Concurrent segmentation of the prostate on MRI and CT via linked statistical shape models for radiotherapy planning

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Purpose: Prostate gland segmentation is a critical step in prostate radiotherapy planning, where dose plans are typically formulated on CT. Pretreatment MRI is now beginning to be acquired at several medical centers. Delineation of the prostate on MRI is acknowledged as being significantly simpler to perform, compared to delineation on CT. In this work, the authors present a novel framework for building a linked statistical shape model (LSSM), a statistical shape model (SSM) that links the shape variation of a structure of interest (SOI) across multiple imaging modalities. This framework is particularly relevant in scenarios where accurate boundary delineations of the SOI on one of the modalities may not be readily available, or difficult to obtain, for training a SSM. In this work the authors apply the LSSM in the context of multimodal prostate segmentation for radiotherapy planning, where the prostate is concurrently segmented on MRI and CT.

Methods: The framework comprises a number of logically connected steps. The first step utilizes multimodal registration of MRI and CT to map 2D boundary delineations of the prostate from MRI onto corresponding CT images, for a set of training studies. Hence, the scheme obviates the need for expert delineations of the gland on CT for explicitly constructing a SSM for prostate segmentation on CT. The delineations of the prostate gland on MRI and CT allows for 3D reconstruction of the prostate shape which facilitates the building of the LSSM. In order to perform concurrent prostate MRI and CT segmentation using the LSSM, the authors employ a region-based level set approach where the authors deform the evolving prostate boundary to simultaneously fit to MRI and CT images in which voxels are classified to be either part of the prostate or outside the prostate. The classification is facilitated by using a combination of MRI-CT probabilistic spatial atlases and a random forest classifier, driven by gradient and Haar features.

Results: The authors acquire a total of 20 MRI-CT patient studies and use the leave-one-out strategy to train and evaluate four different LSSMs. First, a fusion-based LSSM (fLSSM) is built using expert ground truth delineations of the prostate on MRI alone, where the ground truth for the gland on CT is obtained via coregistration of the corresponding MRI and CT slices. The authors compare the fLSSM against another LSSM (xLSSM), where expert delineations of the gland on both MRI and CT are employed in the model building; xLSSM representing the idealized LSSM. The authors also compare the fLSSM against an exclusive CT-based SSM (ctSSM), built from expert delineations of the gland on CT alone. In addition, two LSSMs trained using trainee delineations (tLSSM) on CT are compared with the fLSSM. The results indicate that the xLSSM, tLSSMs, and the fLSSM perform equivalently, all of them out-performing the ctSSM.

Conclusions: The fLSSM provides an accurate alternative to SSMs that require careful expert delineations of the SOI that may be difficult or laborious to obtain. Additionally, the fLSSM has the added benefit of providing concurrent segmentations of the SOI on multiple imaging modalities.

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Key words: MRI, CT, segmentation, statistical shape model, prostate radiotherapy

I. INTRODUCTION

During prostate radiotherapy planning, the prostate gland needs to be delineated on CT.¹ Dose planning is done by calculating the attenuation of radiation by the tissue, and only CT images provide the electron density data that are required for this calculation.¹ Localizing the radiation to the prostate alone, with higher accuracy, can lead to more effective dose planning, thereby reducing radiation toxicity to the rectum and bladder.^{2,3} Currently, the clinical standard for targeting the prostate is to manually delineate the prostate gland on CT. CT has poor soft tissue contrast which causes the boundary between the prostate and surrounding organs to often be nearly indistinguishable [Figs. 1(c) and (d)]. In comparison, the corresponding gland boundary on *in vivo* MRI [Fig. 1(a)] is far more distinguishable from the surrounding tissue. The lack of radiological difference between adjacent tissues⁴ leads to intensity homogeneity on the pelvic CT images. Studies have shown that the prostate volume is largely overestimated on CT.⁵ Gao *et al.*⁶ reported that physicians are generally concerned with unintentional inclusion of rectal tissue when delineating prostate boundary on CT, hence they tend to miss delineating parts of the prostate that are close to the rectal boundary. Physicians are also likely to overextend the anterior boundary of the prostate to encompass bladder tissue.⁶ Further, manual segmentation of the prostate on CT is not only tedious but is also prone to high interobserver variability,⁷ with inaccuracies close to the bladder and rectum. On the other hand, MRI provides better resolution,⁸ better contrast of soft tissue,⁹ and better target delineation,^{5,9} compared to CT. By registering MR images to their corresponding CT images, it is possible to transfer the prostate boundary delineation from MRI to CT, thereby obviating the need for delineating the gland boundary on CT. Consequently, it would be useful if a segmentation algorithm could leverage MRI-CT fusion (i.e., MRI-CT registration) to map the prostate boundary from MRI onto CT and use this information to segment the prostate on CT. Sannazzari *et al.*¹⁰ reported that using MRI-CT fusion methods to map prostate delineations from MRI to CT made it possible to spare approximately 10% of the rectal volume in the radiation field and approximately 5% of bladder and femoral head volumes, compared to a purely CT-based segmentation. In Ref. 10, a rigid registration scheme was employed, involving alignment of anatomical fiducial markers. The superposition of

the fiducial markers was reported to be within 1.5 mm of each other.

Several methods have been proposed to segment the prostate on CT imagery.^{11–18} One method is to use statistical shape models (SSM). The most popular SSM for shape segmentation is the classical active shape model (ASM),¹⁹ which uses principal component analysis (PCA) to model the variation across several presegmented training shapes represented as points. Variants of the ASM (Refs. 12–14 and 18) have been used on prostate CT for segmentation, primarily to constrain shape evolution. Rousson *et al.*¹⁴ presented a coupled segmentation framework for both the prostate and bladder on CT imagery. A Bayesian inference framework was defined to impose shape constraints on the prostate using an ASM. Feng *et al.*¹² employed the ASM to model both inter and inpatient shape variation in the prostate in order to segment it on CT imagery. Over 300 training studies were employed to construct the shape model. Chen *et al.*¹³ constructed an ASM in conjunction with patient-specific anatomical constraints to segment the prostate on CT, using 178 training studies.

On account of the aforementioned difficulties in delineating the gland boundary on CT, constructing a prostate SSM on CT is particularly challenging compared to building it on MRI. While Feng *et al.*¹² and Chen *et al.*¹³ employed hundreds of training instances for constructing their SSM, manual delineation of the gland on CT is a laborious, exhaustive, and error prone task, one subject to high interobserver variability. In addition, since Feng *et al.*¹² included inpatient variation in their shape model, manual delineation of the prostate on the initial planning CT for each patient had to be obtained as well. Potential inaccuracies in expert manual delineations were not discussed and interobserver variability experiments were not conducted either.^{12,13}

ASMs have also been used to segment the prostate on MRI.^{20–25} Toth *et al.*²⁰ evolved an ASM driven by a MR spectroscopy based initialization scheme to segment the prostate on T2-weighted MRI. Martin *et al.*²¹ utilized a combination of a probabilistic atlas and an ASM to segment the prostate on MRI. Although the methods mentioned above represent shapes discretely using landmark points, the level set framework for representing shapes has been gaining popularity, especially for the problem of representing multiple shapes.^{14,23,26,27} The advantage of using level sets is that they provide an accurate continuous shape representation and allow for implicit handling of topology.²³ Tsai *et al.*²³ constructed a coupled ASM from

FIG. 1. (a) MR image with prostate gland boundary delineated in 2D. (b) 3D rendering of the prostate shape as seen on MRI. (c) 2D CT image of the prostate, and (d) 2D CT image with delineation of the prostate gland overlaid. (e) 3D rendering of the prostate as seen on CT.

level sets to segment multiple structures from pelvic MR images. To optimize the segmentation boundary, they used a mutual information (MI) based cost functional that takes into account region-based intensity statistics of the training images. Tsai *et al.*²³ coupled the shape variation between adjacent organs on the same modality to allow for simultaneous segmentation of multiple structures of interest (SOI) on a MRI.

Van Assen *et al.*²⁸ proposed to train a SSM on MRI that would then be directly employed for prostate segmentation on CT imagery. Such an approach, however, may not be able to deal with the significant nonlinear deformations that may occur due to the use of an endorectal coil during prostate MRI acquisition. Figure 1 illustrates this difference in prostate shape by comparing 2D slices as well as the 3D shapes of the prostate as seen on the CT and MRI modalities, respectively. Notice that the shape of the prostate on MRI [Figs. 1(a) and 1(b)] are different compared to the corresponding CT views [Figs. 1(d) and 1(e)]. One of the key motivations of this work is to build a SSM that would allow for a segmentation which is capable of handling of extreme deformations on the CT.

Several registration methods have been presented previously to facilitate segmentation of structures on CT via MRI. These methods include using implanted fiducials to aid a rigid registration method⁸ and using the iterative closest points (ICP) algorithm on presegmented MRI and CT fiducials.²⁹ Most of these 2D registration schemes are typically challenged in their ability to account for the nonlinear differences in prostate shape between MRI and CT; motivating the need for an elastic registration scheme. More recently, Chappelow *et al.*³⁰ presented a multimodal 2D registration scheme for MRI and CT that uses a combination of affine and elastic registration. The MRI-CT registration method³⁰ requires intermediate steps such as determining MRI-CT slice correspondences and manually placing control points on MRI and CT (although it would still be faster, easier and possibly more accurate than manually delineating the prostate on CT). However, we can avoid this problem by leveraging 2D MRI-CT registration to map delineations of the prostate on MRI onto CT, reconstructing the delineations into 3D shapes, and then defining an implicit multimodal shape correlation within a SSM. Every shape generated by the SSM on the MRI will then have a corresponding shape generated on the CT. This would only require 2D MRI-CT registration to be performed once on the corresponding MRI-CT data used to train the SSM. The prostate segmentation on CT could then be determined in 3D without additional time-consuming steps and, more importantly, without having to rely on manual delineations of the gland on CT.

In this work, we present a framework for multimodal segmentation of a SOI, concurrently on MRI and CT (A preliminary version of this work appeared in Ref. 31). The framework involves construction and application of a linked SSM (LSSM), which we define as a SSM that incorporates shape information from multiple imaging modalities to link the SOI's shape variation across the different modalities. We extend the Tsai method²³ to allow SSMs to link shape variations of a sin-

gle SOI across multiple imaging modalities, thus allowing concurrent segmentation of the SOI on the different modalities.

For applications such as prostate radiotherapy planning, the LSSM can be used to find prostate boundaries on a patient's CT by concurrently leveraging corresponding MRI data. In its construction, the LSSM employs the previously mentioned MRI-CT registration method³⁰ to map prostate boundary delineations on MRI onto the corresponding CT image. The LSSM is thus trained using corresponding prostate shape data from both MRI (expert prostate delineations) and CT (delineations mapped onto CT from MRI using MRI-CT registration) which are stacked together when determining the shape variation by employing PCA. Hence, image registration (from MRI to CT) is employed as a conduit to SSM-based segmentation of the prostate on CT.

To the best of our knowledge, our work is the first time that a multimodal SSM has been built for concurrent segmentation on MRI and CT. The closest related work on multimodal SOI segmentation was done by Naqa *et al.*³² Their work applied deformable active contours (AC) for concurrent segmentation of a SOI on 2D MRI, CT, and PET images. The multimodal images are first registered using an MI-based rigid registration algorithm followed by manually delineating a coarse initialization for the AC model.

The rest of the paper is organized as follows. In Sec. II, we give a brief overview of our methodology followed by an in-depth description of LSSM construction in Sec. III. Section IV then describes the application of the LSSM for concurrent segmentation of the prostate on MRI and CT. In Sec. V, we describe the experimental design, followed by the results and discussion in Secs. VI and VII, respectively. In Sec. VIII, we present our concluding remarks and future directions.

II. BRIEF SYSTEM OVERVIEW AND DATA DESCRIPTION

II.A. Notation

We define I to be a two-dimensional image where $I \in \mathcal{I}$, the three-dimensional volumetric image. Let $I = (C, f)$, where C is a finite 2D rectangular grid of pixels with intensity $f(c)$ where $c \in C$ and $f(c) \in \mathbb{R}$. Let the volumetric counterpart $\mathcal{I} = (\mathcal{C}, f)$, where $\mathcal{C}$ is a finite 3D grid of voxels with intensity $f(h)$ where $h \in \mathcal{C}$ and $f(h) \in \mathbb{R}$. We also define a label at h as $\mathcal{L}(h) \in \{0, 1\}$ such that $\mathcal{L}(h) = 1$ if the voxel belongs to the foreground and $\mathcal{L}(h) = 0$ if it belongs to the background. Additionally, we define a K -dimensional feature vector $F(h) \in \mathbb{R}^K$. For each patient study, a set of small FOV MRI (diagnostic MRI), large FOV MRI (planning MRI), and CT were acquired. The corresponding 2D slices are denoted as I^d , I^p , and I^{CT} , respectively. These images are defined on independent coordinate grids C^d , C^p , and C^{CT} . $B(I^d)$, $B(I^p)$, and $B(I^{CT})$ refer to the boundary delineations of the prostate on the respective 2D slices. We define S_d as the training set of diagnostic MRI volumes $\mathcal{I}^d$ such that $S_d = \{\mathcal{I}_i^d : i \in \{1, \dots, N\}\}$. We also define S_{CT} as the training set of planning CT volumes $\mathcal{I}^{CT}$ such that $S_{CT} = \{\mathcal{I}_i^{CT} : i \in \{1, \dots, N\}\}$. S_V is denoted as the training set of binary volumes $V \in \Omega$ (the SOI's) such that

TABLE I. Table of commonly used notation.

Symbol	Description	Symbol	Description
$\mathcal{I}$	3D Volumetric image. $\mathcal{I} = (\mathcal{C}, f)$	$\bar{\varphi}$	Mean of φ across N patients on modality j
I	2D Image scene $I = (\mathcal{C}, f)$. $I \in \mathcal{I}$	$\tilde{\varphi}$	Mean-offset function where $\bar{\varphi}$ is subtracted from φ
$\mathcal{C}$	Finite grid of pixels in a 2D image I	$\mathbf{M}$	Matrix of all training data
$\mathcal{C}$	Finite grid of voxels in a 3D image $\mathcal{I}$	γ	Set of eigenvectors defining shape variation in $\mathbf{M}$
c, e	Single pixel in $\mathcal{C}$	λ	Set of eigenvalues corresponding to γ
h	Single voxel in $\mathcal{C}$	w	Shape vector that weights λ to generate a new shape
$f(\cdot)$	Intensity at c, e or h ; $f(\cdot) \in \mathbb{R}$	ϕ	New shape instance.
$F(h)$	K -dimensional feature vector of a voxel h	D	Marginal entropy $D(\cdot)$, joint entropy $D(\cdot, \cdot)$
V	Binary volume	$\mathcal{L}(h)$	Label of $h \in \{0, 1\}$
$T^{\alpha\beta}$	Transformation for mapping from $\mathcal{C}^\alpha$ to $\mathcal{C}^\beta$	$\mathcal{T}$	Subset of voxels $\in \mathcal{I}^d$
φ	Signed distance function of V	$\tilde{I}$	Transformed image $T^{\alpha\beta}(I)$

$S_V = \{V_i^j : i \in \{1, \dots, N\}, j \in \{1, 2\}\}$, where N is the number of patient studies, V_i^1 corresponds to MRI and V_i^2 corresponds to CT. Commonly used notation in this paper is summarized in Table I.

II.B. Data description

Both of the diagnostic and planning MRIs from each patient were 1.5 T, T2-weighted, axial prostate images, acquired using an endorectal coil. A corresponding planning CT was also acquired for each of those patients. The diagnostic MRI provides the best resolution of the prostate with voxel dimensions of $0.5 \times 0.5 \times 4 \text{ mm}^3$. The planning MRI has voxel dimensions of about $0.9 \times 0.9 \times 6 \text{ mm}^3$, which is a similar FOV to the CT where the voxel dimensions are $1 \times 1 \times 1.5 \text{ mm}^3$. The total image dimensions for each imaging modality are shown below in Table II, along with a summary of the data description. Examples of the diagnostic MRI, planning MRI, and CT are shown in Fig. 2.

II.C. Methodological overview

Below, we present a brief overview of our fusion-based LSSM (fLSSM) methodology applied to the problem of simultaneous, concurrent segmentation of the prostate gland on MRI and CT. Figure 3 shows a flowchart which illustrates the three main modules of our framework, briefly described below.

- **Module 1: MRI-CT Registration** The goal of this step is to transfer expert delineated prostate boundaries on diagnostic MRI onto planning CT. As illustrated in panel 1 of Fig. 3, a combination of affine registration between diagnostic MRI and planning MRI, and elastic registration between planning MRI and planning CT is used to register, on a slice-by-slice basis, diagnostic MRI to planning CT. The result after the affine registration of diagnostic to planning MRI is shown via a checkerboard pattern. As can be appreciated, the checkered image shows continuity between the prostate and surrounding structures. The resulting elastic registration of planning MRI to planning CT is shown via an overlay. Note that the overlay shows good contrast of both bone and soft tissue. The transformation parameters obtained from this registration can be used to transfer the expert delineated prostate boundary from diagnostic MRI onto planning CT. Slice correspondences

between diagnostic MRI, planning MRI, and planning CT are determined by an expert.

- **Module 2: Construction of fLSSM** By leveraging the prostate delineations on 2D MRI and CT slices, 3D shapes of the prostate on MRI and CT are then reconstructed. 3D prostate shape on MRI is reconstructed from the 2D expert delineated prostate boundaries, while the 3D prostate shape on CT is reconstructed from the MRI-CT registration mapped prostate delineations on CT. As shown in panel 2 of Fig. 3, the MRI-CT LSSM (fLSSM) is then constructed to link the shape variations between diagnostic MRI and CT via PCA on the combined MRI-CT data.
- **Module 3: Concurrent segmentation of prostate on MRI and CT via fLSSM** As illustrated in panel 3 of Fig. 3, different kinds of features are extracted from each of the MRI and CT images, in order to train a random forest³³ classifier. The classifier is used in conjunction with a probabilistic spatial atlas of the prostate on MRI and CT to coarsely localize the prostate. Our fLSSM is then concurrently fit to the coarse prostate segmentations on MRI and CT to produce the final prostate segmentations.

III. CONSTRUCTION OF FLSSM

III.A. Error analysis and motivation for fLSSM

The analysis below illustrates the sources of errors associated with the fLSSM and a CT-based SSM.

- We define as $\epsilon^{\delta_{MRI}}$, the error associated with $B(I^d)$ due to errors in delineating the SOI.
- $B(I^{CT})$ will have an error $\epsilon^{\mathcal{F}}$ associated with it due to MRI-CT fusion error.
- The fLSSM $L(MRI, CT)$ will result in some associated error ϵ^L in the final prostate CT segmentation.
- Hence, total possible error for the fLSSM, $\epsilon^{LSSM} = \epsilon^{\delta_{MRI}} + \epsilon^{\mathcal{F}} + \epsilon^L$.

TABLE II. Summary of the prostate image data sets acquired for each of 20 patients considered in this study.

Image slice	Modality	Description	Voxel (mm^3)
I^d	T2-w 1.5 T MRI	Diagnostic MRI	$0.5 \times 0.5 \times 4$
I^p	T2-w 1.5 T MRI	Planning MRI	$0.9 \times 0.9 \times 6$
I^{CT}	CT	Planning CT	$1 \times 1 \times 1.5$

FIG. 2. Examples of (a) small FOV diagnostic MRI, (b) large FOV planning MRI, and (c) planning CT images of the prostate. Note that unlike in Figs. 2(a) and 2(b), the prostate is not discernible on the CT [Fig. 2(c)]. The planning MRI serves as a conduit, by overcoming the differences in FOV between CT and diagnostic MRI, to register the diagnostic MRI with the corresponding planning CT.

In contrast, a purely CT-based SSM (ctSSM) would have the following errors associated with it:

- Delineation error $\epsilon^{\delta_{CT}}$ associated with $B(I^{CT})$.
- The ctSSM will result in some associated error ϵ^{CT} in the final prostate CT segmentation.
- Hence, total error for ctSSM $\epsilon^{ctSSM} = \epsilon^{\delta_{CT}} + \epsilon^{CT}$.

The dominant contribution in ϵ^{LSSM} would arise from $\epsilon^{\mathcal{F}}$ due to the parts of the prostate which are nonlinearly deformed. On the other hand, most of the error from ϵ^{ctSSM} would be due to $\epsilon^{\delta_{CT}}$, since accurate delineation of the prostate gland on CT is very difficult. Assuming that an accurate registration scheme is employed, it is reasonable that $\epsilon^{\mathcal{F}} < \epsilon^{\delta_{CT}}$. Additionally, one can assume that since $\epsilon^{\delta_{MRI}}$ is small (given the high resolution of MRI), that $\epsilon^{\mathcal{F}} + \epsilon^{\delta_{MRI}} < \epsilon^{\delta_{CT}}$. Further assuming that $\epsilon^{\mathcal{L}} \approx \epsilon^{CT}$, since ϵ^{CT} is a function of the training/delineation error $\epsilon^{\delta_{CT}}$, it follows that $\epsilon^{LSSM} \leq \epsilon^{ctSSM}$. This then provides the motivation for employing the fLSSM over the ctSSM for segmentation of the gland on CT. Additionally, note that the fLSSM, unlike the ctSSM, provides for concurrent segmentation of the SOI on both modalities simultaneously.

III.B. Preprocessing of binary images and construction of shape variability matrix

- **Step 1:** For each modality j , align $V_1^j, \dots, V_N^j$ to the common coordinate frame of a template volume V_T^j . This was done using a 3D affine registration with normalized mutual information³⁴ (NMI) being employed as the similarity measure. The template that we used was one of the binary segmentations of the prostate which was visually inspected and identified as a representative prostate shape with a high overlap with other prostate shapes in the dataset.
- **Step 2:** For each aligned volume V_i^j , where $i \in \{1, \dots, N\}$ and $j \in \{1, 2\}$, compute the signed distance function (SDF) to obtain ϕ_i^j . The SDF transforms the volume such that each voxel takes the value, in millimeters (mm), of the minimum distance from the voxel to the closest point on the surface of V_i^j . The values inside and outside the SOI are negative and positive distances, respectively.
- **Step 3:** For each modality j , subtract the mean $\bar{\phi} = \frac{1}{N} \sum_{i=1}^N \phi_i^j$ from each ϕ_i^j , to get a mean-offset function $\tilde{\phi}_i^j$.

- **Step 4:** Create a matrix $\mathbf{M}$ from all the data from $\tilde{\phi}_i^j$. This matrix has i columns such that all the mean-offset data from a single patient are stacked column-wise to create a column in $\mathbf{M}$. In each column i in $\mathbf{M}$, all the data from $\tilde{\phi}_i^2$ would be stacked column-wise underneath the data from $\tilde{\phi}_i^1$, which are also stacked in an identical fashion. Thus

$$\mathbf{M} = \begin{bmatrix} \tilde{\phi}_i^1 \\ \tilde{\phi}_i^2 \end{bmatrix}.$$

III.C. PCA and new shape generation

- **Step 1:** Perform PCA on $\mathbf{M}$ to obtain the magnitude of variation λ , and select q eigenvectors γ that capture 95% of the shape variability.
- **Step 2:** Due to the large size of the matrix, we employ an efficient technique, the method of Turk *et al.*,³⁵ to perform the eigenvalue decomposition step. PCA on $\mathbf{M}$ is done by performing the eigenvalue decomposition on $\frac{1}{N} \mathbf{M} \mathbf{M}^T$, but the eigenvectors and eigenvalues can also be computed from a smaller matrix $\frac{1}{N} \mathbf{M}^T \mathbf{M}$. Thus, if we define the eigenvector obtained from the eigenvalue decomposition of $\frac{1}{N} \mathbf{M}^T \mathbf{M}$ as ℓ , then $\gamma = \mathbf{M} \ell$.
- **Step 3:** The values of γ represent variation in both MRI and CT shape data. The respective eigenvectors from MRI (γ^1) and CT (γ^2) shape data are thus separated from the total set of eigenvectors γ . For additional details on this, we refer the reader to Ref. 23.
- **Step 4:** For each modality j , a new shape instance ϕ^j can now be generated by calculating the linear combination:

$$\phi = \bar{\phi} + \sum_{i=1}^q w_i \gamma_i, \quad (1)$$

where

$$\phi = \begin{bmatrix} \phi^1 \\ \phi^2 \end{bmatrix}, \quad \gamma = \begin{bmatrix} \gamma^1 \\ \gamma^2 \end{bmatrix}, \quad \bar{\phi} = \begin{bmatrix} \bar{\phi}^1 \\ \bar{\phi}^2 \end{bmatrix},$$

and the shape vector w is the weighted standard deviation of the eigenvalues λ such that it has a value ranging $-3\sqrt{\lambda}$ to $+3\sqrt{\lambda}$. Hence

$$\begin{bmatrix} \phi^1 \\ \phi^2 \end{bmatrix} = \begin{bmatrix} \bar{\phi}^1 \\ \bar{\phi}^2 \end{bmatrix} + \sum_{i=1}^q w_i \begin{bmatrix} \gamma_i^1 \\ \gamma_i^2 \end{bmatrix}. \quad (2)$$

FIG. 3. Summary of the fLSSM strategy for prostate segmentation on CT and MRI. The first step (module 1) shows the fusion of MR and CT imagery. The diagnostic and planning MRI are first affinely registered (shown via a checker-board form) followed by an elastic registration of planning MRI to corresponding CT. The diagnostic MRI can then be transformed to the planning CT (shown as overlaid images). The second step (module 2) shows the construction of the fLSSM where PCA is performed on aligned training samples of prostates from both CT and MRI such that their shape variations are then linked together. Thus, for any standard deviation from the mean shape, two different but corresponding prostate shapes can be generated on MRI and CT. The last step (module 3) illustrates the fLSSM-based MRI-CT segmentation process, where we extract different kinds of features from each image to train a random forest classifier which is combined with a probabilistic atlas to identify voxels that are likely to be inside the prostate. The fLSSM, which is concurrently initialized on the classification result on both MRI and CT, is subsequently evolved to yield concurrent segmentations on both modalities.

III.D. Linking variation of prostate shape on multiple modalities

As PCA is performed on all the data from both imaging modalities for all the patient studies, the variability of prostate shape across all patients is linked with the λ and γ

obtained from PCA. $w \in \{-3\sqrt{\lambda}, \dots, 3\sqrt{\lambda}\}$ modulates the magnitude given to the unit length directional eigenvectors γ . Since the same w is used to calculate new shape instances on each modality (by weighing the separated eigenvectors γ^j), this allows the generation of corresponding shapes. For

example, ϕ^1 that is calculated using w is linked to ϕ^2 (calculated using the same w), since they represent shapes corresponding to the same SOI on two different modalities. This is illustrated in the panel 2 of Fig. 3.

IV. APPLICATION OF LSSM TO SEGMENT PROSTATE ON MRI-CT IMAGERY

IV.A. Diagnostic MRI to planning MRI 2D registration

In order to bring each 2D diagnostic MR image I^d into the coordinate space of I^p , I^d was registered to I^p (2D affine registration), via maximization of NMI, to determine the mapping $\mathbf{T}^{dp} : C^d \mapsto C^p$:

$$\mathbf{T}^{dp} = \underset{\mathbf{T}}{\operatorname{argmax}} [\operatorname{NMI}(I^p, \mathbf{T}(I^d))], \quad (3)$$

where $\mathbf{T}(I^d) = (C^p, f^d)$ so that every $c \in C^d$ is mapped to new spatial location $e \in C^p$ (i.e., $\mathbf{T}(c) \Rightarrow e$ and $\mathbf{T}^{-1}(e) \Rightarrow c$). The NMI between I^p and $\mathbf{T}(I^d)$ is given as,

$$\operatorname{NMI}(I^p, \mathbf{T}(I^d)) = \frac{D(I^p) + D(\mathbf{T}(I^d))}{D(I^p, \mathbf{T}(I^d))}, \quad (4)$$

in terms of marginal and joint entropies,

$$D(I^p) = - \sum_{e \in C^p} p^p(f^p(e)) \log p^p(f^p(e)), \quad (5)$$

$$D(\mathbf{T}(I^d)) = - \sum_{e \in C^p} p^d(f^d(\mathbf{T}^{-1}(e))) \log p^d(f^d(\mathbf{T}^{-1}(e))), \quad (6)$$

$$D(I^p, \mathbf{T}(I^d)) = - \sum_{e \in C^p} p^{pd}(f^p(e), f^d(\mathbf{T}^{-1}(e))) \log p^{pd}(f^p(e), f^d(\mathbf{T}^{-1}(e))), \quad (7)$$

where $p^p(\cdot)$ and $p^d(\cdot)$ are the graylevel probability density estimates, and $p^{pd}(\cdot, \cdot)$ is the joint density estimate, calculated from histograms. Note that the similarity measure is calculated over all the pixels in C^p , the coordinate grid of I^p . Despite the small FOV of I^d and the large FOV of I^p , an affine transformation is sufficient since the different FOV MRIs are acquired in the same scanning session with minimal patient movement between acquisitions. Since both types of MRIs are also similar in terms of intensity characteristics, NMI is effective in establishing optimal spatial alignment.

IV.B. 2D Registration of planning MRI to CT

An elastic registration was performed between I^p and I^{CT} using control point-driven TPS to determine the mapping $\mathbf{T}^{pC} : C^p \rightarrow C^{CT}$. This was also done in 2D for corresponding slices which contained the prostate, using an interactive point-and-click graphical interface. Corresponding anatomical landmarks on slices I^p and I^{CT} were selected via the point-and-click setup. These landmarks included the femoral head, pelvic bone, left and right obturator muscles, and locations near the rectum and bladder which showed significant deformation between the images. Note that $\mathbf{T}^{pC}(c)$ is a non-parametric deformation field which elastically maps each

coordinate in C^p to C^{CT} , while $\mathbf{T}^{dp}(e)$ from the previous step is obtained via an affine transformation. The elastic deformation is essential to correct for the nonlinear deformation of the prostate shape on MRI on account of the use of an endorectal coil on MRI.

IV.C. Combination of transformations

The direct mapping $\mathbf{T}^{dC}(c) : C^d \mapsto C^{CT}$ of coordinates of I^d to I^{CT} was obtained by the successive application of $\mathbf{T}^{dp}$ and $\mathbf{T}^{pC}$

$$\mathbf{T}^{dC}(c) = \mathbf{T}^{pC}(\mathbf{T}^{dp}(c)). \quad (8)$$

Thus, using $\mathbf{T}^{dC}(c)$, each $c \in C^d$ was mapped into corresponding spatial grid C^{CT} . This transformation was then applied to $B(I^d)$, to map the prostate delineation onto CT to obtain $B(I^{CT})$.

In summary, the procedure described above was used to obtain the following spatial transformations: (1) $\mathbf{T}^{dp}$ mapping from C^d to C^p , (2) $\mathbf{T}^{pC}$ mapping from C^p to C^{CT} , and (3) $\mathbf{T}^{dC}$ mapping from C^d to C^{CT} . Using $\mathbf{T}^{dC}$ and $\mathbf{T}^{pC}$, the diagnostic and planning MRI that are in alignment with CT are obtained as $\tilde{I}^d = \mathbf{T}^{dC}(I^d) = (C^{CT}, f^d)$ and $\mathbf{T}^{pC}(I^p) = (C^{CT}, f^p)$, respectively.

This module is minimally interactive, where user interaction is limited solely to the elastic registration step. This step involves selecting the corresponding anatomical landmarks on slices I^p and I^{CT} , selected via the point-and-click setup. Interaction time per slice varies with the experience of the user, but for a semi-experienced user, it would take approximately 30–60 s per slice depending primarily on the resolution of the images. On average, each patient study had about eight corresponding slices of MRI and CT, hence total interaction time was approximately 4–8 min. Note that image registration was only performed on slices containing the prostate, where 2D–2D slice correspondence across $\mathcal{I}^d$, $\mathcal{I}^p$, and $\mathcal{I}^{CT}$ had been previously determined manually by an expert.

IV.D. Construction of MRI-CT fLSSM

Since 2D mapping via the aforementioned three steps were performed only on those slices for which slice correspondence had been established across $\mathcal{I}^d$, $\mathcal{I}^p$, and $\mathcal{I}^{CT}$, only a subset of the delineations were mapped onto CT. Shape-based interpolation³⁶ between the slices was performed in order to identify delineations for slices which were not in correspondence across $\mathcal{I}^d$, $\mathcal{I}^p$, and $\mathcal{I}^{CT}$. 3D binary volumes V_i^1 and V_i^2 were then reconstructed out of the 2D masks from both modalities. The model construction method described in Sec. III was then leveraged to build the MRI-CT based fLSSM.

IV.E. Initial prostate segmentation on MRI and CT

IV.E.1. Feature extraction

From all $\mathcal{I}^d \in S_d$ and $\mathcal{I}^{CT} \in S_{CT}$, K -dimensional features $F(h)$ were extracted for each voxel h . A total of 104 features ($K=104$) were used and they consisted of the original

FIG. 4. Representative gradient feature images (a) and (b) on MRI, (c) and (d) on CT.

intensity image, gradient features and Haar³⁷ features. Since some types of gradients are characteristic to edges between the prostate and extra-prostatic structures, while others are characteristic to edges between intraprostatic structures, a number of different gradient features were extracted to aid in the classification process. Some example visualizations of these features are shown on Fig. 4. In this work, the features were employed, in conjunction with a classifier, for detecting the approximate location of the prostate on multimodal imaging. We calculated multilevel 2D stationary wavelet decompositions using Haar wavelets³⁷ to obtain six levels of Haar features for the original intensity image. Four Sobel operators were also convolved with each I^d and I^{CT} to detect horizontal, vertical, and diagonal edges. Three Kirsch operators were convolved with each I^d and I^{CT} to detect strength of edges in the various directions. Additional horizontal, vertical and diagonal gradient detectors were also convolved with I^d and I^{CT} to detect fine gradients.

IV.E.2. Classifier construction

We define $\mathcal{T}$ to be a random set of R voxels that are sampled from our training images such that $\mathcal{T} = \{h_r | r \in \{1, \dots, R\}\}$. The foreground voxels $\mathcal{T}_{fg} \subseteq \mathcal{T}$ are defined as $\mathcal{T}_{fg} = \{h | h \in \mathcal{T}, \mathcal{L}(h) = 1\}$ and the background voxels $\mathcal{T}_{bg} \subseteq \mathcal{T}$ are defined as $\mathcal{T}_{bg} = \{h | h \in \mathcal{T}, \mathcal{L}(h) = 0\}$. The feature vectors $F_{\mathcal{T}_{fg}}(h)$ (corresponding to $\mathcal{T}_{fg}$) and $F_{\mathcal{T}_{bg}}(h)$ (corresponding to $\mathcal{T}_{bg}$) were used as a training set for a random forest classifier³³ to determine the probability of any $F(h)$ (on an independent test image) belonging to the foreground ($P(F(h)|\mathcal{L}(h) = 1)$) or the background ($P(F(h)|\mathcal{L}(h) = 0)$), i.e., inside or outside the prostate. This process was performed for both MRI and CT. The resulting probability map provides for an initial pre-segmentation of locations within and outside the prostate.

IV.E.3. Constructing probabilistic atlases for prostate on MRI and CT

From all the training images $\mathcal{I}^d \in S_d$ and $\mathcal{I}^{CT} \in S_{CT}$, a spatial probabilistic atlas P_{ATLAS} of the prostate was constructed, as illustrated in Eqs. (9) and (10)

$$P_{ATLAS_{in}}^j = \frac{1}{N} \sum_{i=1}^N V_i^j, \quad (9)$$

$$P_{ATLAS_{out}}^j = \frac{1}{N} \sum_{i=1}^N (1 - V_i^j), \quad (10)$$

where N is the number of training studies, and $j = 1$ refers to an MRI atlas and $j = 2$ refers to a CT atlas.

This probabilistic atlas was then combined with the probability map obtained from random forest classification (Sec. IV E 2) of a test image on MRI or CT (using matrix multiplication). This process of combining random forest classification and a probabilistic atlas aids in reducing the number of false positive and false negative errors in classification, compared to only using the classifier output.³⁸

IV.E.4. Combining classifier and atlas for presegmenting prostate on MRI and CT

For every voxel h in $\mathcal{I}_{test}^d$, the MRI on which the prostate is to be segmented, and $\mathcal{I}_{test}^{CT}$, the CT image on which the prostate is to be segmented, we extracted a corresponding K -dimensional feature vector $F(h)$ (Sec. IV E 1). We then applied the random forest classifier (Sec. IV E 2) to $F(h)$, where $h \in \mathcal{I}_{test}$, to obtain the resulting probabilities of a voxel h belonging to the foreground or background on each modality. The probabilities obtained from the classifier and the probabilistic atlas were then incorporated into a Bayesian conditional model. We aim to determine whether $P(\mathcal{L}(h) = 1 | F(h), P_{ATLAS_{in}}^j) > P(\mathcal{L}(h) = 0 | F(h), P_{ATLAS_{out}}^j) + \eta$, where η is a threshold parameter, determined empirically. Bayes rule is employed with log likelihoods, such that

$$\log P_{fg} = \log P(F^j(h)), \quad P_{ATLAS_{in}}^j | (\mathcal{L}^j(h) = 1), \quad (11)$$

$$\log P_{bg} = \log P(F^j(h)), \quad P_{ATLAS_{out}}^j | (\mathcal{L}^j(h) = 0), \quad (12)$$

$$\tilde{V}^j(h) = \begin{cases} \text{if } \log P_{fg} + \log P((\mathcal{L}^j(h) = 1)) \\ 1 - \log P_{bg} + \log P((\mathcal{L}^j(h) = 0)) \\ > \eta \\ \text{if } \log P_{fg} + \log P((\mathcal{L}^j(h) = 1)) \\ 0 - \log P_{bg} + \log P((\mathcal{L}^j(h) = 0)) \\ \leq \eta \end{cases}, \quad (13)$$

where the prior probabilities $P(\mathcal{L}^j(h) = 1)$ and $P(\mathcal{L}^j(h) = 0)$ are given as $|\mathcal{T}_{fg}^j|/|\mathcal{T}^j|$ and $|\mathcal{T}_{bg}^j|/|\mathcal{T}^j|$, respectively.

Additionally, $j \in \{1, 2\}$ where $\tilde{V}^1(h)$ refers to the binary classification of a voxel on MRI, while $\tilde{V}^2(h)$ refers to the binary classification of a voxel on CT.

IV.F. Concurrent 3D segmentation of the prostate on MRI and CT

To initialize the prostate segmentation, the mean of the MRI and CT prostate training shapes (represented as SDFs) were placed at the approximate center of the prostate on MRI and CT, respectively. We then fit the LSSM to both $\tilde{V}^1$ and $\tilde{V}^2$ by simultaneously registering (using 3D affine registration) and deforming (by weighing the eigenvectors γ^1 and γ^2) the initialization of the segmentation (iteratively), on both MRI and CT, until convergence. Equation (14) illustrates the energy functional which would need to be minimized to fit a SSM to either $\tilde{V}^1$ or $\tilde{V}^2$. Equation (15) represents a linear combination of the energy functional required for segmentation of the SOI on each of the individual modalities. The minimization of Eq. (15) was performed using an active set algorithm³⁹

$$E^j(w, t^j, s) = \frac{1}{|\mathcal{C}^j|} \left(\int_{\Omega} \tilde{V}^j H(-\phi_{kw,t^j,s}^j) + \int_{\Omega} \tilde{V}^j H(\phi_{kw,t^j,s}^j) \right), \quad (14)$$

where w is the shape parameter, t is the translation parameter, s is the scaling parameter, H is the Heaviside step function, k refers to the iteration index, and $j \in \{1, 2\}$

$$E(w, t^1, t^2, s) = E^1(w, t^1, s) + E^2(w, t^2, s), \quad (15)$$

According to Eq. (2), the shape parameter w being optimized in Eq. (15), to segment the prostate, is relevant for segmentation on both MRI and CT. The scaling parameter s is also identical. On the other hand, the translation parameter t needs to be scaled according to the pixel spacing in the MRI and CT images. Thus, $t^2 = t^1 \times \left(\frac{ps^1}{ps^2}\right)$, where ps^1 and ps^2 are the pixel spacings (in millimeters) of the MRI and CT, respectively. During optimization of Eq. (15), as the segmentation $\phi_{w,t^1,s}^1$ is iteratively determined, a concurrent optimization determines the corresponding CT segmentation $\phi_{w,t^2,s}^2$.

IV.G. Implementation details

IV.G.1. MRI-CT preprocessing

All MR images were corrected for bias field inhomogeneity using the automatic low-pass filter based technique developed by Cohen *et al.*⁴⁰ All the bias field corrected MR images were subsequently intensity standardized to the same range of intensities.^{41,42} This was done via the image intensity histogram normalization technique⁴³ to standardize the contrast of each image to a template image. The CT images were preprocessed using the histogram normalization technique.⁴³

IV.G.2. Transforming and resampling images

Prior to extracting features and performing segmentation, we resampled each $V_j^i \in S_V$, $\mathcal{I}_i^d \in S_d$, and $\mathcal{I}_i^{CT} \in S_{CT}$ to the

maximum number of slices of any given image volume such that difference in number of slices does not affect our segmentation algorithm. In addition, we also transformed all the MRI and CT images (separately) to a common coordinate frame by using a 3D affine registration with NMI (Ref. 34) being employed as the similarity measure. The template that was used was the same template patient study that we used for the affine registration of the binary segmentations. However, this time, the intensity images were used as the template instead of binary segmentations. After performing segmentation on the transformed, resampled image, the segmentation result was, respectively, transformed and resampled back to its original location and slice number to yield the final segmentation result. Placing all the images on the same coordinate frame and resampling to the same number of slices prior to feature extraction and segmentation greatly aids in improving the segmentation accuracy.

V. EXPERIMENTAL DESIGN

V.A. Types of ground truth

We define expert delineated prostate boundary on CT as $\mathcal{G}_{xCT}$ while expert delineated boundary on MRI is defined as $\mathcal{G}_{MRI}$. Furthermore, prostate ground truth delineations that were mapped from MRI onto CT by employing MRI-CT registration (fusion) is denoted as $\mathcal{G}_{fCT}$ and delineations on CT performed by a trainee is termed $\mathcal{G}_{iCT}$.

V.B. Summary of experimental comparison and evaluation

The four different types of SSMs that were employed and compared in this study are described below:

1. **ctSSM**: CT-based SSM built using $\mathcal{G}_{xCT}$ on CT only.
2. **xLSSM**: LSSM built using $\mathcal{G}_{MRI}$ on MRI and $\mathcal{G}_{xCT}$ on CT. This represents the idealized LSSM.
3. **tLSSM**: LSSM built using $\mathcal{G}_{MRI}$ on MRI and $\mathcal{G}_{iCT}$ (by nonexpert resident or medical student) on CT. Two tLSSMs (tLSSM⁽¹⁾ and tLSSM⁽²⁾) were constructed via prostate delineations on CT, obtained from two different trainees.
4. **fLSSM**: LSSM built using $\mathcal{G}_{MRI}$ on MRI and $\mathcal{G}_{fCT}$ on CT. This represents our new model, which leverages 2D MRI-CT registration,³⁰ to map expert delineated prostate boundaries on the MRI onto CT.

We employed the leave-one-out strategy to evaluate the five SSMs using a total of 20 patient studies (see Table II for a summary of the data). On MRI, the segmentation results of the xLSSM, tLSSM, and fLSSM were evaluated against $\mathcal{G}_{MRI}$. On CT, the segmentation results of all SSMs were evaluated against $\mathcal{G}_{xCT}$. Note, however, that the ctSSM and the xLSSM have an advantage over the fLSSM and the tLSSMs which do not employ $\mathcal{G}_{xCT}$ in their construction. The types of ground truth used for training and evaluation are summarized in Fig. 5. The left side of Fig. 5 illustrates the different types of ground truth used for training the various SSMs, while the right side illustrates the evaluation of

FIG. 5. Summary of the different types of ground truth used for training and testing the various SSMs considered in this study. Expert, trainee and MRI-CT registration based ground truth are shown on the left side of the figure (respectively in red, green and blue). The right side of the figure shows the automatic segmentations via the different SSMs compared against the expert ground truth, the automated segmentations are shown in yellow.

automated segmentation results against expert-based ground truth only.

VI.C. Performance measures

The prostate segmentation results for all the SSMs were evaluated quantitatively using the dice similarity coefficient¹² (DSC) and the mean absolute distance (MAD) (Ref. 20) on both MRI and CT. Two-tailed paired t-tests were performed to identify whether there were statistically significant differences in DSC between the xLSSM, fLSSM, and tLSSMs against the ctSSM, the null hypothesis being that there was no improvement in performance via the use of a LSSM, over the ctSSM, on CT. A p -value less than 0.05 indicates statistically significant improvement in performance of the LSSM in question over the ctSSM.

VI. RESULTS

VI.A. Qualitative results

Our qualitative evaluation of the five SSMs are shown in Fig. 6 as 3D renderings of the prostate segmentation overlaid on the corresponding MRI or CT 3D volume. The error (in millimeter) from each point s of the segmented prostate surface boundary to the closest point g on the associated prostate ground truth segmentation is calculated and every surface point s is assigned an error ϵ_s . This error is rendered on the 3D prostate with a color reflecting the magnitude of ϵ_s where small errors are assigned “cooler colors,” and large errors are assigned “warmer” colors. The particular orienta-

tion angle of the images were chosen to reflect areas of the prostate with most error.

Figures 6(a)–6(e) show the prostate CT segmentation errors when using the ctSSM, xLSSM, fLSSM, tLSSM⁽¹⁾, and tLSSM⁽²⁾, respectively, while Fig. 6(f) shows the prostate MRI segmentation errors for any given LSSM.

VI.B. Evaluating MRI-CT registration

We evaluated our MRI-CT registration, over the 20 patient studies, by comparing the final mapped 3D prostate shapes on CT obtained for each patient study, with $\mathcal{G}_{xCT}$. The mean registration results in terms of DSC and MAD, along with their associated standard deviations are reported on Table III.

VI.C. Evaluating LSSM-based segmentation

In order to assess the feasibility of using the LSSM, it was evaluated via a leave-one-out reconstruction scheme, where reconstruction accuracy was determined, in terms of DSC. The following steps describe how the accuracy was assessed:

- Leave out a particular patient study and train a LSSM using the remaining datasets.
- Let ϕ_r represent the reconstructed prostate shapes on MRI and CT.
- Find the optimal w which minimizes the least-squares reconstruction error between ϕ_r and ϕ from Eq. (1): $\min_w \|\phi - \phi_r\|$.
- In this case, ϕ represents the left-out MRI and CT prostate ground truth shapes.
- Reconstruct the MRI and CT shape, as SDFs, using this w :

$$\begin{bmatrix} \phi_r^1 \\ \phi_r^2 \end{bmatrix} = \begin{bmatrix} \bar{\phi}^1 \\ \bar{\phi}^2 \end{bmatrix} + \sum_{i=1}^q w_i \begin{bmatrix} \gamma_i^1 \\ \gamma_i^2 \end{bmatrix}$$

- Convert the SDFs into binary masks where $\phi_r^i \leq 0 = 1$ and $\phi_r^i > 0 = 0$.
- Calculate the accuracy in terms of DSC in between the reconstructed binary masks and the ground truth binary shapes that were left out.

Using the above methodology, we found a mean reconstruction DSC accuracy of $82.93 \pm 5.83\%$ on MRI and $86.72 \pm 3.57\%$ on CT. Figure 7 shows the reconstruction accuracy obtained using the left-out MRI and CT prostate shape for each patient study.

In order to evaluate the robustness of the fLSSM to centroid initialization, we repeated the fLSSM segmentation experiment by adding random perturbations to the centroid initialization (in addition to the random sampling of voxels for the random forest classifier), for each of the ten runs. Figure 8 shows the average DSC obtained over ten runs when evolving the fLSSM on each patient study. The error bars represent the standard deviation in DSC for the ten runs on each patient study. This figure shows that in spite of the random perturbations of the centroid location, the standard deviation of the resulting DSC for each study is small.

FIG. 6. 3D renderings of MRI and CT segmentation results for a patient study, where the surface is colored to reflect the surface errors (in mm) between prostate surface segmentation and the associated $\mathcal{G}_{CT}$. Segmentation of prostate on (a) CT using the ctSSM evaluated against $\mathcal{G}_{CT}$, (b) CT using the xLSSM evaluated against $\mathcal{G}_{CT}$, (c) CT using fLSSM evaluated against $\mathcal{G}_{CT}$, (d) CT using tLSSM⁽¹⁾ evaluated against $\mathcal{G}_{CT}$, (e) CT using tLSSM⁽²⁾ evaluated against $\mathcal{G}_{CT}$, and (f) MRI using any LSSM evaluated against $\mathcal{G}_{MRI}$.

The xLSSM, fLSSM, and the two tLSSMs were evolved on both MRI and CT images, while the ctSSM was only evolved on the CT images from 20 patient studies. The difference in DSC results between any given pair of LSSMs was not statistically significant for prostate MRI segmentation ($p > 0.05$). Similarly, the evaluation also showed that the LSSMs performed equivalently for prostate CT segmentation. Comparing the performance of each LSSM against the ctSSM showed that all the LSSMs, except tLSSM⁽¹⁾, significantly outperformed the ctSSM ($p < 0.05$).

TABLE III. Mean DSC and MAD for prostate MRI to CT registration, along with their associated standard deviations, calculated over all 20 patient studies.

DSC (%)	MAD (mm)
82.83 ± 4.35	1.88 ± 0.56

Figure 9 and Tables IV and V summarize the quantitative results of prostate segmentation using the: (1) ctSSM, (2) xLSSM, (3) fLSSM, (4) tLSSM⁽¹⁾, and (5) tLSSM⁽²⁾. Figure 9 in particular shows the specific mean DSC values (averaged over ten separate runs due to the random sampling of voxels during the classification process) obtained for each patient study where the X-axis refers to patient index and the Y-axis refers to corresponding mean DSC values. Each of the different colored bars corresponds to a particular SSM. The error bars represent the standard deviation of the DSC values over ten runs. Table VI shows the corresponding p -values when comparing the different LSSMs against the ctSSM and against each other, in terms of DSC, for statistical significance.

VII. DISCUSSION

From Table V, we see that our fLSSM, the idealized xLSSM, and the two tLSSMs perform similarly, for prostate CT segmentation, in terms of DSC and MAD. This is very

FIG. 7. Leave-one-out reconstruction accuracy obtained for each patient study using both MRI and CT shapes. The bars on the left for a patient study represent the DSC obtained on MRI, while the bars on the right represent the DSC obtained on CT.

encouraging since the fLSSM, which is trained with delineations mapped from MRI to CT using image registration, performed just as well as the idealized xLSSM and the tLSSMs. This indicates that the MRI-CT registration scheme employed in our framework is an accurate alternative to manual delineation of the prostate on CT by an expert or trainee, for constructing a LSSM.

The comparison of the xLSSM, fLSSM, and the two tLSSMs against the ctSSM showed superior prostate CT segmentation accuracy in terms of both DSC and MAD. Figure 6(a) reveals that prostate CT segmentation errors associated with the ctSSM occur near the prostate-bladder and prostate-rectum boundary. Figures 6(b) and 6(c) reveal that the prostate CT segmentation errors associated with the xLSSM and fLSSM, respectively, are not as large as the ctSSM near the bladder and rectal boundaries, but mostly occur at the prostate-levator muscle interfaces. Figures 6(d) and 6(e) show that the prostate CT segmentation errors associated with tLSSM⁽¹⁾ and tLSSM⁽²⁾, respectively, occur near the levator muscles, but also

close to the prostate-rectum interface at the base and apex of the prostate. A comparison of Figs. 6(a) and 6(b)–6(e) reveals that the concurrent segmentation of the gland on MRI and CT using the LSSMs aids in reducing segmentation errors near the prostate-bladder and prostate-rectum interface, these errors being more prevalent when employing the ctSSM. This may perhaps be on account of the ability of the LSSMs to exploit the better soft tissue contrast in MRI compared to CT, allowing for discrimination between the prostate, bladder, and rectum, usually indistinguishable on CT.⁴

We see from Table IV that the MRI segmentation results using the various LSSMs are very similar. Qualitatively, it was seen that the prostate MRI segmentation errors occurred in the same locations for all four LSSMs. This is illustrated in Fig. 6(f) where most of the prostate MRI segmentation errors from using any of the LSSMs arise near the prostate-levator muscle interfaces.

Figures 6(b)–6(e), reveal that the latter four prostate CT segmentations yield errors in similar locations relative to the

FIG. 8. The average DSC obtained over ten runs when evolving the fLSSM on each patient study. For each of the ten runs, a random subset of voxels was sampled for the random forest classifier and a random perturbation was added to the centroid initialization. The bars on the left for a patient study represent the DSC obtained on MRI, while the bars on the right represent the DSC obtained on CT. The error bars represent the standard deviation in DSC for the ten runs on each patient study.

FIG. 9. Prostate CT segmentation results for each of the 20 patient studies used in this study. Error bars representing the standard deviation in DSC over ten runs are also shown.

prostate MRI segmentation in Fig. 6(f). This suggests that although the LSSM aids in reducing segmentation errors near the bladder and rectal boundaries, MRI segmentation errors are also propagated onto the CT segmentation. Figures 6(d) and 6(e) also reveal some segmentation errors near the apical rectal and bladder boundary. The apical slices of the prostate are generally the toughest to delineate, especially for less experienced readers, due to: (1) similar attenuation coefficients of the tissues present near the apex of the prostate,⁴⁴ (2) the proximity of the apex of the prostate with the adjoining external urethral sphincter and surrounding fibrous tissue which further increases delineation error,⁴⁵ (3) lower prevalence or absence of fatty tissue which aids in increasing contrast between the prostate and surrounding tissue.⁴⁴ Hence, it is likely that the errors in delineating the prostate near the apex propagated to the prostate CT segmentation when using the tLSSMs.

Table III reveals that prostate CT segmentation, performed via MRI-CT registration, yielded DSC and MAD values comparable to CT segmentation results reported in the literature.^{12–14} This suggests that it may be possible to employ MRI-CT registration for localizing the prostate on CT by transferring the prostate delineations from the associated MRI.

Additionally, our prostate MRI segmentation results using LSSMs performed as well as and even better than some recent state-of-the-art methods in terms of DSC and MAD. The LSSMs outperformed the method proposed by Toth *et al.*,²⁰ and yielded results comparable to that of Martin *et al.*²¹ and Klein *et al.*⁴⁶

Our prostate CT segmentation using the LSSMs performed comparably to several state-of-the-art CT segmentation methods such as those proposed by Stough *et al.*¹¹ and Feng *et al.*¹² While the prostate CT segmentation results

reported in this paper are certainly encouraging, we believe they could be even further improved by incorporating additional domain specific and patient-specific constraints such as in Refs. 11–13. Acquiring a larger training cohort and higher resolution MRIs should improve prostate segmentation results, on both MRI and CT, as well.

In addition, we would like to note that the prostate segmentation results obtained using the fLSSM were very similar to the results obtained via the leave-one-out reconstruction experiment. However, when we take a closer look at the data and compare the DSC of the fLSSM prostate segmentation on CT with the prostate reconstruction accuracy on CT, there are still individual studies where the fLSSM yields a higher DSC compared to the leave-one-out experiments. We attribute this behavior to differences in implementation of the leave-one-out reconstruction experiment and the fLSSM segmentation scheme. The key difference between the implementations is that the fLSSM scheme performs a “fitting” of the shape model to the presegmented MRI and CT prostate shapes after centroid initialization, while the reconstruction experiment does not perform any sort of fitting and simply reconstructs the shape after centroid initialization. Thus, the fLSSM scheme is essentially trying to correct any errors in centroid initialization by optimizing the fitting, whereas the leave-one-out reconstruction scheme simply propagates those errors into the reconstruction accuracy calculation. We believe that this difference in the implementations is the cause of the higher DSC on a few isolated studies, when using the fLSSM scheme.

VIII. CONCLUDING REMARKS

The primary contributions of this work were: (1) a new framework for constructing a linked statistical shape model

TABLE IV. Mean DSC and MAD for prostate MRI segmentation using the different LSSMs.

Reference	DSC (%)	MAD (mm)
xLSSM	82.83 ± 5.69	2.60 ± 0.56
fLSSM	82.56 ± 5.63	2.61 ± 0.58
tLSSM ⁽¹⁾	79.25 ± 5.96	2.75 ± 0.64
tLSSM ⁽²⁾	81.22 ± 5.60	2.66 ± 0.57

TABLE V. Mean DSC and MAD for prostate CT segmentation using the different SSMs.

Reference	DSC (%)	MAD (mm)
ctSSM	81.37 ± 9.64	2.16 ± 1.06
xLSSM	86.43 ± 9.75	2.11 ± 0.98
fLSSM	85.38 ± 7.66	2.02 ± 0.67
tLSSM ⁽¹⁾	85.12 ± 9.23	2.04 ± 0.81
tLSSM ⁽²⁾	85.44 ± 8.02	2.07 ± 0.67

TABLE VI. p -values from two-tailed paired t-tests to identify whether there are statistically significant differences between CT segmentation results (in terms of DSC) of different pairs of SSMs.

	ctSSM	xLSSM	fLSSM	tLSSM ⁽¹⁾	tLSSM ⁽²⁾
ctSSM	—	0.0007**	0.0365*	0.0834	0.0300*
xLSSM	—	—	0.5433	0.5794	0.5846
fLSSM	—	—	—	0.7911	0.9338
tLSSM ⁽¹⁾	—	—	—	—	0.6699

Note: Significant values where $p < 0.05$ are signified by one asterisk while values where $p < 0.01$ are identified via two asterisks.

(LSSM) which links the shape variability of a structure across different imaging modalities, (2) constructing a SSM in the absence of ground truth boundary delineations on one of two modalities used, and (3) application of the LSSM to segment the prostate concurrently on both MRI and CT for radiotherapy planning. To the best of our knowledge, this is the first time a multimodal SSM has been built for concurrent segmentation on multiple imaging modalities. Prostate delineations on MRI are much more accurate and easier to obtain compared to CT. Hence, we leverage prostate delineations on MRI for prostate segmentation on CT (for radiotherapy planning) by using a LSSM.

Our experiments indicated that an exclusive ctSSM did not perform as well as the fLSSM. The fLSSM, which was built using expert delineations on MRI, and MRI-CT registration mapped delineations on CT, yielded prostate MRI and CT segmentation results that were equivalent to corresponding results from our xLSSM and tLSSM schemes (built using expert and trainee delineations of the prostate on CT, respectively). The fLSSM, xLSSM, and the tLSSMs all easily outperformed the ctSSM.

Note that the fLSSM was deliberately handicapped against xLSSM since the same ground truth used in constructing the xLSSM was used in evaluating the xLSSM and the fLSSM. Constructing a xLSSM, tLSSM, or a ctSSM is far more difficult and time-consuming compared to the fLSSM, and are also contingent on the availability of ground truth annotations, which in most cases is very difficult to obtain on CT. Our study yielded some very encouraging results which suggest that the fLSSM is a feasible method for prostate segmentation on CT and MRI in the context of radiotherapy planning. Future directions will include improving the LSSM by: (1) employing additional training studies, (2) incorporating a 3D MRI-CT registration algorithm requiring less user intervention via automated determination of slice correspondences, (3) use of higher resolution MRI, and (4) incorporating additional domain specific constraints into the model.

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