Int. J. Radiation Oncology Biol. Phys., Vol. ■, No. ■, pp. 1–6, 2009

0360-3016/09/$–see front matter

ELSEVIER

doi:10.1016/j.ijrobp.2009.04.041

CLINICAL INVESTIGATION

A PROSPECTIVE STUDY OF INTRAFRACTION PROSTATE MOTION IN THE PRONE VS. SUPINE POSITION

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Purpose: To prospectively analyze prostate intrafraction motion in the prone vs. supine position and to assess patient satisfaction with these two positions.
Methods and Materials: Fifteen prostate cancer patients underwent implantation of five fiducial gold seeds in their prostate for localization. Patients were treated with high-dose-rate brachytherapy to 2,200 cGy followed by intensity-modulated radiation therapy (IMRT) to 5,040 cGy. Patients underwent computed tomography simulation and IMRT in the prone position. For the first five IMRT treatments, an electronic portal imaging system was used to acquire anteroposterior (AP) and lateral images pretreatment and posttreatment. We then repositioned each patient supine and repeated the process, resulting in 600 images.
Results: Mean ± standard deviation intrafraction prostate motion was 2.1 ± 1.2 mm and 1.7 ± 1.4 mm (AP, $p = 0.47$), 2.2 ± 2.0 mm and 1.6 ± 1.8 mm (superoinferior, $p = 0.16$), and 1.0 ± 1.2 mm and 0.6 ± 0.9 mm (left-right, $p = 0.03$) in the prone and supine positions, respectively. Eighty percent of patients stated that they were more comfortable in the supine position ($p = 0.02$).
Conclusions: Prone and supine positions resulted in a similar magnitude of AP and superoinferior intrafraction prostate motion (2 mm). Because there was no significant difference in the magnitude of AP and superoinferior prostate motion prone vs. supine and patients were more comfortable in the supine position, patients now undergo IMRT to the prostate and seminal vesicles at our center in the supine position.

Intrafraction, Prostate, Motion, Prone, Supine.

INTRODUCTION

Online image guidance to account for interfraction movement of the prostate has become routine clinical practice in many radiotherapy departments. Although this allows for a substantial reduction of planning target volume (PTV) margins around the prostate (1, 2), residual errors remain because of inaccuracies of the imaging and repositioning system and intrafraction prostate motion (3). For example, intrafraction prostate motion accounts for approximately 2 mm of the PTV margins with intensity-modulated radiation therapy (IMRT) (4–7).

The purpose of this study is to determine the magnitude of intrafraction motion of the prostate in the prone vs. supine position for IMRT and to assess patient satisfaction with these two positions.

METHODS AND MATERIALS

Implantation of fiducial gold seeds

Between December 2007 and March 2008, 15 consecutive early-stage prostate cancer patients underwent transrectal implantation of five fiducial gold seeds (diameter, 1 mm; length, 5 mm; Alpha-Omega Services, Inc., Bellflower, CA) in their prostate. A urologist performed the seed implantation using ultrasound guidance with a Hitachi EUB-6000 ultrasound scanner (Hitachi Medical Corporation, Tokyo, Japan), local anesthesia, and a 17-gauge needle. Seeds were placed at the following positions in the prostate: (*1*) base, (*2*) right lateral, (*3*) posterior mid-gland, (*4*) left lateral, and (*5*) apex. All of the seeds were placed in the periphery of the prostate.

Patient immobilization, simulation, treatment planning, and treatment

Patients emptied their bladder 15 minutes before simulation and treatment. We placed patients on a low-residue diet (8), but did not require emptying of the rectum before simulation and treatment. We immobilized patients for IMRT in the prone or supine position using a Velcro strap around their feet. We also placed a Styrofoam wedge under patients' shins when they were treated prone vs. under their knees when they were treated supine.

Patients underwent computed tomography simulation with 3-mm slices on a General Electric Discovery ST 16 (*GE* Healthcare, Milwaukee, WI). We used the SIMUPLAN treatment planning

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Presented at the 50th Annual Meeting of the American Society for Therapeutic Radiology and Oncology, September 21–25, 2008, Boston, MA.

Conflict of interest: none.

Received Dec 23, 2008, and in revised form April 22, 2009. Accepted for publication April 23, 2009.

system (Advanced Brachytherapy Solutions, Madrid, Spain) for high-dose-rate brachytherapy and the Varian Eclipse treatment planning system (Varian Medical Systems, Palo Alto, CA) for IMRT. If the risk of pelvic lymph node involvement was ≤15% according to the formula % lymph node risk = 2/3 × PSA + ([Gleason score – 6] × 10), then the clinical target volume (CTV) for IMRT was the prostate gland and inferomedial 10 mm of the seminal vesicles (9). The CTV was treated to 5,040 cGy using daily 180 cGy fractions. The PTV included variable margins up to 10 mm on the CTV. At least 98% of the PTV received 100% of the prescribed dose. If the risk of pelvic lymph node involvement was >15%, the initial IMRT CTV also included the pelvic lymph nodes, as defined by Hsu *et al*. (10). In such cases, we delivered 4,500 cGy to the initial CTV using daily 180 cGy fractions. We then administered three daily 180 cGy fractions to the final CTV consisting of the prostate and inferomedial 10 mm of the seminal vesicles.

We treated patients with an iridium-192 high-dose-rate brachytherapy remote afterloader (Nucletron, Veenendaal, The Netherlands) to 2,200 cGy in four fractions (twice-daily fractions were delivered 1 week apart). We treated patients with IMRT to 5,040 cGy in 28 fractions in the prone position. IMRT began 1–4 days after the completion of high-dose-rate brachytherapy. Patients were treated with IMRT on a Varian 23iX linear accelerator (Varian Medical Systems) using 6-MV photons. The linear accelerator's gantry sag ranged from 0.5 mm to 1.0 mm at isocenter between 0° and 180°.

Adjustment for interfraction prostate motion

We used the Varian On-Board Imager, a gantry-mounted digital kilovoltage (kV) imaging system, to acquire AP and lateral localization images before each IMRT treatment. The On-Board Imager consists of a kV x-ray source, an amorphous silicon kV digital image detector, and two robotic arms that independently position the kV source and imager orthogonal to the treatment beam. Seed positions were determined on radiographs and aligned to reference positions on simulation radiographs. Therapists used online, computer-controlled couch adjustment to account for interfraction motion of the prostate by adjusting the day-to-day isocenter to the simulation isocenter (11). Therapists adjusted patients to the simulation isocenter prior to each treatment. If the prostate gland had rotated, therapists aligned the patient based on the posterior mid-gland fiducial gold seed.

Intrafraction prostate motion detection

For the first 5 IMRT treatments, we used the gantry-mounted digital kilovoltage electronic portal imaging system to acquire anteroposterior (AP) and lateral localization images pretreatment (first set) and posttreatment (second set) in the prone position. Immediately after treatment, we repositioned each patient supine. We then acquired a fourth and final set of AP and lateral images of the patient each day 11 min after the third set of AP and lateral images to simulate IMRT treatment time in the supine position. We obtained a total of 600 prone and supine images and used an in-house image analysis program to assess prostate displacement offline based on the ‘‘center of mass’’ of the prostate relative to isocenter. The center of mass of the prostate at the beginning and end of each 11-min period was calculated based on the x, y, and z coordinates of the five fiducial gold seeds. Center of mass is defined here as the average of the x, y, and z coordinates of the five gold seeds. Negative values for the ranges in Table 1 indicate prostate motion in the posterior, inferior, or right directions. Means and standard deviations in Table 1 were calculated based on absolute values of prostate motion.

Patient questionnaire

Patients were interviewed with a standardized questionnaire asking if they were more comfortable in the prone or supine position.

Statistical analysis

Systematic error represents the average displacement of the prostate's position at treatment relative to its position at simulation (*i.e*., the standard deviation of the means per patient of the absolute values of prostate motion, Σ) (4). Systematic error is due to prostate motion and setup error. Random error is the variation of the prostate's position at treatment about its mean value (*i.e*., the square root of the mean of the variances of the absolute values of prostate motion per patient, σ) (4).

We calculated the mean and standard deviation of intrafraction prostate motion based on the absolute values of measurements in the AP, superoinferior (SI), and left-right (LR) dimensions. For each patient, we also calculated means of the absolute values for prostate motion in the AP, SI, and LR dimensions in the prone vs. supine position. This resulted in 15 mean values for prostate motion in the prone position and 15 in the supine position for each dimension of prostate motion. We compared means in the prone vs. supine position using a two-tailed Wilcoxon signed rank test (12). We used the Pearson correlation (13) to determine if the direction of prostate motion (anterior or posterior) in the prone vs. supine position was consistent across patients.

We analyzed patient questionnaires using a binomial test (14) with a null hypothesis that patients are equally comfortable in the prone or supine position.

RESULTS

Intrafraction prostate motion in the prone and supine positions is presented in Table 1. Mean ± standard deviation intrafraction prostate motion was 2.1 ± 1.2 mm and 1.7 ± 1.4 mm (AP, p = 0.47), 2.2 ± 2.0 mm and 1.6 ± 1.8 mm (SI, p = 0.16), and 1.0 ± 1.2 mm and 0.6 ± 0.9 mm (LR, p = 0.03) in the prone and supine positions, respectively. Intrafraction prostate motion to the left occurred to a lesser degree in the supine position.

In the prone position, AP and SI motion >2 mm occurred in 35% and 49% of treatments, respectively. In the supine position, AP and SI motion >2 mm occurred in 25% and 45% of cases, respectively. The largest absolute values for intrafraction prostate motion in the AP direction were 8 mm and 6 mm in the prone and supine positions, respectively. Similarly, the largest absolute values for intrafraction prostate motion in the SI direction were 7 mm and 6 mm in the prone and supine positions, respectively.

In the prone position, the systematic error of AP intrafraction prostate motion was 1.2 mm and the random error was 2.0 mm. In the supine position, the systematic error of AP intrafraction prostate motion was 0.9 mm and the random error was 1.3 mm.

In the prone position, prostate motion was typically in the anterior direction (Table 1). In contrast, in the supine position, prostate motion was typically in the posterior direction (p = 0.02).

Twelve of 15 (80%) patients stated that they were more comfortable in the supine position (p = 0.02).

Table 1. Intrafraction prostate motion in the prone and supine positions

Prone									
	Anterior-Posterior			Superior-Inferior			Left-Right		
		Absolute values of prostate motion			Absolute values of prostate motion			Absolute values of prostate motion	
Patient	Range (mm)	Mean (mm)	SD (mm)	Range (mm)	Mean (mm)	SD (mm)	Range (mm)	Mean (mm)	SD (mm)
1	–3.0 to –1.0	1.6	0.9	–4.7 to 4.7	3.2	2.0	–1.1 to 3.0	1.3	1.1
2	0.0 to 3.0	1.2	0.0	–5.6 to 0.0	2.9	2.1	–1.9 to 1.9	1.4	0.8
3	–1.0 to 1.0	0.5	0.5	–3.9 to 0.0	1.6	1.7	0.0 to 2.1	0.8	1.1
4	–2.3 to 2.0	1.2	0.4	–3.2 to 1.1	2.1	0.7	0.0 to 0.0	0.0	0.0
5	0.8 to 8.0	5.2	5.1	–2.0 to 3.9	2.8	0.9	–2.3 to 3.2	2.1	0.8
6	–3.0 to 4.0	1.6	0.7	–3.7 to 0.0	1.3	1.8	–2.6 to 0.0	1.7	1.0
7	–5.0 to 6.0	3.4	2.8	–5.8 to 0.0	2.1	2.4	–2.8 to 0.0	0.8	1.2
8	0.0 to 4.0	2.0	0.7	0.0 to 2.8	0.6	1.3	–1.7 to 1.7	0.7	0.9
9	–2.0 to 4.0	1.9	1.1	–4.9 to 2.6	2.8	1.8	–1.5 to 6.0	1.8	2.5
10	–4.5 to 0.0	1.9	2.8	–6.0 to 2.8	2.3	2.3	–1.5 to 2.4	0.8	1.1
11	–2.0 to 8.0	3.2	4.9	–4.5 to 0.0	2.5	2.3	–3.2 to 0.0	1.4	1.4
12	–3.0 to 0.0	1.6	1.4	–3.2 to 0.0	1.0	1.5	0.0 to 2.9	1.0	1.4
13	–1.0 to 2.0	0.8	0.7	–4.0 to 0.0	0.8	1.8	–2.2 to 2.5	0.9	1.3
14	0.0 to 8.0	3.4	3.5	–6.0 to 0.0	2.4	2.5	–1.5 to 0.0	0.3	0.7
15	–5.0 to 2.0	2.4	2.8	–7.3 to 0.0	4.1	3.1	–2.2 to 1.1	0.7	1.0

Supine									
	Anterior-Posterior			Superior-Inferior			Left-Right		
		Absolute values of prostate motion			Absolute values of prostate motion			Absolute values of prostate motion	
Patient	Range (mm)	Mean (mm)	SD (mm)	Range (mm)	Mean (mm)	SD (mm)	Range (mm)	Mean (mm)	SD (mm)
1	–6.0 to 2.8	4.2	1.6	–6.0 to 0.0	3.9	2.4	–2.6 to 0.0	1.3	1.2
2	–2.0 to 1.0	0.7	1.0	–2.6 to 0.0	0.7	1.1	–1.1 to 0.0	0.2	0.5
3	–2.0 to 1.0	1.6	0.7	–3.2 to 0.0	2.3	1.3	0.0 to 3.0	1.1	1.5
4	–3.2 to -0.3	2.0	0.1	–2.6 to 0.0	1.0	1.3	–1.5 to 0.0	0.3	0.7
5	–0.8 to 1.0	0.7	0.0	–2.1 to 1.5	0.7	1.0	–1.3 to 1.7	0.6	0.8
6	–2.0 to 4.0	1.4	0.7	–3.4 to 4.0	2.0	1.9	0.0 to 2.1	0.8	1.1
7	–3.0 to 1.0	1.6	0.7	–5.0 to 0.0	1.6	2.3	–1.5 to 0.0	0.8	0.8
8	–3.0 to –1.0	2.0	0.7	–3.2 to 0.0	1.5	1.5	–1.3 to 1.7	0.6	0.8
9	–3.0 to 1.3	1.5	0.9	–2.1 to 3.2	1.7	1.2	0.0 to 2.1	0.8	1.1
10	–5.8 to 0.0	2.6	2.8	–6.2 to 0.0	1.7	2.7	–1.5 to 0.0	0.8	0.8
11	–3.0 to 0.0	1.4	2.1	0.0 to 0.0	0.0	0.0	0.0 to 2.1	1.1	1.0
12	–1.0 to 0.0	–0.1	0.8	–2.6 to 0.0	1.4	1.3	0.0 to 1.9	0.6	0.9
13	–6.0 to 0.0	2.0	1.4	–4.5 to 3.6	2.5	1.7	0.0 to 0.0	0.0	0.0
14	–2.0 to 0.0	1.2	0.0	–5.1 to 0.0	1.7	2.4	–1.5 to 0.0	0.3	0.7
15	–3.0 to –1.0	1.8	0.0	–3.3 to 0.0	1.7	1.6	–1.9 to 0.0	0.6	0.9

Abbreviations: mm = millimeter; SD = standard deviation.
Negative values for the range indicate prostate motion in the posterior, inferior, or right directions.

DISCUSSION

Some groups localize the prostate using tattoos and bony anatomy (15, 16) or ultrasound (17). These approaches suffer from a number of shortcomings. For example, the use of ultrasound is limited by bladder filling, the therapist's experience with interpretation of the images, and the amount of pressure applied against the patient's abdominal wall. Consequently, we used gold seeds and electronic portal images for localization of the prostate, realizing that there can sometimes be limited visibility of the seeds on lateral radiographs and there is a lack of volumetric information with this approach.

Many studies of intrafraction prostate motion have used pretreatment and posttreatment electronic portal images rather than cone-beam computed tomography scans of gold seeds implanted in the prostate (11, 16, 18–21). It would have taken an additional 24 min to perform four cone-beam computed tomography scans per patient. This was not feasible in our busy clinic. Consequently, we elected to use electronic portal images. If we had taken an additional 24 min to study intrafraction prostate motion with cone-beam computed tomography scans, measurements would have been less representative of the motion that occurs with current IMRT treatment times. We realize that real-time, continuous intrafraction imaging of the prostate is a more accurate approach (22). However, intrafraction imaging is not available at most centers and its cost-effectiveness remains unclear (2, 23).

Bony and internal organ movement causes intrafraction prostate motion (24). For example, leg motion and clenching of pelvic floor muscles can lead to prostate motion (25). Respiration can also result in prostate motion in the prone position (26). In addition, the type of immobilization device used can affect prostate motion. Because thermoplastic shells may result in significant intrafraction motion of the prostate when patients are treated prone (27, 28), we used a Styrofoam wedge and a Velcro strap for immobilization. Moreover, bladder and, to a greater degree, rectal filling can cause prostate motion (29). Prostate motion correlates strongly with rectal volume increases caused by gas in the rectum (30–34). Because we were interested in assessing intrafraction prostate motion, no attempt was made to immobilize the prostate, for example, with a rectal balloon.

Table 1 shows that there was significant variation in translational prostate motion among patients as observed by others (23, 35). We did not measure rotational or deformational changes of the prostate since they are small relative to translational changes (36).

Intrafraction prostate motion is less than interfraction prostate motion (16, 21, 32, 33, 37–40). Because interfraction prostate motion can be accounted for using implanted fiducial seeds and computer-controlled couch adjustment, intrafraction motion has become the most important factor limiting PTV margin reduction around the prostate (16, 41, 42).

Rectal toxicity limits the total dose of radiotherapy that can be administered for prostate cancer (43–45), suggesting that one needs to pay particular attention to intrafraction prostate motion in the AP and SI dimensions. In accordance with other groups (16, 37–39), we observed that intrafraction motion of the prostate is greater in the AP and SI dimensions than the LR dimension. In this study, intrafraction prostate motion was typically in the anterior direction when patients were treated in the prone position (Table 1). In contrast, prostate motion was typically in the posterior direction when patients were treated in the supine position ($p = 0.02$). Similarly, Nederveen *et al.* (7) reported that intrafraction prostate motion is typically in the posterior direction when patients are treated supine. Gravity may have accounted for the 0.9–1.2 mm systematic error (6) and rectal gas may have accounted for the 1.3–2.0 mm random error (4, 24) in prostate motion.

We exclude pelvic nodes from the PTV of our IMRT treatment plans if the risk of nodal involvement is ≤15% (9, 46, 47). Two thirds of our prostate cancer patients have a risk of pelvic lymph node involvement ≤15%. When IMRT is delivered to the prostate and seminal vesicles alone, intrafraction prostate motion and patient comfort are key factors in determining whether to treat patients in the prone or supine position. The prone and supine positions resulted in a similar magnitude of AP and SI intrafraction prostate motion (mean, 2 mm). Patients were more comfortable in the supine position. Because there was no significant difference in the magnitude of intrafraction prostate motion when patients were treated prone vs. supine and patients were more comfortable in the supine position, patients now undergo IMRT to the prostate and seminal vesicles at our center in the supine position.

In summary, intrafraction prostate motion is the main factor limiting PTV margin reduction around the prostate. The magnitude of intrafraction prostate motion correlates with radiotherapy delivery time (48). For an IMRT delivery time of 11 minutes, we observed AP and SI intrafraction prostate motion >2 mm in 25% and 45% of fractions in the supine position, respectively. Padhani *et al.* (25) observed that 57% of intrafraction prostate movements lasted less than 20 s and only two movements lasted more than 60 s. Reduction of IMRT delivery time to ~3 min with novel methods such as intensity-modulated arc therapy or volumetric-modulated arc therapy should reduce intrafraction prostate motion (24, 49), thereby facilitating PTV margin reduction.

REFERENCES

1. Chung PW, 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. *Int J Radiat Oncol Biol Phys* 2004;60:329–334.
2. Shimizu S, Shirato H, Kitamura K, *et al*. Use of an implanted marker and real-time tracking of the marker for the positioning of prostate and bladder cancers. *Int J Radiat Oncol Biol Phys* 2000;48:1591–1597.
3. Mansson Haska T, Honore H, Muren LP, *et al*. Intrafraction changes of prostate position and geometrical errors studied by continuous electronic portal imaging. *Acta Oncol* 2008;47:1351–1357.
4. Kotte AN, Hofman P, Lagendijk JJ, *et al*. Intrafraction motion of the prostate during external-beam radiation therapy: analysis of 427 patients with implanted fiducial markers. *Int J Radiat Oncol Biol Phys* 2007;69:419–425.
5. Li HS, Chetty IJ, Enke CA, *et al*. Dosimetric consequences of intrafraction prostate motion. *Int J Radiat Oncol Biol Phys* 2008;71:801–812.
6. Madsen BL, Hsi RA, Pham HT, *et al*. Intrafractional stability of the prostate using a stereotactic radiotherapy technique. *Int J Radiat Oncol Biol Phys* 2003;57:1285–1291.
7. Nederveen AJ, van der Heide UA, Dehnad H, *et al*. Measurements and clinical consequences of prostate motion during a radiotherapy fraction. *Int J Radiat Oncol Biol Phys* 2002;53:206–214.
8. Smitsmans MH, Pos FJ, de Bois J, *et al*. The influence of a dietary protocol on cone beam CT-guided radiotherapy for prostate cancer patients. *Int J Radiat Oncol Biol Phys* 2008;71:1279–1286.
9. Roach M 3rd, Marquez C, Yuo HS, *et al*. Predicting the risk of lymph node involvement using the pre-treatment prostate

specific antigen and Gleason score in men with clinically localized prostate cancer. *Int J Radiat Oncol Biol Phys* 1994;28:33–37.
10. Hsu A, Pawlicki T, Luxton G, *et al*. A study of image-guided intensity-modulated radiotherapy with fiducials for localized prostate cancer including pelvic lymph nodes. *Int J Radiat Oncol Biol Phys* 2007;68:898–902.
11. McNair HA, Hansen VN, Parker SI, *et al*. A comparison of the use of bony anatomy and internal markers for offline verification and an evaluation of the potential benefit of online and offline verification protocols for prostate radiotherapy. *Int J Radiat Oncol Biol Phys* 2008;71:41–50.
12. Cassidy LD. Basic concepts of statistical analysis for surgical research. *J Surg Res* 2005;128:199–206.
13. Artusi R, Verderio P, Marubini E. Bravais-Pearson and Spearman correlation coefficients: Meaning, test of hypothesis and confidence interval. *Int J Biol Markers* 2002;17:148–151.
14. Lei X, Davis D, Kuan L, *et al*. The conditional binomial test revisited for clinical trials. *J Biopharm Stat* 1998;8:533–543.
15. Alonso-Arrizabalaga S, Brualla Gonzalez L, Rosello Ferrando JV, *et al*. Prostate planning treatment volume margin calculation based on the ExacTrac X-Ray 6D image-guided system: Margins for various clinical implementations. *Int J Radiat Oncol Biol Phys* 2007;69:936–943.
16. Beltran C, Herman MG, Davis BJ. Planning target margin calculations for prostate radiotherapy based on intrafraction and interfraction motion using four localization methods. *Int J Radiat Oncol Biol Phys* 2008;70:289–295.
17. Serago CF, Buskirk SJ, Igel TC, *et al*. Comparison of daily megavoltage electronic portal imaging or kilovoltage imaging with marker seeds to ultrasound imaging or skin marks for prostate localization and treatment positioning in patients with prostate cancer. *Int J Radiat Oncol Biol Phys* 2006;65:1585–1592.
18. Cheung P, Sixel K, Morton G, *et al*. Individualized planning target volumes for intrafraction motion during hypofractionated intensity-modulated radiotherapy boost for prostate cancer. *Int J Radiat Oncol Biol Phys* 2005;62:418–425.
19. Greer PB, Dahl K, Ebert MA, *et al*. Assessment of a daily online implanted fiducial marker-guided prostate radiotherapy process. *J Med Imaging Radiat Oncol* 2008;52:517–524.
20. Pawlicki T, Kim GY, Hsu A, *et al*. Investigation of linac-based image-guided hypofractionated prostate radiotherapy. *Med Dosim* 2007;32:71–79.
21. Rosewall T, Chung P, Bayley A, *et al*. A randomized comparison of interfraction and intrafraction prostate motion with and without abdominal compression. *Radiother Oncol* 2008;88:88–94.
22. Noel C, Parikh PJ, Roy M, *et al*. Prediction of intrafraction prostate motion: Accuracy of pre- and post-treatment imaging and intermittent imaging. *Int J Radiat Oncol Biol Phys* 2008.
23. Kupelian PA, Langen KM, Willoughby TR, *et al*. Image-guided radiotherapy for localized prostate cancer: Treating a moving target. *Semin Radiat Oncol* 2008;18:58–66.
24. Boda-Heggemann J, Kohler FM, Wertz H, *et al*. Intrafraction motion of the prostate during an IMRT session: A fiducial-based 3D measurement with Cone-beam CT. *Radiat Oncol* 2008;3:37.
25. Padhani AR, Khoo VS, Suckling J, *et al*. Evaluating the effect of rectal distension and rectal movement on prostate gland position using cine MRI. *Int J Radiat Oncol Biol Phys* 1999;44:525–533.
26. Kitamura K, Shirato H, Seppenwoolde Y, *et al*. Three-dimensional intrafractional movement of prostate measured during real-time tumor-tracking radiotherapy in supine and prone treatment positions. *Int J Radiat Oncol Biol Phys* 2002;53:1117–1123.
27. Dawson LA, Litzenberg DW, Brock KK, *et al*. A comparison of ventilatory prostate movement in four treatment positions. *Int J Radiat Oncol Biol Phys* 2000;48:319–323.
28. Malone S, Crook JM, Kendal WS, *et al*. Respiratory-induced prostate motion: Quantification and characterization. *Int J Radiat Oncol Biol Phys* 2000;48:105–109.
29. Bentel GC, Munley MT, Marks LB, *et al*. The effect of pressure from the table top and patient position on pelvic organ location in patients with prostate cancer. *Int J Radiat Oncol Biol Phys* 2000;47:247–253.
30. Beard CJ, Kijewski P, Bussiere M, *et al*. Analysis of prostate and seminal vesicle motion: Implications for treatment planning. *Int J Radiat Oncol Biol Phys* 1996;34:451–458.
31. de Crevoisier R, Melancon AD, Kuban DA, *et al*. Changes in the pelvic anatomy after an IMRT treatment fraction of prostate cancer. *Int J Radiat Oncol Biol Phys* 2007;68:1529–1536.
32. Ghilezan MJ, Jaffray DA, Siewerdsen JH, *et al*. Prostate gland motion assessed with cine-magnetic resonance imaging (cine-MRI). *Int J Radiat Oncol Biol Phys* 2005;62:406–417.
33. Mah D, Freedman G, Milestone B, *et al*. Measurement of intrafractional prostate motion using magnetic resonance imaging. *Int J Radiat Oncol Biol Phys* 2002;54:568–575.
34. Nichol AM, Brock KK, Lockwood GA, *et al*. A magnetic resonance imaging study of prostate deformation relative to implanted gold fiducial markers. *Int J Radiat Oncol Biol Phys* 2007;67:48–56.
35. Langen KM, Willoughby TR, Meeks SL, *et al*. Observations on real-time prostate gland motion using electromagnetic tracking. *Int J Radiat Oncol Biol Phys* 2008;71:1084–1090.
36. Deurloo KE, Steenbakkers RJ, Zijp LJ, *et al*. Quantification of shape variation of prostate and seminal vesicles during external beam radiotherapy. *Int J Radiat Oncol Biol Phys* 2005;61:228–238.
37. 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. *Int J Radiat Oncol Biol Phys* 2004;60:30–39.
38. Britton KR, Takai Y, Mitsuya M, *et al*. Evaluation of inter- and intrafraction organ motion during intensity modulated radiation therapy (IMRT) for localized prostate cancer measured by a newly developed on-board image-guided system. *Radiat Med* 2005;23:14–24.
39. Huang E, Dong L, Chandra A, *et al*. Intrafraction prostate motion during IMRT for prostate cancer. *Int J Radiat Oncol Biol Phys* 2002;53:261–268.
40. Pinkawa M, Pursch-Lee M, Asadpour B, *et al*. Image-guided radiotherapy for prostate cancer: Implementation of ultrasound-based prostate localization for the analysis of inter- and intrafraction organ motion. *Strahlenther Onkol* 2008;184:679–685.
41. Letourneau D, Martinez AA, Lockman D, *et al*. Assessment of residual error for online cone-beam CT-guided treatment of prostate cancer patients. *Int J Radiat Oncol Biol Phys* 2005;62:1239–1246.
42. Soete G, De Cock M, Verellen D, *et al*. X-ray-assisted positioning of patients treated by conformal arc radiotherapy for prostate cancer: Comparison of setup accuracy using implanted markers versus bony structures. *Int J Radiat Oncol Biol Phys* 2007;67:823–827.
43. Kuban D, Pollack A, Huang E, *et al*. Hazards of dose escalation in prostate cancer radiotherapy. *Int J Radiat Oncol Biol Phys* 2003;57:1260–1268.
44. Schultheiss TE, Lee WR, Hunt MA, *et al*. Late GI and GU complications in the treatment of prostate cancer. *Int J Radiat Oncol Biol Phys* 1997;37:3–11.

45. Zelefsky MJ, Fuks Z, Hunt M, *et al*. High-dose intensity modulated radiation therapy for prostate cancer: Early toxicity and biochemical outcome in 772 patients. *Int J Radiat Oncol Biol Phys* 2002;53:1111–1116.
46. Lawton CA, DeSilvio M, Roach M 3rd, *et al*. An update of the phase III trial comparing whole pelvic to prostate only radiotherapy and neoadjuvant to adjuvant total androgen suppression: Updated analysis of RTOG 94-13, with emphasis on unexpected hormone/radiation interactions. *Int J Radiat Oncol Biol Phys* 2007;69:646–655.
47. Pommier P, Chabaud S, Lagrange JL, *et al*. Is there a role for pelvic irradiation in localized prostate adenocarcinoma? Preliminary results of GETUG-01. *J Clin Oncol* 2007;25:5366–5373.
48. Padhani AR, Gapinski CJ, Macvicar DA, *et al*. Dynamic contrast enhanced MRI of prostate cancer: Correlation with morphology and tumour stage, histological grade and PSA. *Clin Radiol* 2000;55:99–109.
49. Otto K. Volumetric modulated arc therapy: IMRT in a single gantry arc. *Med Phys* 2008;35:310–317.