Prostate Bed Motion During Post Prostatectomy Radiotherapy

by

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Graduate Program in Medical Physics
Duke University

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Q. Jackie Wu, Supervisor

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Shiva Das

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Devon Godfrey

Thesis submitted in partial fulfillment of the requirements for the degree of Master of Science in the Graduate Program in Medical Physics in the Graduate School of Duke University

2012
ABSTRACT

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Abstract

Purpose: To report the inter-fractional prostate bed motion (PBM), and its correlation to the mean anterior rectal wall and mean posterior bladder wall shifts during post prostatectomy radiotherapy using cone-beam computed tomography (CBCT).

Methods and Materials: A total of 70 CBCT and 8 planning CT scans from 8 patients treated with prostate bed radiotherapy were retrospectively analyzed. For each CBCT-CT pair, two rigid image registrations were performed: one based on surgical clips and the other based on pelvic bony anatomy. Each registration gave a displacement vector. The difference between the two registration displacements represented the PBM. In addition, rectum/bladder contours on CT and CBCT scans were compared to identify the organ wall motion. Shifts of the anterior rectal wall and posterior bladder wall were assessed by averaging the slice-by-slice distances between contours on two image sets, measured along an anterior-posterior line passing through the symphysis pubis. The correlation between the organ wall motions and PBM were calculated by the Pearson’s correlation coefficient. The difference between the cranial and caudal half of the anterior rectal wall shifts was evaluated using
Kruskal-Wallis test. The derived PTV-CTV margin was calculated using Marcel van Herk’s margin recipe[1].

**Results:** The mean prostate bed motion (PBM) in the left-right (LR), anterior-posterior (AP) and superior-inferior (SI) directions were \((0.1\pm0.8)\)mm, \((0.9\pm1.5)\)mm, and \((-0.4\pm1.8)\)mm, respectively. Pearson’s correlation coefficients between PBM and anterior rectal wall (whole length) shifts, between PBM and anterior rectal wall (cranial half) shifts, and between PBM and posterior bladder wall shifts, were 0.43, 0.47, and 0.67, respectively. Significant difference was found between cranial and caudal half of the anterior rectal wall shifts \((p<0.01)\). The derived PTV-CTV margin for LR, AP and SI motion was 3mm, 5mm, and 6mm, respectively, assuming daily radiographic alignment to bone.

**Conclusion:** The magnitude of PBM relative to pelvic bony anatomy in all three directions was small. The correlation between average anterior rectal wall shifts and PBM was weak-to-moderate, which may be due to rectum contouring inconsistency on the CBCT images. Possible sources for this inconsistency include: non-uniform rectal wall motion through its length, low soft tissue contrast on CBCT image, and artifacts caused by rectal filling and surgical clips. Significant correlation between average posterior bladder wall shifts and PBM
suggests bladder wall motion may also be a suitable surrogate for PBM in the AP direction.
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Lastly, I would like to thank my parents. They have been supporting me all the time.
1. Introduction

1.1 Background

In recent years, prostate bed radiation therapy after radical prostatectomy has been proven to improve biochemical relapse-free survival. For post radical prostatectomy, there is a 3% gain in biochemical-free survival per incremental Gray[2].

Dose escalation requires target delineation and delivery accuracy. As the target region is designed to tightly conform to the prostate bed prostate bed, small prostate bed motion may cause significant target miss or higher toxicity to critical structures. Although the European Organization for Research and Treatment of Cancer (EORTC) radiation oncology group proposed guidelines for target volume definition in post-operative radiotherapy[3], it is difficult to identify the soft-tissue structures on electronic portal imaging devices (EPID), orthogonal kV or even CBCT images. An array of studies on prostate bed motion (PBM) using rectal wall motion and/or surgical clips as surrogates have been published[3-5]. Piet Ost et al used the anterior rectal wall as the surrogate for the posterior border of the prostate bed[6]. By applying this indirect approach on CBCT images, Piet Ost et al[6] quantified the PBM and suggested 6-8 mm planning target volume (PTV) margins. Kupelian et al[7] used surgical clips as the surrogate for prostate bed on megavoltage CBCT images. This study reported that the magnitude of PBM is small and significant motion (>3mm) is infrequent. Ajay Sandhu et al[8] used surgical clips as the surrogate for prostate bed and monitored the PBM on orthogonal kV images.
using an on board imaging (OBI™) system (Varian Medical Systems, Palo Alto, CA). This study reported that, using surgical clips for image registration instead of bony anatomy, PTV margin could be reduced by 1-2mm. Tracy Klayton et al reported that localization and real-time tracking of the prostate bed via implanted Calypso® transponders can be used to improve the accuracy of plan delivery[9].

The aim of the present study is to report the inter-fractional prostate bed motion using CBCT imaging. In addition, the correlations between PBM and anterior rectal wall and posterior bladder wall shifts are assessed in the anterior-posterior (AP) direction.

1.2 Problem Description

In the current study, we have collected CT/CBCT image sets from 8 patients who were treated with post-prostatectomy radiotherapy. Before the treatment, positioning and immobilization were performed to match the skin marks. Then, CBCT images were acquired for PBM measurement and analysis, including the derivation of a suggested PTV-CTV margin[1, 6]. Because of the anatomical relationships among the surgical clips, posterior bladder wall, and anterior rectal wall (Figure.1), critical organ wall shifts are expected to affect the clips’ positions. Therefore, we measured the critical organ (bladder and rectum) wall shifts and their correlations to the PBM in the AP direction.
1.3 Disposition

Chapter 1 briefly introduced several related work on PBM and its relationship with critical organ wall shifts. In addition, a simple project description was presented.

Chapter 2 illustrates the important concepts relevant to this thesis, describes the background of this research project and methodologies. Chapter 3 introduces the methodology [Note: Looks like methodology is listed in both chap 3 and chap 4 which is confusing] and research resources specifically used in this thesis study. Chapter 4 presents the analysis results for PBM and critical organ wall shifts. Chapter 5 discusses PTV-CTV margin and issues/problems related to this study.
2. Basic Concepts

2.1 Radiotherapy for Prostate Bed
Approximately 15% to 25%[18] of patients who undergo radical prostatectomy for the treatment of localized prostate cancer will suffer cancer recurrence, manifested initially as the increase of serum prostate-specific antigen (PSA) level. Emerging evidence suggests that the initial pattern of failure with recurrent disease after prostatectomy is predominantly local[18] such as prostate bed or pelvic lymph nodes. Postoperative treatment strategies that target local persistence or recurrence may reduce the risk of systematic progression[19].

2.2 Prostate Bed
Though the definition of prostate bed is not the key issue in current work and we may even weaken the anatomical definition by using surgical clips as the surrogate for prostate bed[7], the definition of prostate bed helps us to have a better understanding of its relationship with surrounding soft-tissues.
2.2.1 Anatomical Definition

After radical prostatectomy, the prostate bed occupies mostly the area corresponding to the prostatic apex, with the bladder filling the space where the prostate was, and the rectum distending mostly superior to the apical area where the prostate bed is[7] (Figure 2).

![Anatomical changes after prostate is removed: rectum distends superiorly to apical area; bladder fills where the prostate was. (Photo courtesy of A.D.A.M. Medical Illustration Team)](image)

2.2.1.1 EORTC Guidelines

In 2007, EORTC[3] proposed guidelines (Appendix A) for target volume definition in post-operative 3DCRT for prostate cancer. The recommendations for the CTV are areas at the greatest risk for relapse after prostatectomy. Figure 3 illustrates a CTV contour example following EORTC guidelines.

Cranially: the bladder neck (Figure 3D) and seminal vesicles (Figure 3A, E-F);
Caudally: including the apex (15mm cranially from the penile bulb, Figure 3B);

Anteriorly: including the anastomosis and the urethral axis (Figure 3B, C).

Posteriorly: up to but not including the outer rectal wall (Figure 3D);

Laterally: up to the neurovascular bundles (if removed up to the ilio-obturator muscles) (Figure 3C, D);

---

Figure 3: Contouring example[3] for CTV for postoperative radiotherapy based on EORTC’s guidelines. A: sagittal plane; B-F: transverse planes from inferior to superior. 1: inferior margin at apex; 2: seminal vesicle remnants or fibrosis; 3: superior margin at bladder neck; 4: lateral margin at ilio-obturator muscles; 5: anterior margin includes urethral axis; 6: posterior margin near anterior rectal wall.

2.2.1.2 Radiation Therapy Oncology Group (RTOG) Guidelines

In 2010, the RTOG0534 protocol[10] proposed the definition of prostate bed for 3DCRT and IMRT(Appendix B). The CTV will extend from the top of the penile bulb inferiorly to just above the pubic symphysis superiorly. Laterally, the CTV will extend from the medial edge of one obturator internus muscle to the other. Anteriorly, the CTV will
include the entire bladder neck until above the pubic symphysis, where a gradual reduction off of the anterior bladder is made. Superiorly, above the pubic symphysis, at least the posterior 2 cm of bladder should be included in the CTV, as well as the area between the bladder and rectum, to the anterior rectal wall. The CTV should extend superiorly to cover any clips in the seminal vesicle bed and the seminal vesicle remnants if present and should extend at least 2 cm above the pubic symphysis. Posteriorly, the CTV is defined by the anterior-most aspects of the anus-rectum. In this clinical trial, the seminal vesicles or remnants that can be identified on CT scans should be included. Compared with EORTC guidelines, RTOG0534 provides more specific CTV definition. And there are some differences between EORTC guidelines and RTOG0534 in each direction.

Also mentioned in the protocol, the CTV may be increased based on the CT or CBCT scans during treatment. In addition to the definition of prostate bed for 3DCRT, RTOG0534 defined CTV for IMRT which is the same as that of 3DCRT[10].

2.2.2 Delineating Prostate Bed on CT/CBCT

Although the EORTC guidelines provide specific anatomical definitions for the prostate bed, difficulties exist in identifying the prostate bed from CT scans. Piet Ost et al[11] used CT alone to delineate the prostate bed following EORTC guidelines and showed only moderate observer agreement. Compared with CT, CBCT has higher background
noise and lower image contrast. Therefore, it is expected to be more difficult to
discriminate and delineate soft-tissue structures in CBCT.

Piet Ost et al suggest instead using postoperative features recommended by RTOG and
Wiltshire et al\cite{10, 12} guidelines. For example, they recommend a location 8mm below
vesicourethral anastomosis to define the caudal/inferior margin for prostate bed instead
of the apex\cite{13}.

### 2.3 Surgical Clips as the Surrogate for Prostate Bed

A viable marker for image-guided radiotherapy (IGRT) should have the following
characteristics: it should be identified easily and reproducibly, it should be stable over
the course of the treatment, and it should represent the target well\cite{14}. Kupelian et al\cite{7}
used surgical clips for CT/megavoltage CT (MVCT) images alignment. Though the clips
were mostly superior to the actual anastomosis, and defined a broader anatomic location,
Kupelian et al considered the clips as a surrogate for the general location of a typical
post prostatectomy radiotherapy target area. They also assessed the uncertainty of the
surgical clips to bone using an anthropomorphic phantom (-0.6±0.4 mm, 0.5±1.0 mm,
0.2±0.7 mm in the LR, SI, and AP directions, respectively).

### 2.4 Cone-beam CT (CBCT)

Cone-beam CT (CBCT) based on flat-panel technology is integrated with a medical
LINAC for therapy guidance\cite{15}. By comparing against planning CT, CBCT images may
be used to verify and correct the patient setup before dose delivery. Both kV and MV
beams have been utilized for cone beam imaging. On-board CBCT is becoming an integrated imaging technology that can yield unambiguous soft-tissue details at the time of treatment[16]. Figure 4 is an example of medical LINAC integrated with CBCT.

Figure 4: Varian Medical LINAC integrated with CBCT (Photo courtesy of Varian Medical Systems, Palo Alto, California, Inc. All rights reserved.)

2.5 Image Registration

One important step in imaging guide radiation therapy (IGRT) is registration of the planning CT and on-board CBCT. Various image registration algorithms have been proposed for clinical use[17]. During the registration process, the CBCT image is defined as the moving image and planning CT is defined as the target image. Moving image is registered with target image through the use of either manual or automated 3D image registration software (e.g, Smart Adapt®Varian, Velocity AI®). The rigid-body image registration process provides image shifts in x, y, and z directions (depending on the manufacturer, rotations can also be included)[17]. The movements acquired after the registration represent the corrections that should be applied to align the patient to the same treatment position.
3. Methods and Materials

A total of 70 CBCT and 8 planning CT scans from 8 patients treated with prostate bed radiotherapy were retrospectively analyzed. Five patients have received IMRT, and the other three received 3DCRT. Every patient received a prescribed dose of 66 Gy and was instructed to keep his bladder full and rectum empty before treatment. Contours on planning CTs were drawn by dosimetrists and attending physicians, while contours on CBCT images were drawn by dosimetrists and physicists. Contouring for CBCT was only performed for the purpose of this study and was not utilized for clinic treatment.

3.1 Rigid Image Registration

Velocity AI® was employed to perform rigid-body image registrations. Rigid-body registration in Velocity AI® reports translational and rotational corrections, but only the translational corrections were used in this study. Each registration yields a displacement in three directions (LR, AP, SI). Both pelvic bony anatomy and clips are reproduced with high contrast in CT/CBCT scans. Therefore, in order to improve the registration quality, it was necessary to adjust the contrast window to select the specific objects of interest for registration.
3.1.1 Rigid Image Registration Based on Pelvic Bony Anatomy

For registration based on pelvic bony anatomy, ROI should include femoral heads, pubic arch, sacrum, ischium, and ilium (Figure 6).

Figure 6: ROI for rigid-body registration based on pelvic bony anatomy. (a) transversal; (b) coronal

The contrast window was adjusted so that only bony anatomy was displayed (Figure 7.3). Velocity AI® was then used for automatic image registration between planning CT and CBCT image sets.
Figure 7: Flow chart for rigid-body image registration based on pelvic bony anatomy

After the registration, we reset the rotational correction and recorded the translational correction in three directions. We defined this vector ($[X_{SE}, Y_{SE}, Z_{SE}]$) as setup error (SE).

### 3.1.2 Rigid Image Registration Based on Surgical Clips

After the bony registration, registration was performed based upon surgical clips. A coarse registration without a selected VOI was initially performed to roughly align the image volumes, and then the final registration was performed with the VOI coned down to only include the region containing the surgical clips. Because clips in CBCT scans may be affected by artifacts, automatic registration based on clips was adjusted manually. An illustration for rigid-body registration based on surgical clips is shown in Figure 8.
The clips-based registration yielded a registration vector with 3 translational shifts and 3 rotations. The rotations were discarded, leaving only the translational shift components, which were defined as the total error (TE) vector ([X_{TE}, Y_{TE}, Z_{TE}]).

### 3.1.3 Prostate Bed Motion Measurement and Analysis

Total error (TE) and setup error (SE) from the two described types of image registrations were used for the PBM calculation[7, 8, 20].

$$\text{PBM measurement} = \text{TE-SE} = [X_{TE}, Y_{TE}, Z_{TE}] - [X_{SE}, Y_{SE}, Z_{SE}] \quad \text{Eq. 1}$$

For each patient had 7-9 CBCT images from which we computed 7-9 PBM measurements. We calculated the average and standard deviation of PBM measurements for each patient, and defined them as PBM_{pti} (Eq .2) and SD_{pti} (Eq .3).
Then we calculated the standard deviation of dataset PBM\(_{pti}\) \((i=1,2...8)\), and defined it as the standard deviation of systematic errors, \(\Sigma\) [1](Eq.4). We calculated the root mean square of dataset SD\(_{pti}\) \((i=1,2...8)\), and defined it as the standard deviation of random errors, \(\sigma\) [1](Eq.5).

\[
\Sigma = \sqrt{\frac{\sum_{i=1}^{8}(PBM_{pti} - \bar{PBM}_{pti})^2}{N - 1}}, N = 8 \quad \text{Eq.4}
\]

\[
\sigma = \sqrt{\frac{SD_{pti}^2 + SD_{pt2}^2 + \ldots + SD_{pt8}^2}{N}}, N = 8 \quad \text{Eq.5}
\]

Finally, the Van-Herk PTV-CTV margin recipe[1, 6] based on \(\Sigma\) and \(\sigma\) was used to calculate the PTV-CTV margin.

\[
\text{Margin} = 2.5 \Sigma + 0.7\sigma \quad \text{Eq.6[1]}
\]
3.2 Measurement of the Anterior Rectal Wall Shift

After the rigid image registration based on pelvic bony anatomy was performed, rectum contours on CT and CBCT scans were compared to identify the anterior rectal wall shift.

The anterior rectal wall shift was assessed by averaging the slice-by-slice distances between contours on two image sets along an anterior-posterior line passing through the symphysis pubis and spine (Figure 9a). We sampled the same length from all rectum contours in the image sets (Figure 9c-d) of a given patient, and calculated the average anterior rectal wall shift for each CBCT scan (Figure 9e-f).

![Flow chart for anterior rectal wall shift measurement](image)

Figure 9: Flow chart for anterior rectal wall shift measurement

For rectum contours in all CBCT scans, the contouring range was defined as follows:
superiorly: 0.75cm above the cranial PTV border; inferiorly: 0.75cm below the caudal PTV border (Figure 9b).

### 3.3 Measurement of the Cranial Half of the Anterior Rectal Wall Shift

Hoogman et al[21] separated the rectum into a caudal and a cranial part. The caudal part starts at the CT slice in which the levator ani muscle encloses the rectum and ends at the anus. The cranial part is the remaining part of the rectum. Hoogman et al claimed that the slice in which the levator ani muscle starts enclosing the outer rectal wall is easily recognizable.

We adopted Hoogman et al’s method in this study. In figure 10, slice “a” and “c” are two adjacent slices on CT (slice thickness is 2.5mm). In slice “a”, the levator ani muscle is still free from the rectum while it encloses the rectum in slice “c”. As such, we separate the rectum at slice “a” level (Figure 10.b).
Figure 10. Images (a) and (c) are adjacent axial CT slices (slice thickness = 2.5mm), whose levels are displayed with a dashed line in the corresponding sagittal views of images (b) and (d). The rectum and levator ani muscle (white arrows) can be identified on both axial slices. In slice “a”, the levator ani muscle is still free from the rectum. In slice “c”, it encloses the rectum. Hence, slice “a” belongs to the cranial rectum while slice “c” belongs to the caudal rectum.

For each patient, we plotted all the CBCT rectum contours and transferred them to the planning CT images (Figure 11); separated the rectum volume at the level where levator ani muscle starts enclosing the outer rectal wall on the CT image (as seen in the axial plane); and then measured the average cranial/caudal half of the anterior rectal wall shifts using the method described in section 3.2.
Since the distribution of the anterior rectal wall shifts was not necessarily the normal distribution, we applied the Kruskal-Wallis test to evaluate the differences among the average shifts of cranial half, caudal half and the whole length of the anterior rectal wall.

3.4 Measurement of the Posterior Bladder Wall Shift

After the rigid image registration based on pelvic bony anatomy, the posterior bladder wall shift was measured using the same method as section 3.2. (Figure 12)
Figure 12: Flow chart for posterior bladder wall shift measurement
4. Results.

4.1 Prostate Bed Motion

From 8 patients in this study, we acquired 70 PBM measurements; results are shown in Table 1.

Table 1: Mean, standard deviation of systematic errors, standard deviation of random errors and derived PTV-CTV margin

<table>
<thead>
<tr>
<th>PBM</th>
<th>$M_1$</th>
<th>$\Sigma$</th>
<th>$\sigma$</th>
<th>Margin</th>
</tr>
</thead>
<tbody>
<tr>
<td>LR (mm)</td>
<td>0.1</td>
<td>0.8</td>
<td>0.8</td>
<td>3</td>
</tr>
<tr>
<td>AP (mm)</td>
<td>0.9</td>
<td>1.5</td>
<td>1.2</td>
<td>5</td>
</tr>
<tr>
<td>SI (mm)</td>
<td>-0.4</td>
<td>1.8</td>
<td>1.3</td>
<td>6</td>
</tr>
</tbody>
</table>

Abbreviations: $M_1$=mean of PBM; $\Sigma$=standard deviation of systematic errors[1]; $\sigma$=standard deviation of random errors[1]; LR=left-right; AP=anterior-posterior; SI=superior-inferior.

Positive values indicate left, anterior or superior shift; margin recipe: $2.5 \Sigma+0.7 \sigma$ [1]

The PBM magnitudes in all directions are listed in Table 2.

Table 2: Mean magnitude of PBM

<table>
<thead>
<tr>
<th>PBM</th>
<th>$M_2$</th>
<th>$\geq2\text{mm}$</th>
<th>$\geq3\text{mm}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>LR (mm)</td>
<td>0.6</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>AP (mm)</td>
<td>1.5</td>
<td>23%</td>
<td>7%</td>
</tr>
<tr>
<td>SI (mm)</td>
<td>1.5</td>
<td>16%</td>
<td>17%</td>
</tr>
</tbody>
</table>

Abbreviations: $M_2$=mean shifts (magnitudes)

Figures 13-15 display the distributions of PBM in three directions.
Figure 13: PBM distribution in the LR direction. For the x axis, bar “-1” means 0<PBM <-1; bar “0” means 0<PBM <1; bar “1” means 1<PBM <2 etc.

Figure 14: PBM distribution in the AP direction

Figure 15: PBM distribution in the SI direction
The results of previous PBM studies are summarized in Table 3. The imaging technique and prostate bed surrogates used in each study are listed for clarity.

**Table 3: Overview of published data and current study**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Image Modality &amp; PB Surrogate</th>
<th>Patients Number/ CBCT scans</th>
<th>LR(mm)</th>
<th>AP(mm)</th>
<th>SI(mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mean of PBM</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Schiffner[20] et al</td>
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*Abbreviation: SD = standard deviation*
4.2 Anterior Rectal Wall Shifts

The correlation between average anterior rectal wall shift over whole length and PBM in AP direction for each patient is shown in Figure 16.

Figure 16: Correlation between anterior rectal wall shift (whole length) and PBM in AP direction.
The aggregate correlation between total anterior rectal wall shifts and PBM for all patients is displayed in figure 17.

![Correlation between anterior rectal wall shifts and PBM in the AP direction for all 8 patients](image)

**Figure 17**: Correlation between anterior rectal wall shifts and PBM in the AP direction for all 8 patients

### 4.3 Cranial Half of the Anterior Rectal Wall Shifts

The correlation between cranial anterior rectal wall shifts and PBM in the AP direction for all 8 patients is shown in figure 18.
Figure 18: Correlation between the cranial half of the anterior rectal wall shift and PBM in the AP direction.

The aggregate correlation between cranial anterior rectal wall shifts and PBM for all patients is displayed in figure 19.
Figure 19: Correlation between cranial half of the anterior rectal wall shifts and prostate bed motion in anterior-posterior direction for all 8 patients

For different parts of anterior rectal wall (whole length, cranial half, caudal half), shifts were plotted in figure 20. The anterior rectal wall shift of the caudal half, the cranial half, and the whole rectum is \(-0.29\pm1.19 \text{cm}, 0.37\pm0.63 \text{cm}, 0.16\pm0.53 \text{ cm}\), respectively.
Figure 20: Anterior rectal wall shifts of different rectum parts in CBCT scans. ‘-‘: posterior; ‘+‘: anterior

4.3 Posterior Bladder Wall Shifts

The correlation between average posterior bladder wall shift over its whole length and PBM in the AP direction is shown for each patient in figure 21.
Figure 21: Correlation between posterior bladder wall shift and PBM in the AP direction

The aggregate correlation between posterior bladder wall shifts and PBM for all 8 patients is displayed in figure 22.
Figure 22: Correlation between posterior bladder wall shifts and PBM in the AP direction for all 8 patients

\[ R^2 = 0.4394 \]

PBM in AP (mm)

Posterior bladder wall shifts (cm)

PBM-posterior.. bladder wall shift
5. Discussion

5.1 Prostate Bed Motion

This study shows a small systematic PBM shift in each direction (LR: 0.1±0.8mm, AP: 0.9±1.5mm, SI: -0.4±1.8mm). Our results, combined with PBM measurements from other studies (Table 3), indicate that the systematic displacements between prostate bed and pelvic bony anatomy in the LR, AP, and SI directions are small. In the LR direction, there was no PBM magnitude larger than 2mm; the maximum was 1.8mm. Ninety three percent of PBM magnitudes in the AP direction (maximum: 3.8mm) and 83% of PBM magnitudes in the SI direction (maximum: 4.3mm) were smaller than 3mm. PBM in these two directions may have been due to day-to-day bladder and/or rectum filling variations[9]. In the current study, the matching of surgical clips employed both automatic registration based on contrast and manual adjustment. This is because clips on CBCT are sometimes blurred or distorted (Figure 23), causing inaccuracy in automatic rigid registration.

Figure 23: Artifacts of surgical clips on CBCT
5.1.1 PTV-CTV Margin

PBM should be considered when assigning treatment margins. Our margin calculation suggests a relatively small but anisotropic PTV-CTV margin (LR: 3mm; AP: 5mm; SI: 6mm), assuming daily bony alignment via on-board imaging. Since the PBM is anisotropic in three directions (LR, AP, SI), a non-uniform PTV margin is recommended for reducing dose to critical organs/normal structures.

5.1.2 PBM vs. Anterior Rectal Wall

This study employed C. Fiorino’s beam’s eye view (BEV) projection[5] method to measure the organ wall shift and Hoogman’s method to separate the rectum volume. The average anterior rectal wall shifts (cranial half, caudal half, and whole length) were measured, and correlated with PBM in the AP direction. The correlation between PBM in the AP direction and the anterior rectal wall shift (whole length) is weakly-moderate (|r|=0.43). The correlation between PBM in the AP direction and the cranial half of the anterior rectal wall is also weakly moderate (|r|=0.47).

Differences between the shifts found in the cranial and caudal halves of the rectal wall are significant (p<0.01). Likewise, differences between shifts found in the caudal half of the rectal wall and those in its whole length are significant (p<0.01). No significant difference was observed in the shifts of the cranial half of the rectal wall and the entire length of the rectum (p>0.05). These results indicate that separating the rectum volume at mid symphysis pubis level is acceptable.
One problem during rectal wall contouring is human contouring inconsistency. This may be due to low image contrast and artifacts. Since rectal wall, filling and surrounding soft-tissues are of a similar contrast range, the rectal wall can be difficult to differentiate without any contrast adjustment (Figure 24, 25).

Figure 24: Adjusted image contrast by which rectal wall can be identified and correctly contoured. a: rectum contour on CT; b: rectum contour on CBCT

Figure 25: Potential rectum contouring inconsistency in adjacent slices due to low image contrast between filling and rectal wall

In addition, gas filling may cause artifacts which affect the CBCT image quality (Figure 26). Different contrast settings on the displayed CBCT images may lead to different interpretations when differentiating the rectal wall boundary. As shown in figure 26, the contrast settings may contribute to the difference between contours on CBCT (yellow)
and CT (red), which is about 1 cm in the example (white arrow, Figure 26a&c). In figure 26b, the contrast window is set to minimize the artifacts’ effect so that the rectal wall can be visually identified. The difference between the adjusted contour from CBCT (green) and the contour from CT (red) is reduced to 0.2 cm (black arrow, Figure 26c). By appropriate image contrast adjustment, we can partly correct for the human contour inconsistency. Therefore, the anterior rectal wall shift measurement will be more accurate.

Figure 26. a: Artifacts due to filling in CBCT. Red contour is rectum contour on CT, yellow contour was original rectum on CBCT; b: Green contour is the adjusted contour for rectum on CBCT; c: White arrow: anterior rectal wall shift based on original rectum contour on CBCT and CT; Black arrow: anterior rectal wall shift based on adjusted rectum contour on CBCT and CT.

One reason that may explain the weakly moderate correlation between PBM in the AP direction and anterior rectal wall shifts is the non-uniform rectal wall motion along the longitudinal axis (cranial-caudal). Filling in the cranial half of the rectum (Figure 27a, d) may cause large anterior rectal wall shift in this part of the rectum, while the caudal half of the rectum remains unchanged. In addition, in some cases, surgical clips were
implanted to lateral sides away from the rectal wall, and they may have different
displacement magnitude compared to the anterior rectal wall shift (Figure 27b).

Figure 27. a-b: Rectum contours on CT (yellow) and CBCT (red); c: Rectum contour on
CT scan (a little filling in rectum); d: Rectum contour on CBCT scan at the same level.

5.1.3 PBM vs. Posterior Bladder Wall

The correlation results of the current study suggest that the posterior bladder wall may
also be a reasonable surrogate for PBM in the AP direction. Based on our observation of
all bladder contours, there is no significant non-uniform shift caused by fecal content
along the posterior bladder wall. This may be a primary reason for the better correlation
between PBM in the AP direction and the posterior bladder wall.
6. Future Work

Future studies might focus on the dosimetrical distribution changes caused by the PBM measured in this study. In addition, the dosimetrical data could be used to calculate the tumor control probability (TCP) and normal tissue complication probability (NTCP) that would have resulted without correction for PBM.
Appendix A
EORTC guideline for target volume definition in post-operative radiotherapy for prostate cancer

Centrally: the urethra-vesical anatomosis;

Cranially: the bladder neck;

Caudally: including the apex(15mm cranially from the penile bulb);

Posteriorly: up to but not including the outer rectal wall, cranially including the most posterior part of the bladder neck;

Laterally: up to the neurovascular bundles(if removed up to the ilio-obturator muscles);

Anteriorly: including the anatomosis and the urethral axis.

In addition to the above high risk areas, EORTC also offered proposed margins:

a. 5mm in all directions(except the rectal wall) to account for microscopical extension;

b. Supplementary 5mm in posterior and lateral directions in the presence of incompletely respected extracapsular tumor extension (ECE), but excluding the rectal wall;

c. supplementary 5mm in the direction of microscopically involved tumor margins as reported by pathologist(except the rectal wall)

In all cases, the original site of the base of the seminal vesicles should be included. If cancer cells involved seminal vesicles, the guideline suggests including the original position and/or remnants of seminal vesicles.
Appendix B
RTOG0543 consensus on definition of prostate bed

1) Superiorly: The prostatic fossa CTV (PF-CTV) should extend superiorly from the level of the caudal vas deferens remnant. In some cases, the vas deferens remnant may be difficult to visualize. In the absence of gross disease or seminal vesicle remnants, the superior limit of the CTV should extend at least 2 cm and need not extend more than 3-4 cm above the level of the pubic symphysis. The consensus definition calls for “inclusion of the seminal vesicle remnants, if present, in the CTV if there is pathologic evidence of their involvement. However, inclusion of any seminal vesicle remnants seen is recommended.

2) Inferiorly: The PF-CTV should extend inferiorly to > 8-12 mm inferior to vesicourethral anastomosis (VUA). With axial CT imaging, the VUA can often be seen in the retropubic region as one slice below the most inferior urine-containing image (the bladder must be modestly full). Magnetic resonance (MR) imaging defines this landmark more clearly with the hyperintense urine signal on T2 images. Inferiorly, the border of the CTV should be at least 8-12 mm below the VUA. A sagittal reconstruction facilitates identification of the position of the VUA and the inferior border of the CTV below it. If visualization of the VUA is problematic due to image quality or surgical clip artifacts, the inferior limit of the CTV can extend to a level just above the penile bulb (same border as described above).
It should be noted that there was considerable discussion about this definition versus extending the inferior border of the CTV to just above the penile bulb; both definitions were deemed acceptable.

3) Anteriorly: Below the superior border of the pubic symphysis, the anterior border is at the posterior aspect of the pubis. The CTV extends posteriorly to the rectum where it may be concave at the level of the VUA. At this level the lateral border extends to the levator ani. Above the pubic symphysis the anterior border should encompass the posterior 1-2 cm of the bladder wall at the minimum and posteriorly it is bounded by the mesorectal fascia. At this level the lateral border is the sacrorectogenitopubic fascia. This is not well-defined in textbooks. If in question, the lateral border should extend to the obturator internus muscle.

4) Posteriorly: The CTV extends posteriorly to the anterior rectal wall, but may be somewhat concave around
References


10. Alan Pollack et al. RTOG0543: A Phase III Trial of Short Term and Androgen Deprivation with Pelvic Lymph Node or Prostate Bed Only Radiotherapy (Support) in Prostate Cancer Patients with a Rising PSA After Radical Prostatectomy. (2009).


