A Structural-functional MRI-based Disease Atlas: Application to Computer-aided-Diagnosis of Prostate Cancer

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ABSTRACT
Different imaging modalities or protocols of a single patient may convey different types of information regarding a disease for the same anatomical organ/tissue. On the other hand, multi-modal/multi-protocol medical images from several different patients can also provide spatial statistics of the disease occurrence, which in turn can greatly aid in disease diagnosis and aid in improved, accurate biopsy and targeted treatment. It is therefore important to not only integrate medical images from multiple patients into a common coordinate frame (in the form of a population-based atlas), but also find the correlation between these multi-modal/multi-protocol data features and the disease spatial distribution in order to identify different quantitative structural and functional disease signatures. Most previous work on construction of anatomical atlases has focused on deriving a population-based atlas for the purpose of deriving the spatial statistics. Moreover, these models are typically derived from normal or healthy subjects, either explicitly or implicitly, where it is assumed that the inter-patient pathological variation is not large. These methods are not suitable for constructing a disease atlas, where significant differences between patients on account of disease related variations can be expected. In this paper, we present a novel framework for the construction of a multi-parametric MRI-based data-driven disease atlas consisting of multi-modal and multi-protocol data from across multiple patient studies. Our disease atlas contains 3 Tesla structural (T2) and functional (dynamic contrast enhanced (DCE)) prostate \textit{in vivo} MRI with corresponding whole mount histology specimens obtained via radical prostatectomy. Our atlas construction framework comprises 3 distinct modules: (a) determination of disease spatial extent on the multi-protocol MR imagery for each patient, (b) construction of a multi-protocol MR imaging spatial atlas which captures the geographical proclivity of the disease, and (c) feature extraction and the construction of the data-driven multi-protocol MRI based prostate cancer atlas. The marriage of data driven and spatial atlases could serve as a useful tool for clinicians to identifying structural and functional imaging disease signatures so as to make better, more informed diagnoses. Each spatial location in this atlas can be associated with a high dimensional multi-attribute quantitative feature vector. Additionally, since the feature vectors are extracted from across multiple patient studies, each spatial location in the data-driven atlas can be characterized by a feature distribution (in turn characterized by a mean and standard deviation). Preliminary investigation in quantitatively correlating the disease signatures from across the spatial and data driven atlases suggests that our quantitative atlas framework could emerge as a powerful tool for discovering prostate cancer imaging signatures.

Keywords: Disease atlas, prostate cancer, MRI, computer-aided-diagnosis, multi-functional, multi-modal, T2, DCE, population atlas, data driven atlas, 3 Tesla

1. INTRODUCTION
As different medical images convey different types of information regarding the disease in the same anatomical organ/tissue, it is important to align and correlate these images so that complementary information about the disease can be combined. On the other hand, since uni-modal medical images of multiple patients accurately reflect the spatial extent of disease, aligning these images into a common coordinate frame can provide an overview of the spatial distribution of the disease, allowing for the construction of population-based atlas. For instance, from empirical evidence, it is known that more prostate cancers originate within the peripheral zone of the gland compared the central zone [1]. A spatial population atlas could provide additional and precise insight into spatial
tendency (if any) of disease occurrence [2]. Additionally, the incorporation of a multi-modal, multi-protocol imaging data into a population based atlas would allow for a quantitative study of disease signatures. Clearly, a spatial disease atlas that simultaneously encapsulates population based statistics of functional, structural, and metabolic imagery signatures on a per voxel basis would be hugely significant. For example, a radiologist might find it useful to quantitatively study and analyze the mean and variance of wash-in and wash-out values of contrast on dynamic contrast enhanced (DCE) MRI on voxel by voxel basis in cancer and non-cancer areas. This would be particularly relevant for purposes of training and teaching radiology residents and fellows who could take advantage of spatial and image derived information simultaneously encoded within a single 3D atlas volume, instead of individually and serially studying imaging studies from different patients. By correlating spatial presence of disease on the spatial atlas with corresponding feature distributions on the data-driven atlas, radiology residents could learn to identify the most relevant imaging markers for disease. With the help of this atlas, clinicians could potentially discover new structural-functional disease signatures that are able to best distinguish diseased and normal areas. Yet, another application of such an integrated spatial and data-driven population based atlas would be in training a computer-aided diagnosis (CAD) system for predicting precise location and extent of disease on images from a new patient. While the framework we present is general and not disease or modality specific, in this paper we focus on building a multi-functional MRI-based in vivo prostate cancer atlas.

Prostate cancer (CaP) is the most common malignancy among men and the second leading cancer related cause of death after lung cancer [3] [4]. The current protocol for CaP diagnosis is a screening test based on elevated levels of the Prostate Specific Antigen (PSA) in the blood. Typically, when high levels of PSA are detected, a blinded transrectal ultrasound (TRUS) guided needle biopsy is carried out, and the extracted pathological tissues samples are then examined in detail for disease presence by a pathologist. However, TRUS biopsies have been associated with a low CaP detection accuracy due to (a) the low specificity of the PSA test and (b) poor image resolution of ultrasound [5]. Therefore, researchers have turned to non-invasive medical imaging modalities such as MRI to identify CaP patterns [6]. Some groups have been active in the development MRI-based CAD systems to detect CaP in vivo [7] [8] [9] [10].

In this paper, we present a comprehensive and quantitative framework for the construction of a disease atlas. In particular, for the construction of a disease based spatial atlas, we present a novel method for the registration of the images from different patients with large pathological variations. Our method does not require a biomechanical model. It involves the registration of the images from different patients through adaptive modification of control points, so that rather than placing control points evenly over the images, more control points are added to the non-diseased regions rather than to the diseased regions. Consequently, non-diseased regions in the two images can have larger impact on the final registration result than the diseased regions. Additionally, to determine spatial extent of disease on the radiological imaging modalities, a deformable registration scheme is leveraged to align multi-functional imaging data with corresponding histological specimens for each patient.

We demonstrate the utility of our atlas construction framework in building a population based prostate cancer atlas consisting of structural and functional 3 Tesla MRI data. A total of 15 patients with documented CaP were first imaged using T2 and DCE MRI protocols, which provide structural and functional disease information, respectively. Then these patients underwent radical prostatectomy, and each of the excised prostates was sectioned and then examined by the pathologists, who outlined the cancerous regions on each prostate histological section. Spatial extent of CaP on the MR imaging is determined by manually establishing slice correspondences with whole mount histology sections. Subsequently, the corresponding MRI and whole mount histology sections are registered with one another. Our prostate cancer atlas allows for computing different parametric representations of functional and structural MR imaging data from a population and enables visualization of statistical disease variations in terms of these parameters across multiple subjects. Our preliminary data analysis reveals that using our prostate cancer atlas, certain feature representations obtained by integrating functional and structural data appears to yield greater CaP-benign class separation compared to individual imaging attributes.

The rest of this paper is organized as follows. In Section 2, we describe the relevant previous work and provide an overview of our new work. In Section 3, we discuss our methodology for the construction of an MRI-based prostate disease atlas. In section 4, we demonstrate the utility of our disease atlas construction framework. Concluding remarks and future directions are presented in Section 5.
2. PREVIOUS LITERATURE AND OVERVIEW

2.1 Previous relevant work

Research has been carried out on medical atlases for the purposes of surgery planning [11], image segmentation [12], targeted biopsy [2], and statistical analysis of anatomical structures [13]. With these methods, the aim has been to obtain a spatial statistical model of organs or diseased conditions. Most atlas construction methods either explicitly or implicitly assume that the sample images are from one single subject or from a number of normal or healthy subjects. Thus, typically the variation in image appearance on account of pathology between different subjects considered in building these atlases is small. However, during the construction of a disease atlas, large pathological variations often exist among different subjects, hence most of the existing atlas construction methods are not suitable for this task, and this may also explain why relatively few attempts have been made to construct a disease atlas. Additionally, we are not aware of any existing work on the construction of a data-driven atlas, one that may be used to find the disease-related data features through integrating multi-modal/multi-protocol data into a common coordinate frame and then analyzing the fused data against the spatial distribution of disease.

In order to build our integrated spatial and data-driven population-based disease atlas, we first need to accurately determine spatial extent of disease on the imaging. Hence for every patient, disease extent acquired from histology needs to be mapped (via intra-patient image registration) onto corresponding radiological modalities (T2, DCE). There are quite a few papers on intra-patient data registration, and [14] [15] offer a comprehensive review of the field. In particular, for the multi-modal or multi-protocol image registration, where a non-linear relationship between voxel intensities in the two images may exist, the non-linear and statistical measures of image similarity such as mutual information (MI) [16] [17], entropy correlation coefficient (ECC) [17] and normalized mutual information (NMI) [18] are often adopted. Nevertheless, these measures are still limited in their ability to handle intensity artifacts and highly dissimilar modalities [23]. To address these problems, we have previously presented some new feature-driven registration schemes, Combined Feature Ensemble Mutual Information (COFEMI) [23] and COLlection of Image-derived Non-linear Attributes for Registration Using Splines (COLLINARUS) [24].

A second important step in constructing a data-driven disease atlas is to integrate the multi-modal data from multiple patients into a common coordinate frame (inter-patient data registration). Compared with the abundance of registration methods for the intra-patient data registration, there are relatively few robust, reliable registration methods available for the inter-patient data alignment. The prostate atlas constructed by Shen et al [2] relied solely on aligning the whole mount histological specimens from a large number of patients, and they only employed the normal prostate surface data for the registration. Pitiot et al [19] realized the impact of the inherent difference between images on the final registration result. While they only considered the impact of physical changes on the resulting images and changes on account of pathological variation was not considered. Mohamed et al [20] worked on the registration of brain tumor images, which have noticeable pathological differences. However, their registration method was based on a biomechanical mass-effect model of the brain tumor. Unfortunately, such biomechanical models are not available for a lot of other tissues/organs (such as prostate). Park et al [21] also noticed the effect of the inherent difference between images during image registration. However, differences on account of larger pathological variations between patients were not considered. Some scientists have proposed registration of images with large pathological variations by allowing the pixels/voxels in the pathologically similar regions (e.g. common anatomical features) to have a greater impact on registration result than the pixels/voxels in the pathologically dissimilar regions (e.g. tissue with different level and spatial distribution of the disease). Zacharaki et al [22] used this approach to register brain tumor images where the tumor regions was used as a mask in order to avoid the mismatch due to the pathological difference between the tumor and non-tumor areas.

2.2 Overview of new work

We present a novel quantitative framework for the construction of a prostate cancer atlas. Our framework consists of 3 modules: (1) determination of spatial disease extent on the radiological imaging, (2) construction of spatial atlas, and (3) feature extraction to construct data-driven disease atlas. For each of these modules, our contributions are as follows:
<table>
<thead>
<tr>
<th>Module</th>
<th>Description</th>
<th>Method</th>
</tr>
</thead>
<tbody>
<tr>
<td>Construction of spatial atlas</td>
<td>T2 MRI - T2 MRI</td>
<td>TPS-based control point modification</td>
</tr>
<tr>
<td>Determination of disease spatial extent on MRI</td>
<td>Histology - T2 MRI</td>
<td>COLLINARUS [24]</td>
</tr>
<tr>
<td></td>
<td>DCE MRI - T2 MRI</td>
<td>COLLINARUS</td>
</tr>
<tr>
<td>Feature extraction to construct data-driven atlas</td>
<td>Structural (T2 MRI)</td>
<td>Mean, standard deviation</td>
</tr>
<tr>
<td></td>
<td>Functional (DCE MRI)</td>
<td>Mean, standard deviation</td>
</tr>
<tr>
<td></td>
<td>Structural and functional (fused T2 MRI and the wash-in value of the fused DCE MRI)</td>
<td>Covariance</td>
</tr>
</tbody>
</table>

1. **Determination of spatial disease extent of disease on multi-protocol MR imaging**: We use COLLINARUS [24] for the non-rigid multi-modal intra-patient MRI data registration. COLLINARUS is a spline based non-linear image registration procedure utilizing multiple representations of the original image. It obtains an improved similarity measure for driving image registration through image feature selection and feature combination.

2. **Construction of spatial atlas of disease**: We present a novel method for the registration of the inter-patient data with significant pathological variations between patients. Our method is based on the thin plate spline (TPS) registration strategy [25]. It registers the images from different patients through adaptive modification of control points, so that rather than placing control points evenly over the whole images, more control points are gradually added to the pathologically similar regions than those added to the pathologically dissimilar regions. In this way, pathologically similar regions in the two images can have larger impact on the final registration result than the pathologically different regions. To differentiate the pathologically similar regions from the pathologically different regions, the ground truth CaP masks outlined on the corresponding histological specimens are utilized. The cancerous regions inside the CaP contours are identified and our method can then reduce the influence of these pathologically different regions on the final registration result.

3. **Construction of data-driven atlas**: After the multi-modal data are registered into a common coordinate frame, each voxel may be associated with a number of feature distributions. In this work, we have limited ourselves to exploring the associations between only 3 different multi-protocol MR imaging features, namely T2 intensity and signal wash-in and wash-out characteristics. However, one could imagine quantitatively extracting $N$ other features (e.g. textural attributes [7] [23]). The feature data accumulated from multiple patients could allow for definition of $N$ feature distributions (characterized by a mean and standard deviation) at every voxel within the data-driven atlas.

4. **Correlation of disease signature between spatial and data-driven atlas**: Each of the $N$ feature distributions (via mean and standard deviation) in the data-driven atlas can be quantitatively correlated on a voxel-by-voxel basis with the spatial distributions for disease on the spatial atlas. This could be used to identify the most important imaging markers (functional, structural, metabolic) for disease (in this context, prostate cancer) characterization.

### 3. DESIGN OF DISEASE ATLAS AND EXPERIMENTAL RESULTS

#### 3.1 Data description

Figure 1 gives the flowchart for the construction of the MRI-based prostate disease atlas. Table 1 summarizes all the 3 modules necessary for the prostate atlas construction.

#### 3.2 Determination of disease spatial extent on MR imaging

We use COLLINARUS for the registration between T2 MRI and DCE MRI as well as for the registration between T2 MRI and the histological specimen. The whole registration procedure is comprised of rigid and non-rigid registration steps, where COFEMI [23] and COLLINARUS [24] are used in the global rigid registration and the
Figure 1. Flowchart of the framework to construct an integrated data and population driven prostate cancer atlas.

local non-rigid registration components, respectively. For two images $A$ and $B$, the global transformation $T_{\text{rigid}}$ is determined by maximizing the following function,

$$T_{\text{rigid}} = \arg\max_{\mathbf{T}} \psi(A, \Phi(B, \mathbf{T})), \quad (1)$$

where $\psi$ is an image similarity measure such as conventional intensity-driven MI or the feature ensemble-driven measure from COFEMI [23], $\mathbf{T}$ stands for a coordinate transformation, and $\Phi$ represents a generic image transformation. Application of $T_{\text{rigid}}$ to $B$ gives the rigidly registered target image $B^r$:

$$B^r = \Phi(B, T_{\text{rigid}}). \quad (2)$$

Similarly, the non-rigid transformation $T_{\text{nrigid}}$ and the final non-rigidly registered target image $B^{nr}$ are determined as:

$$T_{\text{nrigid}} = \arg\max_{\mathbf{T}} \psi(A, \Phi(B^r, \mathbf{T})), \quad (3)$$

and

$$B^{nr} = \Phi(B^r, T_{\text{nrigid}}). \quad (4)$$

In order to achieve the optimization of $T_{\text{nrigid}}$ in Eq. 3, the following steps are taken [24]:

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1. Use a feature ensemble-driven similarity measure for $\psi$, which is obtained via the techniques for feature extraction, selection, and combination that are associated with COFEMI [23].

2. Define $T_{n_{\text{rigid}}}$ as the 2D tensor product of the cubic B-splines [26] [27] to allow local non-rigid image deformation [24].

3. Maximize $\psi$ using a multi-level control point grid approach to achieve B-spline deformation at multiple scales [24].

Figure 2 shows the intra-patient data registration result using COLLINARUS [24] to align the T2 MRI, DCE MRI and histology images for each patient, where we chose T2 MRI as the template image and images from other protocols were used as target images to be registered to the template. Figure 2 reveals our intra-patient data registration step. Not only are the DCE MR and histological images accurately aligned to the T2 MR image, cancer masks determined in histology have also been accurately mapped onto the corresponding T2 MRI so that they can be utilized to guide the distribution of control points for driving the subsequent inter-patient data registration.

3.3 Construction of a spatial atlas for disease

To construct the disease spatial atlas, the two images from different patients are first registered through an affine registration step. As described in Section 2.2, and similar to the approach presented in [22], we aim to put control points within non-diseased regions to drive the TPS registration between the images. Our assumption is that since non-diseased regions in the 2 patient images will be more similar to each other compared to corresponding diseased regions, we deliberately avoid placing control points within the cancer masks obtained from histology. To non-rigidly register the T2 MR images from two patients, TPS-based registration strategy is adopted. An initial set of control points are evenly placed in the non-cancerous regions in two images, then the simplex search
Figure 3. Illustrative example of the inter-patient data registration through modification of TPS control points. (a)-(c) Target image and the distribution of control points over 3 iterations. Red contours indicate the cancer masks on the template image, and green contours indicate the cancer masks on the target image. Note that additional control points are only iteratively placed outside the cancer masks.

is performed to find the optimal displacement for the control point by maximizing the MI between the target and template images.

In order to allow for a more flexible non-rigid transformation, the number of TPS control points gradually increases over successive iterations by evenly decreading the spacing between the control points. Moreover, during each iteration, the cancer mask in the target image is deformed according to the non-rigid transformation parameters that are recovered during the previous iteration, while the additional control points continue to be placed outside the cancer mask. The complete inter-patient data registration is captured via the algorithm below:

**Input**: Template image $A$, target image $B$, initial control points $\Lambda_1$, number of iteration $M$.

**Output**: Non-rigidly transformed target image $B'$.

BEGIN

Apply affine registration: $\theta(B \rightarrow A) \Rightarrow B'$.

for $i = 1$ to $M$

Simplex search to find the optimal displacement for control points $\Delta\Lambda_i$.

$\Lambda_i + \Delta\Lambda_i \Rightarrow \Lambda_i$.

Apply TPS transformation to update the target image: $\theta_{TPS}(B' \rightarrow A) \Rightarrow B'$.

Evenly increase the number of TPS control points in the non-cancerous regions of the two images: $\Lambda_i \Rightarrow \Lambda_{i+1}$

end

END

Figure 3 gives an illustrative example of the inter-patient registration through the adaptive modification of TPS control points. The number of control points gradually increases over 3 iterations (as shown in Figure 3(a) to Figure 3(c), respectively). The red contours indicate the cancer masks on the template image, and green contours indicate the cancer masks on the target image.

Following the registration of the T2 MR image from 14 patients to the selected template T2 MR image, the DCE MR images of these 14 patients were also registered to the template DCE MR images. Figure 4 gives an example of this type of inter-patient data registration of T2 MRI, where Figure 4(a) is the template image, Figure 4(b) is the target image, Figure 4(c) is the registration result, and Figure 4(d) shows the overlay of the two images using checkerboard pattern after registration. It can be seen that after the non-rigid inter-patient data registration, the two images have been conformed into a common spatial coordinate frame. With all the multi-modal/multi-protocol data across multiple patients now in this frame, further analysis of these atlas data can be carried out.
3.4 Constructing a data-driven atlas

3.4.1 Feature extraction

Following the intra- and inter-patient data registration, a number of image attributes can be extracted from every voxel in the multi-functional data atlas. While one could associate each voxel in the data atlas with several hundreds of features (e.g. textural attributes in [7] [23]), in this work, we limit ourselves to extracting and exploring (a) T2-w pixel intensity, (b) wash-in and (c) wash-out rates of the contrast agent on DCE MRI.

3.4.2 Parametric representation of features within disease spatial atlas

For each type of image feature $\Psi$ in the atlas, we have a fused image $C^\Psi = (C, f^\Psi)$, where $C$ is a set of spatial coordinates $c \in C$ and $f^\Psi(c)$ represents the feature distribution for each image feature $\Psi$ across $K$ patients. Formally this can be expressed as $f^\Psi(c) = \{f^\Psi_i(c) | i \in \{1, \ldots, K\}\}$, where $f^\Psi_i(c)$ represents the feature value obtained at location $c \in C$ for $i^{th}$ patient study. Figure 5 give an example. In Figure 5(a) the image feature $\Psi$ is the intensity of T2 MRI and in Figure 5(b) the image feature is the wash-out value computed from DCE MRI.

Since $f^\Psi(c)$ represents a feature distribution for multiple observations $f^\Psi_i(c), i \in \{1, \ldots, K\}$, it can be described via a mean $E(f^\Psi(c))$ and standard deviation $\sigma(f^\Psi(c))$:

$$E(f^\Psi(c)) = \frac{1}{K} \sum_{i=1}^{K} f^\Psi_i(c), \quad (5)$$

$$\sigma(f^\Psi(c)) = \sqrt{\frac{1}{K} \sum_{i=1}^{K} (f^\Psi_i(c) - E(f^\Psi(c)))^2}. \quad (6)$$

Additionally, for two different features ($\Psi_1$ and $\Psi_2$), we can explore the covariance $\Sigma(f^\Psi_1(c), f^\Psi_2(c))$ between feature distributions $f^\Psi_1(c)$ and $f^\Psi_2(c)$ at every $c \in C$:

$$\Pi(f^\Psi_1(c), f^\Psi_2(c)) = E((f^\Psi_1(c) - E(f^\Psi_1(c))) \cdot (f^\Psi_2(c) - E(f^\Psi_2(c)))). \quad (7)$$

3.4.3 Correlation of disease signatures between data driven and spatial atlases

Following construction of the spatial and data-driven atlases, we wished to explore which, if any, of the parametric disease representations are highly correlated to the spatial disease probability map (Figure 6(d)). Figure 6(d) shows the prostate cancer spatial atlas together with representative examples of the cancer masks from different patients (Figures 6(a)-(c)). For example, in this cancer spatial atlas, the cancerous regions are more likely to appear in the left and bottom left of the prostate (note the relatively brighter regions in Figure 6(d) which are also highlighted by red arrows) while the cancer is less likely to occur in the central region of the prostate (note the darker regions in Figure 6(d) highlighted by white arrow).
Figure 5. Feature distribution for (a) image intensity for 3 Tesla T2 MRI, and (b) wash-out value for 3 Tesla DCE MRI.

Figure 6. Construction of the spatial atlas (d) by aggregating images with overlaid cancer masks from different patients ((a)-(c)). The image intensity in the spatial atlas (d) represents the spatial frequency of disease occurrence at every voxel, where darker intensities reflect lower probability of cancer occurrence (as indicated by the white arrow) and higher intensities reflect higher probability of cancer occurrence (as indicated by the red arrows).

Figure 7 shows our preliminary investigations in identifying the most discriminatory multi-functional MR imaging signatures for prostate cancer. Note that the aim of the experiments was to demonstrate the utility of our atlas framework to facilitate disease signature discovery. We do not claim to have necessarily identified these signatures in this work. Figures 7(a)-(d) show the colormaps for the standard deviation of the wash-out value for DCE MRI, the mean wash-in value for DCE MRI, the covariance between the T2 MRI and the wash-in value for DCE MRI, and the standard deviation of the wash-in value for DCE MRI, respectively obtained across 15 studies. In each of Figures 7(a)-(d), the brighter color (red and yellow) indicates a higher value than the darker color (cyan and blue). Note that unlike the cancer spatial atlas shown in Figure 6(d), these figures are only parametric representations of image features and not cancer likelihood maps. For the purposes of comparison, the prostate cancer spatial atlas shown previously in Figure 6(d) is reproduced in Figure 7(e). Figure 7(f) shows the cancer detection result on DCE MRI using the 3 Time Point (3TP) scheme [29], which is based on pharmacokinetic curve fitting to identify wash-in and wash-out points (i.e. time points at which the lesion begins to take up and flush out the contrast agent). Based on the rate of the contrast agent uptake and wash out, the 3TP classifier assigns a red (malignant), blue (benign), or green (indeterminate) label to each pixel. Note that regions identified as cancerous by the 3TP classifier do not show very good correlation with the spatial atlas in Figure 7(e).

Standard deviations of the wash-out value (Figure 7(a)) and the mean wash-in value for DCE MRI (Figure 7(b)) do not appear to correlate well with disease patterns on the spatial atlas in Figure 7(e). Nevertheless, features on the other hand do appear to be better correlated with the prostate cancer extent (covariance between the T2 MRI and the wash-in value for DCE MRI shown in Figure 7(c)). Similarly, the standard deviation of
The wash-in value for DCE MRI (shown in Figure 7(d)) appears to be well correlated with regions of higher probability of cancer occurrence (as indicated by red arrows in Figure 7(e)).

4. CONCLUDING REMARKS

A spatial disease atlas that simultaneously encapsulates population based statistics of functional, structural, and metabolic data on a per voxel basis is very useful for a quantitative study and discovery of imaging markers for disease. Such an atlas would be highly relevant for educational purposes of training and teaching radiology residents and fellows imaging signatures of disease. Moreover, such an integrated spatial and data-driven population based atlas can be used in training a computer-aided diagnosis (CAD) system for predicting precise location and extent of disease in patients.

In this paper, we presented a comprehensive, quantitative framework for the construction of a disease atlas from multi-protocol, structural and functional imaging data. The framework comprises 3 modules: (a) determination of disease spatial extent, (b) construction of disease spatial atlas, and (c) feature extraction to construct the data-driven atlas. In particular, we also presented a novel inter-patient data registration method for handling large pathological variations. In this work, we applied our framework to the specific problem of constructing a structural-functional, in vivo, high resolution MRI prostate cancer atlas. Preliminary results showing the efficacy of our atlas construction methods, including intra-, inter-patient data registration, and parametric data visualization were presented in the context of 15 patient data sets. Preliminary experiments with various parametric representations of the prostate cancer atlas data appear to suggest that some MRI-based structural-functional disease signatures might be more indicative of the CaP patterns than the traditional 3TP scheme. Nevertheless, as we gradually include additional patient data into this disease atlas as well as evaluate alternative parametric...
representations of the atlas data, we expect that better imaging signatures for prostate cancer will begin to be discovered.

While the experiments with the cancer atlas were in 2D, our methods are extensible to 3D. In constructing the spatial and data driven atlases for the prostate, a single 2D slice from the mid-gland of the prostate was selected by a pathologist, with an image from one patient being chosen as the template, and all other images being registered to the template. A more appropriate approach may be the groupwise registration of all the sample images [30], an approach we intend to explore in future work.

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