω_t^{pg} such that nodes on the boundary of the FE mesh, $\mathbf{n}_b = [\mathbf{n}_{b,1}, \dots, \mathbf{n}_{b,N}]$, are located on the prostate boundary, $\partial\Omega_t^{pg}$. Internal mesh nodes $\mathbf{n}_i = [\mathbf{n}_{i,1}, \dots, \mathbf{n}_{i,M}]$ are distributed over Ω_t^{pg} . We also create a distance map $D(\mathbf{x}) = \text{dist}(\mathbf{x}, \partial\Omega_r^{pg})$ which defines the distance between a point and the prostate boundary in the intra-procedural image.

Our aim is to find an elastic deformation $\mathbf{u} = [\mathbf{u}_{b,1}, \dots, \mathbf{u}_{b,N}, \mathbf{u}_{i,1}, \dots, \mathbf{u}_{i,M}]$ of the mesh so that boundary nodes align with $\partial\Omega_r^{pg}$. We formulate the registration problem in a probabilistic framework where the posterior distribution over the deformation of the boundary nodes is defined as follows:

$$\Pr(\mathbf{u}_b | \mathbf{m}; D) \propto \Pr(\mathbf{m} | \mathbf{u}_b; D) \Pr(\mathbf{u}_b; \mathbf{m}) \quad (1)$$

The likelihood is defined as a force which attracts the boundary nodes of the mesh to $\partial\Omega_t^{pg}$:

$$\Pr(\mathbf{m} | \mathbf{u}_b; D) = \prod_{j=1}^N \mathcal{N}(D(\mathbf{n}_{b,j} + \mathbf{u}_{b,j}), 0, \sigma^2), \quad (2)$$

where $\mathcal{N}$ is a zero mean normal distribution with a variance of σ^2 which models how confident we are in the segmentations.

The prior restricts the deformation of the mesh to conform to an elastic material:

$$\Pr(\mathbf{u}_b; \mathbf{m}) = \frac{1}{Z} e^{-\frac{E(\mathbf{u}_b, \mathbf{m})}{T}}, \quad (3)$$

where $E(\mathbf{u}_b, \mathbf{m})$ solves for the elastic movements of $\mathbf{u}_i$ given the boundary conditions $\mathbf{u}_b$ and returns the elastic energy. The energy is converted to a probability by way of the Boltzmann distribution modeled with temperature T .

2.2. Sampling the Posterior Distribution

Because of large voxel sizes and time restrictions during the labeling process, there might be a considerable uncertainty in the prostate segmentation (labeling) which can be reflected in the registration results. Conventional registration methods are not capable of modeling the uncertainty of the labels (Ω^{pz} , Ω^{cg}) while conventional optimization methods are not capable of quantifying the registration uncertainty. We model the label uncertainty with the variance of the likelihood and propose to fully characterize the posterior distribution over deformations by generating samples from the posterior with a Markov Chain Monte Carlo (MCMC) (Metropolis-Hastings) method. The MCMC method constructs a Markov chain that asymptotically has the posterior distribution as its equilibrium distribution. In practice, we start with an initial estimate of the deformation, $\mathbf{u}_b^0$, and generate candidate samples from a Gaussian proposal distribution centered on the previous sample $\widehat{\mathbf{u}}_b \sim \mathcal{N}(\mathbf{u}_b^t, \sigma_*^2)$. Candidate

samples are accepted with probability $A(\widehat{\mathbf{u}}_b, \mathbf{u}_b^t) = \min(1, \frac{\Pr(\widehat{\mathbf{u}}_b | \mathbf{m})}{\Pr(\mathbf{u}_b^t | \mathbf{m})})$. If a sample is accepted we set $\mathbf{u}_b^{t+1} = \widehat{\mathbf{u}}_b$, otherwise $\mathbf{u}_b^{t+1} = \mathbf{u}_b^t$.

2.3. Summarizing the Posterior Distribution

After running the MCMC simulation, the resulting set of deformation samples $\mathbf{u}^0, \dots, \mathbf{u}^{\mathcal{T}}$ define the posterior distribution over deformations. The mode of the distribution defines the most probable deformation while the dispersion of the distribution can be used as a measure of the registration uncertainty [8]. In this paper we describe two ways of summarizing the uncertainty: 1) The inter quartile range (IQR) measures the dispersion (uncertainty) of a distribution. We use it to summarize the marginal posterior distributions over each node. The FE machinery can be used to interpolate the uncertainty at inter-nodal positions. 2) Assume we have defined points in the pre-procedural image where we plan to place a radioactive seed or a biopsy needle. By transforming this point with each of the sampled deformations $\mathbf{u}^0, \dots, \mathbf{u}^{\mathcal{T}}$, we can build a marginal distribution of the position of the transformed point in the intra-procedural image. Both of these uncertainty summaries are shown in Fig. 2.

3. RESULTS

3.1. Data

We validated the method on the dataset depicted in Fig. 1. The pre-procedural image is a 3T FRFSE T2MR image while the intra-procedural image is a 3T TSE T2 MR image. The spatial resolution of the pre- and intra-procedural images are $0.31 \times 0.31 \times 3.0$ mm and $0.44 \times 0.44 \times 3.0$ mm respectively. A clinician contoured the central gland (CG) and the peripheral zone (PZ) in both images. The labelmaps were rigidly registered to establish an approximate initial alignment of the datasets. We note that the objective of this research is to develop registration technology to support both MR-guided biopsy and brachytherapy procedures. However, because of lack of data from brachytherapy procedures, this paper only evaluates the method on images collected during an MR-guided biopsy procedure.

3.2. Experiments

We generated a FE mesh with 944 nodes, 2148 surface triangles and 3887 elements where the elements conform to the CG and PZ. To our knowledge, exact values for the elastic parameters of prostate tissue has not been established. We used values from Bharatha et al. [6] and modeled the CG with a higher (stiffer) Young's modulus E , but lower (more compressible) Poisson's ratio ν , than PZ (CG: $E = 30\text{kPa}$, $\nu = 0.2$; PZ: $E = 3\text{kPa}$, $\nu = 0.4$). The variance of the likelihood was set to $\sigma^2 = 0.2$, while the temperature of the Boltzmann equation was determined experimentally and set to $T = 6000$. With a variance of $\sigma_*^2 = 0.01$ for the sampling kernel, we generated $\mathcal{T} = 10^5$ samples from the posterior and computed the mode as well as the uncertainty (IQR) of the marginal distributions. Our sampler generated approximately 5 samples per second, thus the total computation time was approximately 6 hours. Qualitative results can be seen in Fig. 2. Quantitative results from the registration are included in Tbl. 2. We also computed the Dice Similarity Coefficient (DSC) between the different labels before and after registration and summarize the results in Tbl. 1.

4. CONCLUSION

This paper introduced a probabilistic framework for registration of pre- to intra-procedural images of the prostate. The framework estimates an elastic deformation which matches a pre-procedural segmentation of the prostate with a corresponding intra-procedural segmentation of the same prostate. The probabilistic approach allowed us to include the uncertainty of the prostate segmentation in the likelihood model. We used clinical MR images from a prostate biopsy procedure to validate the method and showed that the registration accuracy is comparable to other published methods in terms of the DSC of registered labels (PZ, CG and PG). From the posterior distribution we can extract the mode (most probable deformation) and the corresponding uncertainty. Registration uncertainty can be valuable information to portray to a surgeon/interventionist, especially when important clinical decisions are based on the registered data.

Several studies have shown that the clinical outcome in prostate brachytherapy correlates with the dose coverage parameters, in particular the dose delivered to 90% of the prostate volume (D_{90}) and the percentage of the target volume receiving 100% of the prescribed dose (V_{100}) [10]. The registration uncertainty may be used to estimate the likely variation in the dose coverage parameters, allowing for better judgment of the clinical dose coverage and possible outcome.

In biopsy procedures, target points are defined in the pre-procedural image and transformed into the intra-procedural image space to guide the surgeon during the procedure. It is important to understand that there is an uncertainty associated with the estimated

transformation and consequently the transformed points. In this paper we have shown how to summarize this uncertainty in terms of the IQR and marginal posterior distributions. Being able to quantify the registration uncertainty comes at a high computational cost. With approximately 6 hours of running time, the method does not currently lend itself to intra-procedural use. We anticipate that with better modeling, parallelization and faster computers it should be possible to approach intra-procedural running times in the future.

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(a) Pre-procedural MRI (I_t) (b) Intra-procedural MRI (I_r) (c) Pre-procedural labels (L_t) (e) FE-mesh ($\mathbf{m}$).**Fig. 1.**

(a) High resolution 3T MRI of the prostate before treatment. (b) 3T MRI of the prostate during treatment. (c) Labelmap of the pre-procedural prostate. The bright label denotes the PZ while the dark label denotes the CG. (e) Rendering of the FE-mesh used in the experiments. Red elements correspond to the CG while green elements correspond to PZ.

(a) Marginal point distribution

(b) IQR

(c) CG difference

(d) PZ difference

Fig. 2.

(a) Assume we have defined the position where we want to insert a radioactive seed, or biopsy needle, in the pre-procedural image. Conventional registration methods can only show the most probable position after registration. Here we visualize the marginal distribution of a point in the PZ deformed to the intra-procedural space overlaid on the intra-procedural image. Notice the considerable spread of the distribution which indicates a large uncertainty. (b) A plot of the sum of the IQR for each dimension (x, y, z) of the marginal posterior distributions over deformations. The brightest point has an IQR of 3.0 mm. (c) Difference between the deformed CG label and the intra-procedural CG. (d) Difference between the deformed PZ label and the intra-procedural PZ.

Table 1

Registration results in terms of the Dice Similarity Coefficient (DSC) between different segmented regions after rigid and non-rigid registration. A value of 0 indicates no overlap; a value of 1 indicates a perfect agreement. Using a different dataset, Bharatha[6] reported DSC values of 0.94, 0.86 and 0.76 for PG, CG and PZ respectively.

Label	Rigid	Non-Rigid
PG	0.79	0.93
CG	0.79	0.87
PZ	0.63	0.81

Table 2

Registration results in terms of the distance between the deformed boundary nodes ($\mathbf{n}_b + \mathbf{u}_b$) and $\partial\Omega_r^{Pg}$.

Percentiles	Distance (mm)
100th (max)	1.40
95th	1.01
85th	0.83
50th (median)	0.56