**Assessment of a daily on-line implanted fiducial marker guided prostate
radiotherapy process**

P.B. Greer^{1,2}, K. Dahl¹, M.A. Ebert^{1,2}, M. White, C. Wratten^{1,2}, P. Ostwald^{1,2}, P.
5 Pichler¹ and J.W. Denham^{1,2}

- 1. Calvary Mater Newcastle Hospital, Newcastle, New South Wales, Australia*
- 2. University of Newcastle, Newcastle, New South Wales, Australia*

10

Corresponding Author

Dr Peter Greer

Dept. of Radiation Oncology

Calvary Mater Newcastle Hospital

15 Locked Bag 7

Hunter Region Mail Centre

NSW 2310

AUSTRALIA

Tel: +61 (0)417 870 071

20 Fax: +61 (0)2 4960 2566

Email: peter.greer@mater.health.nsw.gov.au

ABSTRACT

25 *Aim*

To investigate whether intra-fraction prostate motion can affect the accuracy of on-line prostate positioning using implanted fiducial markers and determine the effect of prostate rotations on the accuracy of the software predicted setup correction shifts.

Methods

30 Eleven patients were treated with implanted prostate fiducial markers and on-line setup corrections. Orthogonal electronic portal images (EPI's) were acquired to determine couch shifts before treatment. Verification images were also acquired during-treatment to assess whether intra-fraction motion had occurred. A limitation of the on-line image registration software is that it does not allow for in-plane prostate
35 rotations (evident on lateral portal images) when aligning marker positions. The accuracy of couch shifts was assessed by repeating the registration measurements with separate software that incorporates full in-plane prostate rotations. Additional treatment time required for on-line positioning was also measured.

Results

40 For the patient group the overall post-alignment systematic prostate errors were less than 1.5 mm (1 standard deviation) in all directions (range 0.2–3.9 mm). The random prostate errors ranged from 0.8 to 3.3 mm (1 SD). One patient exhibited intra-fraction prostate motion resulting in a post-alignment prostate setup error of over 10 mm for one fraction. In 14 of the 35 fractions the post-alignment prostate setup error was
45 greater than 5 mm in the anterior-posterior direction for this patient. Maximum prostate rotations measured from the lateral images varied from 2 to 20 degrees for the patients. The differences between setup shifts determined by the on-line software without in-plane rotations to align markers, and with rotations applied, was less than 1 mm (root-mean-square), with a maximum difference of 4.1 mm.

50 *Conclusions*

Intra-fraction prostate motion was found to reduce the effectiveness of the on-line setup for one of the patients. A larger study is required to determine the magnitude of this problem for the patient population. The inability in the current software to incorporate inplane prostate rotations is a limitation that should not introduce large
55 errors provided that the treatment isocentre is positioned near the centre of the prostate.

INTRODUCTION

The aim of prostate external beam radiotherapy is to deliver a high dose of radiation to the prostate while sparing surrounding normal tissues. As the prostate is a mobile organ, to determine the position before each daily radiotherapy treatment and hence target the beams to the prostate location is advantageous. This could lead to reduced margins and potentially higher doses. The prostate can not be seen directly on standard electronic portal images taken prior to daily radiotherapy treatment.. However small gold markers or seeds implanted within the prostate are visible. These can then be used with image registration software to determine couch shifts to target the treatment beams to the prostate by comparison with reference images created during treatment planning. These reference images show the location of the seeds within the prostate relative to the field borders.

The feasibility of localization of the prostate with implanted seeds and radiographic film was reported as early as 1995 by Balter *et al.*¹ Even earlier, radio-opaque markers were implanted within the prostate and visualized on portal images to aid in determining the prostate apex². Daily implanted marker guided treatment relies on the stability of the marker position within the prostate throughout the course of radiotherapy. This stability has been measured by a number of authors^{3 4 5 6 7 8}.

Intra-fraction motion of the prostate has major consequences for implanted marker guidance, as motion of the prostate could potentially occur between initial positioning and treatment, or during the treatment delivery itself. Two studies acquired portal images before and subsequent to the radiotherapy treatments using implanted markers. In the first, 47 patients were studied with an average of 5 fractions per patient imaged. They found a maximum standard deviation of 2.0 mm for intra-fraction prostate motion. The second study with 18 patients reported the standard deviations of random and systematic prostate displacements were less than 1.4 mm and 0.7 mm. and found only very small prostate movements^{9 10}. However a study of intra-fraction prostate motion of the prostate for 10 patients found marker (prostate) displacements as large as 9.5 mm in one fraction¹¹. A study using the Calypso system found that during 8 min, 2 of 11 patients showed significant prostate motion (>1 cm), with some motion lasting longer than 1 min¹². In order to define potential reductions of treatment

90 planning margins an understanding of the magnitudes and frequencies of intra-fraction prostate motion during on-line image guided radiation therapy is needed.

Rotations of the prostate can also occur and there are two aspects to prostate rotations that must be considered. The first aspect is the accuracy of prostate misalignment
95 measurements in the presence of prostate rotations. The commercial software used at our centre (Varian VaRis, Palo Alto, CA, USA) permits only 2D translations to align markers. When in-plane prostate rotation occurs (which are apparent in lateral portal images,) the markers can not be completely aligned with the marker positions in the reference images - digitally reconstructed radiograph (DRRs). The couch shifts
100 (translations) to accurately position the prostate for treatment could potentially then be inaccurate. We therefore investigated in this work whether the errors in setup shifts when in-plane rotations of the markers (prostate) are not incorporated into the registration procedure are significant.

105 The second aspect is correcting for prostate rotations by rotating the three-dimensional dose distribution within the patient to match the prostate rotation. This is a complex procedure and would require rotation of lateral beam collimator angles or MLC positions, combined with angulation of anterior-posterior fields using a combination of couch and gantry rotations. As depth to the prostate could change
110 along with potential doses to normal tissues, this approach is not generally employed, and the implications not well understood. We minimize the necessity to correct for prostate rotations in our treatment procedure by positioning the isocentre at the centre of the prostate. Therefore the translation and rotation corrections become nearly independent. The displacement of the borders of the prostate due to rotations are
115 relatively small and easily encompassed by our treatment margins (following translation corrections).

The aim of this prospective pilot study was to report the initial observations of an online implanted fiducial marker guided prostate radiotherapy process. Two major
120 aspects of the process were investigated - the effect of intra-fraction motion on the accuracy of the alignment procedure was determined by acquiring verification images during-treatment, and the errors introduced in the reported couch shifts due to the inability to incorporate in-plane prostate rotations were investigated.

METHODS AND MATERIALS

125 DATA ACQUISITION

Gold Marker Insertion

Three 24 carat 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. Ethical approval was obtained for the protocol from the local
130 Hunter Area Health Ethics Committee. The sterile markers were pre-loaded into the needles just prior to insertion and the needle-end sealed with sterile bone wax to keep the seeds in place during the insertion. The seeds were placed with two located in the base of the prostate laterally and one near the apex. A local anaesthetic was used in all cases.

135

CT Planning

CT scanning was performed 1 week after the marker insertion. To ensure a full bladder for simulation and each treatment fraction, patients were instructed to empty their bladder 1 hour prior to the appointment. They were then asked to drink 2 glasses
140 of water (approx 500 mls) and to hold this in their bladder until the appointment was complete. A 2.5 mm CT slice thickness was used. The bowel preparation protocol during their treatment course consisted of a laxative each evening, at least 6 glasses of water per day, and a high fibre diet. Patient setup was supine on a flat couch top. Urethral contrast (10 cc) was used to assist with determining the apex of the prostate.
145 A four-field conformal box technique with 18 MV photons was planned with the isocentre placed approximately in the centre of the prostate. The prescribed dose was 70 Gy in 35 fractions. The CTV to PTV margins were the conservative margins used for our conventional bony anatomy based setup of 1.5 cm laterally/anteriorly and 1.0 cm posteriorly. As this was a pilot study of a new technique we retained the
150 conventional margins. One of the aims of the study (not reported here) was to determine appropriate margins for this setup technique based on measurements of our on-line prostate setup accuracy. DRRs were produced for all four fields that incorporated both bony anatomy and gold markers for prostate position using the Pinnacle treatment planning system Version 6.2 (Philips Medical Systems, WI, USA).

155

On-line setup procedure

The patients were setup supine on a solid carbon fibre couch top. No pelvic immobilization devices were used. Ankle-stocks were used to ensure consistent leg positioning, along with knee cushions (Med-tec, Orange City, IA). The medial-lateral isocentre position was set by aligning the in-room lasers with the anterior-posterior (AP) tattoo placed on the midline of the patient above the isocentre. The superior-inferior (SI) isocentre position was set by aligning the lasers with the AP and lateral tattoos. The anterior-posterior isocentre position was set with the couch-height technique where the couch top is positioned at a reference height below the isocentre.

Orthogonal anterior-posterior (AP) and Right-Lateral (RL) portal images were acquired prior to treatment with an amorphous silicon EPID (Varian aS500, Palo Alto, USA). These were acquired with the treatment energy (18 MV), and the treatment field aperture using 2-3 monitor units (MU). These MU delivered for imaging were subtracted from the treatment beam MU so that no additional dose was delivered due to the on-line imaging procedure.

The image registration software (Varis 4D console, Varian, Palo Alto, USA) was then used to determine couch shifts using the implanted prostate markers. With this software method the portal image and DRR are overlaid and a blend tool is used to simultaneously view the seed locations in both images. The portal image can then be translated to align the seeds. The central axis location in the DRR is stored with the DRR image. The central axis location from the portal image is determined by a field edge detection and an overlay of the planned MLC aperture with this detected edge.

Following the seed alignment the displacement of the central axes is used to determine the couch shifts. Aligning the markers corrects for the combined patient setup error and prostate internal displacements from the planned position. No rotations in the plane of the image are possible within this software so only translations were measured and corrected. In some cases prostate rotation was apparent in the lateral images, and the markers could not be accurately aligned with the markers in the reference image (Figure 1). In these cases the markers at the base of the prostate were aligned. The accuracy of the reported translations is investigated in this work by comparison to translation results obtained when prostate rotation is included in the matching procedure, and all markers are aligned.

The patient position was then corrected using the couch coordinates reported by the image registration software. These were manually applied by the radiation therapists within the treatment room, as remote couch shifting capability was not available. The treatment was performed with the gantry rotating anticlockwise, in the order posterior-anterior (PA), left-lateral (LL), AP and RL. Images were acquired during the first two treatment beams the PA and LL beams. The software would not allow the previous beams to be re-imaged so the opposite direction beams were used. The isocentre of this linear accelerator is encompassed by a sphere of less than 1.5 mm diameter, with smaller difference between the beam axes for opposing lateral fields. As the isocentre is positioned in the centre of the prostate the effect of comparing results from opposing portals is likely to be very small. For each patient the time required for the on-line setup process was measured using the time-stamps of the first pre-treatment image acquired and the first treatment beam image. The time-interval defined by these time-stamps represents the extra time required for on-line setup of the patient. Although off-line corrections to the pre-treatment setup position were also applied according to our standard off-line protocol, the effect of these shifts were removed from the data, and have no bearing on the results.

DATA ANALYSIS

Prostate setup accuracy and intra-fraction motion

The setup accuracy obtained with the on-line setup process was evaluated by quantifying the random and systematic errors according to standard methods. The individual patient prostate systematic errors were quantified by the mean displacement over the treatment course. The individual patient random errors were calculated by the standard deviation of the daily displacements. The group systematic error is defined as the standard deviation of the individual patient systematic errors. This quantifies the spread or size of the systematic errors. The overall mean of the individual patient systematic errors was also calculated and should be close to zero, as systematic deviations in either direction should be equally likely. The group random errors are calculated from the root-mean-square (RMS) of the individual patient random errors. The pre-alignment prostate individual patient systematic errors were determined by comparison of the pre-treatment AP and RL images and their respective DRRs. The post-alignment systematic prostate deviations were derived

from comparison of the PA and LL during-treatment images with their respective
225 DRRs. The residual post alignment prostate displacements are used to evaluate intra-
fraction prostate motion.

Inability to perform inplane rotation for image registration

To determine the magnitude of errors that might be introduced by the software
230 limitations on in-plane rotations, the image registrations for all of the pre-treatment
images were repeated with software that allows in-plane rotations to be applied
(Vision, Varian, Palo Alto, USA). In this case all of the markers in the DRR and EPI
can be aligned, and the software then reports the setup displacements and the rotation.
These results were compared to the on-line 4D console image registration results
235 without the ability to rotate in-plane. The on-line results were to the nearest mm as
only the couch coordinates are recorded. A total of 380 setup shifts were compared for
the 11 patients. Data from five fractions were not recorded due to imaging failure or
missed images on these days.

Marker Migration

To assess whether the markers were migrating the inter-marker distances were
measured for each patient for every third treatment fraction. These were measured
with the Vision software ruler tool for the pre-treatment images. In this case the
measured distance is scaled to the isocentre plane based on the recorded EPID
245 distance. The standard deviation of the inter-marker distances for each patient were
calculated.

RESULTS

Prostate setup accuracy and intra-fraction motion

250 Overall the post-alignment systematic prostate deviations for the group were -0.1 ± 0.5
mm, 0.8 ± 1.4 mm and 0.6 ± 1.4 mm (mean $\pm$ 1 SD) in the medial-lateral (ML),
superior-inferior (SI) and anterior-posterior (AP) directions respectively. The
systematic error comparison is shown in Figure 2. Apart from one case for the lateral
fields the systematic errors after alignment are all within 2 mm in all directions. The
255 larger error was due to intra-fraction prostate motion and is discussed below.

The group prostate random setup errors after alignment were 1.2, 1.9 and 1.7 mm (1 standard deviation) in the ML, SI and AP directions respectively. The range was 0.8 to 3.3 mm. The actual treatment field errors measured at each treatment fraction pre- and post- on-line correction are shown in Figure 3 for both the anterior-posterior fields and the lateral fields.

Patient 10 exhibited poorer treatment accuracy than the other patients following fiducial marker alignment for the lateral fields. To determine whether this was due to intra-fraction patient or internal prostate motion, the difference in bony anatomy position pre-treatment and during-treatment was assessed, removing the effect of any setup shifts. These positions differed by a RMS difference of 1.0 mm (1 standard deviation) showing that the patient position was stable during the treatments. Intra-fraction prostate motion could then be identified as the cause. Figure 4 shows an example from one of the treatment fractions of the movement of the prostate between pre-treatment imaging and treatment imaging that occurred for this patient. While the bony anatomy position within the field aperture is consistent, the prostate has moved inferiorly and posteriorly from the initial setup position. This patient had a maximum prostate setup error from the verification images in one fraction of 10.2 mm in the SI direction and 7.9 mm in the AP direction. In 14 of the 35 fractions the treatment error was greater than 5 mm in the AP direction.

Figure 5 shows a histogram of the additional time required for the on-line setup procedure. The average time overhead for the patients was 5 minutes (range of averages 3.8-6.0 min), with a minimum time observed for any of the treatment fractions of 2.2 minutes, and a maximum of 10.3 minutes. The first and second days of treatment for each patient were excluded from these data, as longer setup times are common particularly for the first treatment day.

Inability to perform inplane rotation for image registration

Six of the patients had maximum prostate rotations measured from the lateral images of greater than 5 degrees. The average and maximum prostate rotations measured from these fields for the patients are given in Table 1. These show that the prostate rotations can be significant, and the inability of the software to allow for inplane rotations is clearly an unnecessary limitation. The RMS standard deviations of the

differences in the image registration results with and without inplane rotation applied were 0.9, 1.0 and 1.1 mm in the ML, SI and AP directions respectively. A maximum difference of 4.1 mm was found.

295 *Marker Migration*

The RMS standard deviation for the inter-marker distances was 0.7 mm (range 0.4-1.1 mm). Some small systematic changes in the inter-marker distances were apparent visually for four of the patients, however these were a maximum drift of 2 mm. From these results the markers can be used as a reliable surrogate for prostate position.

300

DISCUSSION

The pre-treatment systematic errors for the medial-lateral direction were mainly to the patient right. This was due to bony anatomy positioning, not displacement of the prostate. The reason that most patients were initially setup with the fields too far to the right is unclear and is currently being investigated. Studies previously performed of bony anatomy setup accuracy for prostate patients at our center have not shown this trend.

Where intra-fraction prostate motion does not occur, the on-line correction procedure was found to result in small systematic errors. The size of the errors suggest that significant margin reductions could be made for future patients treated with on-line fiducial guidance. Potential margins for these patient are to be examined in a separate report. For the patient that exhibited intra-fraction prostate motion, the prostate systematic error was still reduced by the correction procedure. For one of the patients a post-alignment systematic error in the superior direction of 3.9 mm was found from the left lateral field data (Figure 2b) whereas for the posterior field data the systematic error was 1.7 mm. The intra-fraction motion could be the cause of this discrepancy, as the left lateral field is imaged later than the posterior field. The systematic errors in the SI direction for all the other patients showed agreement between the left-lateral and posterior fields of within 1.1 mm. The patient numbers in this study are not sufficient to determine what percentage of patients exhibit intra-fraction prostate motion that is sufficiently large to compromise the on-line setup procedure.

Whether the amount of intra-fraction prostate motion depends on the time elapsed
325 between initial imaging and treatment imaging is of interest. Masden *et al.*⁹ presented
analysis of radiographs at 6-min intervals for 6 patients showing the greatest prostate
motion occurred between 0-6 min. Ghilezan *et al.*¹³ used cine MRI to examine the
time course of prostate motion. They found a 10% probability of moving more than 3
mm in a time frame of ~1 min if the rectum is full vs. ~20 min if the rectum is empty.
330 There is insufficient data at present to know whether reducing the time between initial
imaging and treatment will reduce the probability of prostate motion. In our study the
first two treatment beams were imaged, whereas potentially imaging the latter two
treatment beams would result in a greater prostate motion due to the longer elapsed
time.

335 The treated prostate random errors were small being less than 2 mm in all directions.
This shows the effectiveness of on-line alignments where random positioning errors
are corrected, as opposed to off-line corrections. In a study where off-line corrections
using seeds were used¹⁴, the random errors were similar to bony anatomy based
340 positioning being 3.0 mm (1 SD) in the superior-inferior direction and 4.0 mm in the
anterior-posterior direction. On-line positioning will therefore allow further margin
reduction than off-line protocols.

The time overhead for on-line positioning found here is greater than that reported by
345 Herman *et al.*¹⁵ which was 2.0 minutes longer than patients without pre-treatment
imaging and Chung *et al.*¹⁶ who found an additional 3 minutes of treatment time was
required. Both of these on-line correction protocols used thresholds for correction, so
that on some treatment days no correction would be made, which would reduce the
time overhead for that fraction significantly. Herman *et al.* corrected only 53% of
350 daily treatments. We corrected 100% of displacements in this study and therefore the
time overhead is greater. The use of a threshold value is currently being considered.
The time overhead results were for a system without remote couch shifting capability,
the radiation therapists had to re-enter the room to reposition the couch. Newer
accelerator and on-board imaging systems have this capability and we would expect
355 this to reduce the time. Moreover greater experience with this technique is also likely
to reduce the time overhead.

There are three main approaches to image registration measurements with implanted fiducial markers. The most rigorous is full three-dimensional image registration where the 3D coordinates of each seed are calculated from two or more images, and the displacements from the 3D planned positions determined. The next approach is a 2D method usually based on template matching where the planned marker positions are aligned with the markers on each individual portal image by rotations and translations. This method does not account for out-of-plane rotations. A third even less robust method is available with some commercial on-line software modules that only allows in-plane translations. Our software used the third approach, however we have found that accurate translations are still made. This is due to the fact that we position the centre of the prostate close to the isocentre. This minimizes errors in the translation results due to the inability to rotate in-plane.

The degree of prostate rotation found in this study is significant. Both ankle stocks and knee-cushions were used to ensure stable patient position and minimize rotations. Therefore the rotations are likely to be due to changes in internal anatomy such as bladder filling. Without cone-beam CT information no definitive conclusions can be drawn.

CONCLUSIONS

The aim of this work was to report the initial observations of an online implanted fiducial marker guided prostate radiotherapy process and determine the effect of prostate rotations on the accuracy of the setup correction shifts. Intra-fraction prostate motion was found to reduce the effectiveness of the on-line setup for one of the patients. Further study is required, potentially in a multi-centre setting to determine what percentage of patients exhibit this motion, and to develop better strategies to deal with it. The inability in the current software to incorporate inplane prostate rotations during the matching procedure did not introduce large errors in translation measurements with the treatment isocentre positioned near the centre of the prostate. The dosimetric implications of rotational misalignments has not however been explored.

390 **ACKNOWLEDGEMENTS**

This work was kindly supported by the Cancer Council NSW, Project Grant RG 07-06.

395 **FIGURES**

Figure 1

An image illustrating the limitation in the image-registration procedure where in-plane prostate rotation can not be accounted for in the measurement process, and only
400 two of the prostate seeds are aligned with the planning DRR template.

Figure 2

Prostate systematic errors before and after the on-line correction procedure, for a) the AP/PA fields and (b) the lateral fields.

405

Figure 3

Prostate treatment displacements from the planned position for (a) pre-treatment anterior-posterior fields, b) post-alignment anterior-posterior fields, c) pre-treatment lateral fields, d) post-alignment lateral fields.

410

Figure 4

Example of the intra-fraction prostate motion observed for one of the patients, with (a) pre-treatment anterior-posterior image, and (b) during treatment posterior-anterior image, acquired after patient repositioning, c) pre-treatment right lateral image, and
415 (d) during treatment left-lateral image The movement of the prostate relative to bony anatomy between these images is apparent.

Figure 5

Histogram of the time overheads for the on-line setup that are in addition to the
420 normal treatment time.

TABLES

Table 1

425 Prostate rotations measured from the lateral fields for the patients. Positive indicates rotation of the apex of the prostate toward the posterior, and base of the prostate toward the anterior.

Patient	Average prostate rotation (degrees)	Maximum prostate rotation (degrees)
1	1.5	13.6
2	0.1	-2.0
3	0.5	-4.0
4	0.3	4.0
5	0.4	-4.6
6	1.5	6.2
7	0.7	-3.0
8	0.9	-5.0
9	3.0	10.3
10	10.0	-19.9
11	3.1	-17.0

430

Figure 1

435

Figure 2

440

(a)

(b)

(c)

(d)

Figure 3

455

460

465 (a)

(b)

(c)

(d)

470 **Figure 4**

475 **Figure 5**

REFERENCES

1. Balter JM, Lam KL, Sandler HM, *et al.* Automated localization of the prostate at the time of treatment using implanted radiopaque markers: Technical feasibility. *International Journal of Radiation Oncology Biology Physics* 1995;33:1281-1286.
2. Sandler HM, Bree RL, McLaughlin PW, *et al.* Localization of the prostatic apex for radiation therapy using implanted markers. *International Journal of Radiation Oncology Biology Physics* 1993;27:915-919.
3. Dehnad H, Nederveen AJ, Van Der Heide UA, *et al.* Clinical feasibility study for the use of implanted gold seeds in the prostate as reliable positioning markers during megavoltage irradiation. *Radiotherapy and Oncology* 2003;67:295-302.
4. Kitamura K, Shirato H, Shimizu S, *et al.* Registration accuracy and possible migration of internal fiducial gold marker implanted in prostate and liver treated with real-time tumor-tracking radiation therapy (RTRT). *Radiotherapy and Oncology* 2002;62:275-281.
5. Pouliot J, Aubin M, Langen KM, *et al.* (Non)-migration of radiopaque markers used for on-line localization of the prostate with an electronic portal imaging device. *International Journal of Radiation Oncology Biology Physics* 2003;56:862-866.
6. Kupelian PA, Willoughby TR, Meeks SL, *et al.* Intraprostatic fiducials for localization of the prostate gland: Monitoring intermarker distances during radiation therapy to test for marker stability. *International Journal of Radiation Oncology Biology Physics* 2005;62:1291-1296.
7. Schallenkamp JM, Herman MG, Kruse JJ, *et al.* Prostate position relative to pelvic bony anatomy based on intraprostatic gold markers and electronic portal imaging. *International Journal of Radiation Oncology Biology Physics* 2005;63:800-811.
8. van der Heide UA, Kotte ANTJ, Dehnad H, *et al.* Analysis of fiducial marker-based position verification in the external beam radiotherapy of patients with prostate cancer. *Radiotherapy and Oncology* 2007;82:38-45.
9. Madsen BL, Hsi RA, Pham HT, *et al.* Intrafractional stability of the prostate using a stereotactic radiotherapy technique. *International Journal of Radiation Oncology Biology Physics* 2003;57:1285-1291.
10. Aubry JF, Beaulieu L, Girouard LM, *et al.* Measurements of intrafraction motion and interfraction and intrafraction rotation of prostate by three-dimensional analysis of daily portal imaging with radiopaque markers. *International Journal of Radiation Oncology Biology Physics* 2004;60:30-39.
11. Nederveen AJ, Heide UAv, Dehnad H, *et al.* Measurements and clinical consequences of prostate motion during a radiotherapy fraction. *International Journal of Radiation Oncology Biology Physics* 2002;53:206-214.
12. Willoughby TR, Kupelian PA, Pouliot J, *et al.* Target localization and real-time tracking using the Calypso 4D localization system in patients with localized prostate cancer. *International Journal of Radiation Oncology Biology Physics* 2006;65:528-534.
13. Ghilezan MJ, Jaffray DA, Siewerdsen JH, *et al.* Prostate gland motion assessed with cine-magnetic resonance imaging (cine-MRI). *International Journal of Radiation Oncology Biology Physics* 2005;62:406-417.

14. Nederveen AJ, Dehnad H, Van Der Heide UA, *et al.* Comparison of megavoltage position verification for prostate irradiation based on bony anatomy and implanted fiducials. *Radiotherapy and Oncology* 2003;68:81-88.
- 530 15. Herman MG, Pisansky TM, Kruse JJ, *et al.* Technical aspects of daily online positioning of the prostate for three-dimensional conformal radiotherapy using an electronic portal imaging device. *International Journal of Radiation Oncology Biology Physics* 2003;57:1131-1140.
- 535 16. Chung PWM, Haycocks T, Brown T, *et al.* On-line aSi portal imaging of implanted fiducial markers for the reduction of interfraction error during conformal radiotherapy of prostate carcinoma. *International Journal of Radiation Oncology Biology Physics* 2004;60:329-334.