KJU Korean Journal of Urology

www.kjurology.org
http://dx.doi.org/10.4111/kju.2014.55.1.23

Original Article - Urological Oncology

Interfraction Prostate Movement in Bone Alignment After Rectal Enema for Radiotherapy

Young Eun Seo, Tae Hyo Kim, Ki Soo Lee, Won Yeol Cho, Hyung-Sik Lee[1], Won-Joo Hur[1], Youngmin Choi[1]

Departments of Urology and [1]Radiation Oncology, Dong-A University College of Medicine, Busan, Korea

Purpose: To assess the effect of a rectal enema on interfraction prostate movement in bone alignment (BA) for prostate radiotherapy (RT), we analyzed the spatial difference in prostates in a bone-matched setup.

Materials and Methods: We performed BA retrospectively with data from prostate cancer patients who underwent image-guided RT (IGRT). The prostate was identified with implanted fiducial markers. The setup for the IGRT was conducted with the matching of three fiducial markers on RT planning computed tomography images and those on two oblique kV x-ray images. Offline BA was performed at the same position. The coordinates of a virtual prostate in BA and a real prostate were obtained by use of the ExaxTrac/NovalisBody system, and the distance between them was calculated as the spatial difference. Interfraction prostate displacement was drawn from the comparison of the spatial differences.

Results: A total of 15 patients with localized prostate cancer treated with curative hypofractionated IGRT were enrolled. A total of 420 fractions were analyzed. The mean of the interfraction prostate displacements after BA was 3.12±2.00 mm (range, 0.20–10.53 mm). The directional difference was profound in the anterior-posterior and supero-inferior directions (2.14±1.73 mm and 1.97±1.44 mm, respectively) compared with the right-left direction (0.26±0.22 mm, $p<0.05$). The required margin around the clinical target volume was 4.97 mm with the formula of van Herk et al.

Conclusions: The interfraction prostate displacement was less frequent when a rectal enema was performed before the procedure. A rectal enema can be used to reduce interfraction prostate displacement and resulting clinical target volume-to-planning target volume margin.

Keywords: *Displacement; Enema; Image guided radiotherapy; Prostate neoplasms*

Article History:
received 12 July, 2013
accepted 28 August, 2013

Corresponding Author:
Youngmin Choi
Department of Radiation Oncology, Dong-A University Hospital, 26 Daesingongwon-ro, Seo-gu, Busan 602-715, Korea
TEL: +82-51-240-5380
FAX: +82-51-254-5889
E-mail: cymin00@dau.ac.kr

INTRODUCTION

The prostate is in front of the rectum and is separated by just a fascia. As a result, the location of the prostate is significantly affected by rectal volume [1,2]. In particular, the location of the peripheral zone can be easily affected by a change in rectal volume because the peripheral zone abuts the anterior wall of the rectum. About two-thirds of prostate cancers occur in the peripheral zone [3]. Therefore, it is necessary to include the peripheral zone in a radiotherapy (RT) field. When the rectum is distended, it can push the prostate anteriorly, especially the peripheral zone, and give rise to inadequate irradiation in some portion of the prostate. Increased risk of biochemical and local failures was reported in patients whose rectums were distended on RT planning (RTP) computed tomography (CT) for prostate cancers [4,5]. Hence, it is recommended that a patient undergo RTP CT again after rectal emptying if the patient had a distended rectum at the time of a RTP CT scan.

Rectal emptying can reduce the degree of prostate motion [6,7] and additionally intrafractional motion [8]. In one study, a 10% probability of prostate movement of more than 3 mm occurred in 1 and 20 minutes in full and empty rectum groups, respectively [6]. Accordingly, we decided to apply a rectal enema before each RT fraction to limit the inter- and intrafraction prostate movements resulting from changes in rectal volume.

Setup uncertainty could be reduced markedly with the use of image-guided RT (IGRT), which uses the prostate itself for the RT setup, compared with conventional RT, which uses skin markers or pelvic bones for the RT setup. Among the methods for IGRT, prostate alignment with implanted fiducial markers results in the least interuser disagreement compared with that with anatomy or contours [9]. In as much as the implanted fiducial markers can be used as a surrogate for a prostate, their position stands for the location of the prostate. IGRT with implanted fiducial markers can improve prostate alignment further over that with bony pelvis or soft tissues [9,10].

Although the implanted fiducial markers can increase the accuracy of the prostate setup for RT, they are not used routinely in Korea because of their invasive nature. Some radiation oncologists implement IGRT with pelvic bones or soft tissues instead. There may be a larger discrepancy in prostate locations between RT setup with pelvic bones or soft tissues and that with implanted fiducial markers.

Despite the effect of rectal volume on a prostate position, studies about the spatial difference of prostates after RT setup have generally not dealt with alterations in rectal volume [11-13]. A larger change in rectal volume can evoke greater prostate movement.

We were intrigued about the discrepancy of prostate locations after rectal emptying. In the present study, to limit the change in rectal volume, a rectal enema was administered before every RT fraction. To investigate the difference in prostate locations at pelvic bone alignment after rectal emptying, we retrospectively analyzed the data of patients who received IGRT after a rectal enema.

MATERIALS AND METHODS

1. Patients

From October 2010 to September 2012, 15 consecutive patients with localized prostate adenocarcinoma who received curative IGRT at Dong-A University Hospital, Busan, South Korea, were enrolled in this retrospective analysis. Prior to IGRT, three gold fiducial markers (Civco, Kalona, IA, USA) were implanted under transrectal ultrasound guidance. The markers were 0.8 mm in diameter and 3 mm in length, and their surface was knurled to prevent migration.

Rectal enemas with 50 mL of 50% glycerin were administered to all patients before RTP CT and each RT fraction to make rectal volumes less variable. Glycerin did not disturb the dose distribution of RT. RTP CT was taken more than 1 week after marker implantation to avoid the temporary distortion of the prostate shape due to inflammation or edema. Patients lay supine with an ankle immobilization device and underwent RTP CT from the fourth lumbar vertebra to about 3 cm below the ischial tuberosities with a slice interval of 2–3 mm.

2. Radiotherapy

The clinical target volume (CTV) was defined as the prostate plus seminal vesicles according to patient characteristics. The planning target volume (PTV) was built with the CTV plus a 5-mm margin except for the posterior expansion of 4 mm. All patients received a PTV dose of 70.0 Gy in 28 fractions with intensity-modulated RT plans by use of iPlan 3.0 (BrainLAB, Feldkirchen, Germany).

Two oblique kV x-rays were taken before each RT fraction passing through the isocenter of the patient in directions from floor to ceiling. The radio-opaque implanted fiducial markers were used as the surrogate of the prostate. The implanted fiducial markers on the two oblique kV x-ray images were fused with those on the digitally reconstructed radiographs of RTP CT by use of the ExaxTrac/NovalisBody system (BrainLAB) for the IGRT setup. Patient setups were approved when the difference between them was less than 1 mm in each right-left (RL), supero-inferior (SI), and antero-posterior (AP) direction (Fig. 1).

3. Off-line bone alignment and interfraction prostate displacement

We proceeded to off-line bone alignment virtually at the position of approved fiducial marker alignment. Coordinates of a virtual prostate at bone alignment and those of an actual prostate at implanted fiducial marker alignment were calculated automatically with the ExaxTrac/NovalisBody system. The spatial difference between them was produced from the difference in coordinate locations between them. The result was as follows:

$$spatial\,difference = \sqrt{(x-x')^2+(y-y')^2+(z-z')^2}$$

where x, y, and z represented the RL, SI, and AP directions, respectively (Fig. 2). Interfraction prostate displacement was drawn from all the spatial differences after bone alignments in all RT fractions, and the directional analysis (RL, SI, and AP directions) was performed.

4. Margins around CTV for interfraction prostate displacement

The mean and standard deviation (SD) of the interfraction prostate displacements were analyzed. Then systematic and random errors were produced from the SD (Σ) of the means and root mean square (σ) of the SDs, respectively. We calculated required margins around the CTV for the interfraction prostate displacement after bone alignment according to the recipe of van Herk et al. [14]: 2.5 times Σ plus 0.7 times σ, which was devised to deliver a minimum cumulative CTV dose of at least 95% of the prescribed dose for 90% of the patients.

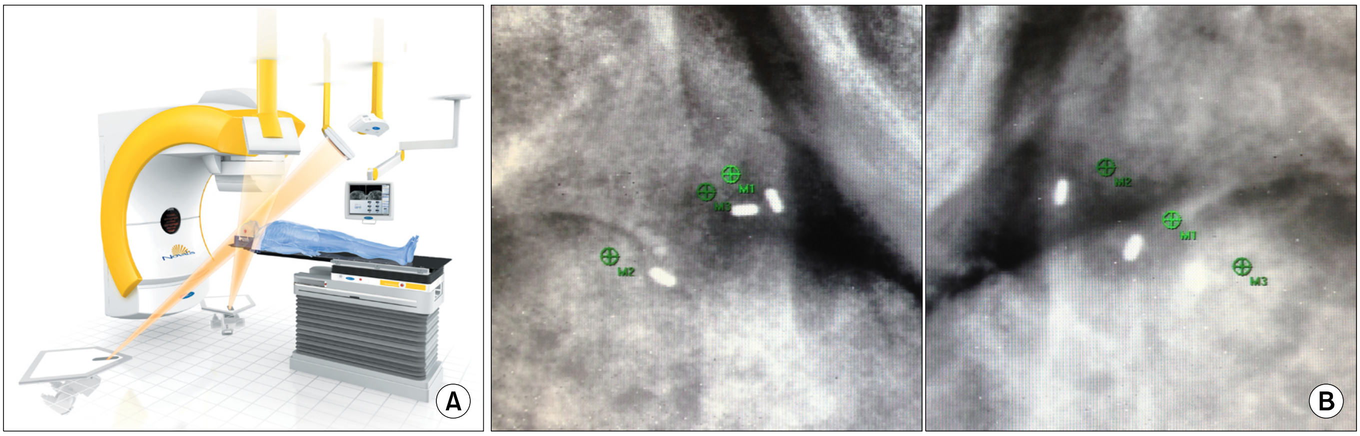

FIG. 1. ExacTrac/NovalisBody system. (A) Two oblique kV x-rays were taken from floor to ceiling via the iso-center of radiotherapy. (B) Fiducial markers on the kV x-ray images (radio-opaque) were fused with those on the digitally reconstructed radiographs from radiotherapy planning computed tomography (round markers).

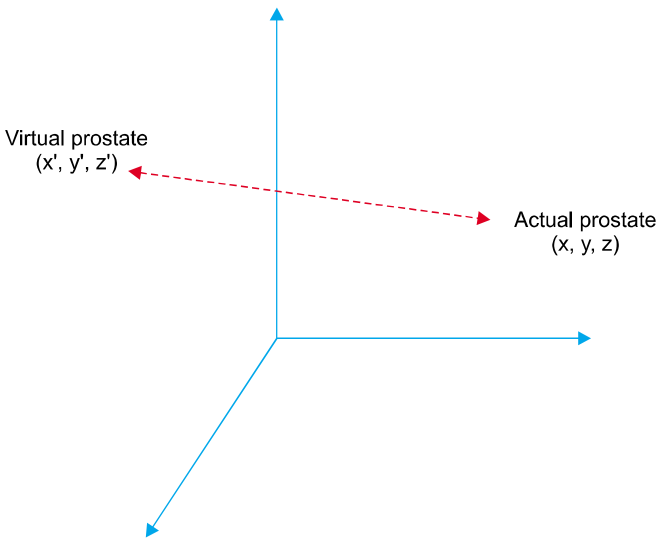

FIG. 2. Distance between an actual prostate and a virtual prostate after a bone alignment.

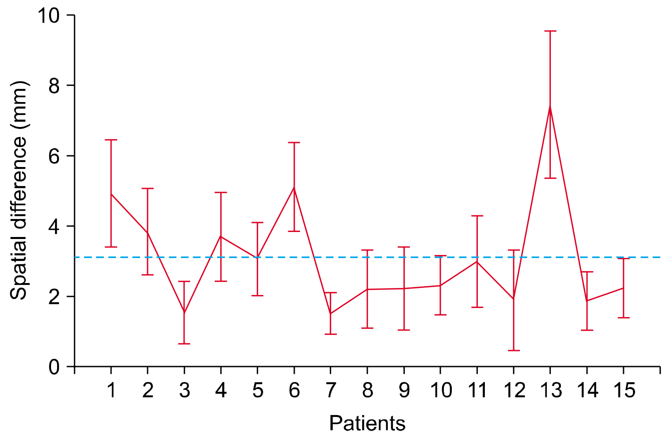

FIG. 3. Interfraction prostate displacements after bone alignment in prostate cancer patients who received a rectal enema prior to each radiotherapy fraction (mean±1 standard deviation). The dotted line indicates the mean of interfraction prostate movement.

5. Statistical analysis

The directional vectors of the interfraction prostate displacement were compared with a paired t-test. A p-value of $\leq$0.05 was regarded as being statistically significant. Statistical analysis was carried out with IBM SPSS ver. 21 (IBM Co., Armonk, NY, USA).

RESULTS

1. Interfraction prostate displacement after bone alignment

A total of 420 fractions were analyzed from 15 prostate cancer patients. The mean of interfraction prostate movements after bone alignment was 3.12±2.00 mm (Fig. 3). More than 3 mm and 5 mm of prostate displacements were found in 44.0% and 15.7% of all RT fractions, respectively. The interfraction prostate movement in 90% of RT fractions reached up to 5.85 mm. The directional analysis showed that the displacements in the AP and SI directions were greater than those in the RL direction ($p<0.05$) (Table 1).

2. Required margins around CTV

The required margin for CTV-to-PTV expansion with the formula of van Herk et al was 4.97 mm after a bone matched setup in the prostate cancer patients who received a rectal enema before each RT fraction. From the directional analysis, the required CTV-to-PTV margins in the RL, AP, and SI directions were 0.41 mm, 4.35 mm, and 3.50 mm, respectively.

DISCUSSION

Distension of the rectum and bladder is the main factor influencing interfraction prostate movement [13,15,16].

Table 1. Interfraction prostate movement after bone alignment

Variable	No. of fractions	Range (mm)	Mean±SD (mm)	p-value
Prostate movement	420	0.20–10.53	3.12±2.00	
Directional analysis				<0.05[a]
Right-left	420	0–1.33	0.26±0.22	
Antero-posterior	420	0–8.41	2.14±1.73	
Supero-inferior	420	0–6.41	1.97±1.44	

SD, standard deviation.
[a]:Right-left versus antero-posterior and supero-inferior.

Table 2. Difference of prostate locations after bone alignment

Author	No.	Prostate identification	Rectal emptying	Spatial difference (mm)	Directional analysis (mm)		
					Right-left	Antero-posterior	Supero-inferior
Zelefsky et al. 1999 [18]	50	Contour	Before RTP CT		−0.6 (0.8)	−1.2 (2.9)	−0.5 (3.3)
Frank et al. 2008 [17]	15	Contour	Before RTP CT	4.6 (3.5)	0.2 (1.2)	0.1 (3.0)	−0.5 (2.1)
Ogino et al. 2008 [6]	76	Contour		4.4 (2.6)			
	42		Evacuation of gas	3.9[a] (2.3)	0 (0.9)	−0.3 (3.7)	−0.2 (2.4)
	34		No	4.9[a] (2.9)	0.1 (1.2)	−0.3 (4.7)	0.3 (3.0)
Kudchadker et al. 2009 [22]	10	Contour	No		−0.05 (0.67)	−0.21 (2.81)	−0.08 (2.41)
Tanyi et al. 2010 [20]	14	Implanted transducers	No		−0.08 (0.69)	0.30 (3.96)	0.77 (3.51)
Peng et al. 2011 [19]	20	Contour	Yes	5.8 (3.1)			
Present study	15	Implanted markers	Rectal enema	3.12 (2.00)	0.26 (0.22)	2.14 (1.73)	1.97 (1.44)

Values are presented as mean (standard deviation).
RTP CT, radiotherapy planning computed tomography.
[a]:$p < 0.05$.

Rectal filling has a greater correlation with the extent of prostate motion than does bladder filling [11,13]. Therefore, it was reasonable to assume that reducing rectal volume could decrease the interfraction prostate movement. Accordingly, we administered a rectal enema before every IGRT fraction in localized prostate cancer patients in this study.

The interfraction prostate displacement after bone matching ranged from 3.9±2.3 mm to 5.8±3.1 mm in some studies (Table 2). Although implanted fiducial markers are known to make the least interobserver difference compared with contours or anatomies for prostate identification [9], various methods were used in previous studies. To reduce the risk of prostate misidentification as much as possible, implanted fiducial markers were utilized in this study.

Despite the well known effect of rectal filling on prostate motion, rectal volume was not regulated in any of the studies of interfraction prostate displacement. Some used rectal emptying before initial RTP CT acquisition but not before RT fractions [17,18]. The effect of rectal emptying was suggested by Ogino et al. [6], who evaluated the effect of rectal gas on interfraction prostate displacement. Those authors found that the interfraction prostate movement was reduced in the patients who evacuated rectal gas compared with those who did not. We thought that a rectal enema could evacuate feces as well as gas out of the rectum. Therefore, we expected that a rectal enema before every RT fraction would reduce the interfraction prostate displacement. The interfraction prostate motion after bone alignment was smaller in this study, which used a rectal enema before each RT fraction, 3.18±2.03 mm, than in other studies that did not use rectal emptying, with values of more than 4.6 mm. Peng et al. [19] also used rectal emptying prior to each RT fraction, but the interfraction prostate displacement seemed a little larger than in other studies that did not used rectal emptying. We discovered that in the study by Peng et al. [19], rectal emptying was performed by the patients after they received instruction. Thus, we suspect that the unexpectedly larger interfraction prostate motion may be attributed to some degree to inadequate rectal emptying.

In clinical practice, defining a target volume is complicated. A larger expansion around a tumor results in fewer misses in irradiating the tumor but greater potential for damaging normal tissues. Therefore, the margin on the tumor should be determined after full consideration of the probability of normal tissue damage. In terms of the necessary margin that would account for interfraction prostate movement after bone alignment, the required margins in the RL direction have been reported to be significantly smaller than those in the SI and AP directions [20,21], with values ranging from 1.6 to 3.1 mm in the RL direction, from 8.9 to 8.92 mm in the SI direction, and from 10.2 to 10.7 mm in the AP direction. The required margin in the RL direction was less than in other directions in the present study also, but the magnitudes were smaller than in other studies.

As a retrospective study, the lack of control patients produced several limiting factors. The interfraction prostate motion without rectal enema was borrowed from other studies and was compared with the results of this study [17,18,20,22]. The absence of results of rectal volume alteration and prostate shape before and after rectal enema was another limitation. Merrick et al. [23] reported that the lateral dimension of the distended rectum was reduced after rectal evacuation with a rectal enema. They also found that the posterior border of the prostate became flat over most of the length of the prostate gland. From those findings, we considered that a rectal enema could reduce the rectal volume and make the prostate shape unaffected by the rectal distension. Therefore, we conceived that a rectal enema could be useful for prostate RT setup.

Compared with other bone alignment studies, the interfraction prostate displacement and resultant required PTV margins were less in this study, which seems to be the effect of the rectal enema before each RT fraction. In future studies on the effectiveness of a rectal enema on the interfraction prostate movement, we can confidently reduce the PTV margin with the use of a rectal enema in prostate cancer patients.

CONCLUSIONS

In the current study, interfraction prostate displacement was less frequently observed when a rectal enema was performed prior to the procedure. A rectal enema can be used to reduce interfraction prostate displacement and the resulting CTV-to-PTV margin.

CONFLICTS OF INTEREST

The authors have nothing to disclose.

ACKNOWLEDGMENTS

This work was supported by the Dong-A University research fund.

REFERENCES

1. Antolak JA, Rosen II, Childress CH, Zagars GK, Pollack A. Prostate target volume variations during a course of radiotherapy. Int J Radiat Oncol Biol Phys 1998;42:661-72.
2. Melian E, Mageras GS, Fuks Z, Leibel SA, Niehaus A, Lorant H, et al. Variation in prostate position quantitation and implications for three-dimensional conformal treatment planning. Int J Radiat Oncol Biol Phys 1997;38:73-81.
3. McNeal JE, Redwine EA, Freiha FS, Stamey TA. Zonal distribution of prostatic adenocarcinoma. Correlation with histologic pattern and direction of spread. Am J Surg Pathol 1988;12:897-906.
4. de Crevoisier R, Tucker SL, Dong L, Mohan R, Cheung R, Cox JD, et al. Increased risk of biochemical and local failure in patients with distended rectum on the planning CT for prostate cancer radiotherapy. Int J Radiat Oncol Biol Phys 2005;62:965-73.
5. Heemsbergen WD, Hoogeman MS, Witte MG, Peeters ST, Incrocci L, Lebesque JV. Increased risk of biochemical and clinical failure for prostate patients with a large rectum at radiotherapy planning: results from the Dutch trial of 68 GY versus 78 Gy. Int J Radiat Oncol Biol Phys 2007;67:1418-24.
6. Ogino I, Uemura H, Inoue T, Kubota Y, Nomura K, Okamoto N. Reduction of prostate motion by removal of gas in rectum during radiotherapy. Int J Radiat Oncol Biol Phys 2008;72:456-66.
7. Fiorino C, Di Muzio N, Broggi S, Cozzarini C, Maggiulli E, Alongi F, et al. Evidence of limited motion of the prostate by carefully emptying the rectum as assessed by daily MVCT image guidance with helical tomotherapy. Int J Radiat Oncol Biol Phys 2008;71:611-7.
8. Ghilezan MJ, Jaffray DA, Siewerdsen JH, Van Herk M, Shetty A, Sharpe MB, et al. Prostate gland motion assessed with cine-magnetic resonance imaging (cine-MRI). Int J Radiat Oncol Biol Phys 2005;62:406-17.
9. Langen KM, Zhang Y, Andrews RD, Hurley ME, Meeks SL, Poole DO, et al. Initial experience with megavoltage (MV) CT guidance for daily prostate alignments. Int J Radiat Oncol Biol Phys 2005;62:1517-24.
10. Moseley DJ, White EA, Wiltshire KL, Rosewall T, Sharpe MB, Siewerdsen JH, et al. Comparison of localization performance with implanted fiducial markers and cone-beam computed tomography for on-line image-guided radiotherapy of the prostate. Int J Radiat Oncol Biol Phys 2007;67:942-53.
11. Beard CJ, Kijewski P, Bussiere M, Gelman R, Gladstone D, Shaffer K, et al. Analysis of prostate and seminal vesicle motion: implications for treatment planning. Int J Radiat Oncol Biol Phys 1996;34:451-8.
12. Roeske JC, Forman JD, Mesina CF, He T, Pelizzari CA, Fontenla E, et al. Evaluation of changes in the size and location of the prostate, seminal vesicles, bladder, and rectum during a course of external beam radiation therapy. Int J Radiat Oncol Biol Phys 1995;33:1321-9.
13. van Herk M, Bruce A, Kroes AP, Shouman T, Touw A, Lebesque JV. Quantification of organ motion during conformal radiotherapy of the prostate by three dimensional image registration. Int J Radiat Oncol Biol Phys 1995;33:1311-20.
14. van Herk M, Remeijer P, Rasch C, Lebesque JV. The probability of correct target dosage: dose-population histograms for deriving treatment margins in radiotherapy. Int J Radiat Oncol Biol Phys 2000;47:1121-35.
15. Ten Haken RK, Forman JD, Heimburger DK, Gerhardsson A, McShan DL, Perez-Tamayo C, et al. Treatment planning issues related to prostate movement in response to differential filling of the rectum and bladder. Int J Radiat Oncol Biol Phys 1991;20:1317-24.
16. Schild SE, Casale HE, Bellefontaine LP. Movements of the prostate due to rectal and bladder distension: implications for radiotherapy. Med Dosim 1993;18:13-5.
17. Frank SJ, Dong L, Kudchadker RJ, De Crevoisier R, Lee AK, Cheung R, et al. Quantification of prostate and seminal vesicle interfraction variation during IMRT. Int J Radiat Oncol Biol Phys 2008;71:813-20.
18. Zelefsky MJ, Crean D, Mageras GS, Lyass O, Happersett L, Ling CC, et al. Quantification and predictors of prostate position variability in 50 patients evaluated with multiple CT scans during con-

formal radiotherapy. Radiother Oncol 1999;50:225-34.
19. Peng C, Ahunbay E, Chen G, Anderson S, Lawton C, Li XA. Characterizing interfraction variations and their dosimetric effects in prostate cancer radiotherapy. Int J Radiat Oncol Biol Phys 2011;79:909-14.
20. Tanyi JA, He T, Summers PA, Mburu RG, Kato CM, Rhodes SM, et al. Assessment of planning target volume margins for intensity-modulated radiotherapy of the prostate gland: role of daily inter- and intrafraction motion. Int J Radiat Oncol Biol Phys 2010;78:1579-85.
21. 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;70:289-95.
22. Kudchadker RJ, Lee AK, Yu ZH, Johnson JL, Zhang L, Zhang Y, et al. Effectiveness of using fewer implanted fiducial markers for prostate target alignment. Int J Radiat Oncol Biol Phys 2009;74:1283-9.
23. Merrick GS, Butler WM, Dorsey AT, Dorsey JT 3rd. The effect of constipation on rectal dosimetry following prostate brachytherapy. Med Dosim 2000;25:237-41.