Gold seed fiducial markers for prostate radiation therapy: Describing prostate motion

Abstract ***Purpose:*** Gold seed fiducial markers can be used to accurately define daily treatment field placement for prostate cancer patients. In 2007, a small study was undertaken to evaluate the effectiveness of using gold seed fiducial markers. ***Methods:*** Eleven patients who attended for treatment had three gold fiducial markers inserted into their prostate. Daily megavoltage (MV) and kilovoltage (kV) orthogonal images were taken throughout treatment. Online correction was applied for the kV images matched to the fiducial markers daily, and the MV images were matched offline using pelvic bone anatomy. ***Results:*** 850 sets of orthogonal images were reviewed from the 11 patients. When comparing the bony anatomy imaging with the fiducial marker imaging, all patients would have had at least five treatments where the displacement exceeded 0.5 cm if treatment verification was undertaken using MV bony anatomy match. There was no trend in prostate movement throughout the patients treatment schedule (0.7 cm early and middle of treatment and 0.8 cm at the end of treatment.) ***Conclusion:*** The results have demonstrated that daily matching to fiducial markers improves treatment field placement compared with MV bony anatomy matching for patients with prostate cancer.

Keywords: gold seed fiducial marker, prostate localisation, imaging.

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Introduction

Gold seed fiducial markers can be used to visualise the prostate gland on images taken immediately prior to radiation treatment. Visualisation of these fiducial markers enables accurate daily treatment field placement, which may allow dose escalation to be confidently performed in an attempt to improve tumour control.[1] Accurate treatment delivery to the prostate gland can minimise irradiation of surrounding organs, especially the rectum and bladder, which reduces the side effects experienced during radiation therapy, as well as potentially minimising long term side effects of treatment.[2]

Standard prostate treatment set-up uses external skin markers (tattoos) for daily positioning, and electronic portal imaging (EPI) verification or kilovoltage (kV) images matched to bony anatomy weekly throughout treatment. The position of the prostate however, varies daily depending largely on the degree of filling of adjacent organs bladder and rectum. Although at our centre, patients are advised to have an empty rectum and a full bladder prior to treatment, external skin markers and anatomy matching on images are likely inadequate in determining the exact prostate position on a daily basis.

The introduction of gold seed fiducial markers into the prostate, allow the prostate gland position to be visualised and appropriate adjustments to the field isocentre made prior to the delivery of each treatment fraction. Precise localisation of the prostate gland is critical if dose escalation, hypofractionated treatment regimens and intensity modulated treatment (IMRT) are being considered.[1,2]

A number of studies have been conducted to evaluate the use of fiducial markers in improving treatment accuracy in the treatment of localised prostate cancer with radiotherapy.[1,3,4–6] However to acquire ongoing funding for new technologies, the accumulation of evidence in order to justify the associated additional costs and to provide quality assurance outcomes for the new technique is required.

In 2007, the department research committee at Westmead Cancer Care Centre (WCCC) supported a small study to be conducted of the initial findings from patients who had previously consented to treatment with gold seed fiducial markers in this single centre. The practice of implanting gold seeds was being introduced into the department as a "routine best practise" technique based on the existing national and international experience.

In particular, this study set out to determine if there was substantial improvement in prostate localisation sufficient to justify the associated expense, the likely discomfort, potential for complications including infection and possible treatment delay resulting from the fiducial marker implant procedure.[7]

Materials and method

Over a 12-month period starting in 2007, 11 patients to be treated with definitive radiation therapy for prostate cancer were eligible if they consented to gold seed fiducial markers and the radiation oncologist considered them suitable for the procedure. Three gold seed fiducial markers were implanted into their prostate under rectal guidance and were positioned in the right base, left lateral mid gland and right apex. Patients were given mild sedation for the procedure and local anaesthetic using 1% lignocaine was injected around the neurovascular bundle bilaterally at the base and apex. The demographics for this group of patients

Table 1: Demographics.

Patient ID	Age	Presenting PSA (ng/ml)	T Stage	Gleason score	Risk grouping	Hormones
1	77	8.4	T1c	3+4=7	Int	No
2	76	7.4	T2a	3+4=7	Int	No
3	58	41	T2a	3+4=7	High	Yes
4	63	24	T2c	4+3=7	High	Yes
5	67	2.4	T1c	3+4=7	Int	No
6	63	4.8	T1c	3+4=7	Int	No
7	72	8.7	T2b	3+4=7	Int	No
8	64	10	T2a	4+5=9	High	Yes
9	72	7	T1c	4+3=7	Int	No
10	75	11	T1c	3+4=7	Int	Yes
11	74	9.7	T1c	3+3=6	Low	No

*Int = intermediate

are shown in Table 1. Nine of 11 had intermediate risk prostate cancer and two patients had high-risk localised disease. The age of the patients ranged from 58 to 77 years with a median age of 72.

All patients were simulated and planned as per the normal department planning procedures with a two-phase 3D conformal radiotherapy technique. A 1 cm margin was used around the prostate gland with a 0.7 cm margin posteriorly. The dose delivered to the prostate only (plus or minus proximal seminal vesicles) was 78 Gy in 39 daily fractions for nine patients and 74 Gy in 37 fractions for two patients treating nine or 10 fractions per fortnight.

A quality assurance research proposal was submitted to Westmead Hospital Human Research Ethics Committee (HREC) and was accepted as a quality assurance project.

Standard departmental procedure for treatment verification:

The department imaging protocol for prostate treatment requires that orthogonal MV EPI images are matched according to bony pelvic anatomy after the first treatment fraction moving the isocentre for the subsequent fraction if necessary. Images are taken for the first three days to determine the average isocentre position and then repeated weekly throughout treatment.

New departmental procedure for treatment verification using fiducial markers:

Patients in whom gold seed fiducial markers were implanted had orthogonal daily MV and kV imaging prior to treatment. The kV imaging was reviewed pre-treatment, and matched to the fiducial markers with moves made using a 0 mm tolerance threshold. The prostate markers were visualised using Varian on board imaging (OBI) equipment in three planes. A cone beam CT (CBCT) was performed on day 1 and then fortnightly throughout treatment. This image was used to determine if there was any seed migration.

kV orthogonal images were taken and matched daily to the fiducial markers with the moves made and recorded in the superior-inferior, anterior–posterior and left–right directions. After the completion of treatment the MV EPI images were matched retrospectively by a single radiation therapist, using anatomical landmarks as per standard departmental protocol. The isocentre shifts from the MV images were recorded separately from the kV images.

For each patient, the overall displacement of the isocentre was calculated as a three dimensional vector for the MV and kV images for every fraction over the treatment course. Adjustments to correct for any isocentre shifts were included for the MV images to give a true indication of treatment according to the department imaging guidelines. For the purpose of comparing accuracy, the kV imaging position was considered the "gold standard" or 'real' position of the prostate, given that the markers appeared not to migrate outside the prostate and were embedded in the gland. Thus, displacements of the MV images from the position determined by the kV images were calculated to evaluate the inaccuracy of using bony landmarks for the purpose of prostate localisation.

The accuracy of the positioning is measured on a given day as the deviation from the planned isocentre to the set-up isocentre. This is given by the formula:

Deviation = $\sqrt{(X_P - X_T)^2 + (Y_P - Y_T)^2 + (Z_P - Z_T)^2}$ where (X_p,Y_p,Z_p) represent the planned isocentre coordinates and (X_T,Y_T,Z_T) are the set-up isocentre coordinates. A similar relation is used to measure the deviation from the planned isocentre coordinates to the treated isocentre coordinates. [8]

In order to examine whether deviations were affected by the part of the treatment course being delivered, the average displacement for the first 10 days (early in treatment) for each patient was calculated and this was then averaged over the 11 patients. This procedure was repeated for the last 10 days (late in treatment). The approximate middle day of treatment was taken to be day 19 and this value was also averaged over the 11 patients.

Results

In total, 850 sets of orthogonal images were taken and reviewed for the 11 patients, (425 sets for kV and 425 sets for MV).

The daily MV displacement is shown in Figure 1 for each patient over the entire treatment course. This is along with the corresponding difference in displacement from the MV image matching to bony landmarks to the kV image calculated displacement. This demonstrates the differences in daily image results using MV imaging (matched to bony anatomy) compared with kV imaging matched to the fiducial markers.

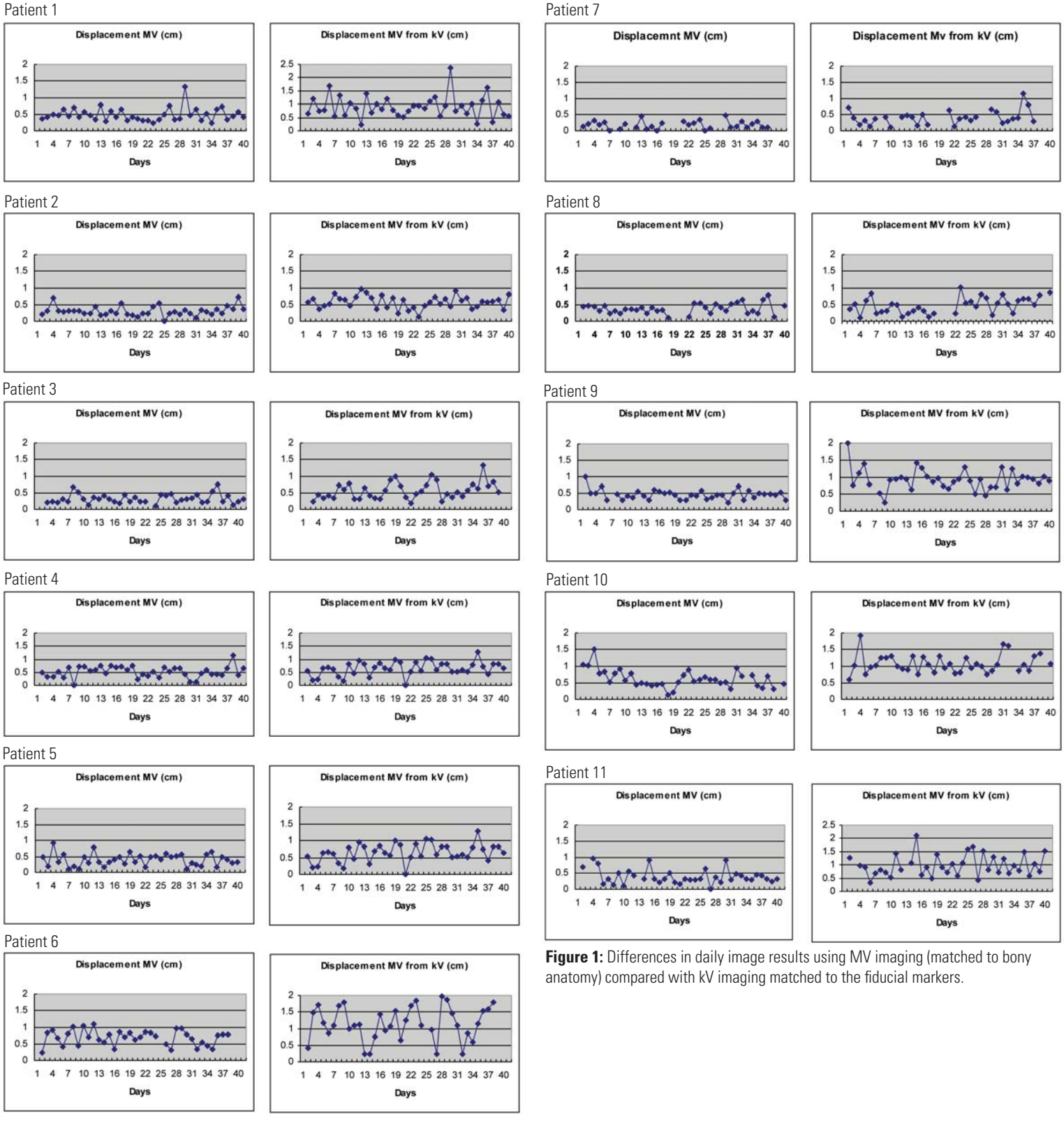

Figure 1: Differences in daily image results using MV imaging (matched to bony anatomy) compared with kV imaging matched to the fiducial markers.

The average displacement early in treatment was 0.7 cm (range: 0.4, 1.2 cm), for late in treatment it was 0.8 cm (range 0.5, 1.2 cm) and in the middle of treatment it was 0.7 cm (range 0.5, 0.9 cm). This suggests that prostate motion is on average similar throughout the treatment period. Figure 1 supports this observation, as there is no apparent discernable trend or regular pattern to prostate motion both within and between the 11 patients in the study as they underwent their course of radiation therapy.

The routine acceptable tolerance for displacement within our department is 0.5 cm when matching to bony landmarks. It was determined in advance that it would be potentially clinically significant,

Table 2: Displacement for > 5 days difference.

Displacement (cm)	Number of patients
> 0.5 cm	11
> 1.0 cm	6
> 1.5 cm	2

Number of patients who would have experienced at least 5 days of treatment with a displacement larger than 0.5 cm, 1 cm and 1.5 cm without fiducial markers.

if a patient was to have at least 5 days of treatment (1 week) for which the prostate position was outside the departmental tolerance threshold. When comparing the bony anatomy imaging with the fiducial marker imaging (fiducial marker positioning considered the gold standard), all patients would have had at least 5 treatments where the displacement exceeded 0.5 cm if treatment verification was undertaken using MV bony anatomy match alone (Table 2). The inaccuracy in positioning was greater than 1.0 cm for 55% of the patients for at least five days of treatment, had MV bony matching been used alone.

Of note, the CBCT did not detect seed migration in any patient. One patient experienced a clinically significant infection that may have been related to the fiducial marker insertion.

Discussion

Our results showed there was a substantial difference in prostate position when using bony anatomy to match for daily field placement verification compared with matching to gold seed fiducial markers. We demonstrated that all patients had at least five days of treatment where the MV bony anatomy image results would have lead to an isocentre deviation of greater than 0.5 cm if kV imaging matching to gold seed fiducial markers had not been used. Over half the patients would have undergone a week or more of treatment where the isocentre displacement was greater than 1.0 cm from the planned isocentre. This degree of inaccuracy could potentially lead to substantial treatment outcomes.

The standard departmental imaging protocol for prostate treatment when matching to bony anatomy on EPI, is to adjust the isocentre if any field placement is > 0.5 cm away from the planning image. Displacements using imaging of fiducial markers varying from those using bony anatomy confirms that the prostate moves independently to the pelvis. This study lends support to the claim that clinicians are not confident in applying dose escalation for patients without fiducial markers.[1]

This study looked for patterns in prostate displacements through the treatment course. The average displacement for the first and last sets of 10 treatments was calculated to determine if there were any trends in prostate motion at the very beginning or end of radiation therapy when compared to half way through. It was thought that perhaps there would be less movement at the beginning of treatment when patients are being diligent with their bladder and bowel preparation. Towards the end of treatment the prostate may become more mobile as patients are experiencing side effects from radiation therapy treatment, and a full bladder prior to treatment may not be maintained. However the average displacement for the first 10 treatments (0.7 cm) did not show any substantial difference from the average displacement for the last 10 treatments (0.8 cm), or from the middle of treatment (0.7 cm). It would therefore be difficult to predict prostate motion without the use of fiducial markers, and daily imaging should be utilised.

The main limitation of this study is the small sample size. Many similar studies have been conducted with a similar study design and small numbers.[3,4,10,11] These studies including the current one provide further observations supporting the routine use of fiducial markers to accurately localise the prostate gland. Large, potentially multi-centre studies would be needed to draw more definitive conclusions. This could be achieved by conducting a meta-analysis.

Conclusion

This small exploratory investigation has demonstrated that at our centre daily matching to fiducial markers improves treatment field placement compared with MV bony anatomy matching. Dose escalation and hypo-fractionated treatment should only be used with patients who have fiducial markers for accurate localisation. Although fiducial markers have an associated increase in expense to the department and pose a small risk of infection to the patient, we believe that the improvements in field placement justify this new procedure and related verification protocols. Our centre now uses fiducial markers routinely for majority of our patients requiring radiation therapy to the prostate gland, especially for those being dose escalated to 78 Gy.

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