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Original Article

Comparison of three-dimensional conformal irradiation techniques for prostate cancer using a low-energy (6 MV) photon beam

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Abstract

Purpose: To evaluate composite coplanar and non-coplanar three-dimensional conformal techniques (3D-CRT) for external-beam prostate radiotherapy using a low-energy (6 MV) photon beam.

Methods and Materials: For treatment-planning purposes, three different planning target volumes (PTV) were defined for ten patients with prostate cancer and as follows: PTV1 (pelvis), PTV2 (prostate + seminal vesicles + 1 cm margin) and PTV3 (prostate + 1 cm margin). Conformal techniques of 2, 3, 4, 5 (coplanar) and 6 (non-coplanar) field techniques have been considered and combined to produce five different plan combinations (i.e. techniques A, B, C, D and E). Treatment plans were generated with a prescription dose of 75 Gy to PTV3, 65 Gy to PTV2 and 45 Gy to PTV1 and were assessed on the basis of 3D dose distributions and dose-volume histograms (DVHs). Normal tissue-dose constraints for the relevant organs at risk (OARs), that is, rectum, bladder and femoral heads, were also considered.

Results: Findings show that all five treatment-plan combinations result in adequate PTV coverage and acceptable OAR irradiated volumes. The greatest rectal spacing in the high-dose region is achieved by technique C; all techniques achieve this, except for technique A, and give approximately the same fraction of volume (of rectum) that receives a dose of 50 Gy (V50) and 60 Gy (V60). When considering the bladder, techniques B, D and E give the best bladder sparing with small absolute differences, whereas technique A results in the lowest dose for femoral heads. Technique E appears to give the best compromise for all three considered OARs, provided the PTV is adequately covered.

Conclusions: Even though the optimum photon-beam energy for conformal prostate radiotherapy is greater than 10 MV, our study shows that a good sparing of OAR can be achieved even with a lower-energy beam (6 MV) and the appropriate plan combination and that the dose to prostate can be as high as 75 Gy.

Keywords

prostate cancer; radiotherapy; 3D conformal techniques

INTRODUCTION

External beam radiation therapy is an effective treatment of localised and locally advanced

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stages of prostate cancer.[1,2] In clinical practice, depending on the irradiation techniques and facilities, the need for high-radiation dose to be given to the tumour is often limited by the inevitable irradiation of the surrounding critical organs and the subsequent side-effects to them. Late side-effects are defined as those that develop and persist for more than 3 months after completion of treatment. In case of prostate radiation treatment, late rectal bleeding and bladder complications are more ''dose-limiting'' effects than acute effects because they are generally permanent and may be progressive in severity.[3,4] Toxicity of late effects depends on the volume of normal tissues irradiated.[3,5,6]

Dose levels in the range of 65 Gy to 70 Gy have been proved to be effective for the external beam radiation therapy of locally advanced prostate cancer patients.[6–10] However, studies with data from patients treated with conventional (non-3D) techniques (administered dose levels ≤70 Gy) have shown 7- to 10-year prostate-specific antigen (PSA) relapse-free survival rates of 65% in T1-T2 disease[11] and 24% in more locally advanced T3 tumours.[6,8,10] Higher doses have shown to improve the outcome, but rectal and bladder complications rates at 6.9%[3,12] have limited the ability to deliver higher doses with conventional techniques.

Three-dimensional conformal techniques (3D-CRT) are based on advanced 3D imaging and tumour visualisation techniques, 3D dose calculations algorithms and advanced beam-shaping technologies. The combined effect enables better conformation of dose distribution to the tumour area and improved sparing of critical organs. Safe administration of higher doses with lower rates of late side-effects may be achieved with 3D-CRT, compared to conventional RT. Several studies in the literature[6,12,13] have shown fewer acute toxic effects and an acceptable degree of late side-effects when the treatment dose to prostate cancer was increased from 65 Gy to 75 Gy or more. Other studies[3,4,14] indicate that a 10% increase in treatment dose may improve the local tumour control by 20% in radiosensitive tumours such as prostate. Intensity-modulated radiotherapy (IMRT) has been used to make possible more dose escalation – up to 85 Gy.[15,16] Although IMRT techniques offer more advantages in dose delivery compared to non-modulated 3D-CRT treatments, the latter remain a predominant method of treatment delivery for many radiotherapy centres around the world.

The optimum photon-beam energy used for 3D conformal prostate radiotherapy is greater than 10 MV. Beam arrangement in conformal techniques varies between centres. The choice of technique is often based on the departmental previous experience and on a preventive balancing of possible side-effects on the critical organs (rectum, bladder and femoral heads). A number of studies have been performed comparing different 3D coplanar and non-coplanar techniques used in prostate radiotherapy with differing results.[17–21]

Our study was initiated mainly for the reason that many radiotherapy centres in our country are equipped with a single, low-energy (e.g. 6 MV), linear accelerator. The question that arises in such a case is, whether a radiotherapy department equipped with a single, low-energy linac is able to provide radical external-beam radiotherapy in prostate cancer patients or a high-energy linac is a prerequisite for such a treatment?

Therefore, the aim of the current study is to compare, in terms of final dose distribution and treatment-planning outcome and evaluation, different combinations of 3D conformal coplanar and non-coplanar techniques using a 6-MV linac beam. Radical radiotherapy of the prostate cancer with 3D-CRT techniques is considered adequate only if the given total dose to the prostate gland is at least 70 Gy; the main challenge for this study is whether or not a total dose of 75 Gy can be applied to the prostate while keeping the dose to the surrounding critical organs at levels considered safe.

METHODS AND MATERIALS

Ten randomly chosen patients with locally advanced prostate cancer histologically staged from T1c to T3b[22] were retrospectively studied. All patients were aligned in supine position and marked for treatment positioning in the department's simulator unit. Standard bilateral leg and knee immobilisation positioners were utilised for all patients. Prior to CT scan and treatment, all patients were advised to have full bladder and empty bowel. An axial CT scan of the pelvic region was used for treatment planning. Acquisition parameters were as follows: 120 kV tube voltage, 256 × 256 pixel matrix size, max 80 slices, 5 mm slice thickness, no interslice gap, field of view 250 × 250 mm^2. CT images were DICOM imported into the Treatment Planning System (TPS; PLATO Sunrise™ v1.8, Nucletron Veenedal, Netherlands).

PTV and OAR contouring

Planning target volume (PTV) and the relevant organs at risk (OARs), that is, rectum, bladder and femoral heads, were contoured according to the recommendations of ICRU.[23,24] Rectum was contoured from anal verge to recto-sigmoid flexure as a solid organ. Bladder was contoured as a whole organ, including the cavity.

The prostate gland was considered as the gross tumour volume (GTV), whereas three clinical target volumes (CTV) were identified for treatment planning purposes. CTV1 included the whole pelvis (prostate, bilateral seminal vesicles, internal iliac lymph nodes and inferior part of common iliac lymph nodes). CTV2 included the prostate, bilateral seminal vesicles, periprostatic tissues and all known areas of tumour extension. CTV3 included the prostate gland alone.

A 3D margin was added to define the corresponding PTVs – PTV1, PTV2 and PTV3 – to account for internal organ motion, patient movement and daily set-up errors. In all phases, except towards the rectum, where 0.5-cm margin was used, 1 cm was added isotropically from CTVi to PTVi.

Treatment techniques

Treatment was delivered in an ELEKTA SL-75-5 linear accelerator (Elekta Hellas EPE, Athens, Greece) with 6-MV photon beam. Treatment plans for each technique were generated in the PLATO TPS. Phase I prescription dose was 45 Gy to PTV1, phase II dose was 65 Gy to PTV2 and phase III dose was 75 Gy to PTV3. PTV contouring and respective phase doses are shown analytically in Table 1.

Five different combinations of treatment techniques have been considered in order to reveal the most efficient one in terms of overall dose distribution while keeping dose constraints to OARs. The considered planning-technique combinations are presented in Table 2. Analytically, in phase I, two techniques were considered: (1) 2-field (AP/PA) and (2) 4-field box. In phase II, three different techniques were considered: (1) 4-field box, (2) 3-field coplanar and (3) 5-field coplanar. In phase III, the 6-field non-coplanar technique was chosen for all combinations. This choice was made for the reason that, in phase III, the PTV3 is expected to be the smallest volume, compared to the PTV1 and PTV2. Moreover, this technique uses a larger number of beams aiming to better target conformity and greater sparing to OARs. In Figure 1 the observer' eye view shows the patient body, the 3D PTV, and the rectum and the beam entries of the 6-field non-coplanar technique. Furthermore, 3D dose distributions were computed using a

Table 1. *CTV and PTV prescription doses*

	CTVi	PTVi	Fractionation	Prescribed Dose
Phase I	Pelvis	CTV1 + 1-cm 3D margin 0.5 cm in rectum	23 fractions, 1.8 Gy/fraction	45 Gy
Phase II	Prostate + BSV	CTV2 + 1-cm 3D margin 0.5 cm in rectum	10 fractions, 2 Gy/fraction	65 Gy
Phase III	Prostate	CTV3 + 1-cm 3D margin 0.5 cm in rectum	10 fractions, 2 Gy/fraction	75 Gy

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Table 2. *3D conformal treatment techniques*

Technique A	
Phase I:	2-field technique (AP/PA fields)
Phase II:	4-field-box technique (AP/PA fields and LT/RT lateral fields)
Phase III:	4-field-box technique (AP/PA fields and LT/RT lateral fields)
Technique B	
Phase I:	4-field-box technique (AP/PA fields and LT/RT lateral fields)
Phase II	4-field-box technique (AP/PA fields and LT/RT lateral fields)
Phase III	4-field-box technique (AP/PA fields and LT/RT lateral fields)
Technique C	
Phase I:	4-field-box technique (AP/PA fields and LT/RT lateral fields)
Phase II:	3-field-technique (AP field and LT/RT lateral fields)
Phase III:	6-field non-coplanar technique. (LT/RT laterals fields + 2 pairs of non-coplanar opposed oblique fields at (G = 45°, G = 225°, couch = 60°; G = 135°, G = 315°, couch = 120°)
Technique D	
Phase I:	4-field-box technique (AP/PA fields and LT/RT lateral fields)
Phase II:	5-field coplanar technique (AP field, LT/RT lateral and oblique at G = 55° and 315°)
Phase III:	6-field non-coplanar technique
Technique E	
Phase I:	4-field-box technique
Phase II:	4-field-box technique
Phase III:	6-field non-coplanar technique

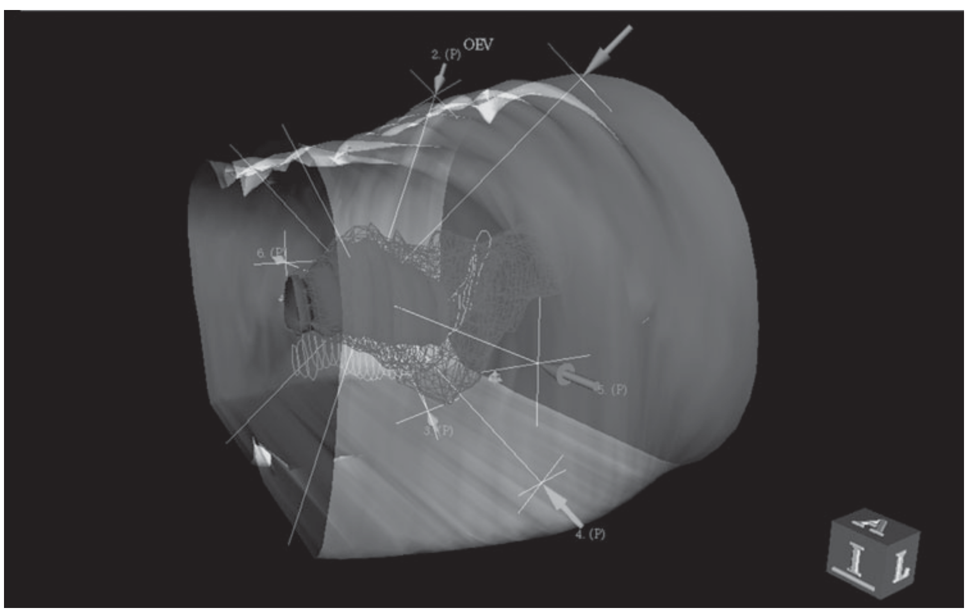

Figure 1. Observer's eye view (OEV) of the 6-field non-coplanar technique.

pencil-beam-based algorithm for the 6 MV photon beam. As the linac is not equipped with a multi-leaf collimator, custom-shaped blocks were used to conform the dose distribution to the PTV. Beam weights and wedge angles were adjusted to achieve dose homogeneity within the PTV, where the minimum requirement for dose homogeneity is defined in such measures as to[23,24] allow for a 12% dose variation. Thus, coverage of the PTV was designed to be between -5% and +7% of the prescribed (isocentric) dose. To compare the

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plans, the dose distributions were normalised to the isocentre, and a reference dose equal to 95% of the isocentre dose was assessed.

In accordance with minimum dose recommended in refs. 23 and 24, maximum dose and mean doses were recorded for the PTV and the OARs. Treatment plans were compared using 3D dose distributions and cumulative dose-volume histograms (cDVH).

Dose constraints to OARs

Dose constraints for the bladder, the rectum and the femoral heads were adopted using ICRU guidelines. Normal tissue limits (dose constraints) for plan generation are outlined in Table 3. The dose constraints for the OARs are assessed as figures of merit, in order to quantitatively compare the DVHs of the rectum, the bladder and the femoral heads.[17–19,25,26]

RESULTS

Treatment plans were evaluated in terms of 3D-dose-distribution comparison and DVH values. Comparable results are summarised in Table 4, using mean statistics. Figures 2 and 3, respectively, illustrate comparisons between different DVH curves for rectum and bladder resulting from all the five techniques applied to a single patient. In Figures 4 and 5, a representative DVH (PTV and OARs) and dose distribution for technique E are presented respectively.

All five treatment-plan combinations satisfied normal tissue dose limits and resulted in adequate PTV coverage. In all cases, more than 95% of the PTV receives 95% of the prescribed dose (0.95 D_{PTV}). The mean PTV were 1150 ± 162 cm^3 (phase I), 269 ± 94.2 cm^3 (phase II) and 149 ± 50.9 cm^3 (phase III), respectively.

In our study, as it can be seen in Table 4, all treatment techniques achieve the goal of rectal-dose constraint, that is, V70 < 30%. Among all techniques, technique C is giving the best rectal sparing, V70 = 21.5 ± 5.9% in the high-dose region. This is due to the relative higher weight of the lateral fields which better spare the rectum. In the lower-dose region, except for technique A all techniques present similar behaviour. In techniques B to E, V50 ranges from 64 to 67% and V60 ranges from 51 to 53% approximately, whereas in technique A the result was as follows: V50 = 98.5 ± 9.7%. It is evident that technique A and B deliver the highest dose to the rectum because they use a posterior field (180°) in all phases (I, II and III).

Regarding bladder sparing, technique A seems to give the best-possible V70 value (V70

Table 3. *Normal tissue dose constraints*

OAR	Dose limit
Rectum	V70 < 25–30%
Bladder	V70 < 50%
Femoral heads	D mean < 52.5 Gy

(V70); fraction of the OAR volumes that receives a dose of 70 Gy.

Table 4. *Summary of DVH data for PTV and all OARs averaged over all ten patients for each of the five treatment-plan combinations*

	(A) 2F + 4F + 4F	(B) 4F + 4F + 4F	(C) 4F + 3F + 6F	(D) 4F + 5F + 6F	(E) 4F + 4F + 6F
PTV V(0.95 D_{PTV})	>95%	>96%	>96%	>96%	>96%
Rectum V70 (%)	26.2 ± 7.1	27.7 ± 5.7	21.5 ± 5.9	22.4 ± 4.8	24.0 ± 5.5
Rectum V50 (%)	98.5 ± 9.7	64.8 ± 8.7	64.8 ± 9.5	67.2 ± 8.9	66.3 ± 8.3
Bladder V70 (%)	34.5 ± 10.5	37.5 ± 9.2	39.5 ± 9.9	36.0 ± 9.1	37.4 ± 8.7
Bladder V50 (%)	90.2 ± 15.3	74.2 ± 14.7	76.9 ± 16.1	75.6 ± 16.5	75.5 ± 15.8
Fem heads D_{mean} (Gy)	27.0 ± 4.4	47.0 ± 3.9	46.0 ± 3.8	48.5 ± 3.3	45 ± 4.1

Mean (±1 SD) statistics are quoted.
V70: percentage of volume (%) irradiated to 70 Gy

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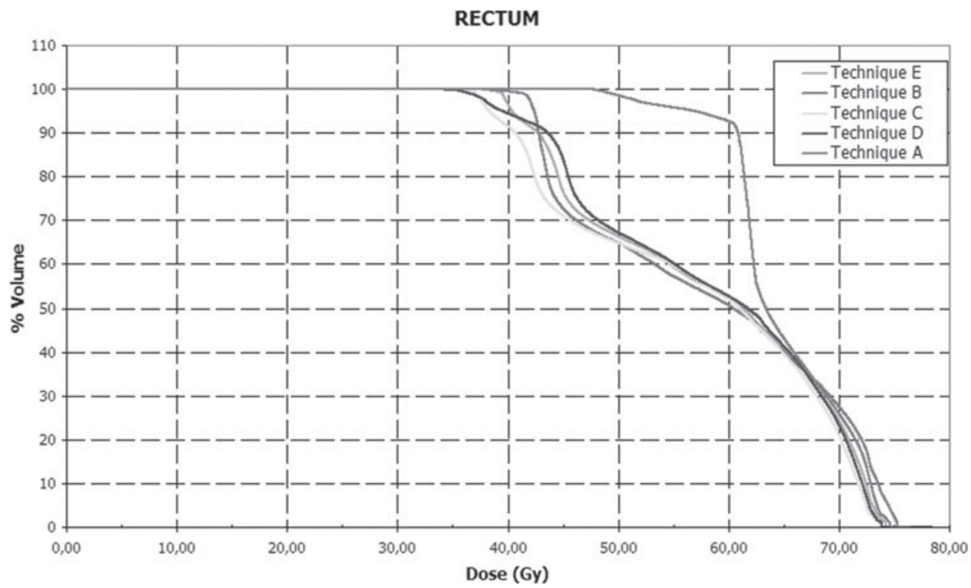

Figure 2. Dose-volume histograms for rectum in a single patient for all five treatment-plan combinations.

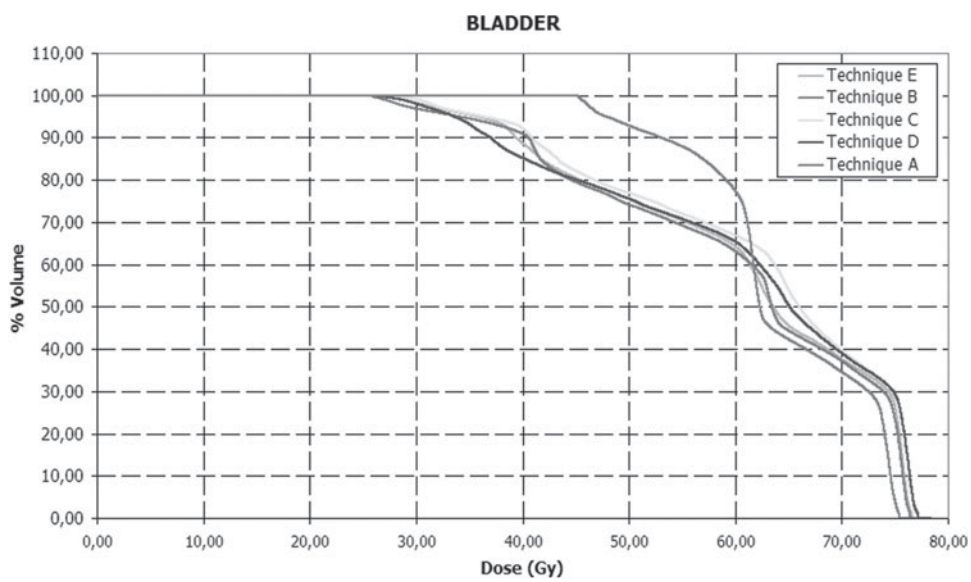

Figure 3. Dose-volume histograms for bladder in a single patient for all five treatment-plan combinations.

= 34.5 ± 10.5%). However, when considering the comparative cDVHs in Figure 3, technique A elicited the poorest efficacy compared to all other techniques. In technique A, much greater volume of bladder receives dosages up to 60 Gy. For technique A, the proportion of the bladder receiving greater than 50 Gy (V50) of the isocentric dose was V50 = 90.2 ± 15.3%, whereas for all other techniques, it was V50 < 77%. Among techniques B, D and E, technique E gives the best bladder sparing: V50 = 75.5 ± 15.8 %. The higher SD values of bladder V70 and V50, corresponding to their respective rectum volumes, are due to the greater variation of bladder filling between patients.

In all cases, the whole femoral head dose does not exceed the 52-Gy threshold. It is evident

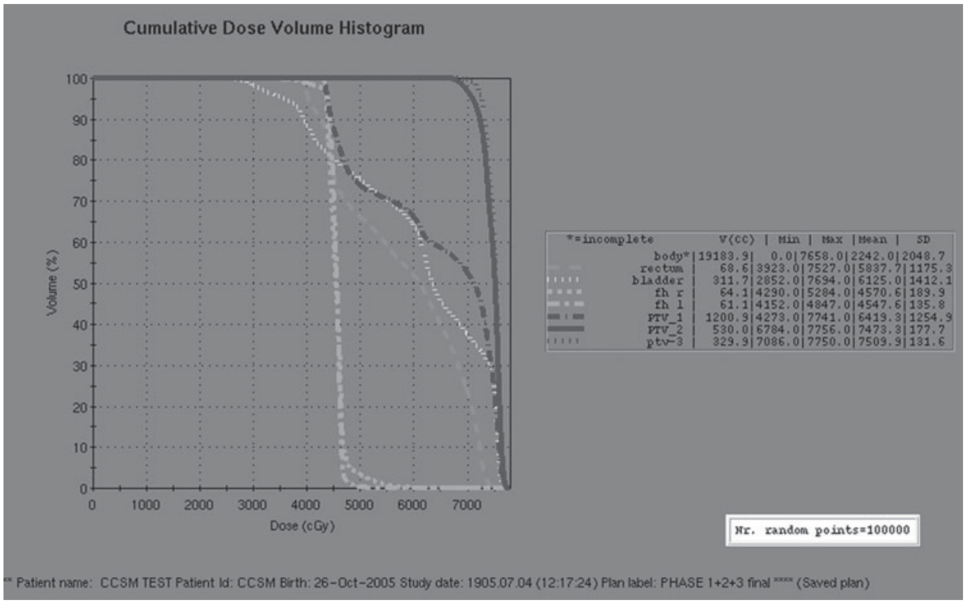

Figure 4. Dose-volume histogram (PTV, rectum, bladder and fem heads) for technique E in a single patient.

(Table 4) that technique A, as it is the only technique that does not use lateral fields for phase I, gives the lowest mean dose, Dm = 27 Gy, to the entire femoral head. Techniques B to E give similar results, with technique E showing the best performance (Dm = 45 Gy).

DISCUSSION

Rectal toxicity appears to be the most clinical relevant and dose-limiting organ for prostate radiotherapy.[9,27,28] The probability of late rectal complications has been reported to increase with larger volumes irradiated to target dose levels. Reports in current literature concerning the radiation-induced toxicity to the rectum note that the percentage of rectal volume exposed to doses higher than 70 Gy is correlated with rectal bleeding.[3,4,6,29,30] Several groups have investigated the risks of rectal toxicity on the basis of dose-volume assessments. For example, Zagars et al.[8] noted a 3% incidence of major recto-sigmoid complications in patients receiving more than 70 Gy in rectal wall. Furthermore, Fiorino et al.[19] noted that V50 below 60 to 65%, V60 below 45 to 50% and V70 below 25 to 30% should keep the rate of late bleeding (grades 2–3) between 5 and 10% for an ICRU dose between 70 and 78 Gy.

Regarding the use of non-coplanar treatment technique, reports in the literature[20,21,31] suggest that such technique provides increase in rectal sparing—a finding which is also confirmed in our study. In fact, when comparing technique B, where all technique combinations are coplanar, with techniques C to E (in phase III, the non-coplanar technique is used) our data show that rectum V70 is reduced by 10 to 20%. In refs. 21,31 a technique involving left and right opposed fields together with two anterior inferior oblique fields is reported and was found to reduce the irradiated volume of rectum and bladder to a level comparable to that provided by opposed lateral fields alone. However, no consistent comparison of non-coplanar techniques has been mentioned in literature.

Bladder toxicity is not as common as rectal toxicity but can be a very late phenomenon, surfacing even several years after therapy. Predictors of late bladder injuries are more elusive due to the longer onset of injury and the more severe volume changes during therapy. The

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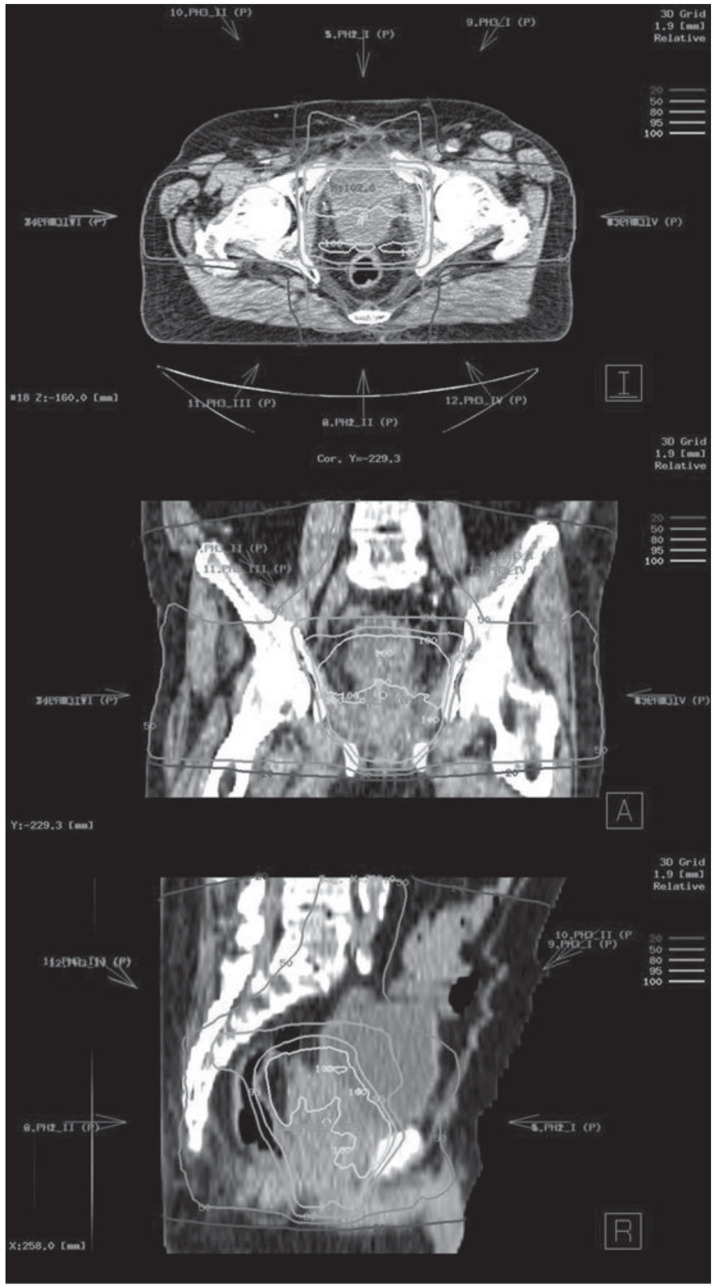

Figure 5. Axial, sagittal and coronal dose distribution through the isocentre in a single patient for technique E. The isodoses (centre outwards) are 100, 95, 80 and 50% of the prescribed dose (75 Gy).

influence of the shape of the bladder on DVHs when considering the filling from one fraction to another is an important problem. This results in a more arbitrary determination of bladder dose constraints. Michalski et al.[9] in 9406 RTOG trial for prostate cancer reported that the relative risk of developing acute or late bladder toxicity increased as the percentage of the bladder receiving more than 65 Gy increased. For doses more than 70 Gy Hanks et al.[7] and Lawton et al.[32] observed a significantly increased incidence of grade 3 and grade 4 urinary toxicity. In general terms, fewer than 5% of patients develop chronic cystitis, but,

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occasionally, with doses higher than 75 Gy, approximately 5% of patients require cystectomy due to hemorrhagic cystitis.[9] Our results are consistent with the reported bladder constraints as mean V70 was less than 40%.

When considering the femoral heads very little data are available on the dose–effect relationship. Using doses of approximately 60 to 64 Gy, a $TD_{5/5} = 52$ Gy for the entire femoral head has been suggested.[17,18,33] In ref. 19 there is a suggestion from clinical experience that small fractions of femoral heads should tolerate relatively high doses (70 Gy). Thus, our data showing a maximum dose of 48.5 Gy to femoral heads (technique D) are consistent with the 52-Gy threshold mentioned in literature.

Overall, provided PTV is adequately covered, techniques B to E achieve the goal of dose constraints to the relevant OAR, whereas technique A proved to be the worst in bladder and rectum sparing in dosages approximately in the region of 40 Gy and 60 Gy (Figures 2 and 3). The influence of the shape and volume of the bladder and the rectum on DVHs becomes an important problem when considering the intrafraction filling and variation of both organs.[5,27,34] Controlling the filling of the bladder would result in significant improvement in the bladder sparing. Moreover, special diet could be advised to patients, in order that regular function of the rectum is maintained throughout the treatment course.

This study suggests that using 6-field non-coplanar treatment-planning techniques in phase III would result in better sparing of both the bladder and the rectum. These techniques are applied using a 6-MV linear accelerator without a multi-leaf collimator. Hence, the large number of beams associated with non-coplanar techniques increase the time taken to generate a plan, to produce custom-shaped blocks for each field and, finally, to deliver the treatment. All these lead to greater cost- and time-related constraints for patient. In routine use, technique B is more preferable to technique E for two reasons: (1) it satisfies adequately the pre-set planning constraints for all three OAR, and (2) it has the advantage of being less expensive in terms of preparation, execution and verification of the treatment.

It is clear that pelvic anatomy varies greatly from patient to patient; perhaps the best way to ensure an optimal treatment technique for a given patient is to evaluate a variety of plans, but this could delay planning.

CONCLUSIONS

In this study, five different combinations of 3D-conformal coplanar and non-coplanar techniques using a 6 MV linac beam have been compared. Provided that the PTV is adequately covered, the choice of the optimal plan arrangement for prostate cancer is always a compromise between dose to all three OAR—rectum, bladder and femoral heads. Although it is desirable to use photon beams of higher energy at 10 MV and higher for conformal prostate radiotherapy, our study shows that even with a lower-energy beam (6 MV) and the appropriate plan combination a good sparing of OAR can be achieved while the dose to prostate can be as high as 75 Gy.

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