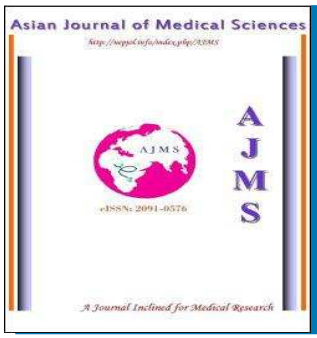

IMAGE GUIDED RADIOTHERAPY BY CBCT BASED POSITION VERIFICATION IN HIGH RISK CARCINOMA PROSTATE- AN INDIAN EXPERIENCE AND REVIEW OF LITERATURE

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[1]Rashi Agrawal, [2]Dinesh Singh, [3]Sudarsan De, [4]Sandeep Agrawal, [5]Sweety Gupta. Depart of Radiation Oncology Galaxy Cancer Institute, Pushpanjali Crosslay Hospital, Ghaziabad, India.

CORRESPONDENCE:

Dr Rashi Agrawal
J 48, Patel Nagar First
Ghaziabad, Uttar pradesh
India-201001
(M): +91-9891483550
Email ID:
drrashi.ag@gmail.com

"Image guided radiotherapy through CBCT led to direct visualization of prostate during treatment.Thus escalated radiation dose for curative treatment of carcinoma prostate can be delivered safely."

ABSTRACT

Introduction-External beam radiotherapy is one of the principle treatment options for locally advanced prostate cancer. Over the past several decades, RT techniques have evolved to allow higher doses of radiation to be administered safely. We report our experience of Image guided intensity modulated radiotherapy (IGRT) and CBCT based position verification.

Material and methods-
In this study we are presenting data of 17 consecutive patients that were treated from august 2009 to october 2010. All patients received 76 -78 Gy Gy to clinical target volume for primary disease. Daily online matching was performed by using KV CBCT scan before treatment. In each patient, soft tissue (prostate) matching was done by the radiation oncologist.

Results – Median Follow up of our patients is 16 months with minimum follow up of 13 months. 3(17.6%) patients developed grade 2 acute rectal toxicity and 4 (23.5%) bladder toxicity. Till date none of our patients had late bladder or rectal toxicity. None of our patient developed local recurrence.

Conclusion-Our study concludes that we can follow the dose escalation with CBCT based position verification **.**With CBCT we can consider entire prostate and normal structures volume for localization.

Key words- Image guided radiotherapy, CBCT scan, Carcinoma prostate, Dose escalation.

INTRODUCTION

Prostate cancer has become a major public health burden, accounting for 29% of new cancer cases in men in 2012 in United states.[1] There has been consistent increase in incidence in most countries of Asia over the last 25 years. At Delhi registry the incidence for prostate cancer has increased from 6.0/100,000 in 1988-89 to 8.1/100,000 in 2002-2003.[2]

Over the past several decades, radiotherapy techniques have evolved to allow higher doses of radiation to be administered safely. Steep dose gradients in intensity-modulated radiation therapy provide better conformity to complex target volumes but this requires accuracy in patient positioning during treatment.

In Image guided radiotherapy, additional verification tool is used to ensure accurate target localization. Here we are representing an Indian experience of Image guided intensity modulated radiotherapy in carcinoma prostate by using cone beam computed tomography (CBCT) imaging as position verification tool.

MATERIALS AND METHODS

In this study we are presenting data of 17 consecutive patients of biopsy proven adenocarcinoma of prostate that were treated from August 2009 to October 2010. After complete history and physical examination all patients underwent laboratory studies including complete blood count, renal and liver function tests and prostate specific antigens (PSA) estimation, Ultrasound upper abdomen, magnetic resonance imaging (MRI) pelvis, chest radiography and bone scan. Patients with Kernofsky performance score ≥80 were included in the study. Based on tumor stage, pretreatment PSA, and Gleason score, prostate cancer is generally grouped according to one of several risk stratification models.[3,4]

High risk group includes clinical stage T3 or Gleason score 8-10 or Serum PSA more than 20ng/ml. Our all patients were of high risk group and their metastatic workup was negative. TNM staging was scored according to the American Joint Committee on Cancer (AJCC) staging guidelines 2007. To determine T-stage, physical examination from digital rectal examination was supplemented with computed tomography (CT) scan and magnetic resonance imaging (MRI) scan data. All patients received concomitant and adjuvant hormonal therapy either in the form of bilateral orchiectomy or luteinizing hormone releasing hormone (LHRH) analogue.

Planning process for all the patients was same that follows the steps as described. For immobilization, thermoplastic mould of lower abdomen was made, both arms were placed over chest. For CT simulation, patients were advised for emptying of rectum and to void completely and take 500ml of water half hour before CT simulation and also to follow same instructions before each treatment. A planning CT scan of the area of interest was taken with 2 mm slice thickness with intravenous non ionic contrast injection. Area of interest extended from L3-L4 junction till mid femur. At the same time all patients underwent MRI scans of the pelvic region. At the time of planning CT scan, fiducial is placed at upper border of pubic symphysis for primary reference point. Then both CT and MRI were imported to our planning system and co registration was done. Brame RS et al reported that some centers do magnetic resonance imaging.[5]

The radiotherapy equipment in our hospital consists of dual energy linear accelerator (Clinac iX, Varian Oncology System) incorporating asymmetric X and Y collimators, 120 leaf millenium-multileaf collimator, amorphous silicon based electronic portal imaging, kilovoltage cone beam CT scanner, 3D beam planning computer workstation (eclipse TPS ver 8.6.17) and networking (Aria network). Target volumes and organ at risk both were contoured by radiation oncologist. All organs at risk were contoured according to Radiation Therapy Oncology Group (RTOG) guidelines. Bladder is contoured from its base to dome, rectum from recto-sigmoid flexure to anal verge. Penile bulb includes the portion of bulbous spongiosum immediately inferior to the genitourinary diaphragm and this structure was drawn with the help of MRI. Both femoral heads were drawn within the acetabulum and neck of femur was not included. Bowel was drawn as a single structure encompassing the peritoneal cavity and any loops of bowel in the pelvis. The upper extent was kept constant at 2 cm superior to the uppermost extent of the pelvic nodal planning target volume (PTV) to have comparability of the dose volume data. All the patients were treated with intensity modulated image guided radiotherapy by nine equiangular beams.

Clinical target volume for primary disease (CTV1) included prostate, extra capsular spread and seminal vesicle. Planning target volume was created by applying 6mm margin craniocaudal, mediolateral and anteriorly and 4 mm posteriorly. The CTV for prophylactic lymph node irradiation was contoured according to the RTOG guidelines. A total dose of 76-78 Gy in 38 -40 fractions was prescribed to CTV1 and 62.7-63.2 Gy in 38-40 fractions to CTV2. DVH constraints for rectum were set at <5-9% of rectum volume to be treated over 70 Gy, <15%, over 65 Gy and <35% over 50 Gy. For bladder, constraints were set at <12 % of bladder volume to be treated over 70 Gy, <20% over 65 Gy and<40% over 50 Gy. Mean intestinal dose was kept at 30 Gy. Less than 5% of both femoral head should receive more than 45 Gy. According to dose prescription and organ at risk constraints, various radiotherapy plans were generated. At the time of planning, isocentre was transferred from primary reference point to treatment volume centre. This coordinate shift was applied to the patient on the first day of implementation. Plans were evaluated by radiation oncologist. Quality assurance tests were done before treatment of each patient. On the day of implementation, patients were positioned by use of a customized external immobilization mould and skin markers with a laser coordination system. KV CBCT and orthogonal X rays of each patient were taken then online matching before treatment is done by the treating oncologist by prostate to prostate (soft tissue) matching. Any vertical, longitudinal or transverse shift was applied to the patient then treatment was started. Before each treatment session KV CBCT was done. For deviations of 5 mm or greater, repeat CBCT scan was obtained before treatment to verify prostate position.

During treatment, weekly review of each patient was done to see treatment related toxicities. Acute and late toxicities were scored according to the RTOG morbidity scoring scale.[6] Acute toxicity was defined as an occurrence of toxicity during or within three months of treatment.[7]

After completion of treatment, for first follow up visit patient was called at 15 days then at two months and subsequently three monthly visits were performed. Clinical examination was done at each visit. Serum PSA was assessed at three monthly interval and MRI pelvis was done at six monthly intervals for first two years.

RESULTS

This was a prospective single arm study in which all of our patients had a minimum follow up of 13 months. Demographic characteristics of patients are presented in Table 1. Median age of our patients was 71 years (range 63-81 years). Pretreatment serum PSA level ranged between 2.38-105.8 ng/ml. The distribution of patients according to 2007 American Joint Committee on Cancer (AJCC) clinical stage was T2:4 (23.5%), T3: 5 (29.4%), and T4:8 (47.1%). All patients had Kernofsky performance score ≥80. Five patients underwent orchiectomy along with tab bicalutamide 50mg once a day. All other patients received gonadotropin releasing hormone along with tab bicalutamide. All patients were treated with intensity modulated image guided radiotherapy to a total dose of either 76 or 78 Gy. Four patients received 78 Gy to clinical target volume and rest 13 patients received 76 Gy with a daily dose of 1.98-2 Gy. All patients received five fractions per week. Gross tumor volume ranged from 23.54 to 227.18cc and clinical target volume ranged from 71.69 to 395.85cc. Two percent volume of clinical target volume received 79.4 Gy. Mean rectum volume was 75.76cc while mean volume of rectum that was inside the PTV was 15.13cc. Ninety point twenty-three percent of rectum and 15.87 % of bladder received 70 Gy. Details are presented in table 2 and 3. Mean intestine dose was 23.7 Gy. All patients completed radiotherapy without any interruption due to radiation related morbidity. Acute toxicity are reported in Table 4. None of our patient had grade 3 acute rectal toxicity while one patient had acute bladder toxicity. Median follow up is 16 months and till date none of our patients had late bladder or rectal toxicity. One patient developed lung metastases after fourteen months of treatment. His pre treatment stage was T4a N0. Another patient expired 23 months after treatment due to natural causes. His age was 81 years and his last serum PSA was within normal limits. All other patients are in regular follow up.

DISCUSSION

In 1970s and 1980s, radiation doses in the range of 70 Gy and two dimensional radiotherapy technique were standard of care for the management of carcinoma

Table 1- Demographic characteristics of patients

Age(years)	
Median	71
Range	63-80
T Stage	
T2b	2 (11.7%)
T2c	2 (11.7%)
T3a	2 (11.7%)
T3b	3(17.6%)
T4a	8 (47%)
Gleason score	
6 or <6	2 (11.7%)
7	4 (23.5%)
8-10	11(64.7%)
Pretreatment PSA level(ng/ml)	
less than or equal to 10	6 (35.2%)
11-20	1 (6%)
>20	10 (58.8%)
Median	23.92
Mean	31.8

Table 2-Volume of target and organ at risk

Target /Organ at risk	Mean Volume(cc)	Median Volume(cc)
Rectum	75.76	65.06
Bladder	326.45	290.03
Gross Tumor Volume	69.49	47.85
Clinical Target Volume	151.79	117.29

Table 3- Dose achieved by organs at risk

Dose achieved(mean)	V70 Gy(%)	V65 Gy(%)	V50 Gy(%)
Rectum	9.23	18.3	38.71
Bladder	15.87	22.43	41.38

prostate. With the advent of CT-based radiation planning, three-dimensional conformal radiotherapy became the standard of care during the 1990s. It resulted in both higher cure rates and lower complication rates compared with two-dimensional radiotherapy.[8] Zelefsky et al conducted a single-institution phase I and II study of dose escalation from 64.8 to 86.4 Gy to the prostate alone.[9] Radiotherapy was delivered by 3DCRT or IMRT to a total of 1,100 patients. 405 patients belong to intermediate and and 416 to unfavorable risk group. 2.5 years after 3D-CRT, prostate biopsy was repeated which were positive in 7% of patients receiving 81.0 Gy, compared to 45% after70.2 Gy, and 57% after 64.8 Gy. Therefore, they proposed dose escalation as a definition of new standard for curative radiotherapy in this disease.

M.D. Anderson dose escalation trial published in 2000 was the first PSA era randomized phase III trial to show the benefit of higher dose in tumor control.[10] The study included 301 patients with clinical stage T1 to T3 disease. The median PSA was 7.8 and Gleason score 8 to 10 was seen in 17% of patients. Radiotherapy was delivered by conventional technique in the 70 Gy arm and in phase 1 of the 78 Gy arm; a conformal boost plan was used in the 78 Gy arm. The 6-year PSA control was 70% versus 64% in favor of the 78 Gy arm (p = 0.03), but no survival difference was observed. Subgroup analysis suggested that the benefit of dose escalation is

Table 4- Acute toxicity

Acute Rectal toxicity	
Grade0	3(17.6%)
Grade1	11(64.7%)
Grade2	3(17.6%)
Grade3	0
Acute Bladder toxicity	
Grade0	3(17.6%)
Grade1	9(52.9%)
Grade2	4(23.5%)
Grade3	1(5%)

primarily in patients with a PSA >10 ng/mL (62% vs. 43%; p = 0.012), rather than when the PSA was ≤10ng/mL (p = 0.46) or any Gleason score. Another randomized trial reported by Zeitmann et al delivered radiotherapy by using a combination of conformal photon and proton beams.[11] A total of 393 patients with T1b-T2b and prostate specific antigen <15ng/ml were assigned to a total dose of either 70.2 gray equivalents or 79.2 GyE. There was a 19% absolute difference in PSA disease-free survival at 5 years post-treatment 61% versus 80%. Although the benefit was same in all risk groups.

In year 2006, Peeters et al compared 664 patients with stage T1b to T4 who were randomized to receive either 68 or 78 Gy.[12] In this trial there was a 10% absolute difference in PSA failure-free survival favoring the high dose arm (64% vs.54%), at 5 years post-treatment. With a median follow-up of 51 months, no difference in clinical failure or overall survival was seen. Kuban et al recently reported long term results of M. D. Anderson trial with median follow up to7.8 years with stage T1-T3b prostate cancer.[13] The authors reported superior freedom from biochemical or clinical failure for the 78-Gy arm. Difference was greater in patients with initial PSA >10 ng/ml (78% vs. 39%, p = 0.001). In light of these findings, the conventional 70 Gy is not considered adequate. On basis of these trials we are treating our high risk carcinoma prostate patients with 76-78 Gy. 17.6% patients had grade 2 acute rectal and 23.5% had grade 2 acute bladder toxicity. No patient experienced acute grade 3 rectal or bladder toxicity and till date none of our patient had late rectal or bladder toxicity. In the Zietman et al. study, only 1% patients receiving conventional-dose and 2% receiving high-dose experienced acute genitourinary (GU)or gastrointestinal (GI) or rectal morbidity of RTOG grade ≥3. Forty two percent patients receiving conventional-dose and 49% patients of high-dose therapy experienced grade 2 acute GU morbidity. The proportions for grade 2 acute GI morbidity were 41% and 57%, respectively (P=0.004). Proportions for grade 2 late GU morbidity were 18% and 20% (not significant). Late grade 2 GI morbidity was doubled (17% vs. 8% P=0.005) in patients treated to the higher dose level of 79.2 GyE. According to Peeters et al there was no difference in late genitourinary or gastrointestinal toxicity of grade 2 or more in conventional or higher dose arm. While Kuban et al showed that GI toxicity of grade 2 or greater occurred twice as often in the high dose patients (26% vs. 13%), although GU toxicity of grade 2 or greater was less and not statistically significantly different. Dose-volume histogram analysis showed that the complication rate could be significantly decreased by reducing the amount of treated rectum.

Xu N published a toxicity analysis of a minor dose escalation in a total of 189 patients.[14] One hundred nineteen patients received 75.6 Gy and 70 received 81.0 Gy. Their analyses showed that only age and radiotherapy dose correlated with acute GU toxicity and only radiotherapy dose correlated with late GU toxicity. Only intensity modulated radiotherapy use correlated with acute GI toxicity; no factors correlated with late GI toxicity or final GU or GI toxicity. Intensity Modulated Radiation Therapy (IMRT) allows a much greater degree of control of the radiation volume, by varying the strength of a beam across its entire area.

The IMRT method allows the high-dose radiation volume to be effectively curved to fit virtually any volume of requirement. It allows for escalation while minimizing toxicity to surrounding organs, such as the rectum and bladder.[15] Integration of more conformal radiation techniques with smaller radiation fields into the clinical setting has necessitated a better understanding of the location of the prostate during treatment. Image-guided radiotherapy (IGRT) refers to the use of additional verification tools in an attempt to ensure proper target localization during the course of radiotherapy. The term IGRT has been widely used to refer to imaging techniques as simple as daily port films to those as complicated as computer-assisted patient repositioning devices. Inter fraction variation can be caused by many factors such as variation in patient positioning, deformation of body tissues ,relative movements of organs e.g. bowel, bladder, rectum, changes in patient weight due to nutritional factors, changes in tumor size due to response. IGRT eliminates inter fraction variation. Jason M. Pawlowski published a trial in which eight prostate cancer patients were treated with IMRT to 76 Gy at 2 Gy per fraction.[16] Daily target localization was performed via intraprostatic fiducials and weekly kV-cone beam computed tomography (CBCT) scans. The dose distributions were calculated using actual treatment plans (an 8-mm PTV margin everywhere except for 6-mm posteriorly) and the feasibility of margin reduction was evaluated by reducing planning margins to 4 mm everywhere except for 3 mm posteriorly. They concluded that for treating smaller PTV volume image guidance is needed. Zelefsky MJ et al also concluded that reduction in dose of bladder rectum can facilitate prostate dose escalation and improved biochemical tumor control.[17] Kilovoltage (kV) Cone beam computed tomography (CBCT) is a sophisticated IGRT technology that produces online, high-quality, three-dimensional images of the prostate gland. Soft-tissue images enable the evaluation of the anatomic variations of other structures such as rectum and bladder. CT system is built into the treatment machine that does not require patient movement and decreases acquisition time. Interfractional displacements of the prostate can be quantified so that daily RT can be accurately delivered.

Daily need of physician input and interuser variability has been noted by this technique. In our institute we are treating our all high risk patients with76-78 Gy.
None of them faced late bladder or rectal toxicity till date. We are using kv cone beam computed tomography for daily imaging and online matching is done by radiation oncologist. Implanted fiducial markers is well established method of localization but their implantation is not without any risk. A patient who requires chronic long-term anticoagulation may benefit from CBCT soft-tissue alignment and invasive procedure of implantation can be avoided Moseley et al showed that with the use of the cone-beam CT images, the interuser variability increases.[18] They concluded that with the uses of soft-tissue images for alignment, as long as minimum treatment margins of 5 to 7 mm are used, it is unlikely that the delivered doses will be affected because of misalignments caused by CT-image interpretation. Brandon M. Barney published their experience with image-guided radiotherapy comparing fiducial markers and cone-beam computed tomography (CBCT) for daily localization of prostate cancer.[19] They concluded that CBCT and kV portal images using fiducials are similar for defining interfraction prostate shifts but one-quarter of shifts differed enough to affect target coverage. They preferred fiducials because this requires less input and physician need to analyze imaging system Ultimately, the main advantage of using CT-based methods is the ability to evaluate soft-tissue changes such as prostate deformation but, more importantly, rectal distention, bladder filling, and other anatomic daily variations that could have an impact on outcomes. A larger series of patients imaged daily with CT scans, with daily target and normal tissue dosimetric evaluations, should be used to correlate these dosimetric variables with ultimate outcomes. Not only is the prostate a moving target, but organs at risk such as the rectum are also structures that are moving.[20]

CONCLUSION

Worldwide, image guided intensity modulated radiotherapy with dose escalation is standard of care for carcinoma prostate. Improvement in dose delivery could potentially be obtained by using more sophisticated localization techniques such as CBCT which consider the entire prostate volume rather than

three implanted seeds and also the bladder rectum volume variation. Our study concludes that we can follow the dose escalation with CBCT based position verification. The relevance of imaging and targeting the prostate gland should be judged by the ultimate clinical outcomes in patients although geometric or dosimetric outcomes play a significant role.

REFERENCES

1. Siegel R, Naishadham D, Jemal A. Cancer statistics. Cancer J Clin 2012; 62:10-29.
2. Yeole BB. Trends in prostate cancer incidence in India.Asian Pacific J Cancer Prev 2008; 9: 141-144.
3. Sylvester JE, Blasko JC, Grimm PD, Meier R, Malmgren JA. Ten-year biochemical relapse-free survival after external beam radiation and brachytherapy for localized prostate cancer: the Seattle experience. Int J Radiat Oncol Biol Phys 2003; 57:944-952.
4. D'Amico AV, Whittington R, Malkowicz SB, Cote K, Loffredo M, Schultz D, et al. Biochemical outcome after radical prostatectomy or external beam radiotherapy for patients with clinically localized prostate carcinoma in the prostate specific antigen era. Cancer 2002; 95:281-286.
5. Brame RS, Zaider M, Zakian KL, Koutcher JA, Shukla-Dave A, Reuter VE, et al. Regarding the focal treatment of prostate cancer: inference of the Gleason grade from magnetic resonance spectroscopic imaging. Int J Radiat Oncol Biol Phys 2009;74:110-114.
6. Cox JD, Stetz J, Pajak TF. Toxicity criteria of the Radiation Therapy Oncology Group (RTOG) and the European Organization for Research and Treatment of Cancer (EORTC). Int J Radiat Oncol Biol Phys 1995, 31:1341-1346.
7. De Meerleer G, Vakaet L, Meersschout S, Villeirs G, Verbaeys A, Oosterlinck W, De Neve W: Intensity-modulated radiotherapy as primary treatment for prostate cancer: acute toxicity in 114 patients. Int J Radiat Oncol Biol Phys 2004; 60:777-787.
8. Corn BW, Hanks GE, Schultheiss TE, Hunt MA, Lee WR, Coia LR. Conformal treatment of prostate cancer with improved targeting: superior prostate-specific antigen response compared to standard treatment. Int J Radiat Biol Phys 1995; 32:325-330.
9. Zelefsky MJ, Fuks Z, Hunt M, Lee HJ, Lombardi D, Ling CC et al. High dose radiation delivered by intensity modulated conformal radiotherapy improves the outcome of localized prostate cancer. J Urol 2001; 166:876–881.
10. Pollack A, Zagars GK, Smith LG, Lee JJ, von Eschenbach AC, Antolak JA, et al. Preliminary results of a randomized. radiotherapy dose-escalation study comparing 70Gy with 78Gy for prostate cancer. J Clin Oncol 2000; 18:3904–3911.
11. Zietman AL, DeSilvio ML, Slater JD, Rossi CJ Jr, Miller DW, Adams JA, et al. Comparison of conventional-dose vs high-dose conformal radiation therapy in clinically localized adenocarcinoma of the prostate: A randomized controlled trial. JAMA 2005; 294:1233-1239.
12. Peeters STH, Heemsbergen WD, Peter CM, Koper PCM, Putten WLJV, Slot A, et al. Dose-response in radiotherapy for localized prostate cancer: Results of the Dutch multicenter randomized phase III trial comparing 68 Gy of radiotherapy with 78 Gy . J Clin Oncol 2006; 24:1190-1196.
13. Kuban DA, Tucker SL, Dong L, Starkschall G, Huang EH, Cheung MR, et al. Long-term results of the M. D. Anderson randomized dose-escalation trial for prostate cancer. Int J Radiat Oncol Biol Phys 2008; 70:67-74.
14. Xu N, Rossi PJ, Jani AB.Toxicity analysis of dose escalation from 75.6 Gy to 81.0 Gy in prostate cancer. Am J Clin Oncol 2011; 34:11-15.
15. Valicenti R, Lu J, Pilepich M, Asbell S, Grignon D. Survival advantage from higher-dose radiation therapy for clinically localized prostate cancer treated on the Radiation Therapy Oncology Group trials. J Clin Oncol 2000; 18:2740–2746.
16. Pawlowski JM, Yang ES, Malcolm AW, Coffey CW, Ding GX. Reduction of dose delivered to organs at risk in prostate cancer patients via image guided radiotherapy. Int. J. Radiation Oncology Biol. Phys 2010; 76: 924–934.
17. Zelefsky MJ, Yamada Y, Fuks Z, Zhang Z, Hunt M, Cahlon O, et al. Long-term results of conformal radiotherapy for prostate cancer: Impact of dose escalation on biochemical tumor control and distant metastases free survival outcomes. Int J Radiat Oncol Biol Phys 2008; 71:1028-1033.
18. Moseley DJ, White EA, Wiltshire KL, Rosewall T, Sharpe MB, Seiwerdsen 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; 67:942-953.
19. Barney BM, Lee RJ, Handrahan D, Welsh KT, Cook JT, Sause WT.Image guided radiotherapy for prostate cancer comparing kV imaging of fiducial markers with cone beam computed tomography.Int J Radiat Oncol Biol Phys 2011;80:301-305.
20. Kupelian PA, Langen KM, Willoughby TR, Zeidan OA, Meeks SL. Image guided radiotherapy for localized prostate cancer: treating a moving target. Semin Radiat Oncol 2008; 18:58-66.

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