A prostate MRI atlas of biochemical failures following cancer treatment

Mirabela Rusua\textsuperscript{a}, John Kurhanewicz\textsuperscript{b}, Ashutosh Tewari\textsuperscript{c}, Anant Madabhushi\textsuperscript{a,*}

\textsuperscript{a}Case Western Reserve University, Cleveland, Ohio; \textsuperscript{b}University of California San Francisco, San Francisco, California; \textsuperscript{c}Icahn School of Medicine at Mount Sinai Hospital, New York, New York; \textsuperscript{*}Corresponding author

ABSTRACT

Radical prostatectomy (RP) and radiation therapy (RT) are the most common treatment options for prostate cancer (PCa). Despite advancements in radiation delivery and surgical procedures, RP and RT can result in failure rates as high as 40% and >25%, respectively. Treatment failure is characterized by biochemical recurrence (BcR), which is defined in terms of prostate specific antigen (PSA) concentrations and its variation following treatment. PSA is expected to decrease following treatment, thereby its presence in even small concentrations (e.g., 0.2 ng/ml for surgery or 2 ng/ml over the nadir PSA for radiation therapy) is indicative of treatment failure. Early identification of treatment failure may enable the use of more aggressive or neo-adjuvant therapies. Moreover, predicting failure prior to treatment may spare the patient from a procedure that is unlikely to be successful. Our goal is to identify differences on pre-treatment MRI between patients who have BcR and those who remain disease-free at 5 years post-treatment. Specifically, we focus on (1) identifying statistically significant differences in MRI intensities, (2) establishing morphological differences in prostatic anatomic structures, and (3) comparing these differences with the natural variability of prostatic structures. In order to attain these objectives, we use an anatomically constrained registration framework to construct BcR and non-BcR statistical atlases based on the pre-treatment magnetic resonance images (MRI) of the prostate. The patients included in the atlas either underwent RP or RT and were followed up for at least 5 years. The BcR atlas was constructed from a combined population of 12 pre-RT 1.5 Tesla (T) MRI and 33 pre-RP 3T MRI from patients with BcR within 5 years of treatment. Similarly, the non-BcR atlas was constructed based on a combined cohort of 20 pre-RT 1.5T MRI and 41 pre-RP 3T MRI from patients who remain disease-free 5 years post treatment. We chose the atlas framework as it enables the mapping of MR images from all subjects into the same canonical space, while constructing both an imaging and a morphological statistical atlas. Such co-registration allowed us to perform voxel-by-voxel comparisons of MRI intensities and capsule and central gland morphology to identify statistically significant differences between the BcR and non-BcR patient populations. To assess whether the morphological differences are valid, we performed an additional experiment where we constructed sub-population atlases by randomly sampling RT patients to construct the BcR and non-BcR atlases. Following these experiments we observed that: (1) statistically significant MRI intensity differences exist between BcR and non-BcR patients, specifically on the border of the central gland; (2) statistically significant morphological differences are visible in the prostate and central gland, specifically in the proximity of the apex, and (3) the differences between the BcR and non-BcR cohorts in terms of shape appeared to be consistent across these sub-population atlases as observed in our RT atlases.

Keywords: gland morphology, biochemical recurrence, MRI atlas, prostate cancer

1. DESCRIPTION OF PURPOSE

Radical prostatectomy (RP) and radiation therapy (RT) are the most common treatment strategies for clinically localized prostate cancer (PCa), accounting for roughly 110,000 annual interventions in US alone.\textsuperscript{1,2} Despite the good prognosis associated with treating low grade PCa, disease recurrence following either treatment occurs frequently. At 5 years post treatment, biochemical recurrence (BcR) occurs in up to 40% of patients\textsuperscript{3} undergoing RP and more than 25% of patients\textsuperscript{4} treated via RT. BcR is generally defined in terms of PSA concentrations and its variations following treatment, although the absolute thresholds vary based on the treatment type. A PSA concentration > 0.2 ng/ml\textsuperscript{5} indicates BcR following RP, while concentrations > 2 ng/ml\textsuperscript{5} from the lowest value post-RT, also referred to as the PSA nadir, indicate BcR following RT.
The early prediction of recurrence is essential, as BcR is prognostic of disease progression, metastasis, and disease-related mortality. Predicting which patients might experience BcR would enable the early administration of more aggressive or neo-adjuvant therapies and may potentially improve patient outcome. Moreover, if obtained prior to treatment, such predictions might facilitate choosing alternative therapies to spare the patient from a procedure that is likely to fail.

Pre-treatment nomograms that employ statistical models based on patient specific risk criteria have been introduced to predict BcR post-treatment. For example, the Kattan nomograms predict 5 year cancer-free likelihood following RP or RT by incorporating pre-treatment PSA, biopsy Gleason score and clinical stage. Additionally, Kattan nomograms predicting BcR post RT also include radiation dose. Other approaches used MRI alone or in combination with magnetic resonance spectroscopy (MRS) or molecular profiles to improve the prediction of BcR. These studies employ qualitative, reader-derived MRI measurements of disease, such as the number of sextants involving the index lesion, tumor volume, extracapsular spread or seminal vesicle invasion. However, to our knowledge, no study to date has investigated characteristics on MRI that are correlated with BcR following RT or RP.

In this study, we focus on identifying imaging and morphological differences associated with BcR that are visible on pre-treatment MRI between patients with and without BcR. The use of treatment planning MRI allows the study of differences independent of the treatment, while facilitating the early intervention to adjust treatment.

In this work, we specifically test the hypothesis that differences exist in the anatomy and tissue appearance of the prostate which may provide clues regarding BcR risk at 5 years after the treatment. Tiwari et al. has shown that MRI can distinguish indolent from aggressive cancers, the latter of which are also more likely to cause BcR. In this work, we test whether BcR can be predicted by pre-treatment MRI intensity or gland shape.
structures by combining anatomic surface and intensity similarity terms in the optimization process. Such anatomic constraints are required to account for the large variability in appearance and shape of the prostate and its anatomical substructures, the central gland and peripheral zone.\textsuperscript{15} The resulting prostate statistical atlas is composed of 1) a statistical MRI intensity atlas, 2) a morphological atlas of the prostate, and 3) a morphological atlas of the central gland.

The prostate atlas, $A_B$, was constructed for the patients who had BcR following either treatment, while $A_{NB}$ included subjects without BcR at 5 years following treatment. Moreover, treatment-specific atlases were constructed from the cohorts stratified by treatment strategy. The RP atlas, $A_B$(RP), was constructed from 33 subjects with BcR within 5 years, while 41 patients were included in the non-BcR atlas, $A_{NB}$(RP). The RT BcR atlas, $A_B$(RT), incorporated 12 patients, whereas 20 patients were included in the non-BcR atlas, $A_{NB}$(RT). The atlas construction procedure allowed us to map both populations into the same canonical space, enabling voxel-by-voxel comparisons via the Wilcoxon test. To assess whether the morphologic and intensity differences ascertained between the BcR and non-BcR atlases for RT were significant, we created atlases from sub-populations within the BcR and non-BcR cohorts and evaluated the differences between these populations. The objective of this experiment was to determine whether differences observed were real or by random chance resulting from the natural variability of the prostate.

The rest of this paper is organized as follows. In Section 2, we describe the anatomically constrained registration framework and its application to construct the BcR and non-BcR atlases. Section 3 introduces and discusses the results of the various comparative experiments performed. Finally, in Section 4 we discuss the implications of our findings.

2. METHODOLOGY AND EXPERIMENTAL DESIGN

2.1 Preprocessing

Bias field correction via low-pass filtering approach described in\textsuperscript{17} was applied to the MRI prior to atlas construction. Moreover, a histogram alignment was performed to correct the inter-patient MRI intensity drift, allowing for per voxel MRI intensity comparisons.

2.2 Atlas construction framework

The construction of the BcR atlas $A_B$ and non-BcR atlas $A_{NB}$ was accomplished using the anatomically constrained registration framework, previously described in.\textsuperscript{15} A summary of the atlas construction framework is provided below, and the notations used in this work are outlined in Table 1. The framework uses an iterative registration approach to simultaneously create the MRI intensity and shape atlases while increasing the degrees of freedom of the optimized transformation from a simple affine to an elastic deformation.

In the first step, the outline of the prostate and central gland are obtained through interactive segmentation using either 3D Slicer\textsuperscript{18} or MeVisLab.\textsuperscript{19} Next, a first atlas is created from all datasets once the MRI is centered and isotropically scaled to ensure a constant prostate volume, defined here as the median prostatic volume in the input cohort. The atlas is created via median filtering of the MRI intensity and the prostate and central gland outline of all subjects. The framework generates 1) an MRI intensity atlas, denoted by $A^M$, 2) a statistical shape atlas of the prostate, $A^{pr}$ and 3) a statistical shape atlas of the central gland $A^{cg}$. This first atlas served as registration template for the second step, affine registration. Following the affine registrations, the atlas is updated and used as a reference template for the deformable registration step. The final atlas is obtained via median filtering of the elastically aligned MRI.

A combination of MRI intensity similarity and regional overlap defined relative to the prostate and central gland shapes are used to drive the registration of every subject $X_i$, $\forall i \in \{1, \ldots, N\}$ to the template atlas $A$:

$$\psi(A, X_i^\sigma) = I_2(A^M, X_i^M) + \sum_{\sigma \in \{cg, pr\}} w^\sigma \cdot \psi^\sigma(A^\sigma, X_i^\sigma),$$

where $X_i^\sigma$, $\forall i \in \{1, \ldots, N\}$, $\sigma \in \{M, cg, pr\}$ represents the MRI intensity, the prostate (pr) and the central gland (cg) shapes of subject $X_i$. $A$ is the template atlas composed of $A^\sigma$, $\sigma \in \{M, cg, pr\}$. The mutual information,\textsuperscript{20}

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\[ I_2 \text{ is used to assess the similarity of MRI intensities, while } \psi^\sigma(\mathcal{A}^\sigma, \mathcal{X}^\sigma_i) \text{ quantifies the alignment of the anatomic structures } \sigma \in \{cg, pr\}, \text{ and } w^\sigma \text{ is an empirically determined weight}.^{15} \text{ In this work, we choose the normalized squared error to evaluate the regional alignment.} \]

### 2.3 BcR and non-BcR atlas construction

The MRI, prostate shape and central gland shape atlases are constructed for the BcR and the non-BcR cohort, resulting in \( \mathcal{A}^\sigma_\theta, \sigma \in \{M, pr, cg\}, \theta \in \{B, NB\} \). Moreover, due to the patient specific criteria for RT or RP, we not only constructed the combined RP+RT atlases, denoted by \( \mathcal{A}_B \) and \( \mathcal{A}_{NB} \) respectively, but we also generated the individual atlases \( \mathcal{A}_B(RP) \) and \( \mathcal{A}_{NB}(RP) \) for the RP cohorts, and \( \mathcal{A}_B(RT) \) and \( \mathcal{A}_{NB}(RT) \) for the RT cohorts (see Table 1).

### 2.4 Experiments

We performed 3 experiments. In experiment E1 (see Section 2.4.1), we investigate the MRI differences that can be identified between patients with or without BcR within 5 years following treatment. Experiment E2 (see Section 2.4.2) was performed to assess the statistically significant differences between the morphology of the prostate and central gland of the BcR vs non-BcR patients. Finally, experiment E3 (see Section 2.4.3) is designed to assess morphological differences within the BcR and non-BcR cohorts independently.

#### 2.4.1 Experiment E1: Voxel-by-voxel comparison of MRI intensities

The atlas construction enables the mapping of all patients within a common canonical space, which allows us to test whether differences exist between MRI intensities of BcR and non-BcR patients on a per-voxel basis. The statistical significance of MRI differences is assessed using the non-parametric Wilcoxon test. Here, we test whether the mean MRI intensity is statistically significantly different between the \( N \) subjects used to generate \( \mathcal{A}_B \) and the \( M \) subjects considered when creating \( \mathcal{A}_{NB} \). The Wilcoxon test was performed for each voxel \( c \in C \), yielding a statistical significance map. We chose a lower significance level \( \alpha = 0.01 \) to account for the large

![Table 1: Symbols and notations employed in this paper.](http://proceedings.spiedigitallibrary.org/)

<table>
<thead>
<tr>
<th>Symbol</th>
<th>Description</th>
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<tbody>
<tr>
<td>( \mathcal{A} )</td>
<td>Prostate atlas, composed of ( \mathcal{A}^\sigma, \sigma \in {M, pr, cg} )</td>
</tr>
<tr>
<td>( \mathcal{A}^{M} )</td>
<td>MRI intensity atlas</td>
</tr>
<tr>
<td>( \mathcal{A}^{N} )</td>
<td>Statistical shape atlas, ( \sigma \in {pr, cg} )</td>
</tr>
<tr>
<td>( \mathcal{X}_i^\sigma = (C, f_i(c)) )</td>
<td>Subject ( i ) scene with ( \forall c \in C, f_i(c) ) represents data at location ( c, \sigma \in {M, pr, cg} )</td>
</tr>
<tr>
<td>( \mathcal{X}_i^{M} )</td>
<td>MRI intensity scene of subject ( \mathcal{X}_i )</td>
</tr>
<tr>
<td>( \mathcal{X}_i^{N} )</td>
<td>Outline scene of the region ( \sigma \in {pr, cg} ) for subject ( \mathcal{X}_i )</td>
</tr>
<tr>
<td>( I_2 )</td>
<td>Mutual information</td>
</tr>
<tr>
<td>( \psi^\sigma )</td>
<td>Surface similarity metric for ( \sigma \in {pr, cg} )</td>
</tr>
<tr>
<td>( w^\sigma )</td>
<td>Weight associated with the surface ( \sigma \in {pr, cg} )</td>
</tr>
<tr>
<td>( N, M )</td>
<td>Subject count in the BcR and non-BcR cohort</td>
</tr>
<tr>
<td>( \mathcal{A}_\theta^\sigma )</td>
<td>Atlas ( \sigma \in {M, pr, cg} ) constructed from the cohort ( \theta \in {B, NB} )</td>
</tr>
<tr>
<td>( \mathcal{A}^B_{B\rightarrow NB} )</td>
<td>Difference between BcR and Non-BcR for ( \sigma \in {M, pr, cg} )</td>
</tr>
<tr>
<td>( \mathcal{A}_B )</td>
<td>BcR atlas of the combined RT + RP patient cohort</td>
</tr>
<tr>
<td>( \mathcal{A}_{NB} )</td>
<td>Non-BcR atlas of the combined RT + RP patient cohort</td>
</tr>
<tr>
<td>( \mathcal{A}_B(RP) )</td>
<td>BcR atlas of the RP patient cohort</td>
</tr>
<tr>
<td>( \mathcal{A}_{NB}(RP) )</td>
<td>Non-BcR atlas of RP patient cohort</td>
</tr>
<tr>
<td>( \mathcal{A}_B(RT) )</td>
<td>BcR atlas of the RT patient cohort</td>
</tr>
<tr>
<td>( \mathcal{A}_{NB}(RT) )</td>
<td>Non-BcR atlas of RT patient cohort</td>
</tr>
<tr>
<td>( \mathcal{A}_{B,k}, k \in {1,...,4} )</td>
<td>Atlas obtained from a subset of BcR subjects</td>
</tr>
<tr>
<td>( \mathcal{A}_{NB,l}, l \in {1,...,4} )</td>
<td>Atlas constructed from a subset of non-BcR subjects</td>
</tr>
</tbody>
</table>

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number of comparisons done in this study. Rejection of the null hypothesis indicates a statistically significant difference in the mean MRI intensities.

Moreover, we also computed the normalized mean difference between the BcR and non-BcR cohorts, and uses it to establish qualitative correlations with the statistical significance map, defined \( \forall c \in C \) by:

\[
D(c) = \frac{1}{M} \sum_{i=1}^{M} f_{B,i}(c) - \frac{1}{M} \sum_{j=1}^{M} f_{NB,j}(c)
\]

where \( f_{B,i}(c) \) and \( f_{NB,j}(c) \) represent the MRI intensities at location \( c \) for subject \( X_i \) from the BcR cohort and \( X_j \) from the non-BcR cohort, respectively. Large \( D(c) \) are expected to correspond to voxels that show statistically significant differences between the BcR and non-BcR patients, while values close to zero indicate similar MRI intensities when comparing BcR and non-BcR subjects.

2.4.2 Experiment E2: Variability in gland morphology

The atlas construction framework allowed us to generate the statistical shape of the prostate and central gland based on the cohorts considered. Statistical shapes of the prostate and central gland were computed for both \( A_B \) and \( A_{NB} \), and distances between these gland shapes were evaluated to estimate the inter-population variability in gland morphology. The non-parametric Wilcoxon test is used to investigate whether the levelset representations of the prostate surfaces and central glands are significantly different between \( A_B \) and \( A_{NB} \) using \( \alpha = 0.01 \). The levelset representation provides a continuous version of the region segmentations corresponding to different anatomic areas. We chose such a representation to limit boundary effects. Two tests were performed for each voxel \( c \), comparing the \( N \) levelset representations of the prostate surface and central gland in \( A_B \) to the \( M \) levelset representations in \( A_{NB} \). As in experiment E1, rejection of the null hypothesis indicates a statistically significant difference in the structural morphology of the gland and anatomical regions.

2.4.3 Experiment E3: Prostate morphological variability assessed within cohort

In order to assess whether the morphological differences observed in experiment E2 are meaningful, we also constructed four sub-atlases \( A_{B,k} \), \( k \in \{1, ..., 4\} \), from a randomly selected subset of patients of the RT BcR set. \( A_{NB,l} \), \( l \in \{1, ..., 4\} \), were constructed from the set of patients that did not have BcR. We estimate the intra-population variability in gland shape based on the four sub-atlases, and we estimate the variability as the average distances to the statistical shape of the prostate gland within each of the sub-population atlases.

2.5 Data Description

Table 2 summarizes the characteristics of the 106 patients included in this study. The 75 subjects included in the RP group had 1) biopsy confirmed cancer, 2) surgery to remove the prostate and 3) 3 Tesla(T) T2 weighted MRI acquired prior to the surgery using an endo-rectal coil. BcR was defined by 0.2 ng/ml PSA concentration. The median follow up period for the BcR patients was 10 months (range: 0-46 months), while the non-BcR patients had a median follow up period of 68 months (range 65-78).

The subjects included in the RT group had biopsy confirmed cancer, underwent either external beam RT or brachytherapy, and had 1.5T T2 weighted endo-rectal MRI acquired prior to treatment. The 12 BcR subjects were followed up for at least 20 months, with a median period of 59 months, and BcR was assessed at a median period of 47 months post treatment using either of the following two criteria: 1) increased PSA concentration of 2ng/ml or more above nadir PSA,\(^5\) or 2) medical evidence that PCa recurred as indicated by medical notes or follow-up intervention, e.g. brachytherapy. The 20 non-BcR subjects either did not have BcR during the entire follow-up period (median 87 months, with minimum 60 months of follow up) or had BcR after 5 years or more following RT (median 89 months with range of 73-118 months).
Table 2: Data description; \(|\) shows Gleason grade stratified as low (\(\leq 6\)), intermediate (7), high (\(\geq 8\)) and not available; \(|\) time provided in months showing median and range in parenthesis; \(|\) included in the non-BcR cohort was a subgroup of patients who had BcR failure later than 5 years (between 73-118 months).

<table>
<thead>
<tr>
<th>Atlas</th>
<th>Cohort</th>
<th>Status</th>
<th>Cohort Size</th>
<th>MRI Strength</th>
<th>Grade</th>
<th>Follow up</th>
<th>Failure time</th>
</tr>
</thead>
<tbody>
<tr>
<td>(A_B(RP))</td>
<td>RP</td>
<td>BcR</td>
<td>33</td>
<td>3.0T</td>
<td>1,25,8,0</td>
<td>46.5 (18-73)</td>
<td>10 (0-46)</td>
</tr>
<tr>
<td>(A_{NB}(RP))</td>
<td>RP</td>
<td>Non-BcR</td>
<td>41</td>
<td>3.0T</td>
<td>3,34,4,0</td>
<td>68 (65-78)</td>
<td></td>
</tr>
<tr>
<td>(A_B(RT))</td>
<td>RT</td>
<td>BcR</td>
<td>12</td>
<td>1.5T</td>
<td>8,3,1,0</td>
<td>59 (20-90)</td>
<td>47 (19-68)</td>
</tr>
<tr>
<td>(A_{NB}(RT))</td>
<td>RT</td>
<td>Non-BcR</td>
<td>20</td>
<td>1.5T</td>
<td>13,6,0,1</td>
<td>87 (60-123)</td>
<td>89 (73-118)</td>
</tr>
<tr>
<td>(A_B)</td>
<td>RT+RP</td>
<td>BcR</td>
<td>45</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>(A_{NB})</td>
<td>RT+RP</td>
<td>Non-BcR</td>
<td>61</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

3. EXPERIMENTAL RESULTS AND DISCUSSION

3.1 Experiment E1: MRI intensity atlas

In experiment E1, we constructed the BcR atlases of the combined cohort \(A_B\) (Figure 2a) and individual cohorts \(A_B(RP)\) (Figure 2e) and \(A_B(RT)\) (Figure 2i), as well as the non-BcR atlases of the combined cohort \(A_{NB}\) (Figure 2b) and individual cohorts \(A_{NB}(RP)\) (Figure 2f) and \(A_{NB}(RT)\) (Figure 2j). By constructing the atlases, the patients were projected in the same canonical space, which allowed us to make per-voxel comparisons of the same anatomic regions. Sharp hypo-intense boundaries of the prostate and the central gland can be observed indicating a good alignment of the anatomic regions (Figure 2a,b,e,f). The smaller number of patients included in the RT BcR cohort caused less defined boundaries within the MRI intensity atlas \(A_B(RT)\) (Figure 2i).
3.2 Experiment E1: MRI intensity differences

Figure 2 also shows the normalized difference $D$ (eq. 2) and the $p$-value to assess the statistical significance of these differences. The normalized mean differences revealed up to 30% differences between $A_M^B$ and $A_M^{NB}$. Furthermore, some of these differences were found to be statistically significant (column 4 in Figure 2). Such statistically significant differences were visible across the entire gland but were consistently found at the boundary of the central gland and peripheral zone, in the proximity of the apex. The RP atlases showed more structured statistically significant differences in MRI intensity particularly at the boundary of the central gland and peripheral zone. Such pronounced differences may be attributed to BcR in those patients that underwent radical prostatectomy. Although MRI differences appear larger when comparing the $A_B(RT)$ and $A_{NB}(RT)$ (Figure 2k), these differences are not typically statistically significant, in part due to the small RT population size.
3.3 Experiment E2: Morphological differences in the prostate

Figure 3 shows the morphological distances for the combined RP+RT cohort (Figures 3a-d) and the RP cohort alone (Figures 3e-h). These morphological distances are measured by the Euclidean distance of the mean regional shapes, $\sigma \in \{pr, cg\}$, obtained via the atlas construction framework. Figure 3 shows the apex of the prostate (Figures 3a,e), the prostate side (Figures 3b,f), the apex of the central gland (Figures 3c,g), and the side of the central gland (Figures 3d,h). Large differences are visible close to the apex for both the prostate and the central gland in both the RP+RT or RP cohorts. Moreover, statistically significant differences are apparent when comparing $A_{pr}^{B\rightarrow NB}(RT)$, $A_{pr}^{B\rightarrow NB}(RP)$, and $A_{CG}^{B\rightarrow NB}(RP)$ (Figure 4). The statistically significantly different regions are visible in the proximity of the apex both the prostate and central gland.

Figure 5 shows the statistically significant differences (Figures 5a-d) of prostate morphological distances $A_{pr}^{B\rightarrow NB}(RT)$ (Figure 5e-h) for the patients who had RT. Distances of up to 2.67 mm can be observed between
the prostate shape, indicating the existence of morphologic gland differences between the two populations. Statistically significant differences are visible on the rectal wall (Figure 5a) and on the prostate side (Figure 5c), while other regions do not show significant differences, attributable to the smaller population size.

3.4 Experiment E3: Morphological differences in the prostate

The intra-class variability in prostate shape was assessed for the BcR cohort via $A_{B,k}$ (Figures 5i-l) and non-BcR cohort via $A_{NB,l}$ (Figures 5m-p), $k, l \in \{1, 2, \ldots, 4\}$. Figures 5i-p indicate that the intra-class variability in gland morphology is larger in $A_{NB}(RT)$ compared to $A_{B}(RT)$. It is important to note that the inter-class morphologic differences (Figure 5e-h) surpass the intra-population variability, which barely reaches 2mm.

4. CONCLUDING REMARKS

In this work, we investigate imaging and morphological differences that may be associated with biochemical recurrence (BcR) following prostate cancer treatment by either radical prostatectomy or radiotherapy. In order to investigate these differences, we constructed prostate atlases for patients with and without BcR 5 years post treatment. Through the atlas construction, the pre-treatment MRI of the subjects were projected into the same canonical space, which allowed us to perform per-voxel comparisons within the spatially normalized images. Such comparisons were done relative to the MRI intensity and the prostate and central gland morphology.

Statistically significant MRI differences were observed between the BcR and non-BcR patients that had radical prostatectomy. These differences were visible at the border of the central gland and peripheral zone close to the apex. Similarly, statistically significant differences were observed near the apex in the atlas constructed from the combined radical prostatectomy and radiotherapy patients. On the other hand, the small sample size in the radiotherapy cohort prevented us from observing statistical significant differences in MRI intensity between the patients that had BcR and those that did not have BcR following radiation therapy. Moreover, morphologic differences in the prostate and the central gland shapes were localized towards the apex and were found to be statistically significant between the BcR and non-BcR populations, regardless of treatment. Furthermore, morphological differences were observed on the rectal wall of the prostate in the radiation therapy patients who had BcR versus those who did not have it 5 years post treatment. In the radiation therapy cohort, the differences between the BcR and non-BcR subjects were larger than the variability within each individual cohort (BcR or non-BcR) which suggests that the observed differences are meaningful. These results suggests that we may be able to predict early BcR even before treatment which may allow for early intervention via more aggressive or neo-adjuvant treatments.

The lack of precise mapping of cancer on MRI prevented us from quantifying the influence of cancer size and shape in assessing gland morphology variability. In future studies, we will attempt to carefully map the extent of tumor from the ex vivo prostatectomy specimens onto the pre-operative MRI for those patients in the radical prostatectomy cohort. Such mapping could allow us to build more detailed atlases for predicting biochemical recurrence following surgery. Moreover, we envision extending the current atlas to incorporate information pertaining to type of treatment, radiation dose, cancer grade or extra-capsular spread to predict risk of biochemical failure.

5. ACKNOWLEDGMENTS

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