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ORIGINAL ARTICLE

Implementing daily soft tissue image guidance with reduced margins for post-prostatectomy radiotherapy: research-based changes to clinical practice

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Abstract

Introduction: We have previously demonstrated that daily soft tissue matching with reduced anisotropic margins provides an ideal balance between prostate bed coverage and meeting organ at risk constraints. The aim of this study was to evaluate the implementation of this approach in clinical practice. **Methods:** Thirty-eight radiation therapists (RTs) completed offline IGRT training involving six patients. After training was completed, this approach was implemented clinically. The first 24 patients were evaluated with a central review of match displacements and geographic miss (GM). An assessment of treatment times and planning parameters was also performed. **Results:** During offline training, the anterior–posterior (AP) match discrepancy had the largest mean variation ranging from −0.46 to 0.06 cm and undetected geographic miss occurred in 17% of alignments. The mean time taken to treat the first 24 patients ranged from 12.2 to 20.6 min. The smaller anisotropic margin resulted in similar target coverage but achieved reduced doses to the bladder (V65Gy from 36% to 27%, V40Gy from 54% to 51%) and rectum (V65Gy from 20% to 19%, V60Gy from 27% to 24%, V40Gy from 42% to 38%). The matches of 806 CBCT images in 24 patients were reviewed. The mean match ranged from −0.12 to 0.17 cm AP, −0.14 to 0.14 cm superior–inferior (SI) and −0.04 to 0.04 cm left–right (LR). An undetected geographic miss was found in the prostate bed in 17 (2.1%) images and lymph nodes in 2 (0.2%) images. **Conclusions:** Daily soft tissue IGRT with reduced anisotropic margins for post-prostatectomy radiotherapy has been successfully implemented. RTs performed better with real-time online matching than they did in offline training, perhaps influenced by having several RTs perform online matching. Daily soft tissue IGRT did not prolong treatment time.

Introduction

Approximately 30-40% of men require post-prostatectomy radiotherapy for rising PSA following a radical prostatectomy.[1] Previously published work from the Northern Sydney Cancer Centre (NSCC) has quantified that the prostate bed inter-fraction motion moves independently of the bony anatomy especially in the superior–inferior (SI) and anterior–posterior (AP) directions.[2] In a retrospective analysis, the degree of movement, the optimal planning target volume (PTV) expansion and best image-guided radiotherapy (IGRT) policy were investigated.[3] Anisotropic PTV expansions were found to decrease the risk of geographic miss with a larger expansion used in the upper portion of the prostate bed where the greatest motion was detected. Daily soft tissue alignment of the prostate bed using cone beam computed tomography (CBCT) also reduced the incidence of geographic miss. A major limitation of this previous study was that it was based on offline matching

by a single investigator and results might vary in the clinical environment.

There is limited literature documenting the accuracy of radiation therapist (RT) soft tissue image matching in post-prostatectomy patients. Campbell et al compared the accuracy of six RT's soft tissue matching of 60 CBCT images with both a radiation oncologist (RO) gold standard and a dual registration tool.[4] More research is required into evaluating the accuracy of RT soft tissue matching prior to changing IGRT policy for these patients.

The IGRT and PTV changes proposed have now been implemented into clinical practice at NSCC, and an evaluation of these changes was required. The aims of this retrospective study were to:

1. evaluate the offline training provided to the RTs,
2. time the effect of soft tissue matching on treatment delivery,
3. measure the degree of benefit of smaller anisotropic PTV expansions on planning parameters and
4. conduct a match accuracy audit of the first 24 patients treated with soft tissue matching and a smaller anisotropic PTV.

Methods

Prior to this study, patients were treated with daily bony anatomy matching with a larger anisotropic PTV margin as described in Table 1. On initiation of this programme, patients were treated with soft tissue matching and smaller anisotropic margins as determined by our previous offline work.[3] Ethics approval to conduct a retrospective implementation evaluation study was granted by the Northern Sydney Local Health District.

The matching technique involved firstly matching the planning computed tomography (CT) scan and CBCT scan to bony anatomy. The match was then adjusted to place the posterior edge of the clinical target volume (CTV) from the planning CT on the anterior rectal wall on the CBCT scan. The match was then further adjusted to align the soft tissue of the prostate bed and any surgical clips located within the prostate bed. Lymph node coverage was also checked if being treated. If staff were unable to cover all of the prostate bed, the patient was removed from the treatment couch and asked to alter their bladder or rectal filling as appropriate. A repeat CBCT was then performed.

Offline training

The RTs were provided with offline soft tissue IGRT training using CBCT images. These one-on-one training sessions were conducted by a single trainer on a training terminal using Offline Review (Varian Medical Systems, Palo Alto, CA, USA). Each training session took approximately 60 min. Firstly, the trainee was guided through the written procedure for the technique. This would take approximately 30 min and included talking through the examples shown in the procedure document and any questions about the technique would be discussed. The second half of the training was completed alone by the trainee. This involved matching six CBCT scans belonging to six different patients, three with surgical clips located in the prostate bed and three without. The images were selected to represent a simple match, a difficult match and a match where a geographic miss could not be avoided and hence a decision to intervene was required to address inadequate bladder and/or bowel preparations, for both the surgical clip and soft tissue patient cohorts. A gold standard match was required to assess the accuracy of the matches completed during training. To generate this, the trainer matched each of the images five times over a number of days. These matches were used to calculate the

Table 1. Post-prostatectomy planning target volume expansion and image guidance protocol

PTV expansion protocol			
Area of prostate bed	Direction of expansion	Previous NSCC PTV (cm)	New smaller anisotropic PTV (cm)
Upper	Anterior	1.5	1.0
	Posterior	1.0	1.0
	Superior	1.0	0.5
	Inferior	0.5	0.5
	Left	1.0	0.5
	Right	1.0	0.5
Lower	Anterior	0.8	0.5
	Posterior	0.8	0.5
	Superior	0.8	0.5
	Inferior	0.8	0.5
	Left	0.8	0.5
	Right	0.8	0.5
IGRT protocol			
		Previous IGRT policy	New IGRT policy
Matching technique		Bones	Soft tissue
Imaging type and frequency		CBCT: 1,2,3,5,10,15,20,25 kV/kV: all other fractions	CBCT: all fractions

cm, centimetre; NSCC, Northern Sydney Cancer Centre; IGRT, image-guided radiotherapy; CBCT, cone beam computed tomography; kV, kilovoltage.

mean of the trainer's intra-observer variability which was used as the match gold standard. After each image match, the trainee was required to document all geographic miss caused by bladder or rectal filling which would require intervention before treatment. A geographic miss was defined as any soft tissue and/or surgical clips contoured within the CTV on the planning CT scan being located outside the PTV on the CBCT scan. Of the six training patients, half were planned with a 2-field volumetric modulated arc radiotherapy (VMAT) technique and half with a 7- to 9-field intensity-modulated radiotherapy (IMRT) technique. A review of the training match accuracy was conducted by comparing the trainee matches with the trainer's mean image match results, and descriptive statistics were used to evaluate any differences.

Dosimetric evaluation

The first eight patients were planned with both the new and old PTV expansions to evaluate the benefit of the reduced margins on organs at risk (OAR) constraints. Seven patients were planned with a 2- to 3-field VMAT technique and one with a 7-field IMRT technique. Average dose volume histogram (DVH) curves were calculated for the CTV and PTV to assess prostate bed coverage, and for the rectum, and bladder.

Online IGRT evaluation

Soft tissue matching was completed online daily prior to treatment by two RTs. The first 24 patients treated with soft tissue matching and reduced anisotropic margins were identified. Twenty of whom were planned using a 2-3 arc VMAT technique and four with a 7- to 11-field IMRT technique. The online matches were reviewed by the trainer to evaluate matching accuracy. The AP, SI and left–right (LR) match discrepancy was recorded, and an assessment of geographic miss was made. This was then compared with the online match used for treatment using descriptive statistics.

Effect on treatment time

To measure the effect of the clinical practice changes in the treatment section, the appointment time recorded in the ARIA Oncology Information System (Varian Medical Systems, Palo Alto, CA, USA) for the first 24 patients was compared to the standard appointment time booked for post-prostatectomy patients.

Microsoft Excel (Microsoft Corporation, Redmond, WA, USA) and GraphPad Prism (GraphPad Software, La Jolla, CA, USA) were used to conduct statistical analyses on the collected data.

Results

Offline training

A total of 38 RTs completed the offline post-prostatectomy soft tissue IGRT training. Thirty-eight matches were completed per patient, with 114 matched to surgical clips and soft tissue, and 114 matched to soft tissue only. The mean and 95% confidence interval (CI) of the offline match discrepancy for each of the 6 patients are displayed in Figure 1. The AP match discrepancy had the largest variation with the mean of the six patients ranging from −0.46 to 0.06 cm. The 95% CI was also largest in this direction. The SI match discrepancy had a mean variation ranging from −0.03 to 0.29 cm. The LR demonstrated the smallest range of −0.07 to 0.03 cm. The match discrepancy was larger in the soft tissue cohort in all directions compared to the surgical clip cohort.

The detection of geographic miss was also assessed during offline training (Table 2). When reviewing all six patients, 16.7% of geographic misses were not detected. In the majority of cases, geographic miss was detected correctly with the exception of patient 5. In this case, the RTs detected a geographic miss when appropriate averaged matching would have avoided this. There was variation in geographic miss detection between the surgical clip and soft tissue matched cohorts with geographic miss detection correct in 96.5% of cases for surgical clip patients compared to 70.2% in soft tissue patients.

The number of matches that were outside of a 0.3 cm tolerance was also assessed (Table 2). In total, 32% of the matches indicated a match discrepancy outside of the 0.3 cm tolerance. There was a lower percentage of discrepancies in the surgical clip cohort with 13 images (11.4%) compared to 60 images (52.6%) in the soft tissue cohort.

The interventions documented by the RTs were investigated when the image matching discrepancy was larger than 0.3 cm (Table 2). Of the 73 images that were outside of the 0.3 cm tolerance, the RT had decided not to treat the patient in 66 (90.4%) of the images, therefore avoiding a geographic miss. The intervention rate was higher in the soft tissue cohort with 93.3% of images outside the 0.3 cm tolerance not being treated compared to 76.9% in the surgical clip cohort.

Dosimetric evaluation

Averaged DVH curves were calculated to determine the effect the new PTV expansion had on target coverage and OAR doses (Fig. 2). There was little effect on the

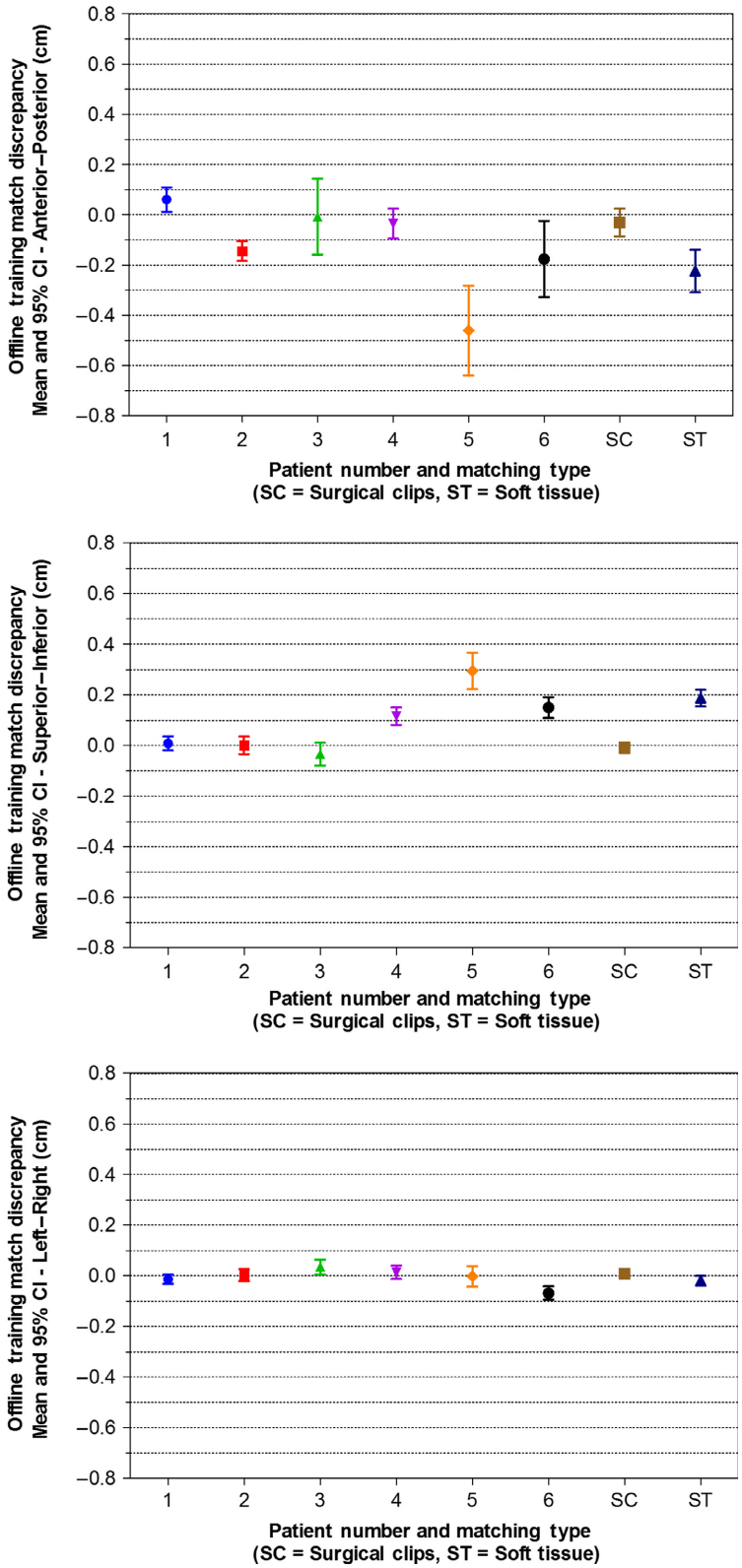

Figure 1. Offline training match accuracy. The offline training match accuracy mean and 95% confidence interval are displayed for the AP, SI and LR directions. The results for each of the patients and for the scans grouped into surgical clip or soft tissue matching techniques have been calculated.

Table 2. Offline training geographic miss and intervention detection

	Correct geographic miss detection	Match discrepancy > ±0.3 cm	Images with a match discrepancy > ±0.3 cm where RT decided not to treat
	Number of images/total images (percentage)	Number of images/total images (percentage)	Number of images/total images (percentage)
All patients	190/228 (83.3%)	73/228 (32%)	66/73 (90.4%)
Patient 1	38/38 (100%)	2/38 (5.3%)	0/2 (0%)
Patient 2	38/38 (100%)	2/38 (5.3%)	1/2 (50%)
Patient 3	34/38 (89.5%)	9/38 (23.7%)	9/9 (100%)
Patient 4	36/38 (94.7%)	4/38 (10.5%)	1/4 (25%)
Patient 5	7/38 (18.4%)	30/38 (78.9%)	29/30 (96.7%)
Patient 6	37/38 (97.4%)	26/38 (68.4%)	26/26 (100%)
Surgical clip cohort	110/114 (96.5%)	13/114 (11.4%)	10/13 (76.9%)
Soft tissue cohort	80/114 (70.2%)	60/114 (52.6%)	56/60 (93.3%)

cm, centimetre; RT, radiation therapist.

target coverage with both the CTV and PTV coverage similar.

The new PTV resulted in a reduction of the bladder V65Gy from 36% to 27% and the V40Gy reduced from 54% to 51%. The rectal V65Gy, V60Gy and V40Gy doses decreased from 20% to 19%, 27% to 24% and from 42% to 38%, respectively, with the use of the new PTV expansions.

Online IGRT evaluation

Eighteen (75%) of the 24 patients had surgical clips in situ that could be used to assist matching. Ten (41.7%) of whom also received lymph node treatment. Gross target volumes (GTV) were located in the prostate bed in 2 (8.3%) men and in the lymph nodes in 4 (16.7%) patients.

A total of 806 pre-treatment online CBCT images were reviewed offline by the trainer. The mean and 95% CI of the online match discrepancy compared to the trainer's offline review for each patient are displayed in Figure 3. The mean match discrepancy for the first 24 patients ranged from −0.12 to 0.17 cm AP, −0.14 to 0.14 cm SI and −0.04 to 0.04 cm LR. When the 24 patients were grouped into surgical clip versus soft tissue matched cohorts, there was little difference in the match discrepancies in all directions.

The image matching discrepancy between the trainer and the treatment RTs was also calculated with a 0.3 cm tolerance threshold used. Of the 806 images, a total of 32 matches (4%) were outside the 0.3 cm tolerance. The soft tissue cohort saw a larger percentage of these with 7% (13 images) compared to the surgical clip cohort with 3% (19 images).

All 806 CBCT images were also reviewed for undetected geographic miss (Table 3). An undetected geographic miss was found in the prostate bed in 17 (2.1%) images, lymph nodes in 2 (0.2%) images and lymph node GTV in 1 (0.1%) image.

Effect on treatment time

The time taken to treat the first 24 patients was calculated to determine the effect on treatment resources (Fig. 4). The standard appointment time slot scheduled for post-prostatectomy patients treated with both IMRT and VMAT is 15 min. The mean times for the first 24 patients ranged from 12.15 to 20.59 min. In total, 54.2% of the mean times achieved for each patient were under 15 min and 83.3% under 16 min. It is important to note that these patients also had post-treatment CBCT images acquired on the first three fractions then once weekly throughout their radiotherapy treatment course which was not previously standard practice. Patients 20 and 23 required a modified imaging protocol using daily dual CBCT and kV/kV orthogonal imaging as their lymph node volumes extended superiorly to include the para-aortic lymph nodes.

Discussion

Our previous work demonstrated that the ideal balance between coverage and OAR constraints was achieved with soft tissue matched IGRT and reduced anisotropic PTV margins.[3] However, this previous research was not performed in the clinical environment and was conducted by a single investigator.

Overall, the offline training demonstrated a relatively high rate of discordance and undetected geographic miss. The overall geographic miss rate on the training patients was 16.7%, with surgical clip patients having a lower rate of miss (3.5%) compared to the soft tissue patients

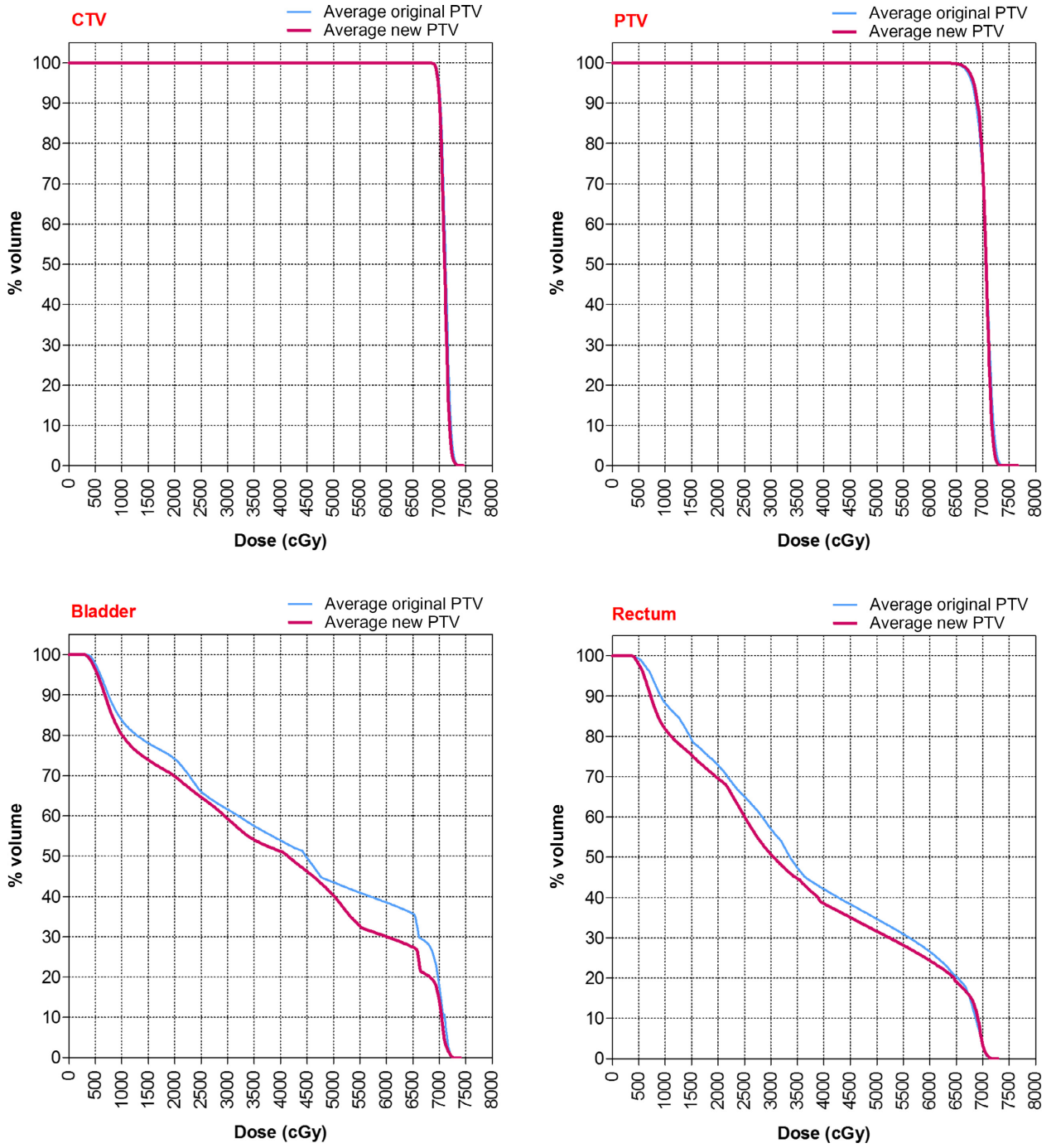

Figure 2. Averaged dose volume histograms for target and organ at risk structures for plans with the original and new planning target volumes. The first 8 patients were planned both with the original (purple) and new (red) PTV expansions. Averaged DVH curves were calculated for the target volumes (CTV and PTV) and organs at risk (bladder and rectum).

(29.8%). The number of matches outside of the 0.3 cm tolerance was also high (32%) with a greater discrepancy seen in the soft tissue matched patients (52.6%) compared to the surgical clip patients (11.4%).

The online evaluation results were more positive and demonstrated better concordance and geographic miss detection. The overall geographic miss rate was only 2.1% in patients with surgical clips in situ. There was also a

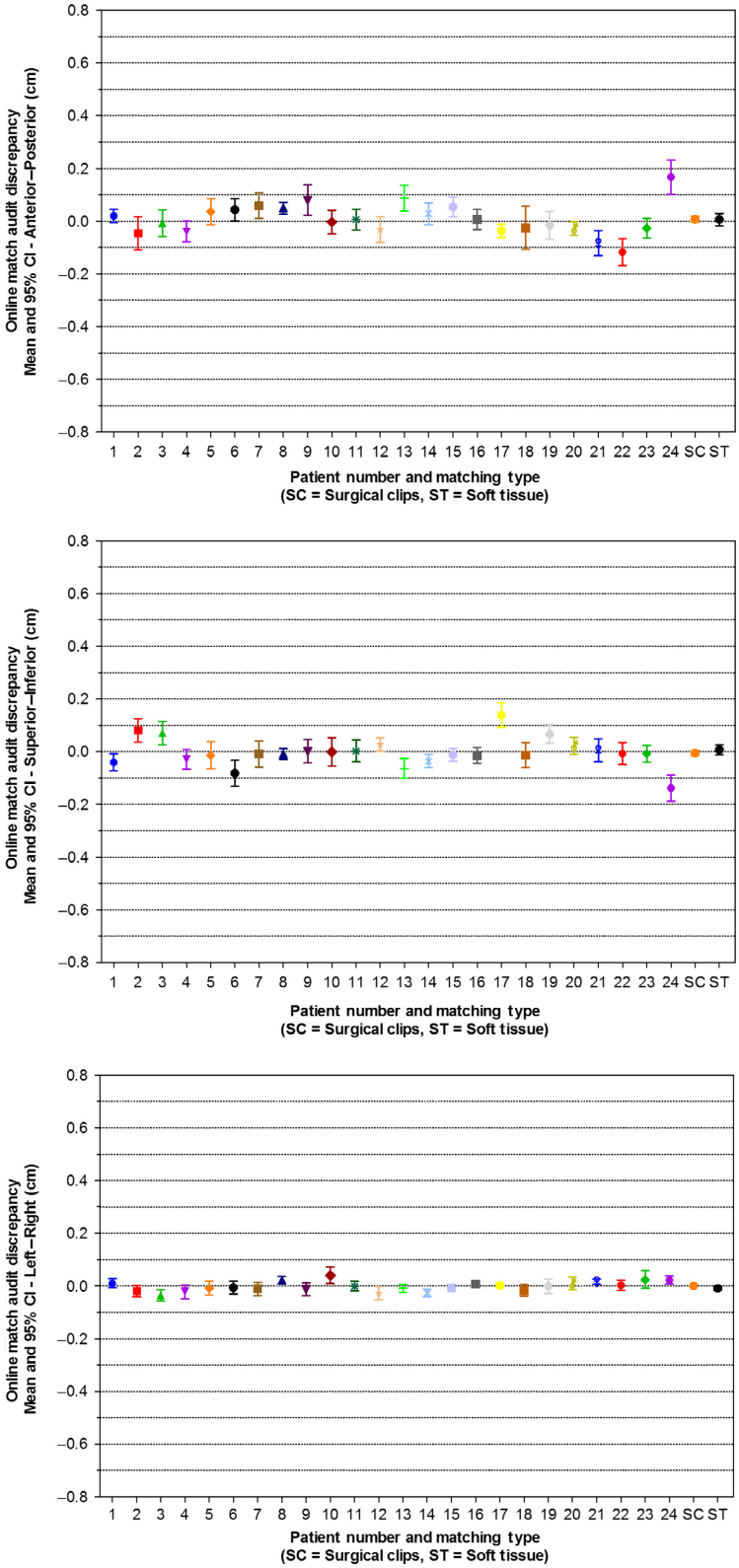

Figure 3. Online match accuracy evaluation. The online match accuracy evaluation mean and 95% confidence interval are displayed for the AP, SI and LR directions. The results for each of the patients and for the patients grouped into surgical clip or soft tissue matching techniques have been calculated.

Table 3. Online evaluation geographic miss and match discrepancy

	Geographic miss detected during match audit	Matches outside of 0.3 cm match tolerance
	Number of images/ total images (percentage)	Number of images/ total images (percentage)
All patients	17/806 (2.1%)	32/806 (4%)
Surgical clip cohort	17/606 (2.8%)	19/606 (3.1%)
Soft tissue cohort	0/200 (0%)	13/200 (6.5%)

cm, centimetre.

much lower rate of match discrepancies in this cohort, with only 4% of images demonstrating a discrepancy larger than 0.3 cm. A lower rate of discrepancy was detected in the surgical clip patients (3%) compared to the soft tissue matched patients (7%).

The differences between the offline training and online audit may have been caused by a number of factors. Firstly, the images selected to be used in the training process were predominately difficult matches. Of the six matches, only two represented 'standard' matches. This made the training challenging but exposed the RTs to these difficult cases offline without the risk of treating the patient incorrectly or the time pressure in vivo. Secondly, the results for patient 5 showed consistent variation from the trainer's gold standard match (Table 2 and Fig. 1). Reviewing this patient's image shows a large rectum and the decision to not treat this patient in 96.7% of cases where the match discrepancy was larger than 0.3 cm was appropriate. Thirdly, the increased online match accuracy might be because the offline matches were completed by one RT, whereas the online matches were completed by two RTs prior to delivering treatment. A number of RTs during training commented that they missed having a second RT to discuss the match as they would on the treatment machine. It can be argued that evaluation of RT matching offline should be done alone to ensure individualised assessment; however, having two RTs treating patients allows for built-in peer review.[5] This suggests that conducting IGRT matching online should remain a task requiring two RTs.

Even though the results from the offline training were worse than the online review, providing training for new techniques is important. RTs are often expected to learn new techniques whilst treating patients; however, this 'hands-on' type of training has been implicated in systematic treatment errors.[6] The offline training for the soft tissue matched IGRT technique was an important step in the implementation of the clinical changes even though the results were not as expected. Simulation-based training has been used previously for RTs and resulted in participants having improved procedural compliance.[7] CBCT matching can be difficult due to the occurrence of anatomical changes that cannot be completely corrected, and the time pressure on treatment means that fast decisions need to be made in these challenging cases.[8]

The offline match accuracy audit indicated that matching was completed more accurately when surgical

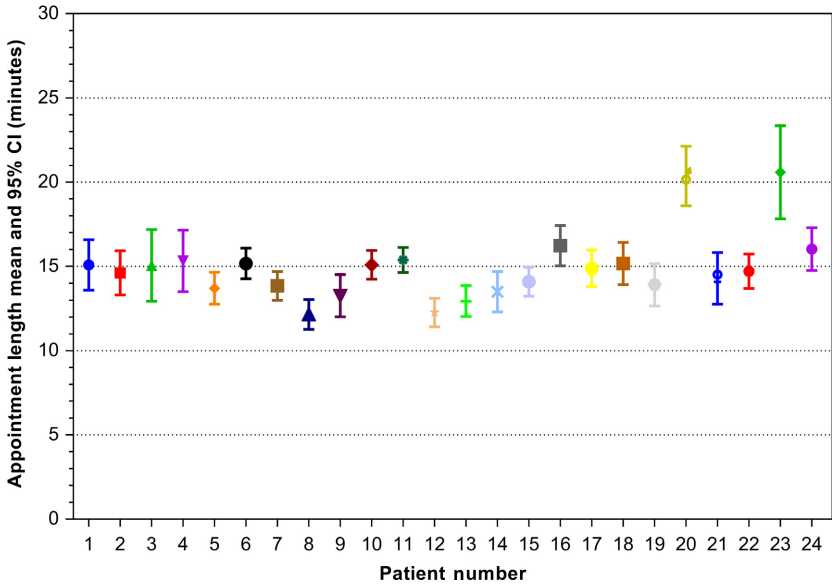

Figure 4. Treatment appointment length. The treatment appointment length mean and 95% confidence level were calculated for each patient. The standard appointment time allocated for post-prostatectomy patients is 15 min.

clips were located in the prostate bed; however, less variance between surgical clip and soft tissue matching was detected online. This might have occurred because 75% of patients in the online match cohort had surgical clips in situ. Match accuracy using fiducial markers has been investigated previously in the definitive prostate setting, and the small differences in match accuracy were found to be within clinically acceptable limits.[9] It is important to exercise caution when using surgical clips as a surrogate for prostate bed motion, as these clips are not inserted for the purpose of localising radiotherapy treatment. Their position is not optimised for IGRT, and the entire prostate bed and nodes might move differently relative to the surgical clips.

There is limited data in the literature examining the accuracy of RT soft tissue image matching in post-prostatectomy patients. Campbell et al compared the accuracy of RT soft tissue matching with both a RO gold standard and a dual registration tool.[4] The percentage of matches within the clinical threshold of 0.3 cm were reviewed for both the ROs to registration tool and the ROs to RT cohorts. The concordance between the ROs and the registration tool was 96.7% in the SI direction, 91.6% in the AP and 100% in the LR direction. The RO and RT concordance was 98.9% (SI), 91.9% (AP) and 100% (LR) in each direction. Overall, they concluded that the accuracy of RT soft tissue matching was acceptable.

In our previously published single investigator study, various PTV expansions and IGRT techniques were evaluated for rates of geographic miss.[3] With a CTV to PTV expansion of 1 and 0.5 cm posteriorly suggested by Sidhom et al.[10], matching to bony anatomy, a geographic miss rate of 15.6% was detected and was reduced to 5.8% if soft tissue IGRT was used. When evaluating soft tissue IGRT with the smaller anisotropic PTV margins (as evaluated in this study), our previous study suggested a geographic miss rate of 5.6%. In the current online audit, this geographic miss rate was measured to be even lower at 2.1% in the clinical environment (Table 3) which is very encouraging.

The changes to clinical practice did not adversely affect resources in the department. Treatment appointment length was not impacted, and the majority of the fractions were delivered within the standard appointment time slots of 15 min. The two patients (patients 20 and 23) that took longer to treat used a dual imaging protocol which is standard departmental practice when the para-aortic lymph nodes are treated in conjunction with prostate bed or definitive patients. This would normally take longer than the standard appointment time slots so this was not deemed to have a detrimental effect on treatment resources.

In some patients, it was noted that the prostate bed would move differently to the lymph node volumes. This has previously been described in definitive prostate radiotherapy.[11] The prostate bed may move differently both in direction and amount than the lymph nodes, which means that the CTV to PTV expansion used on the lymph node volumes needs to be considered to account for the change to alignment to the prostate bed. This is especially important when GTV volumes are located in the lymph nodes. A PTV margin is required around this smaller volume that allows accurate alignment when the primary match is made to the prostate bed.

This study had a number of limitations. The assessment of planning parameters was only completed on the first eight rather than all 24 patients. The decision was made to not dual plan each patient after patient 8 because of the increased clinical resources required. The other limitation of this study is the definition used to determine a geographic miss. A geographic miss was defined as any soft tissue and/or surgical clips contoured within the CTV on the planning CT scan being located outside the PTV on the CBCT. On many occasions, the amount of tissue located outside the PTV was only very small, for example up to 3 mm. It could be argued that this tissue being outside the PTV would have little if any clinical significance because a large percentage of the CTV volume was being covered by the prescribed dose and the same portion of tissue might only be missed for 1 of 32 to 34 fractions. Further, intra-fraction motion has not been considered in this study. Quantifying intra-fraction motion is important when reviewing margin generation and IGRT procedures. Measuring intra-fraction motion in post-prostatectomy radiotherapy is the focus of a current study being conducted in our department and will help further inform treatment parameters for these patients.

Conclusions

Daily soft tissue IGRT with reduced anisotropic PTV expansions for post-prostatectomy radiotherapy has been successfully implemented following offline training, an evaluation of departmental resources which showed no adverse effects, and careful audit of practice with high rates of tumour bed coverage and reduced OAR doses.

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Conflict of Interest

None.

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