Comparison of prostate setup accuracy and margins with off-line bony anatomy corrections, and on-line implanted fiducial based corrections

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Aim

To determine prostate setup accuracy and setup margins with off-line bony anatomy based imaging protocols, compared to on-line implanted fiducial marker based imaging with daily corrections.

Methods

Eleven patients were treated with implanted prostate fiducial markers and on-line setup corrections. Pre-treatment orthogonal electronic portal images (EPI's) were acquired to determine couch shifts and verification images were acquired during treatment to measure residual setup error. The *prostate* setup errors that would result from skin marker setup, off-line bony anatomy based protocols and on-line fiducial marker based corrections were determined. Setup margins were calculated for each setup technique using the percentage of encompassed isocentres and a margin recipe.

Results

The *prostate* systematic setup errors in the medial-lateral, superior-inferior and anterior-posterior directions for skin marker setup were 2.2, 3.6 and 4.5 mm (1 standard deviation). For our bony-anatomy based off-line protocol the prostate systematic setup errors were 1.6, 2.5, and 4.4 mm. For the on-line fiducial based setup the results were 0.5, 1.4 and 1.4 mm. A prostate systematic error of 10.2 mm was uncorrected by the off-line bone protocol in one patient. Setup margins calculated to encompass 98% of prostate setup shifts were 11-14 mm with bone off-line setup, and 4-7 mm with on-line fiducial markers. Margins from the van Herk margin recipe were generally 1-2 mm smaller.

Conclusions

Bony-anatomy based setup protocols improve the group prostate setup error compared to skin marks however large prostate systematic errors can remain undetected, or systematic errors increased for individual patients. The margin required for setup errors was found to be 10-15 mm unless implanted fiducial markers are available for treatment guidance.

INTRODUCTION

The most commonly used setup technique for prostate radiotherapy patients has been to align the beams using external skin marks to treatment room lasers that define the isocentre location. More recently megavoltage images of bony anatomy are acquired and compared to the bony anatomy location relative to the field aperture defined during treatment planning. Several off-line protocols to correct systematic setup errors have been developed including the shrinking action level (SAL)[2], no action level (NAL)[3], and Newcastle model[4]. When these protocols are applied to bony anatomy setup data, the actual prostate position may not be effectively corrected.

There has been significant interest in positioning prostate patients using small fiducial markers or seeds that are implanted within the prostate and can be seen on electronic portal images taken prior to daily radiotherapy treatment. On-line or daily positioning protocols are most common, and various techniques have been reported[5,6,7,8], although off-line protocols to reduce prostate systematic errors have also been applied using the measured prostate position from implanted markers[3].

The prostate markers can also be used to determine the accuracy and required margins for current setup procedures based on skin markers and bony anatomy. Nederveen *et al.*[9] compared the accuracy of prostate positioning with skin marker setup, and off-line positioning protocols based on both implanted markers and bony anatomy for 23 patients. The bony anatomy based off-line protocol was found to reduce the systematic errors in prostate positioning in only two directions compared to skin marker setup and was ineffective in the superior-inferior direction. Moreover the systematic prostate error was increased for 6 of the 23 patients using the off-line protocol.

Our aim in this work is to report on a pilot study of the effectiveness of prostate positioning with three separate off-line bony-anatomy based protocols compared to implanted fiducial based on-line setup, as well as derive setup margins for each treatment setup technique.

METHODS AND MATERIALS

PATIENT DATA ACQUISITION

Eleven patients had gold seed insertion as a component of a pilot study into MRI based treatment planning and fiducial marker guided treatment. Three pure gold seeds of 1 mm diameter by 7 mm length were inserted trans-rectally by a urologist using an 18 gauge brachytherapy needle under trans-rectal ultrasound guidance. The seeds were placed in the base of the prostate laterally and one near the apex. All patients received prophylactic antibiotics and a local anaesthetic. Ethical approval was obtained for the protocol from the local ethics committee. CT scanning was performed 1 week after the marker insertion. The patients were setup supine on a solid carbon fibre couch top and CT scanned with a full bladder. The bowel preparation protocol consisted of a laxative each evening, at least 6 glasses of water per day, and a high fibre diet. Urethral contrast was used to assist with determining the apex of the prostate and ankle-stocks were used to ensure consistent leg positioning. A four-field conformal box technique with 18 MV photons was planned using the Pinnacle (Phillips, Madison, USA, Ver 6.2). The prescribed dose was 70 Gy in 35 fractions to the ICRU point with CTV to PTV margins of 1.5 cm laterally/anteriorly and 1.0 cm posteriorly. Digitally reconstructed radiographs (DRRs) were produced for all four fields incorporating both bony anatomy and gold markers for prostate position using the Pinnacle treatment planning system Version 6.2 (Philips Medical Systems, WI, USA). To produce DRRs that clearly show the gold seeds we used 2.5 mm slice thickness CT scans, and the highest resolution DRR setting. The markers were contoured as a structure on the CT scan so that they were then incoporated into the DRR.

Patients were setup for treatment using tattoos and the couch-height for anterior-posterior positioning. Ankle-stocks were used to ensure consistent leg positioning, along with knee cushions (Med-tec, Orange City, IA). Orthogonal anterior-posterior (AP) and Right-Lateral (RL) portal images were acquired prior to treatment with an amorphous silicon electronic portal imaging device (EPID). These images were field aperture only, and incorporated into the plan, so that no additional dose was delivered to the patient. The image registration software (Varian VaRis 4D Console, Version 7, Varian, Palo Alto, CA) was then used to determine couch shifts using the implanted prostate markers and the patient position was corrected. No threshold for correction was used, all measured displacements were corrected. No rotations in the plane of the image are possible within this software so only translations were measured and corrected. These were manually applied by the radiation therapists within the treatment room. Treatment was initiated with verification images acquired during the first two treatment beams the posterior-anterior (PA), and left-lateral (LL) beams. This version of the software would not allow the previous beams to be re-imaged so the opposite direction beams were used.

DATA ANALYSIS

Bony anatomy setup accuracy with off-line setup protocol using bony anatomy

To ensure that our patient setup techniques based on external skin markers, and off-line bony anatomy based protocol were comparable with accuracies reported in the literature, the *bony anatomy* setup errors were assessed. The pre-treatment bony anatomy setup positions for the first five fractions were input into our in-house off-line protocol software and any recommended setup shifts were recorded. These shifts were then applied to the pre-treatment bony anatomy setups. The resulting bony anatomy positions were then assessed to determine the setup accuracy, compared with no intervention.

The Newcastle model (NM) off-line protocol[4] uses Hotelling T2 sample statistics to determine whether a systematic error is present for the treatment based on a sample of treated positions, in this case 5 measurements. Based on a scatter plot of setup errors for a treatment field, it derives a two-dimensional ellipse that incorporates the patients systematic error with 95% confidence level. If one of the direction axes (zero setup error for a particular direction) does not lie within the ellipse then a non-zero systematic error is diagnosed in that direction. If a systematic error is diagnosed in any direction, then the average position from the 5 measurements in that direction is used as the correction shift applied to all subsequent treatment fractions. We apply the protocol in both week 1 and later in week 4 of treatment in case drifts of position have occurred. We also apply a tolerance of 2 mm to determine whether to reposition the patient. The in-house software is a Windows based system that inputs setup shift result files, and stores them in a database. A graphical interface displays the daily measured positions, confidence ellipse and required setup corrections.

Prostate setup accuracy with off-line setup protocol using bony anatomy

Setup correction (couch) shifts were found by entering the first five treatment days of bony-anatomy setup errors into the NM protocol. These setup shifts were then applied to the measured pre-treatment (uncorrected) prostate positions to determine the *prostate* setup accuracy that would have resulted from using an off-line bone protocol. Systematic and random errors of the prostate position were calculated. This analysis was then repeated for the no-action level (NAL) protocol[3], where the setup correction shift was calculated from the average of the first three days of bony-anatomy setup errors. A third protocol was also applied, where the bony anatomy systematic error was perfectly corrected. This is referred to as an optimal protocol, and gives the ultimate accuracy obtainable with an off-line bone protocol. These simulated results were compared to the treatment prostate setup accuracy that resulted from the daily on-line corrections using the implanted prostate markers. The treated prostate setup accuracy was determined using verification images (post-correction) acquired during the treatment delivery. The results were obtained from alignment of gold seeds in the verification images to the DRR in the Vision software (Version 6.2, Varian, Palo Alto, CA).

Setup Margins

The setup margins required for each setup technique were calculated for each direction. Two methods were used; 1) the margin that encompassed a fixed percentage of prostate setup shifts, in this case 98%, and 2) using the margin recipe derived by van Herk[1], where the margin is given by $2.5\Sigma + 0.7\sigma$ where Σ and σ are the group systematic and random errors respectively. The original van Herk fomular also included an additional margin reduction of a few mm which resulted in a small (~1%) reduction in tumour control probability. We follow common practice here and omit this additional margin reduction.

RESULTS

Bony anatomy setup accuracy with off-line setup protocol using bony anatomy

The results for the *bony anatomy* systematic errors in the medial-lateral, superior-inferior and anterior-posterior directions with skin marker based setup were 1.9 ± 2.8 mm, 0.7 ± 2.4, and -2.4 ± 2.8 mm (mean ± 1 standard deviation) respectively. The results with the NM off-line setup protocol were 1.5 ± 0.9 mm, 0.5 ± 0.8 mm and -0.8 ± 1.5 mm.

Prostate setup accuracy with off-line setup protocol using bony anatomy

Figure 1(a) shows for the medial-lateral direction the *prostate* systematic errors that would result from skin marker based setup, the NM off-line bone setup protocol, and the on-line fiducial marker based setup. The absolute value of the systematic errors are shown for clarity. There is one patient in which the off-line bone protocol increases the systematic prostate error (Patient #1) compared to skin marker setup (no intervention) although this increase is very small. In four other patients the off-line protocol has no effect on the prostate systematic error. In six patients the off-line protocol is beneficial. The on-line setup systematic errors in only one case exceed 2 mm.

The superior-inferior direction results from that anterior and posterior fields are shown in Figure 1(b). For two patients (#9, #10) the off-line bone protocol increases the SI prostate systematic error compared with no intervention, although these increases are again small. In a further three patients the off-line protocol makes no difference and in six patients the protocol reduces the prostate systematic error.

In the anterior-posterior direction shown in Figure 1(c), for two patients (#6, #8) the off-line bone protocol increases the error compared with no intervention. For Patient #8 the error is increased from nearly zero to 5 mm. For seven patients the off-line bone protocol gives no improvement in prostate systematic error including one patient where a prostate systematic error of over 10 mm is not detected by the off-line bone protocol. Only two of the patients showed a benefit from the off-line protocol, however in one case the prostate systematic error was reduced significantly from over 8 mm to just over 1 mm.

Table 1 shows the *prostate* setup accuracy for the patient group for skin marker setup, NM bone off-line protocol, and on-line fiducial based corrections. In the anterior-posterior direction there is no improvement in the systematic errors for the off-line bone protocol compared to skin marker setup. As would be expected the NM protocol has little impact on random errors, in fact these are increased slightly. Table 2 compares the systematic prostate errors with the NM off-line bone protocol, the NAL off-line bone protocol and the optimal bone protocol. These show very similar results for the NM and NAL protocols with a slight improvement for the optimal protocol. The random prostate setup errors were also calculated.

Setup Margins

Figure 2 shows how the percentage of prostate setup shifts encompassed by the setup margin depends on the size of the setup margin for the three directions independently. The setup margins required for covering a particular percentage of prostate displacements can then be selected. The setup margins required to encompass 98% of prostate displacements are approximately 11, 11 and 14 mm in the medial-lateral, superior-inferior and anterior-posterior directions with bony anatomy setup, and 4, 6, and 7 mm in these directions with on-line fiducial markers. Repeating this calculation with the van Herk margin recipe yields setup margins of 6, 9 and 13 mm in the ML, SI and AP directions with the bony anatomy protocol, and 2, 4, and 5 mm in these directions with on-line fiducial markers. These margin calculations only derive the margin component to account for setup errors. Total margin size must also include allowance for target delineation and other planning uncertainties.

DISCUSSION

The results for *bony-anatomy* setup accuracy with the NM off-line protocol are comparable with previously reported values in the literature from other authors[10] and show that this protocol will effectively correct systematic errors based on bony anatomy. However these setup results do not necessarily reflect the target or prostate setup accuracy.

Several authors have reported prostate setup accuracy with skin marker localization. Nederveen[9] reported skin marker setup prostate systematic setup errors of 2.4 mm, 3.7 and 4.4 mm (1 SD) in the medial-lateral, superior-inferior and anterior-posterior directions (1 SD). These are very similar to the setup errors for skin marker setup measured here. Other reports have used different setup accuracy metrics which hampers comparisons[11 12 13].

Nederveen *et al.*[9] also examined improvement in prostate accuracy for a no-action level (NAL) type off-line protocol using both bone and markers. The off-line bone protocol reduced systematic errors to 1.2, 4.1 and 2.4 mm respectively in the ML, SI and AP directions. They found that the bone-based protocol did not reduce prostate setup errors in the superior-inferior direction. Our prostate setup accuracy results are of a similar magnitude, with our systematic errors being 1.6, 2.5, and 4.4 mm. However we found the direction where errors were not reduced by the bone protocol was the anterior-posterior direction. This is obviously of concern, as the rectum is the dose limiting structure immediately posterior to the prostate. These discrepancies could be due to the small sample sizes in both studies, and highlight the need for larger studies in this area. They noted that while the group systematic errors in prostate position decrease with the bony anatomy protocol, individual patients can have their prostate systematic errors increased by the protocol, which was also found here.

Their random prostate positioning errors were not reduced with the off-line marker based setup and remained at 2.4, 3.0 and 4.0 mm. The random errors for our on-line positioning were 1.2, 1.9 and 1.7 mm. The majority of treatment centres now use on-line positioning for prostate setup with fiducial markers, and therefore comparison with on-line setup is most applicable in determining the relative benefit of bony anatomy based setup.

We have also extended the study of off-line bony anatomy protocols to incorporate two clinically used protocols, and an optimal protocol that perfectly corrects systematic bone errors. Even with an optimal bony anatomy setup, large systematic prostate errors will remain undetected, and some individual patients will have their systematic error increased by the off-line protocol. However, for the group overall, the off-line protocol is beneficial compared with skin marker setup, and these protocols should be continued in cases where it is not possible to use on-line fiducial markers.

There is no general agreement in the radiation oncology community on how treatment margins should be calculated, however they should incorporate both setup errors and target delineation uncertainties. In this paper, two separate margin recipes were used. In the first, a margin that incorporated 98% of protate setup shifts was calculated for each direction. Figure 2 also shows how a margin size can be determined with this approach based on a pre-selected percentage value. In the second, the margin recipe of van Herk was used. It is based on achieving for 90% of patients an equivalent uniform dose of 98% of the prescribed isocentre dose. This margin recipe gave less than a 1% reduction in tumour control probablity for the patient population due to geometric errors. It should be noted that there are many assumptions inherent in this margin recipe model. Approximations to the radiobiological model include the assumption of cell density homogeneity, along with an assumed α value in the linear quadratic model. Moreover, the radiobiological effects of fractionation are not included with β set to zero. Only a spherical dose distribution and a conformal prostate dose distribution was considered. Another approximation is that the dose distribution was blurred to account for random setup errors, which does not take fractionation effects into account, particularly for smaller fractionation regimes. The effect of inhomogeneities was also not incorporated.

The margin results show that small margins should not be used when positioning prostate patients using bony anatomy based setup protocols. It has become more common recently to use small margins in the posterior direction of the order of 5 mm. The results here suggest that small margins should only be used if implanted fiducial markers are being used for patient positioning. When bony anatomy is used for patient setup large prostate systematic errors can remain undetected, as the prostate position can move significantly relative to bone between CT simulation and treatment. Margins in the order of 10-15 mm should be utilized when only bony anatomy targeting is available. Clearly definitive margins can not be set based on the small sample size in this study, however these data highlight the problem. The sample size in this study was not based on a statistical analysis, as the intention was to obtain pilot data to determine how future investigations should be undertaken with larger patient populations. More data is required in this area, and a larger study of the patient population would be beneficial. Appropriate margins can then be set using knowledge of the prostate positioning uncertainty combined with delineation uncertainties.

These 7 mm length seeds that we used were slightly longer than is necessary for visibility, but as these were manually loaded into the needle by the urologist, the longer length was required. There were no difficulties encountered due to the seed length in determining setup shifts. Other considerations such as the inability to account for inplane prostate rotations, and hence align all the seeds in the image are more significant issues.

CONCLUSION

We have determined the *prostate* setup accuracy with off-line bony anatomy based imaging protocols, compared to on-line implanted fiducial marker based setup with daily corrections. Bony-anatomy based setup protocols improve the group prostate setup error compared to skin marks however large prostate systematic errors can remain undetected, or systematic errors increased for individual patients. The component of the margin required for setup errors was found to be 10-15 mm unless implanted fiducial markers are used for treatment guidance, with larger studies required to define margin sizes more accurately.

ACKNOWLEDGEMENT

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FIGURES

Figure 1

Prostate systematic errors in the (a) medial-lateral, (b) superior-inferior, and (c) anterior-posterior directions with skin marker setup, off-line NM bony anatomy (BA) based protocol and on-line positioning using fiducial markers (FM).

Figure 2

Percentage of prostate setup shifts encompassed by the setup margin for a) medial-lateral, b) superior-inferior, and c) anterior-posterior directions.

TABLES

Table 1

Prostate systematic (mean ± 1 standard deviation) and random errors (1 standard deviation).

Table 2

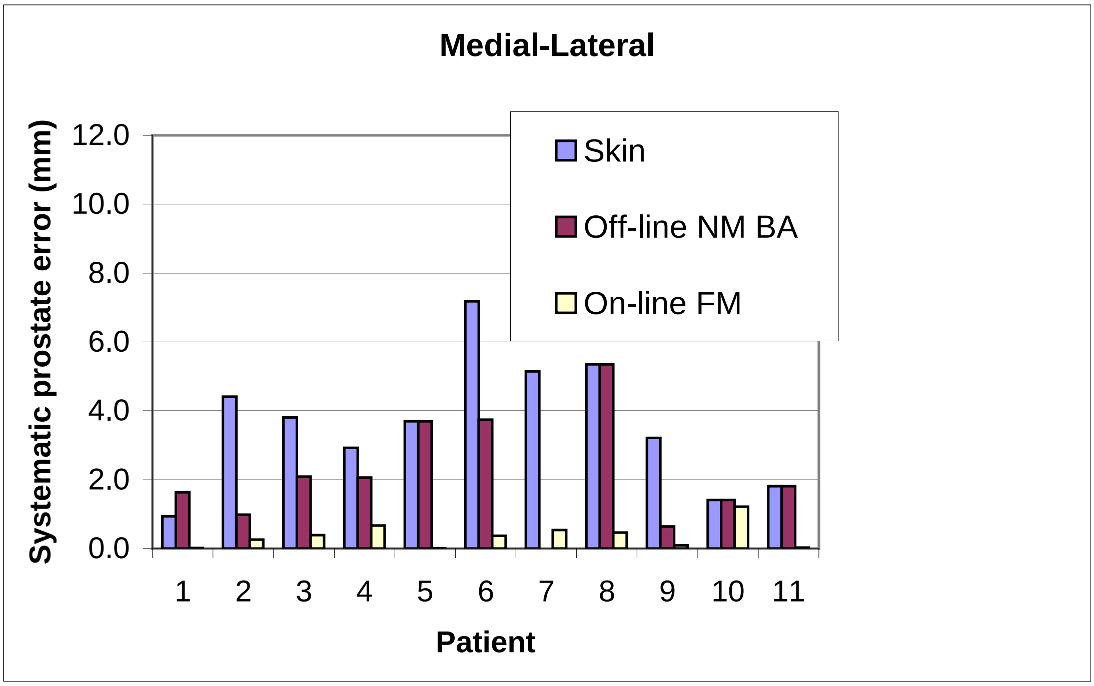
Comparison of *prostate* systematic errors for three off-line protocols using bony anatomy positions, the Newcastle Model, the No Action Level, and an optimal off-line protocol that eliminates systematic error (mean ± 1 standard deviation).

	Skin markers (mm)	Off-line bone protocol (mm)	On-line prostate (mm)
Medial-lateral	3.5 ± 2.2 (2.7)	2.1 ± 1.6 (2.9)	0.1 ± 0.5 (1.2)
Superior-inferior	-0.4 ± 3.6 (3.7)	-0.3 ± 2.5 (4.0)	0.2 ± 0.9 (1.9)
Anterior-posterior	–2.2 ± 4.5 (2.9)	-0.6 ± 4.4 (3.3)	-0.6 ± 1.4 (1.7)

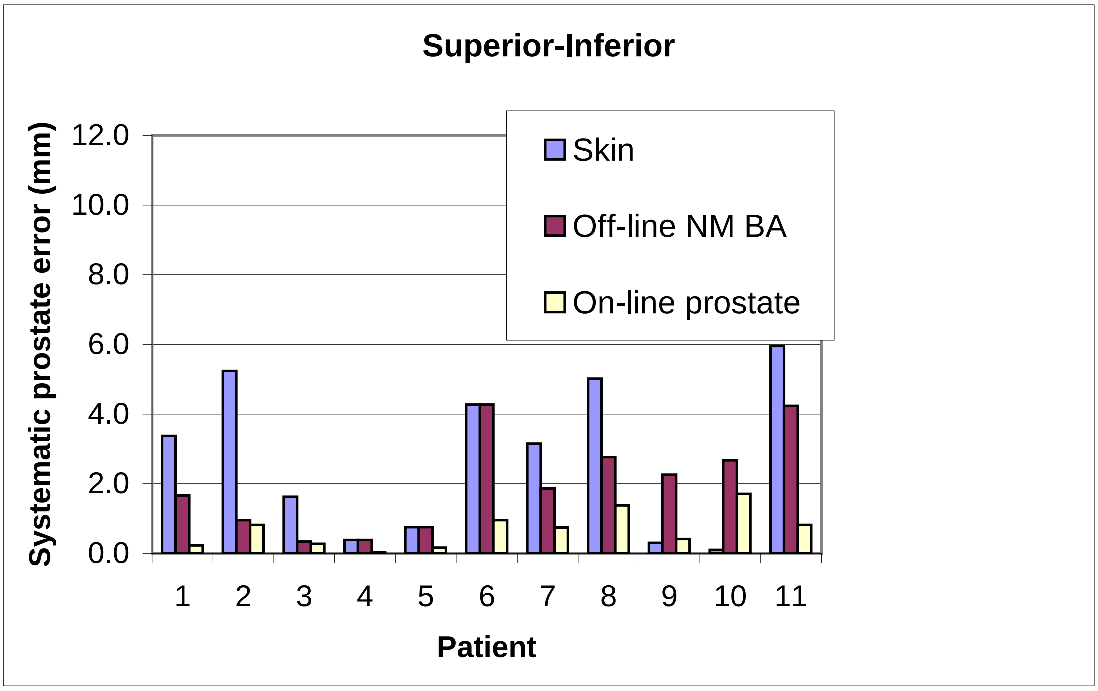
Table 1

	NM Off-line bone protocol	NAL off-line bone protocol	Optimal off-line bone protocol
Medial-lateral	2.1 ± 1.6	1.7 ± 1.4	0.7 ± 1.2
Superior-inferior	-0.3 ± 2.5	-0.7 ± 2.6	-0.8 ± 2.4
Anterior-posterior	-0.6 ± 4.4	-0.1 ± 4.4	0.2 ± 3.6

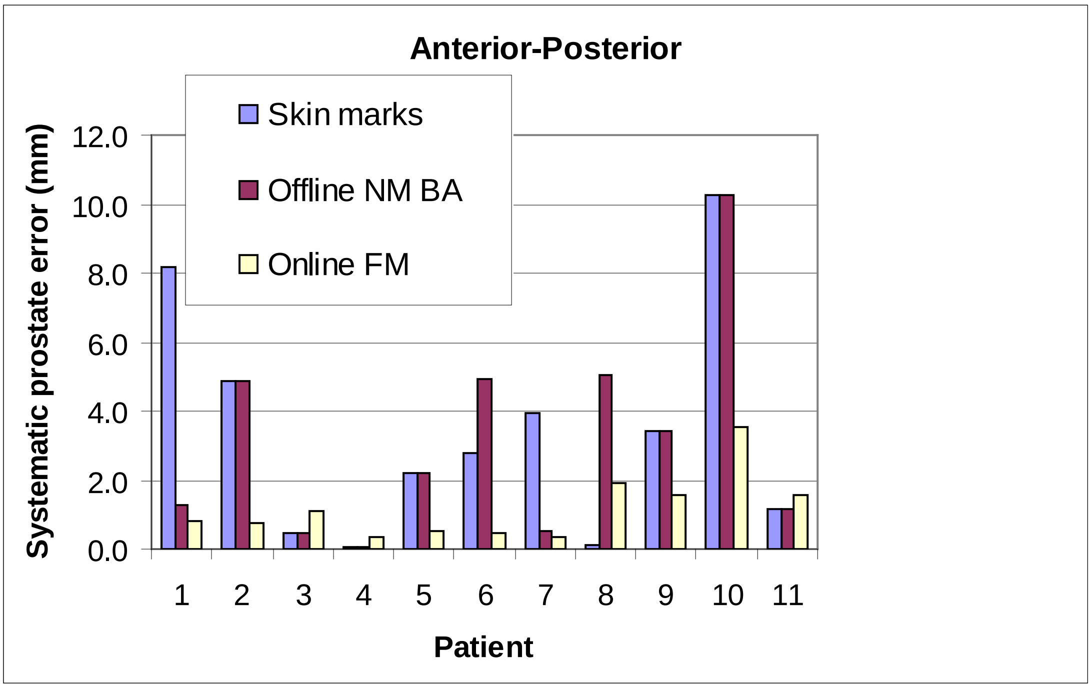
Table 2


Medial-Lateral
Systematic prostate error (mm)
12.0
10.0
8.0
6.0
4.0
2.0
0.0
Skin
Off-line NM BA
On-line FM
1 2 3 4 5 6 7 8 9 10 11
Patient

(a)

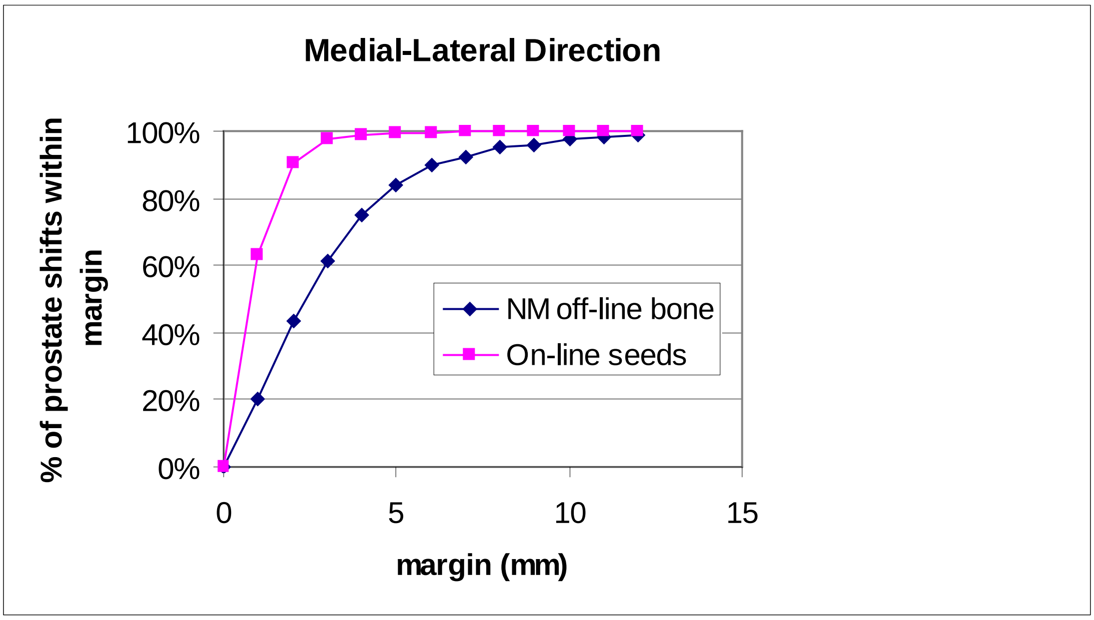

Superior-Inferior
Systematic prostate error (mm)
12.0
10.0
8.0
6.0
4.0
2.0
0.0
Skin
Off-line NM BA
On-line prostate
1 2 3 4 5 6 7 8 9 10 11
Patient

(b)

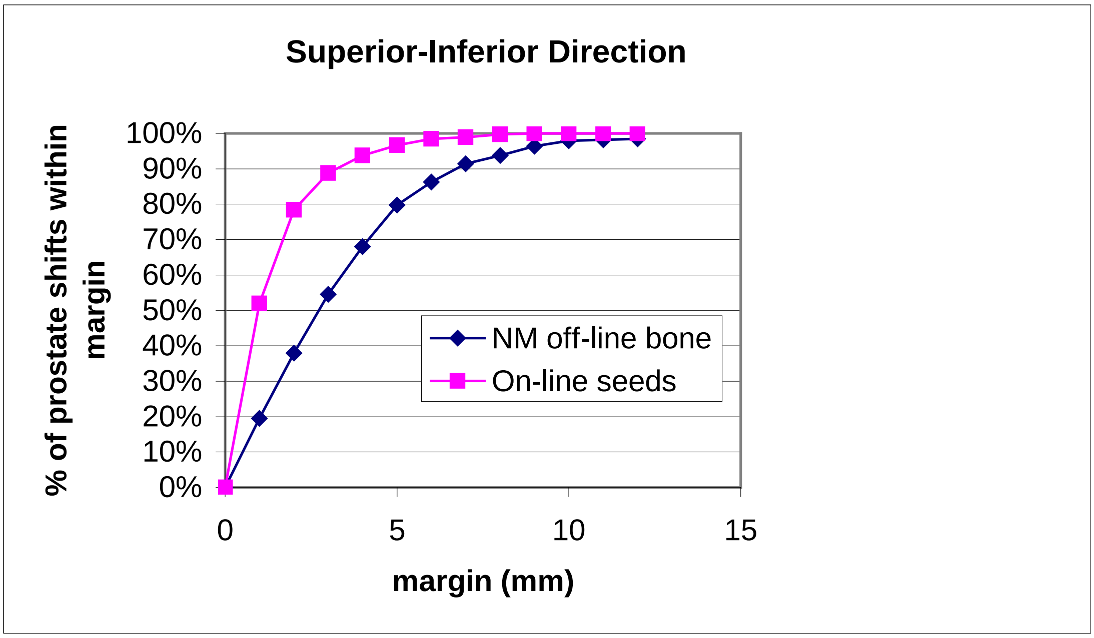

Anterior-Posterior
Skin marks
Offline NM BA
Online FM
Systematic prostate error (mm)
12.0
10.0
8.0
6.0
4.0
2.0
0.0
1
2
3
4
5
6
7
8
9
10
11
Patient

(c)

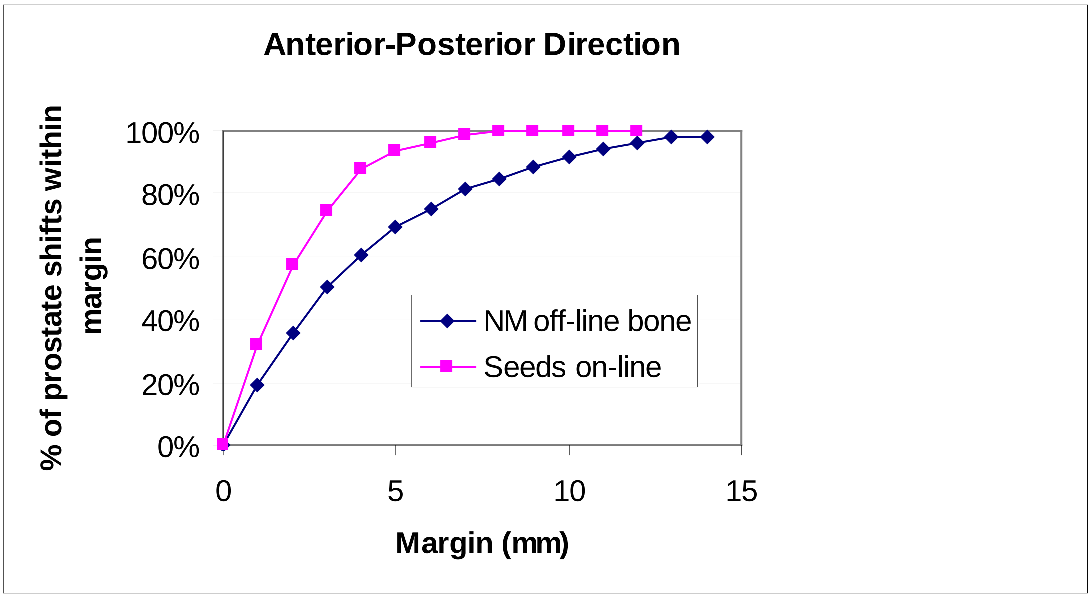
Figure 1


Medial-Lateral Direction
% of prostate shifts within margin
100%
80%
60%
40%
20%
0%
NM off-line bone
On-line seeds
0
5
10
15
margin (mm)

(a)


Superior-Inferior Direction
% of prostate shifts within margin
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
0
5
10
15
margin (mm)
NM off-line bone
On-line seeds

(b)


Anterior-Posterior Direction
% of prostate shifts within margin
100%
80%
60%
40%
20%
0%
0
5
10
15
Margin (mm)
NM off-line bone
Seeds on-line

(c)

Figure 2