Journal of Radiotherapy in Practice

Journal of Radiotherapy in Practice (2010)
9, 41–51

doi:10.1017/S1460396909990185

Original Article

Dose distribution in 3-dimensional conformal radiotherapy for prostate cancer: comparison of femur doses for four treatment techniques

Didem Karaçetin[1], Aydın Çakır[2], Fulya Ağaoğlu[2], Hakan Çamlıca[2], Arzu Ergen[2], Yavuz Dizdar[2], Emin Darendeliler[2]

[1]*Radiation Oncology Clinic, Şişli Etfal Research and Training Hospital, Istanbul, Turkey,* [2]*Oncology Institute, Istanbul University, Istanbul, Turkey*

Abstract

Purpose: Conformal radiotherapy of the prostate is an increasingly common technique in the treatment of prostate cancer. When using 3D conformal radiotherapy (CFRT) methods, it is desirable to protect the vital structures such as bladder, rectum, and femur. In this study, our aim was to compare the femur head doses resulting from co-planar beam arrangements in four-field (4F), five-field (5F), six-field (6F) and seven-field (7F) treatment plans, in a dose-escalated CFRT schedule.

Materials and Methods: From January 2005 to December 2006, at Istanbul University Medical Faculty of Radiation Oncology Clinic, a total of 22 patients with carcinoma of the prostate had been scanned using computed tomography (CT) (0.50 mm) in the supine position. During the CT scanning which used the Sim Pro (CMD–USA) programme, planned target volume (PTV), clinical target volume (CTV), and dose volumes received by the bladder, rectum and femur heads were recorded and dose–volume histogram (DVH) were created. The dose volume relating to prostate and seminal vesicles was termed CTV 1, and the dose volume relating to prostate alone was termed CTV 2. During the formation of PTV, into CTV 1, from the anterior-superior-inferior 8 mm, and from posterior 5 mm tolerance were taken into account. After volume determination is calculated using XiO (CMS-USA) 3D treatment planning computer, each patient 4F ($45^\circ - 25\%$, $135^\circ - 25\%$, $225^\circ - 25\%$, $315^\circ - 25\%$), 5F ($0^\circ - 20\%$, $45^\circ - 20\%$, $90^\circ - 20\%$, $270^\circ - 20\%$, $315^\circ - 20\%$), 6F ($45^\circ - 20\%$, $90^\circ - 10\%$, 135° 20%, $315^\circ - 20\%$, $270^\circ - 10\%$, $225^\circ - 20\%$) and 7F ($0^\circ - 4\%$, $45^\circ - 12.9\%$, $90^\circ - 22.2\%$, $135^\circ - 12.9\%$, $315^\circ - 12.9\%$, $270^\circ - 22.2\%$, $225^\circ - 12.9\%$) was entered; 70 – 76 Gy was calculated to be given to prostate lodge. With the use of Siemes Oncor, 18 MV photons CFRT was applied. In DVH analysis, following were observed: V50, minimum and maximum doses for head of left femur and right femur total doses.

Results: Our statistical evaluation was made using SPSS software, and we found femur doses following; 4F V50 1030 cGy (minimum 58, maximum 1390), 5F V50 2425 cGy (minimum 540, maximum 3631), 6F V50 1769 cGy (minimum 1234, maximum 3912) and 7F V50 3230 cGy (minimum 2150, maximum 4137). In comparing different techniques, the greatest rectal sparing was achieved by the 5F plan. (Rectal: 5F V%25 $= 59.90 \pm 6.8$ Gy, 4F V%25 $= 62.30 \pm 10.3$ Gy, 6F V%25 $= 69.36 \pm 5.7$ Gy, 7F V%25 $= 61.32 \pm 7.3$ Gy). The greatest femoral head sparing was achieved by the 4F techniques. When paired samples *t*-test was made, we found considerable lower femur doses for 4F techniques ($p = 0.05$).

Correspondence to: Diden Karaçetin, Şişli Etfal Research and Training Hospital, Radiation Oncology Clinic, Istanbul, Turkey. Email: didemkaracetin@gmail.com

Conclusion: We concluded that, during radiotherapy to treat carcinoma of the prostate, the dose received by the rectum is the most important factor to consider, given the potential for late toxicity in this organ. However, while using lateral fields (90–270°) so as to protect the rectum, the doses received by the femur heads were observed to be higher. Especially in older patients, the critical doses of 52 Gy for TD5/5 and 65 Gy for TD 50/5 were observed to be not reached late toxicity for 4F, 5F, 6F and 7F.

Keywords

3D conformal radiotherapy; prostate cancer; dose to femur heads; toxicities

INTRODUCTION

Radical radiotherapy is routinely used for the curative treatment of localised prostate cancer. Dearnaley *et al.* recently reported that conformal radiotherapy (CFRT) techniques in the radical treatment of prostate cancer provided significant reduction in late rectal morbidity when compared with conventional open-field techniques.[1] Using prescribed doses of up to 64 Gy, rectal complications greater than or equal to grade 2 as measured on the Radiation Therapy Oncology Group (RTOG) scale were reduced from 15% to <5% ($p = 0.01$). Radiation doses received by the bladder and femur heads were found to be acceptable, and there were no serious complications resulting from these doses. This finding laid the foundation for the randomised Medical Research Council RT-01 trial of dose escalation for localised prostate cancer. This ongoing trial involves the use of CFRT for patients with prostate cancer; the patients are randomly assigned to two groups, one of which receives a dose of 64 Gy and the other an escalated dose of 74 Gy.

On the basis of dose–response data relating to radiotherapy for prostate cancer the Patterns of Care Study suggested that there is improvement in local control with a dose of >70 Gy in stage C tumours,[2] but that this dose is accompanied by an increase in toxicity to normal tissues. However, 3D-CRT studies have shown that doses >70 Gy can be delivered to achieve better local control in prostate tumour with no associated increase in either acute or late toxicity.[3]

Although external beam radiotherapy is commonly used in the treatment of localised prostatic carcinoma, the optimal beam arrangement is still being debated. Traditionally, a four-field 'box' technique has been used, but more recently other approaches have been applied, including three-field (3F), four-field (4F), six-field (6F) and arcing fields. Each of these different treatment plans has its own advantages and disadvantages in terms of sparing of critical structures, delivery of treatment, and ease of verification. Pickett *et al.* concentrated on the 6F technique and found that anterior and posterior oblique beams angled at 35° from the lateral direction, combined with bilateral fields (i.e., gantry angles at 55°, 90°, 125°, 235°, 270° and 305°), provided the best combination of CTV coverage and maximum sparing of the femoral heads, rectum and bladder.[4] Several authors have reported results of comparative studies involving different numbers of fields for prostate radiotherapy. These studies include the one by Lennernäs *et al.*[5] who compared 4F, 5F and 6F techniques. They found that the use of more than four fields did not reduce the dose to the organs at risk, and that if increased sparing of these organs was necessary, it must be achieved through application of reduced tumour margins. This conclusion was supported by Neal *et al.*, who found that, although the use of a larger number of fields reduced the dose to the femoral heads and bladder, the 4F technique was the most advantageous in terms of clinically relevant rectal sparing.[6] Fiorino *et al.* concluded, after comparing 3F, 4F and 6F techniques, that no one technique was better than the others, because sparing of the rectum was always achieved at the expense of increased dose to the femoral heads.[7]

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In this study, our aim was to compare the femur head doses resulting from co-planar beam arrangements relating to various 4F, 5F, 6F and 7F plans in a dose-escalated CFRT schedule for prostate cancer. The aim was to determine which of these plans (4F, 5F or 6F) provides the maximum sparing of femoral heads, while maintaining the radiation doses to the rectum and bladder within acceptable limits.

PATIENTS AND METHODS

Patient characteristics

A total of 22 patients with prostate adenocarcinoma were selected for this study. We used the data from computed tomography (CT) abdomen scans of 22 patients who were treated for prostate cancer in our institute in 2005–2006. All these patients were treated with 3D-CRT. They had undergone complete clinical evaluation and laboratory studies including complete blood count, renal and liver function tests and prostate-specific antigen estimation. CT scan of abdomen and pelvis, chest radiography and bone scan formed part of the staging procedure. The median Gleason score was 7 (range 6–9).

Radiotherapy treatment planning and dose calculation algorithms

For the 3D-CRT procedure the patients were immobilised (pelvis and leg) in a thermoplastic mask system or a vacuum lock fixation device in the supine position. All the patients underwent treatment planning intravenous contrast enhanced CT scans with 5 mm axial contiguous cuts which extended from midpoint of sacroiliac joint to below the lesser trochanter of the femur. The scans were imported through an electronic network. Clinical target volume (CTV) and organs at risk (rectum, bladder and femur heads) were contoured. The CTV included the prostate and seminal vesicles. The lower pelvic nodal areas were included in the CTV for purposes of planning, after which they were contoured only if pre-treatment CT/magnetic resonance imaging scans revealed involvement of the pelvic nodal area. The planned target volume (PTV) was contoured on the basis of the CTV, allowing a margin of 0.5 cm. The dose planned to the prostate was 70–76 Gy, and to the seminal vesicles 50.4–60 Gy; the lower pelvic nodal region received a prophylactic dose of 45 Gy. All treatment planning was normalised to the ICRU reference point.

The prescribed dose was normalised to 100% at the isocentre, and 95% isodose surface covered the PTV.

The doses received by the bladder, rectum and femoral heads were measured for statistical analysis.

Target volumes

For all the patients, the delineation of target(s) and critical structures was done by a single physician with extensive experience in the treatment of prostate cancer. The CTV for each of the patients included 2 cm of seminal vesicles of the peri-prostatic rectum and a 5 mm expansion of the gross tumour volume (prostate only) in all directions, except posteriorly. The prostate planning target volume ($PTV_{prostate}$) was generated by expanding the prostate CTV by a uniform 5 mm in all directions. The nodal CTV included a 1 cm expansion of pelvic lymph nodes in all directions excluding the anterior portion of 1 cm of skin, prostate PTV, bladder, rectum, small bowel, and femoral heads. The nodal PTV volume (PTV_{nodes}) was arrived at by expanding the nodal CTV by 5 mm in all directions excluding prostate PTV and anterior skin 1 cm.

Critical structures

The critical structures included the rectum, bladder, small bowel and femurs. The nodal CTV included a 1 cm expansion of pelvic lymph nodes in all directions prostate PTV, bladder, rectum, small bowel and femoral heads. In addition, the unspecified tissue was also contoured and included in the optimisation.

Statistical analysis

Normal tissue doses for bladder, rectum, femur heads were calculated.

The data were analyzed using the software from Statistical Package for Social Sciences (SPSS 12.0).

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The various 4F, 5F, 6F and 7F plans were compared using mean dose–volume statistics. A two-tail Student's *t*-test was used to verify the significance of differences in the mean results of the treatment plans, after correlation of quantile–quantile plots had shown the data to be normally distributed.

RESULTS

The mean statistical values relating to the 4F, 5F, 6F and 7F plans are shown in Table 1. Each of the optimised plans (4F, 5F, 6F and 7F) improved on its respective reference plan in terms of V50 (Figures 1–4).

We calculated the radiation doses received by the femur under each of the treatment conditions: For the left femur, these were: 4F, V50 1030 cGy (minimum 58, maximum 1390); 5F, V50 2425 cGy (minimum 540, maximum 3631); 6F, V50 1769 cGy (minimum 1234, maximum 3912); and 7F, V50 3230 cGy (minimum 2150, maximum 4137). For the right femur, the doses were: 4F, V50 1040 cGy (minimum 88, maximum 1350); 5F, V50 2325 cGy (minimum 483, maximum 3074); 6F V50 1780 cGy (minimum 1352, maximum 3968); and 7F, V50 3275 cGy (minimum 2250, maximum 4050). The 4F plan irradiated a smaller volume of femoral head than the other three reference plans did.

Table 1. *Mean statistics for each of the 4F, 5F, 6F and 7F plans*

	Left femur 4F	Left femur 5F	Left femur 6F	Left femur 7F	Right femur 4F	Right femur 5F	Right femur 6F	Right femur 7F
N								
Valid	22	22	22	22	22	22	22	22
Missing	0	0	0	0	0	0	0	0
Mean	898.18	2327.5909	1875.5909	3066.6818	912.5909	2179.0000	1870.5909	3095.2273
Minimum	58	540.00	1234.00	2150.00	88.00	483.00	1352.00	2250.00
Maximum	1390	3631.00	3912.00	4137.00	1350.00	3074.00	3968.00	4050.00

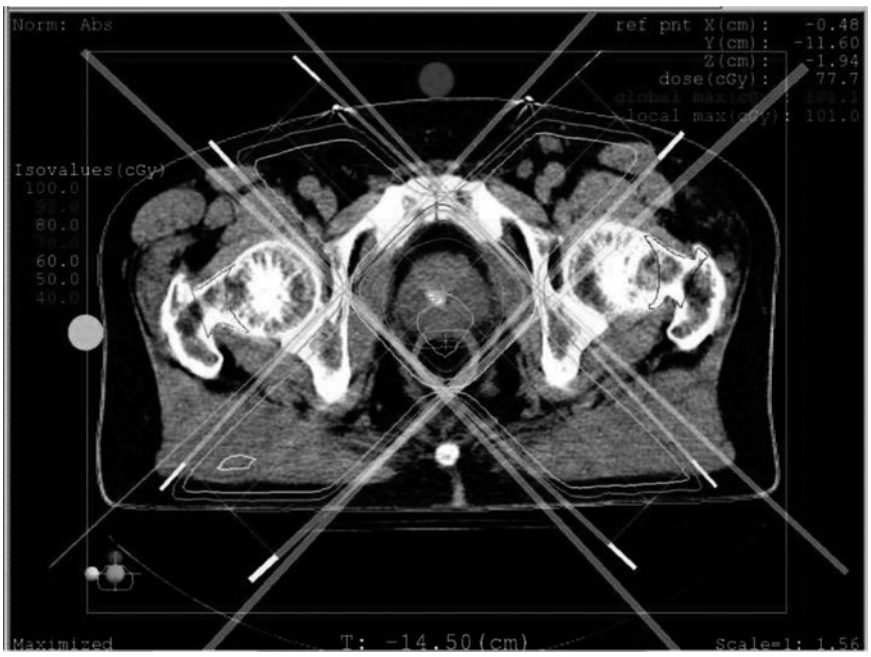

Figure 1. Four-field conformal planning techniques.

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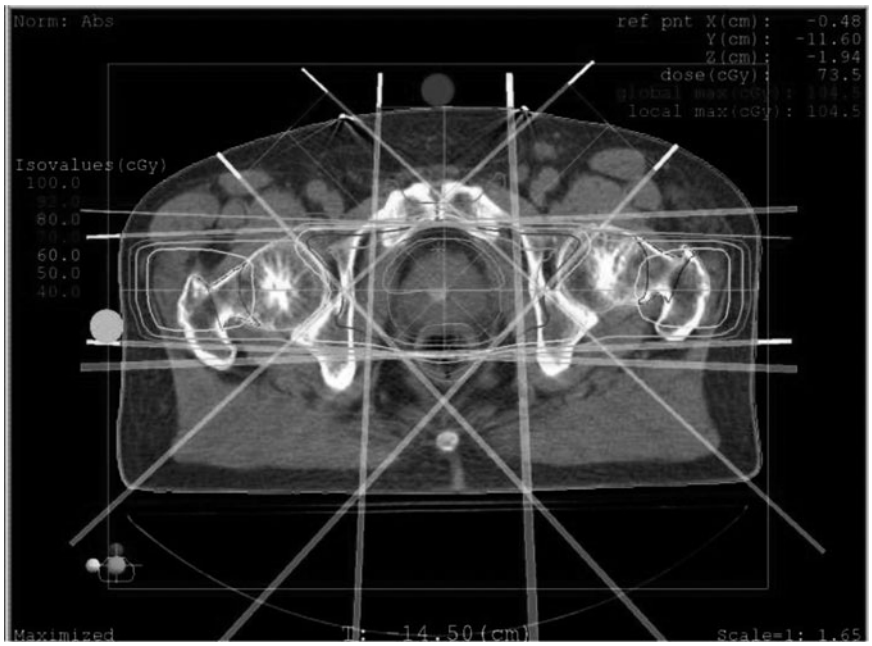

Figure 2. Five-field conformal planning techniques.

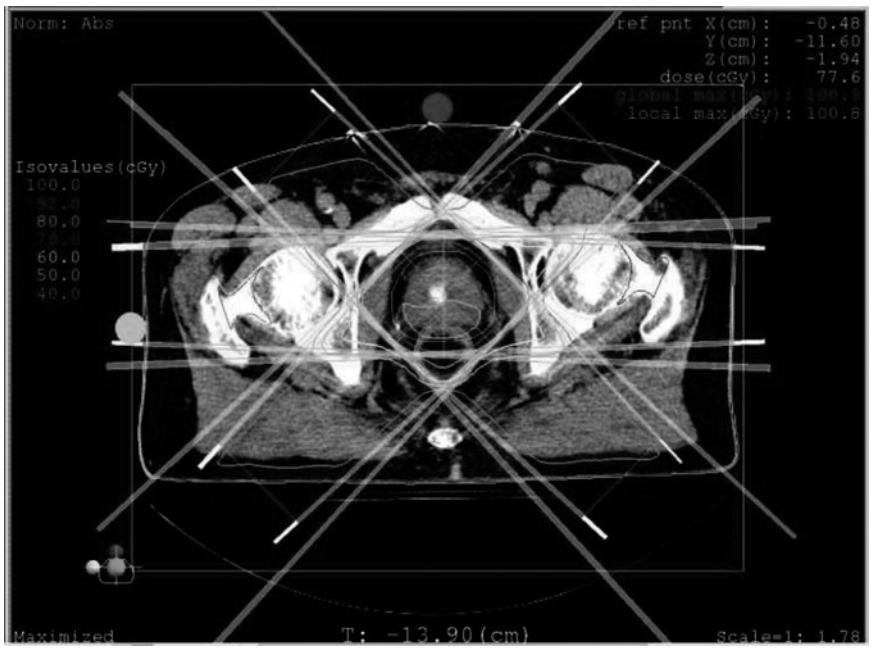

Figure 3. Six-field conformal planning techniques.

When paired samples *t*-test was carried out, we found considerably lower femur doses for 4F techniques ($p = 0.05$). We concluded that, during radiotherapy for prostate carcinoma, the dose received by rectum is the overriding factor to consider, in view of potential for late toxicity in this organ. When lateral fields were used (90–270°) with a view to protecting

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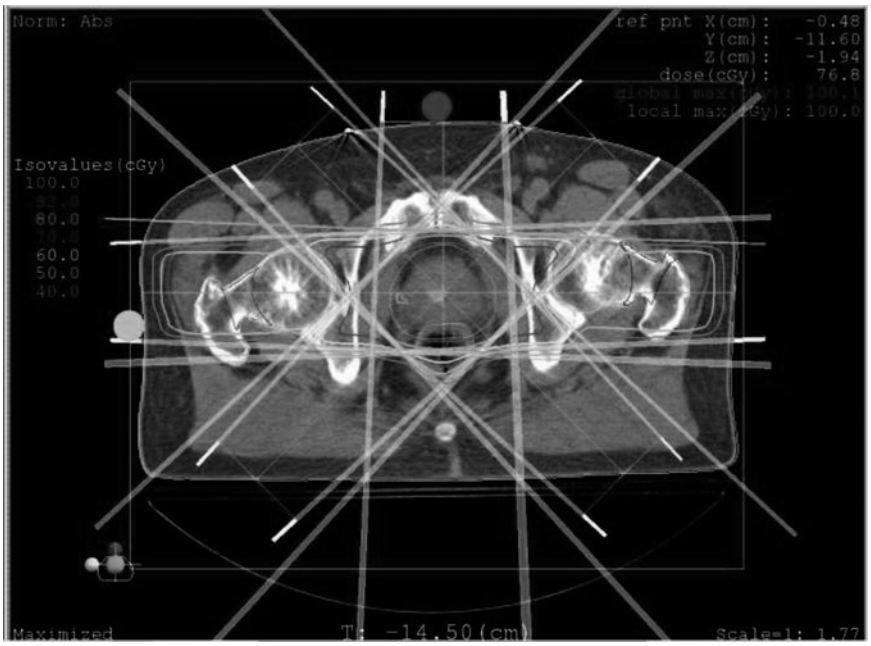

Figure 4. Seven-field conformal planning techniques.

the rectum, the doses received by the femur heads were observed to increase.

Especially in older patients, the critical doses of 52 Gy for TD5/5, 65Gy for TD 50/5 were observed to be not reached late toxicity for 4F, 5F, 6F and 7F.

DISCUSSION

Prostate cancer is the most frequently diagnosed non-skin cancer in the male population in Western countries.[8] The prostate cancer clinical guidelines panel of the American Urological Association recommended radiation therapy as an important option in the management of localised prostate cancer.[9] A comparison of outcomes of external beam therapy versus radical prostatectomy for 382 patients with low-risk prostate carcinoma treated at a single institution revealed similar 7-year rates of biochemical control and cause-specific survival.[10]

The 3D-CRT technique overcomes the limitation of conventional open-field radiotherapy, in that it avoids toxicity to normal tissues. In 3D-CRT, the prescribed radiation doses conform to the outline of planned target volume in its entire 3D configuration. Therefore the risk of under-dosing the target is reduced. Effective exclusion of normal tissues permits dose escalation to the target to high levels.

The standard 3D conformal beam arrangement consists of six co-planar fields, comprising two lateral, two anterior and two posterior oblique beams.[11] Several other beam arrangements have been proposed for 3D-CRT, with the most common being the conformal four-field.[12–15]

Dose–volume histograms (DVHs) were generated for the PTV, femoral heads, and rectal and bladder walls (Figures 5–8). Wherever the bowel was located near the prostate and seminal vesicles, a dose calculation for the bowel was also done. In the Memorial Sloan-Kettering Cancer Center 6F plan, the two lateral beams typically delivered approximately half of the total dose to the isocentre with the four oblique beams contributing the rest. The beam weights of the anterior and posterior oblique beams were adjusted to obtain a uniform dose within the PTV and to place the hot spots away from the rectum. The plan was normalised so that the prescription isodose (100%) covered the PTV with a hot spot of 6–9% within the

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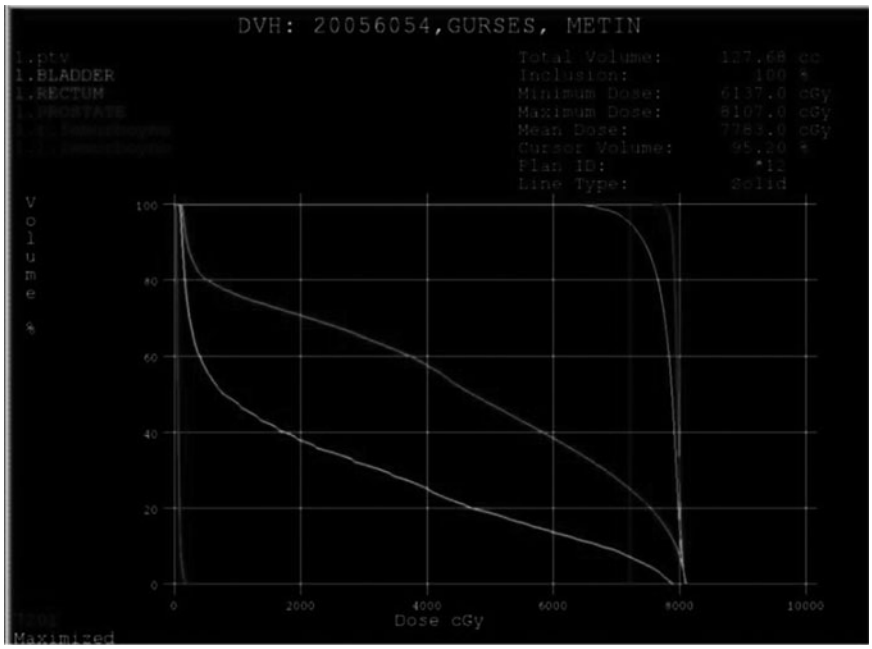

Figure 5. Four-field conformal planning dose–volume histograms.

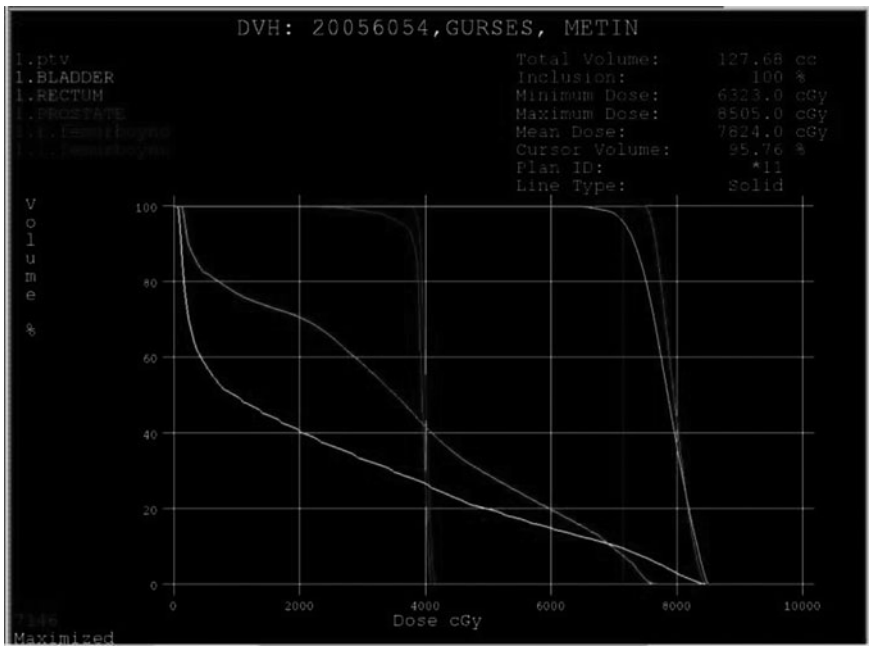

Figure 6. Five-field conformal planning dose–volume histograms.

PTV. Although the portion of the rectal wall enclosed within the PTV was expected to receive the prescription dose, or slightly higher, the rectal wall volume that received 75.6 Gy or more did not exceed 30%. For these 3D-CRT plans, the other dose limits relating to normal tissue included limiting the maximum dose to the femurs to $\leq$68 Gy (90%), the maximum

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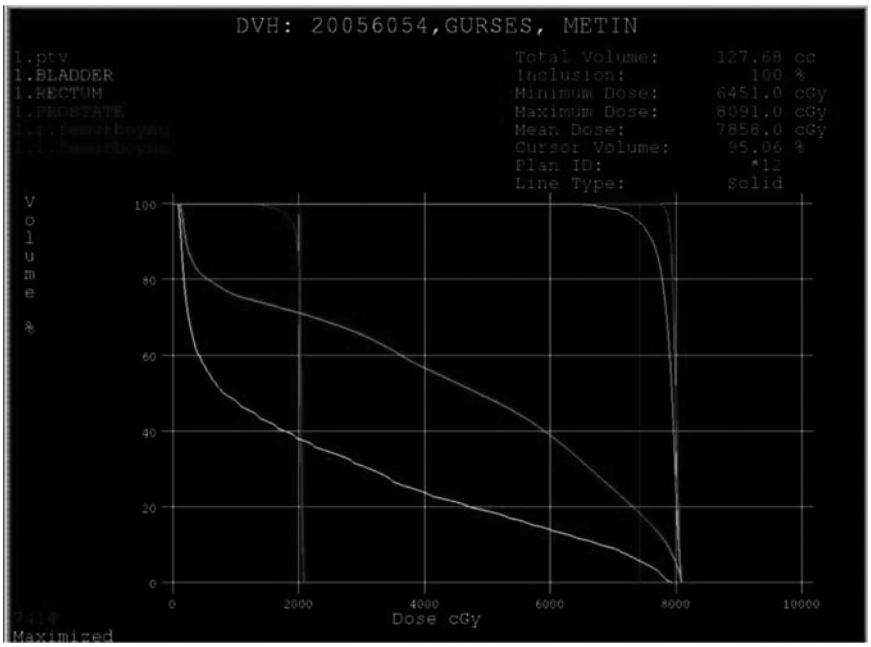

Figure 7. Six-field conformal planning dose–volume histograms.

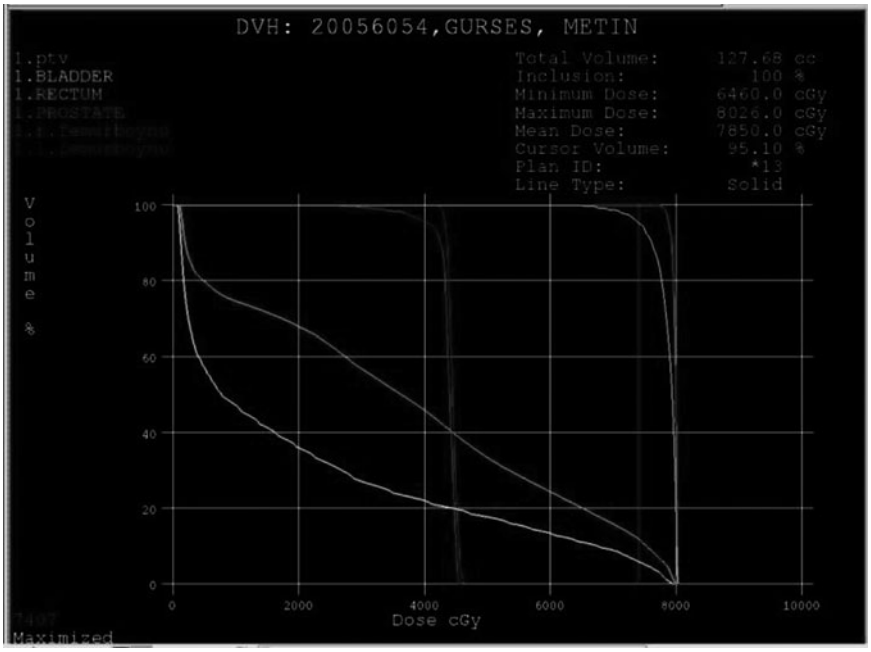

Figure 8. Seven-field conformal planning dose–volume histograms.

dose to the large bowel to ≤60 Gy (79%), and the maximum dose to the small bowel to ≤50 Gy (66%).

The dose tolerance limits of the rectum and bladder have been the main limiting factors for dose escalation in radiotherapy for prostate cancer. After the introduction of 3D-CRT, the early results reveal no significant increase in gastrointestinal and genitourinary toxicity with increased doses of radiation to the prostate. In 96 patients treated with 3D-CRT to a level of

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75.6 Gy or 81 Gy, the occurrence of acute grade II morbidity was 17% for the rectum and 36% for the urinary bladder.[3] All the other patients had either no morbidity at all, or grade I morbidity. No acute grade III side effects were observed. Late rectal morbidity was nil or grade I in 85% of the patients. Grade II morbidity occurred in 15% of the patients. The acute and late effects of high-dose 3D-CRT were studied in the RTOG 9406 prostate cancer trial.[16] In 262 patients with T1T2 prostate cancer who were treated at dose levels of 74 Gy, the tolerance has been found to be better than would be expected on the basis of historical data.

The safety-related constraints regarding dose to the femoral head during radiotherapy for prostate cancer are not yet well established.[17–19] For example, Bedford *et al.* recommend that no more than 10% of the femoral head should receive a dose higher than 52 Gy. Such a conservative upper limit for the tolerable dose was suggested in view of the presumed low α/β ratio for the femoral head.[17] Emami *et al.* suggest that a dose of 52 Gy to the whole femoral head produces a complication probability of 5% at 5 years, i.e., TD5/5 = 52 Gy (tolerance dose, TD).[20] Clinical experience suggests that a higher dose ($\geq$70 Gy) to a small part of the femoral head may be tolerated.[21] Fiorino *et al.* demonstrated, after comparing five techniques (3F, 4F and 6F), that the sparing of the rectum may be achieved at the expense of an increased dose to the femoral heads.[21] They suggest that, in taking dosing decisions, priority should be given to assessing the doses that will be received by the dose-limiting organs such as the rectum and bladder; the dose to the femoral head is of less relative importance.[22] In their study, the 3F and 6F techniques spared the femoral heads to a greater extent than the 4F technique did. Both our study and the study by Tobler *et al.*, the 6F technique offered better sparing of femoral heads as compared with dynamic conformal arc therapy.[23] The increase in the femoral dose was small (10.1%) with the 6F technique, and slightly more (10.9%) with optimised arc therapy. Importantly, in all the situations the femoral head DVH constraints were fulfilled.

A study carried out in France in 306 patients treated with CFRT and randomised to either a 70 Gy or an 80 Gy dose, reported similar rectal, bladder and femoral head toxicity in both groups.[19] A morbidity evaluation report of a 3D-CRT dose-escalation trial at Fox Chase Cancer Centre in 232 patients (median dose of 71.58 Gy and median follow-up of 60 months)[3] showed 5-year grade III and IV gastrointestinal toxicity to be <1%, and there was no toxicity in the femur heads.

In this study, the 4F (45°, 135°, 225°, 315°) plan consistently provided acceptable levels of femoral head doses. It provided better sparing of the femur heads in comparison with the 5F (0, 45°, 90, 270, 315), 6F (45, 90°, 135, 315°, 270°, 225°) and 7F (0°, 45°, 90°, 135°, 315°, 270°, 225°) beam arrangements that are currently used at our institution, with equivalent and acceptable bladder and rectal doses.

Emami had suggested that a dose of 52 Gy to the entire femoral head may result in a 5% probability of necrosis at 5 years (TD5/5 = 52 Gy). This 52 Gy level corresponds to 70% of 74 Gy. In practice, the dose to the whole femoral head seldom exceeds this 52 Gy threshold. The volume of the bladder that received 90% (V90) of the prescribed radiation dose was measured.[20]

A major dose-escalation report relating to radiotherapy for prostate cancer is the one from MD Anderson Cancer Centre. Pollack and Zagars studied 938 men with prostate cancer who received radiotherapy treatment at three dose levels, <67 Gy, 67–77 Gy and >77 Gy. 3D-CRT was employed for doses of 74–78 Gy. The actuarial freedom from failure at 3 years was 61%, 74% and 96%, respectively, for these three dose levels.[24] The dose tolerance levels of the rectum, bladder and femur have been the main limiting factors for radiation dose escalation in prostate cancer. After the introduction of 3D-CRT, the early results have revealed no significant increase in gastrointestinal and genitourinary toxicity with increasing radiation doses to the prostate. In 96 patients treated with 3D-CRT to the level

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of 75.6 Gy or 81 Gy, the acute grade II morbidity was 17% for rectum and 36% for the urinary bladder.[25] All the other patients had either no morbidity or grade I morbidity. No acute grade III side effects were observed. In 85% of the patients, late morbidity of the rectum was nil or grade I. Grade II morbidity occurred in 15% of the patients. The acute and late effects of high-dose 3D-CRT were studied in the RTOG 9406 prostate cancer trial.[16] In 262 patients with T1T2 prostate cancer who were treated at dose levels of 74 Gy, the tolerance has been found to be better than would be expected on the basis of historical data. A study carried out in France in 306 patients treated with CFRT and randomised to either a 70 Gy or an 80 Gy dose, reported similar rectal, bladder and femoral head toxicity in both groups.[19] A morbidity evaluation report of a 3D-CRT dose-escalation trial at Fox Chase Cancer Centre in 232 patients (median dose of 71.58 Gy and median follow-up of 60 months)[3] showed 5-year grade III and IV gastrointestinal toxicity to be <1%, and there was no toxicity in the femur heads.

In this study we compared the outcomes from 4F, 5F, 6F and 7F techniques as regards dose to the femoral heads. The distribution of the mean total dose, the probability of complications to the normal tissues, and the volume of the femoral head receiving radiation indicated that lower parameters were achieved in the case of the 4F technique using beam orientations of 45°, 135°, 225° and 315°. When the lateral fields (90–270°) were used in an effort to protect the rectum, the doses received by the femur heads were observed to increase.

This study has shown that the 4F technique with 18 MV photon energy applied provides the best level of protection for the femoral head. There are no significant differences among the plans evaluated in the study as regards dose distribution in the target (PTV). None of these techniques presented the problem of unacceptable levels of radiation dose leading to morbidity of the femoral heads. The 4F technique with beam orientations as described yielded the best sparing effect for the femoral heads.

References

1. Dearnaley DP, Khoo VS, Norman AR, Meyer L, Nahum A, Tait D, Yarnold J, Horwich A. Comparison of radiation side-effects of conformal and conventional radiotherapy in prostate cancer: a randomised trial. Lancet 1999; 353:267–272.
2. Hanks GE, Martz KL, Diamond JJ. The effect of dose on local control of prostate cancer. Int J Radiat Oncol Biol Phys 1988; 15:1299–1305.
3. Hanks GE, Hanlon AL, Schultheiss TE, Pinover WH, Movsas B, Epstein BE, Hunt MA. Dose escalation with 3D conformal treatment: five year outcomes, treatment optimization, and future directions. Int J Radiat Oncol Biol Phys 1998; 41:501–510.
4. Pickett B, Roach M 3rd, Horine P, Verhey L, Phillips TL. Optimization of the oblique angles in the treatment of prostate cancer during six-field conformal radiotherapy. Med Dosim 1994; 19:237–254.
5. Lennernäs B, Rikner G, Letocha H, Nilsson S. External beam radiotherapy of localized prostatic adenocarcinoma. Evaluation of conformal therapy, field number and target margins. Acta Oncol 1995; 34:953–958.
6. Neal AJ, Oldham M, Dearnaley DP. Comparison of treatment techniques for conformal radiotherapy of the prostate using dose-volume histograms and normal tissue complication probabilities. Radiother Oncol 1995; 37:29–34.
7. Fiorino C, Reni M, Cattaneo GM, Bolognesi A, Calandrino R. Comparing 3-, 4- and 6-fields techniques for conformal irradiation of prostate and seminal vesicles using dose-volume histograms. Radiother Oncol 1997; 44:251–257.
8. Parker SL, Tong T, Bolden S, Wingo PA. Cancer statistics, 1997. CA Cancer J Clin 1997; 47:5–27.
9. Middleton RG, Thompson IM, Austenfeld MS, Cooner WH, Correa RJ, Gibbons RP, Miller HC, Oesterling JE, Resnick MI, Smalley SR. Prostate Cancer Clinical Guidelines Panel Summary report on the management of clinically localized prostate cancer. The American Urological Association. J Urol 1995; 154:2144–2148.
10. Martinez AA, Gonzalez JA, Chung AK, Kestin LL, Balasubramaniam M, Diokno AC, Ziaja EL, Brabbins DS, Vicini FA. A comparison of external beam radiation therapy versus radical prostatectomy for patients with low risk prostate carcinoma diagnosed, staged, and treated at a single institution. Cancer 2000; 88:425–432.
11. Leibel SA, Kutcher GJ, Zelefsky MJ, Burman CM, Mohan R, Ling CC, Fuks Z. 3-D conformal radiotherapy for carcinoma of the prostate. Clinical experience at the Memorial Sloan-Kettering Cancer Center. Front Radiat Ther Oncol 1996; 29:229–237.
12. Lee WR, Hanks GE, Hanlon AL, Schultheiss TE, Hunt MA. Lateral rectal shielding reduces late rectal morbidity following high dose three-dimensional conformal radiation therapy for clinically localized prostate cancer:

https://doi.org/10.1017/S1460396909990185 Published online by Cambridge University Press

further evidence for a significant dose effect. Int J Radiat Oncol Biol Phys 1996; 35:251–257.

13. Marsh LH, Ten Haken RK, Sandler HM. A customized non-axial external beam technique for treatment of prostate carcinomas. Med Dosim 1992; 17:123–127.
14. Perez CA, Michalski JM, Mansur D, Lockett MA. Three-dimensional conformal therapy versus standard radiation therapy in localized carcinoma of prostate: an update. Clin Prostate Cancer 2002; 1:97–104.
15. Ten Haken RK, Perez-Tamayo C, Tesser RJ, McShan DL, Fraass BA, Lichter AS. Boost treatment of the prostate using shaped, fixed fields. Int J Radiat Oncol Biol Phys 1989; 16:193–200.
16. Michalski JM, Winter K, Purdy JA, Perez CA, Ryu JK, Parliament MB, Valicenti RK, Roach M 3rd, Sandler HM, Markoe AM, Cox JD. Toxicity after three-dimensional radiotherapy for prostate cancer with RTOG 9406 dose level IV. Int J Radiat Oncol Biol Phys 2004; 58:735–742.
17. Bedford JL, Khoo VS, Oldham M, Dearnaley DP, Webb S. A comparison of coplanar four-field techniques for conformal radiotherapy of the prostate. Radiother Oncol 1999; 51:225–235.
18. Cheung P, Sixel K, Morton G, Loblaw DA, Tirona R, Pang G, Choo R, Szumacher E, Deboer G, Pignol JP. 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. Beckendorf V, Guérif S, Le Prisé E, Cosset JM, Lefloch O, Chauvet B, Salem N, Chapet O, Bourdin S, Bachaud JM, Maingon P, Lagrange JL, Malissard L, Simon JM, Pommier P, Hay MH, Dubray B, Luporsi E, Bey P. The GETUG 70 Gy vs. 80 Gy randomized trial for localized prostate cancer: feasibility and acute toxicity. Int J Radiat Oncol Biol Phys 2004; 60:1056–1065.
20. Emami B, Lyman J, Brown A, Coia L, Goitein M, Munzenrider JE, Shank B, Solin LJ, Wesson M. Tolerance of normal tissue to therapeutic irradiation. Int J Radiat Oncol Biol Phys 1991; 21:109–122.
21. Fiorino C, Reni M, Cattaneo GM, Bolognesi A, Calandrino R. Comparing 3-, 4- and 6-fields techniques for conformal irradiation of prostate and seminal vesicles using dose-volume histograms. Radiother Oncol 1997; 44:251–257.
22. Chuba PJ, Sharma R, Yudelev M, Duclos M, Shamsa F, Giacalone S, Orton CG, Maughan RL, Forman JD. Hip stiffness following mixed conformal neutron and photon radiotherapy: a dose–volume relationship. Int J Radiat Oncol Biol Phys 1996; 35:267–272.
23. Tobler M, Watson G, Leavitt DD. The application of dynamic field shaping and dynamic dose rate control in conformal rotational treatment of the prostate. Med Dosim 2002; 27:251–254.
24. Pollack A, Zagars GK. External beam radiotherapy dose response of prostate cancer. Int J Radiat Oncol Biol Phys 1997; 39:1011–1018.
25. Zelefsky MJ, Fuks Z, Wolfe T, Kutcher GJ, Burman C, Ling CC, Venkatraman ES, Leibel SA. Locally advanced prostatic cancer: long-term toxicity outcome after three-dimensional conformal radiation therapy – a dose-escalation study. Radiology 1998; 209:169–174.

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