Original Article

Treatment planning comparison between high dose rate and intensity–modulated radiation therapy for prostate cancer as a means of boost dose

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Abstract

Purpose: The main objective of this study was to compare dosimetric characterisation of high-dose-rate brachytherapy (HDR-BT) with external beam intensity-modulated radiation therapy (EX-IMRT) as a means of delivering boost dose.

Materials and methods: Five HDR patients were selected for IMRT planning. Patients underwent ultrasound-guided catheter placement for HDR. Computed tomography (CT) images were obtained and imported into the Nucletron PLATO Brachytherapy system. The prostate, urethra, bladder and rectum were contoured on axial slices. The dose was calculated and optimised by graphical optimisation. The CT images of these structures were exported from the PLATO to Eclipse workstation for IMRT planning. For each patient, the dose–volume histogram (DVH) of HDR and IMRT plans were generated, drawn on the same scale and compared.

Results: The dose distribution in HDR plans was non-uniform and conformed peripherally inside the planned target volume (PTV). A small volume of the prostate received a very high dose from HDR. In IMRT plans, a uniform dose distribution was observed. The DVH curves for PTV dropped sharply and reached to a zero volume of the prostate at about $6 \cdot 4$ Gy. In HDR plans, the DVH curves for PTV showed a long tail up to a very high dose. About 10% of the prostate received about $13 \cdot 3$ Gy, which is 222% of the prescribed dose (6 Gy) in HDR plans. In contrast, the same volume in IMRT plans received <6 Gy (100%). The average dose for V90 was about $6 \cdot 3$ Gy for HDR and $5 \cdot 8$ Gy for IMRT plans. At a prostate volume of V100 level, the average dose in all plans was $5 \cdot 0$ Gy from HDR and $5 \cdot 4$ Gy from IMRT plans. In HDR plan, the V100 dose for urethra varied from $0 \cdot 6$ to $3 \cdot 0$ Gy (average $1 \cdot 8$ Gy). The range in IMRT plans varied from $3 \cdot 6$ to 6 Gy with an average of $4 \cdot 7$ Gy. At V90 level, the dose range in HDR and IMRT plans varied from $2 \cdot 5$ to $4 \cdot 7$ Gy (average $3 \cdot 8$ Gy) and $4 \cdot 8$ to $5 \cdot 4$ Gy (average $5 \cdot 3$ Gy), respectively. In general, the dose to the bladder and rectum was comparatively lower in HDR than in IMRT plans.

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Conclusions: HDR brachytherapy may reduce normal tissue toxicities in prostate boost treatments, even though the dose homogeneity inside the PTV is far worse than in IMRT treatments. Another advantage of HDR over IMRT is that the organ motion is not a significant concern as in IMRT.

Keywords: DVH comparison; HDR brachytherapy; IMRT; prostate cancer

INTRODUCTION

The key to the success of radiation therapy is to deliver prescribed dose precisely to the tumour and to reduce the dose to the normal tissues. At present, there are three types of radiation sources available as a means of delivering the primary as well as boost dose in the treatment of prostate cancer. These are external beam radiation therapy (EBRT) using conventional 3D or IMRT, implants with low dose rate isotopes (I–125 or Pd–103), and remote after loader high–dose–rate brachytherapy (^{192}Ir HDR–BT). Of these procedures, ^{192}Ir HDR–BT is an attractive method to deliver boost dose accurately to the target because of the steep dose gradient to the surrounding tissues and to spare the organs at risk (urethra, bladder and rectum).

Prostate is not stationary and can move during treatments. Because of the systematic and random setup errors, internal organ motion, deformation and organ changes related to treatments, EBRT or EX–IMRT may limit the accuracy of delivering the prescribed dose to the tumour.[1–4] Studies have shown that during external beam treatments, the prostate and the seminal vesicle move from a few mm to 2 cm.[5–12] Patients treated with EBRT or EX–IMRT in combination with HDR–BT boost produced excellent long–term outcomes in terms of biochemical control rates, disease–free survival and cause–specific survival in patients with prostate cancer even for those at highest risk, and minimised the toxicity of the critical structures.[13–15] The local control of prostate adenocarcinoma has been reported[16] directly related to dose.

This study describes a detailed dosimetric characterisation of ^{192}Ir HDR–BT and EX–IMRT treatments in prostate cancer as a boost dose using the Nucletron PLATO and the Varian eclipse treatment planning systems, respectively.

The prostate cancer patients were treated with EBRT or EX–IMRT to a median dose of 45 Gy, in 1·8 Gy/fraction. For a boost dose, the patients were given 18 Gy in 6 Gy/fraction by ^{192}Ir HDR–BT. For our studies, we have selected randomly five prostate patients for IMRT planning who have already been treated with ^{192}Ir HDR–BT. The IMRT planning as a means of delivering the boost dose was performed for comparison purpose only, not to treat the patients.
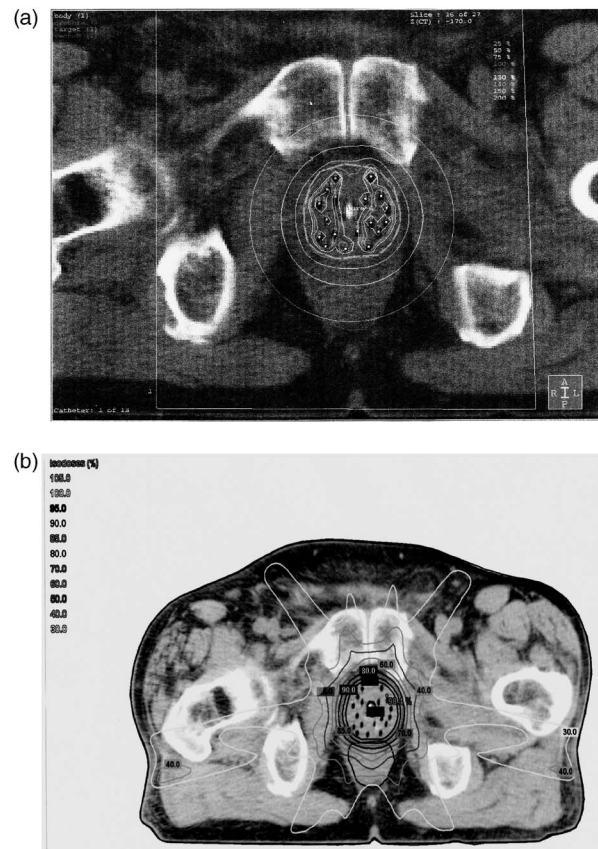

Figure 1. (a) Prostate HDR plan using Nucletron PLATO System. (b) Prostate IMRT plan using Varian Eclipse system. Abbreviations: HDR, high dose rate; IMRT, intensity-modulated radiation therapy.
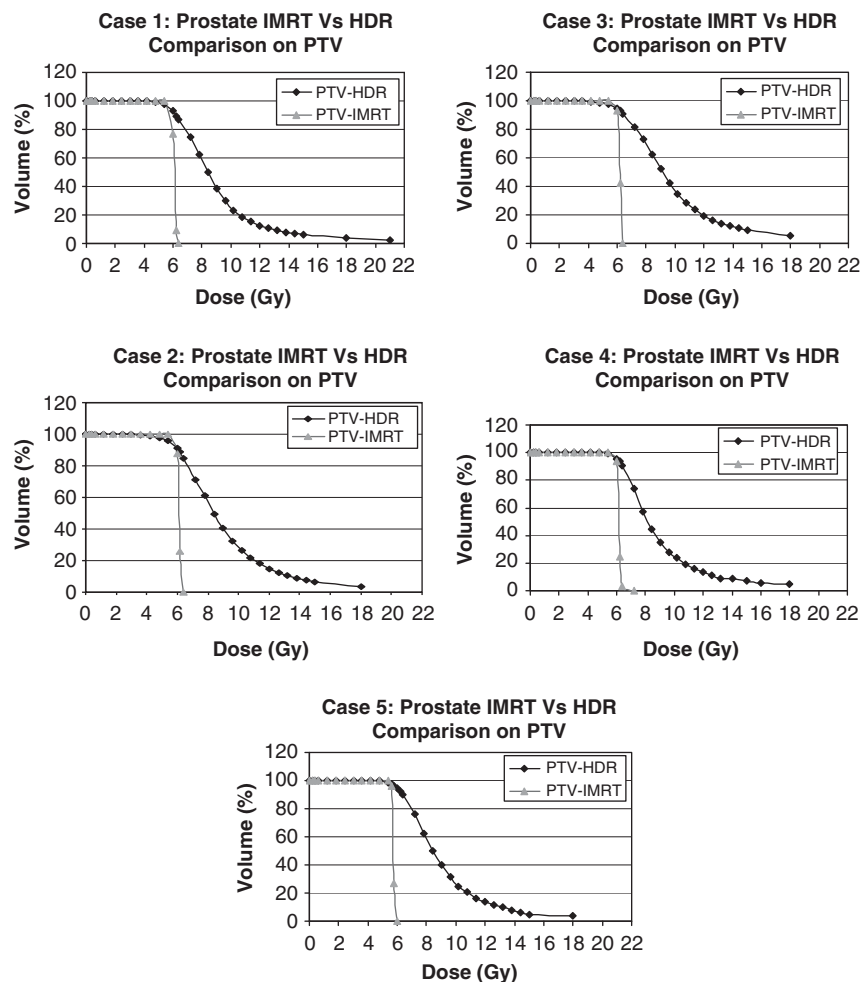
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Figure 2. Prostate (PTV) dose–volume comparison between HDR-BT and IMRT.
Abbreviations: HDR-BT, high-dose-rate brachytherapy; PTV, planned target volume; IMRT, intensity-modulated radiation therapy.

MATERIALS AND METHODS

Brachytherapy

The ^{192}Ir HDR–BT implant procedure was performed within a week after completion of EBRT. Patients underwent transrectal ultrasound–guided catheter placement. The TRUS-guided transperineal implant technique allowed instantaneous visualisation of the relationship between the rectal wall, urethra, bladder and prostate.

The apex and base of the prostate gland were identified using transverse and sagittal images. A rectal template was used for needle placement. The plastic needles (6F pro-guide needles, Nucletron, Tilburg, The Netherlands) were placed uniformly into the prostate avoiding the area around urethra. A fluoroscopy was performed to verify the appropriate needle tip positions. After placing the needles, the patients were allowed to have a recovery period and then a computed tomography (CT) scan was performed for treatment planning. These CT images were imported into the Nucletron PLATO Brachytherapy system version 14·2 (Nucletron Corp., Tilburg, The Netherlands). The prostate [planned target volume (PTV)], urethra, bladder and rectum were contoured on axial slices. The source dwell positions in the needles were digitised manually on each axial plane at 5 mm intervals. The dose was calculated and optimised using geometrical optimisation followed by inverse optimisation, and finally tuned by graphical optimisation. The isodose lines were manually manipulated using
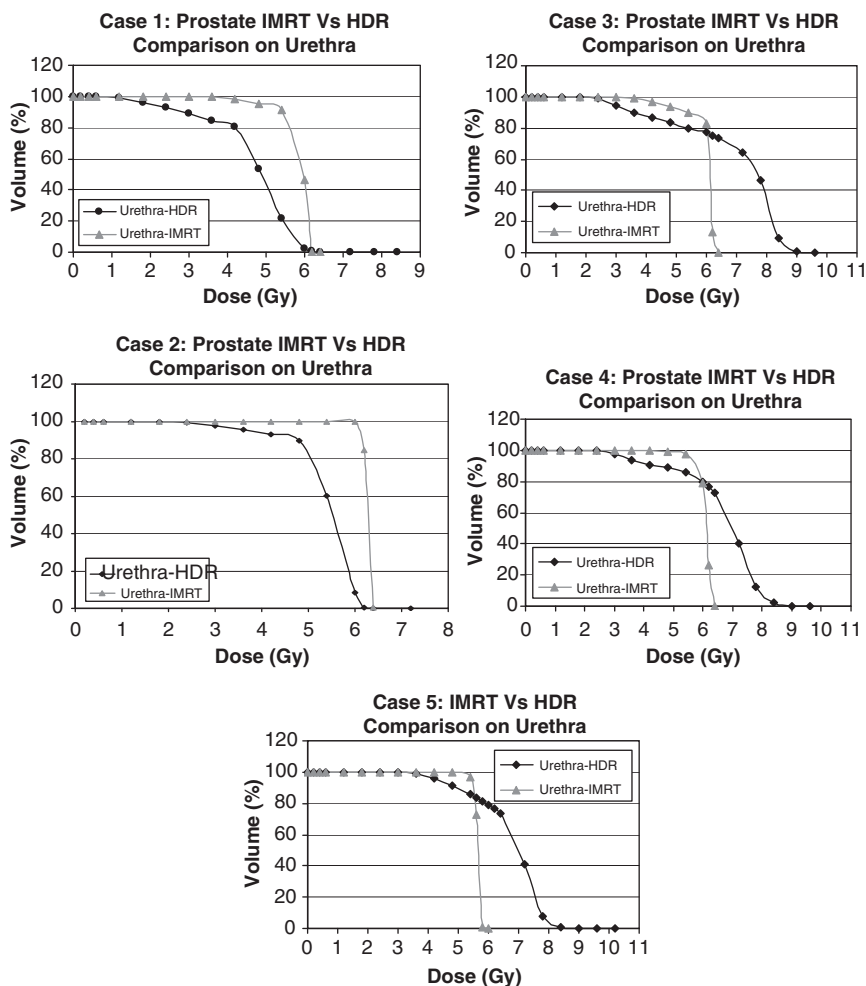
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Figure 3. Urethra dose–volume comparison between HDR-BT and IMRT.
Abbreviations: HDR-BT, high-dose-rate brachytherapy; IMRT, intensity-modulated radiation therapy.

the mouse to customise the shape of isodose distribution so that the target is encompassed with the prescribed dose, and the dose to urethra, bladder and rectum is minimised. After the planning was completed, the treatment delivery was performed using the after loader ^{192}Ir source.

EX-IMRT

As mentioned before that these ^{192}Ir HDR-BT patients who have already received treatments were considered for treatment planning using the IMRT modality for dosimetric comparison between ^{192}Ir HDR-BT and IMRT. Therefore, the CT images containing the same structures (PTV, urethra, bladder and rectum) used in

[192]Ir HDR-BT were exported from the Nucletron PLATO to Varian eclipse workstation for IMRT planning using the PLATO SunRise[TM] dicom software. The PTV margin for IMRT plans were the same as used in HDR plans (PTV + 5 mm). In order to compare dose distribution, the prescription for IMRT planning was adjusted to 6 Gy/fraction. Both HDR and IMRT plans were evaluated to compare dose distribution in PTV, urethra, bladder and rectum.

The dose distributions were evaluated using dose–volume histogram (DVH) of the target, urethra, bladder and rectum. The DVH for PTV, urethra, bladder and rectum was generated separately for each patient and drawn on the same scale.
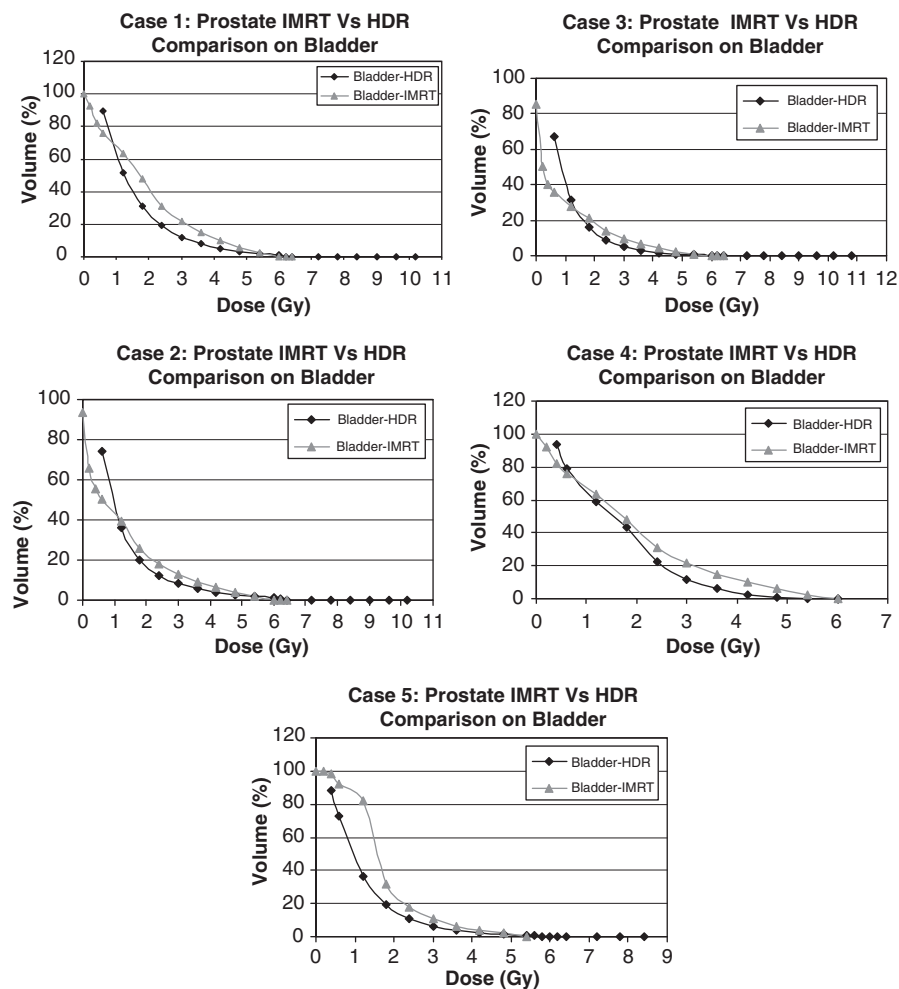
Figure 4. Bladder dose–volume comparison between HDR-BT and IMRT.
Abbreviations: HDR-BT, high-dose-rate brachytherapy; IMRT, intensity-modulated radiation therapy.

RESULTS

The optimised isodose dose distribution on transverse image of a single plan is shown in Figures 1a and 1b for comparison. The dose prescription for IMRT boost treatments was typically 2 Gy/fraction and for HDR treatments was 6 Gy/fraction. In order to compare dose distribution between HDR and IMRT, the dose prescription in IMRT plan was adjusted to 6 Gy/fraction. In HDR plan (Figure 1a), the prescribed dose to PTV (prostate) was conformed peripherally by sparing the urethra. In contrast, the IMRT plan (Figure 1b) showed a uniform dose distribution within the PTV as well as in the urethra. The normal tissue/organ receives more doses in IMRT plan than in HDR plan at a low dose level (shown at 30% isodose line).

The DVH on PTV, urethra, bladder and rectum for each patient is shown separately in Figures 2, 3, 4 and 5, respectively. The dose to PTV was evaluated at V100 (100% of the prostate volume), V90 (90% of the prostate volume) and (10% of the prostate volume). This V10 was defined as an arbitrarily unit to determine the maximum dose for a small volume of the prostate. From Figure 2, it may be seen that the DVH in all IMRT plans dropped sharply and reached to a zero volume of the prostate at about an average value of 6·4 Gy. Contrarily, in all HDR plans the DVH showed a long tail up to a very high dose. On the average, a small volume of the prostate, that is, V10 received about 13·3 Gy, which is about 222% of the prescribed dose (6 Gy). The same volume (V10) in IMRT plans received about 6 Gy (100%).
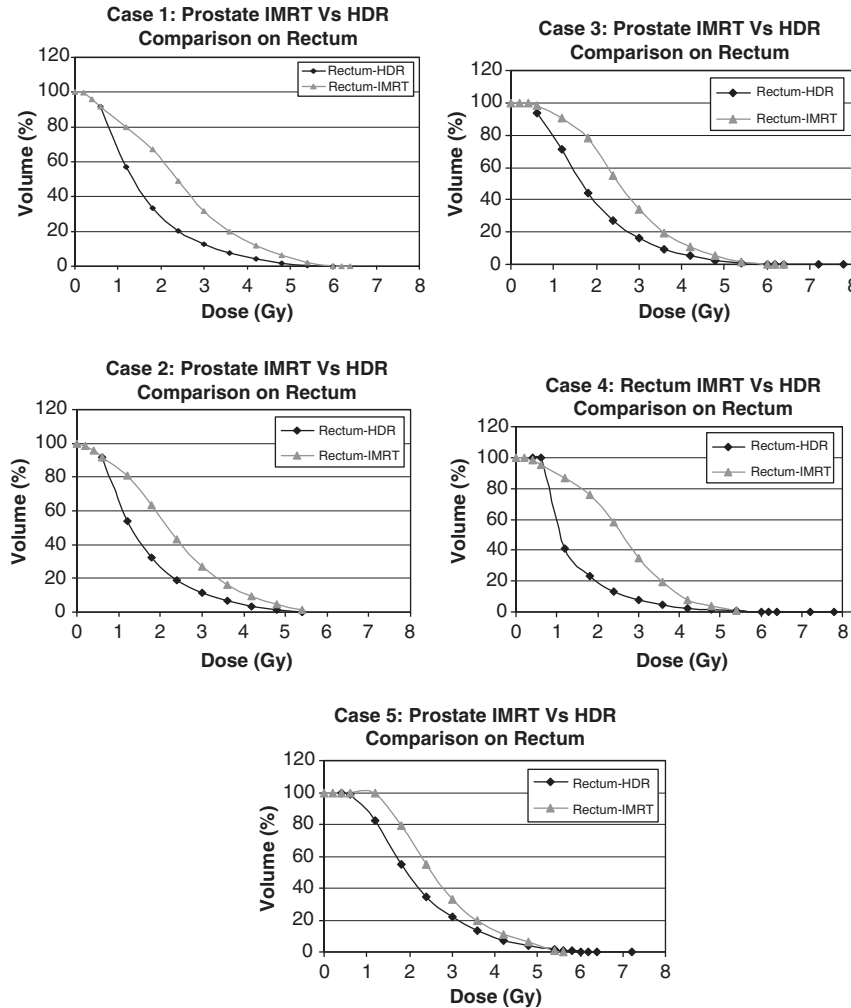
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Figure 5. Rectum dose–volume comparison between HDR-BT and IMRT.
Abbreviations: HDR-BT, high-dose-rate brachytherapy; IMRT, intensity-modulated radiation therapy.

The average dose for V90 was about 6·3 Gy for HDR and 5·8 Gy for IMRT plans. The 100% of the prostate volume (V100) in all plans received an average dose of about 5·0 Gy from HDR and 5·4 Gy from IMRT plans.

Figure 3 shows the DVH comparison on urethra between HDR and IMRT plans. The peak dose in all IMRT plans appeared to be significantly higher than HDR plans. A sharp dose fall off at the prescribed dose was observed in IMRT plans. The dose to urethra was evaluated at V100 and V90 of the urethra volume. In HDR plan, the V100 dose varied from 0·6 to 3·0 Gy (average 1·8 Gy), whereas the range in IMRT plan varied from 3·6 to 6 Gy with an average of 4·7 Gy. At V90 level, the

dose range in HDR and IMRT plans varied from 2·5 to 4·7 Gy (average 3·8 Gy) and 4·8 to 5·4 Gy (average 5·3 Gy), respectively.

The DVH comparison for bladder is shown in Figure 4. The comparisons for bladder were based on fractional volume analysis at a low dose level because at V90, the dose is essentially zero in four cases out of five. The trend of isodose distribution of bladder in IMRT plans is higher than in HDR; however, at 0·6 Gy dose level the bladder volume in HDR is higher (range 67–89%, average 76%) than in IMRT plans (range 36–92, average 66%). dose. With increasing dose from 0·6 to 4·2 Gy, the percentage of bladder volume involved was higher in IMRT than in HDR plans. In both cases, about 5% of

the bladder received <5 Gy, and then at higher doses the isodoses superimposed on the top of each other.

Rectum DVH is presented in Figure 5. The dose in rectum was evaluated at V90, V80 and V10. Generally, the rectum received higher doses from IMRT plans. At V90 level, the dose in both HDR and IMRT plans are very similar. At V80, the dose in IMRT plans was higher ranging from 1·2 to 1·8 Gy (average 1·7 Gy). The dose levels in HDR plans were observed to vary from 0·8 to 1·4 Gy with an average of 1·1 Gy. At a very small volume level (V10), the dose varied from 3·8 to 4·3 Gy (average 4·1 Gy) in IMRT and 2·5 to 3·6 Gy (average 3·1 Gy) in HDR plans.

DISCUSSIONS

In HDR–BT, a small volume is getting a very high dose. This may be attributed to the fact that the dose gradient around each catheter is very high. The catheter was placed from an interval 5 mm to 1 cm peripherally in the prostate. The source dwell position was 5 mm along the catheter. The isodose lines were optimised first graphically and then tuned manually using the mouse. This dose adjustment option allowed delivering a very high dose precisely to the area of interest creating a hot and cold spots inside the PTV. The dose to urethra, bladder and rectum was comparatively lower in HDR than in IMRT plans.

Another significant advantage of HDR over IMRT is the radiobiologic benefit. Prostate cancer tissues have slow cell growth kinetics. The α/β ratio for prostate tumour control is reported to be 1·5.[17,18] Kal et al.[19] reported a higher value of 4. Prostate tumours showed high sensitivity to fractionation for low α/β values.[20] This low α/β ratio is favourable for HDR because the dose per fraction is higher than conventional EX–IMRT, and the treatment duration is short because the number of fraction is reduced.

Martinez et al.[21] reported that for prostate with α/β ratio of as low as 1·2 to 1·5, the

biological effective dose (BED) is very high in the range of 136·3 Gy. This high BED would be extremely difficult to achieve even with IMRT.[22]

CONCLUSIONS

For HDR–BT, it is possible to place needles in the prostate precisely, and the exact location of each needle relative to the disease area in the prostate and the surrounding structures can be determined. As a result, it is possible to deliver accurate dose to the PTV because prostate movements during treatment is not of concern. Therefore, an advantage of HDR over IMRT is that the organ motion is not a significant concern as can be expected in IMRT. In HDR, it is possible to create hot and cold spots within the PTVs. With EBRT or IMRT, the true extent of the target volume may not receive the prescribed dose because of systematic and random setup errors, internal organ motion, deformation and organ changes related to treatments. Therefore, an additional margin will be necessary to accommodate these errors in IMRT plans. HDR may reduce normal tissue toxicities in prostate boost treatments, even though the dose homogeneity inside the PTV is far worse than in IMRT treatments. In general, the HDR plans contributed less doses to urethra, bladder and rectum. The dose distribution was not uniform, but conformed peripherally. This may be an advantage in terms of biological response to kill tumour cells.

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