

3-Dimensional conformal radiotherapy versus intensity modulated radiotherapy for localized prostate cancer: Dosimetric and radiobiologic analysis

A.K. Bhardwaj^{1*}, T.S. Kehwar², S.K. Chakarvarti³, A.S. Oinam¹, S.C. Sharma¹

¹ Department of Radiotherapy, Post-graduate Institute of Medical Education and Research, Chandigarh, 160012 India

² Department of Radiation Oncology, University of Pittsburgh Cancer Institute, Pittsburgh, Pennsylvania, USA

³ Department of Applied Physics, National Institute of Technology, Kurukshetra, 136119 India

Background: To analyze the dosimetric and radiobiologic advantages between intensity modulated radiotherapy (IMRT) and 3 dimensional conformal radiotherapy (3DCRT) and selection of optimal photon energy for IMRT treatments. **Materials and Methods:** 24 patients with localized prostate carcinoma were planned for 3DCRT and IMRT techniques. Radiation dose of 54 Gy with 2 Gy/fraction, was planned to Planning target volume (PTV1) (prostate + seminal vesicle + 1 cm margin) and 72 Gy to PTV2 (prostate + 1 cm margin) respectively. 3DCRT planning was done using 15 MV photon beam while IMRT plans were created using 6 MV and 15MV photons. Treatment plans were analyzed using mean, median, dose maximum and cumulative dose volume histogram for PTV1, PTV2, bladder, and rectum. Tumor control probability (TCP) was calculated for prostate. Normal tissue complication probability (NTCP) was calculated for bladder, rectum, and head of femur. **Results:** Mean dose to prostate was 72.79 ± 0.18 Gy for IMRT 15 MV, 72.16 ± 0.27 Gy for 3DCRT and 72.48 ± 0.19 Gy for IMRT 6 MV. TCP was greater for IMRT 15 MV followed by IMRT 6 MV. The mean value of NTCP was significantly lower ($p = 0.0015$) for IMRT 6 MV compared to 3DCRT for rectum while for bladder all were comparable. **Conclusion:** IMRT techniques shows superiority in sparing surrounding critical organs, thus reducing normal tissue complication rates while maintaining the same or higher tumor control probability. No significant difference was observed between IMRT 6 MV and IMRT 15 MV techniques. Iran. J. Radiat. Res., 2007; 5 (1): 1-8

Keywords: 3DCRT, IMRT, TCP, NTCP.

INTRODUCTION

Confining the radiation dose to the planning target volume (PTV) with minimum spillage of radiation dose out side PTV is the main aim of radiotherapy treatment

planning. 3-dimensional conformal radiotherapy (3DCRT) ⁽¹⁻³⁾ is used to confine the radiation dose to PTV but intensity modulated radiotherapy (IMRT) ⁽⁴⁻⁸⁾ have an additional advantage of sparing the organs at risk (OAR). Many times with 3DCRT, it is difficult to spare the OAR without compromising the PTV coverage. IMRT has the ability to produce the desired dose distributions shaped to the planned target volume with sparing of OARs. Tumor dose escalation and desired dose homogeneity and heterogeneity (simultaneous integrated boost technique) with in PTV are added advantages of IMRT ⁽⁹⁻¹⁰⁾. A number of reports have reported the encouraging early results of IMRT but it is too early to say about clinical outcomes.

Since Intensity modulated radiotherapy is becoming popular for treatment of prostate cancer patients, it is important to analyze its potential benefits over 3DCRT. In the present study, we have compared the different dosimetric and radiobiological parameters between 3DCRT and IMRT treatment plans. The apparent advantages of reduced dose to OAR and increased PTV dose and dose uniformity were analyzed using radiobiological modeling. We also compared the IMRT treatment planning using 15 MV

*Corresponding author:

Dr. Anup Kumar Bhardwaj, Department of Radiation Oncology, Post Graduate Institute of Medical Education and Research, Chandigarh 160012, India.

Fax: +91 1722749338

E-mail: anoop401@rediffmail.com

photon beams, to find any added advantages of using high energy photon beam for IMRT treatments.

MATERIALS AND METHODS

Patient characteristics and data acquisition

Twenty four patients with localized carcinoma of prostate already treated with 3DCRT or IMRT were chosen for this study. The age ranged between 61 to 70 years with mean age 65 years. All the patients belonged to stage 1 disease (TNM classification). Prior to planning, all patients were immobilized in supine position with a 6 clamp thermo plastic, ORFIT® (ORFIT Industries, Wijegem, Belgium) immobilization cast mounted on a pelvic base plate (ORFIT). CT slices were acquired 24 hours after the ORFIT immobilization casts were made. This was done to take care of the setup variations which might occur due to shrinkage of the cast. Tentative external fiducial markers using 2 mm Φ lead balls were fixed to the ORFIT cast on the anterior surface and two lateral surfaces after matching with sagittal and transverse lasers on the simulator-CT Phebus® (version 1.2, Mecaserto, France). CT scans were acquired on a flat table top with a multi slice diagnostic CT scan Light speed+® (version 2.4.2_H2.4MS, GE medical systems, Milwaukee, Wisconsin, USA) which can scan four slices in a single rotation. The slices were taken from the upper border of L-4 vertebral body to 3 cm below the level of lesser trochanter of femur. The slice spacing was 5 mm over the entire treatment area. The CT data was imported to contouring workstation via local area network system.

Target and critical volumes delineation

The planning target volumes and OARs were delineated by radiation oncologist on the CT slices using contouring workstation Soma Vision® (version 7.2.02 M, Varian medical systems, Palo Alto, CA). For each patient two different treatment volumes were defined, planning target volume PTV1 (Gross tumor volume prostate + seminal vesicles

+margin) and PTV2 (prostate + margin). The margins were expanded based on the institutional protocol for 3DCRT, i.e. 1 cm along the transverse direction, 1 cm along the cranial caudal direction, 1 cm anteriorly and 0.6 cm posteriorly.

Dose prescription, planning and treatment delivery machine

The treatment planning was done with Eclipse® (version 7.3.10, Varian medical systems, Palo Alto, CA) treatment planning system by using 6 MV and 15 MV photon beam data. Varian Millennium 80 multileaf collimator fitted in high energy linear accelerator Clinac DHX®, was used for 3DCRT and IMRT treatment delivery. The mean dose of 54 Gy and 72 Gy was given to PTV1 and PTV2 respectively by 2 Gy/fraction and 5 fraction/week in both 3DCRT and IMRT methods. A dose homogeneity of -5% and +7%, was set as initial plan acceptance criterion as recommended by ICRU (11, 12).

Treatment planning techniques

In 3DCRT technique, radiation dose was delivered in two courses using 15 MV photon beam. In first course, the dose of 54 Gy with 2Gy/fraction to PTV1 was delivered with 4 field technique. In second course, radiation dose of 18 Gy in 9 fractions was given to PTV2 by 4 field box technique. Four fields box technique was used for 3DCRT because it is generally followed in our institute. 6 mm margin was given to MLC field apertures from PTV1 and PTV2 using beams eye view for photon fields for penumbra regions. All plans were created using source to axis distance (SAD) isocentric technique.

Radiation dose delivery was planned in 2 courses by IMRT technique. IMRT plans were generated for both 6 MV and 15 MV photon beam using sliding window technique. Radiation dose of 54 Gy and 18 Gy boost with 2 Gy/fraction, was planned to PTV1 and PTV2 respectively. Seven coplanar and equiangular beams were used for IMRT plan optimization. The inverse plan optimization engine Helios (version 7.3.1) of Eclipse planning system was used for IMRT

planning. Appropriate dose-volume constraints for IMRT plan optimization for PTV and critical organs (bladder and rectum) were used. For PTV1 and PTV2, optimization constraints were such that 100% PTV volume should get 100% dose, and dose maxima should be less than 102% for zero % volume. The upper and lower priorities were 100 and 95 respectively. For bladder and rectum the upper dose limit was 50 Gy and 45 Gy respectively for 15 % total organ volume with priority of 65. Depending on the PTV doses (PTV1: 54 Gy; PTV2 boost: 18 Gy), the dose to critical organs was scaled for two IMRT courses. Although for all patients these optimization criteria were not completely satisfied by optimization algorithm and we stopped the optimization process after attaining saturation in optimization process. The optimized photon fluencies were converted to deliverable photon fluencies by the leaf motion calculator program. Dose distributions were computed by applying density corrections using modified Batho formula.

Dosimetric and volumetric analysis

For comparisons between different techniques, plan sum was created for all courses. Plans were compared using the Dose Volume Histogram (DVH) method. The values of mean dose, V45, V50, V55, V60, and V70% defined as percentage of rectum and bladder volumes receiving at least 45, 50, 55, 60 and 70 Gy respectively were considered. V90%, mean, global maximum dose and relative standard deviation for PTV1 and PTV2 were also calculated. The conformity index (CI) was defined for PTV1 and PTV2 as PTV covered by 95% isodose line / PTV, and Over Dose Index (ODI) as PTV covered by 105% isodose line/PTV. Here PTV corresponds to both PTV1 and PTV2.

To find the lower dose to normal tissue called Irradiated volume IrV10 and IrV20 were calculated. IrV10 and IrV20 are the volume of normal tissue receiving radiation dose more than 10 Gy and 20 Gy respectively. To the estimate of dose spillage out side PTV2, treated normal tissue volume IrV36

(volume receiving 50% of prescribed 72 Gy dose) and IrV90 (volume receiving 90% of prescribed dose) were calculated.

Comparison using radiobiological models

Tumor control probability (TCP) and normal tissue complication probability (NTCP) were calculated for all three types of plans i.e. 3DCRT, dynamic IMRT 15 MV and dynamic IMRT 6 MV.

The NTCP model

The normal tissue complication probability NTCP was calculated by Lyman model⁽¹³⁾ for IMRT and 3DCRT techniques. Model parameters given by Burman *et al.*⁽¹⁴⁾ and compiled by Emami *et al.*⁽¹⁵⁾ for high grade complications associated with partial or full organ irradiation were used. The value of n and m were 0.5 and 0.11 for bladder; 0.12 and 0.15 for rectum; 0.25 and 0.12 for head of femur respectively. TD₅₀ was 80 Gy for both bladder & rectum while 65 Gy for head of femur. The NTCP was calculated for bladder, rectum, and head of femur.

The expression of the NTCP model may be written as

$$NTCP = (2\pi)^{-1/2} \int_{-\infty}^t \exp[-t^2/2] dt$$

Where

$$t = [D - TD_{50/5}(V)] / \sigma(V)$$

$$\sigma(V) = m * TD_{50/5}(V)$$

$$TD_{50/5}(V) = TD_{50/5}(1) * V^{-n}$$

TD_{50/5}(V)=5 year, 50% tolerance dose for partial volume V

TD_{50/5}(1)=5 year, 50% tolerance dose for whole organ volume

D=dose to uniformly irradiated reference volume V

1>n>0 for all tissues fitted by Burman *et al.*⁽¹⁴⁾.

But in practical situation, organs are not uniformly irradiated i.e. there are multiple partial volume irradiations to different doses. The effects of partial volume irradiation are computed using Kutcher-Burman⁽¹⁶⁾ effective-volume dose-volume histogram scheme. Considering any partial volume v_i

receiving dose d_i , the effective irradiated volume is given by

$$v_{\text{eff}} = v_i (d_i / d_{\text{ref}})^{-n}, \text{ where } d_{\text{ref}} \text{ is TD50}$$

Total effective volume V for whole organ is given by summing all v_{eff} . Using cumulative dose-volume histogram and above mentioned equations NTCP for different organs was calculated.

The TCP model

The tumor control probability (TCP) is defined by a Poisson statistics model and is written by

$$\text{TCP} = \exp\left[-\sum_{j=1}^K N_{c_j} \exp\{-\alpha \cdot \text{BED}_j\}\right]$$

Where $\text{BED}_j = D_j[1 + d_j/(\alpha/\beta)]$ and $N_{c_j} = v_j \cdot N_c$

" v_j " is fractional volume and " d_j " is corresponding dose per fraction. " N_c " is number of clonogens. " α " is a radio sensitive parameter and is the coefficient of lethal damage, " BED " is the biologically effective dose of a uniformly irradiated tumor. For the calculation purpose we have taken $\alpha=0.1 \text{ Gy}^{-1}$ and $\alpha/\beta = 1.5 \text{ Gy}$. " k " is total number of sub volumes in target.

RESULTS

The PTV1 and PTV2 size varied considerably among patients under study. Bladder and rectum volumes also vary among patients depending on their filling. The amount of bladder and rectum receiving higher doses equal to PTV depends on their volumes. When bladder and rectum volumes are smaller, their distance from PTV reduces and overlap with PTV increases resulting a greater percentage of their volumes lies in high dose areas and vice versa.

Dose-volume histogram analysis

Figure 1 shows the dose volume histogram for PTV2, bladder, and rectum for all three techniques for one of the patients in the study (patient 2). Small bowel and small intestine or

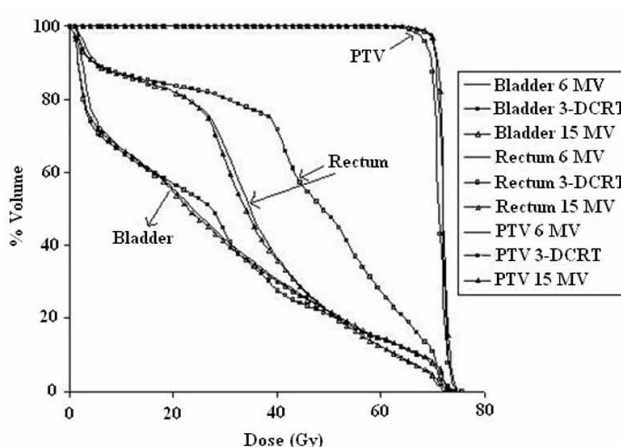


Figure 1. Cumulative dose -volume histogram for PTV2, bladder and rectum for one of treated patient for all three treatment techniques. Data is shown for complete treatment (72 Gy) with IMRT or for 3DCRT techniques.

colon dosimetric data is not reported because the field openings were small and there was hardly any direct dose to these organs. Left femur head and right femur head receives clinically lesser mean dose (~20 Gy from IMRT and 25 Gy from 3DCRT) concerning late complications, so we have not taken them for comparing treatment techniques. However for radiobiological parameters comparison, we calculated NTCP for both. From figure 1 and table 1 it is clear that the bladder doses were higher for 3DCRT as compare to IMRT 6 MV and IMRT 15 MV. Bladder mean dose was slightly higher for IMRT 6 MV while comparing with IMRT 15 MV. The mean bladder doses for 3DCRT, IMRT 15 MV and IMRT 6 MV were 37.10 Gy, 35.08 Gy and 35.48 Gy respectively. Similarly for rectum there was not much difference in case of mean dose between two IMRT techniques but ~ 10% higher mean rectum dose was observed with 3DCRT. In case of both PTV, mean dose was almost similar in all techniques as shown in table 4. Body mean dose was highest for IMRT 6 MV technique among all techniques. In terms of PTV2 coverage both IMRT techniques shows similar results. Dose gradient for bladder and rectum is more sharp in case of IMRT techniques as compare to 3DCRT (tables 1 and 2), which is obviously the advantage of IMRT. In terms of dose homogeneity with in PTV, IMRT techniques are superior to 3DCRT.

Table 1. Mean value and standard deviation (SD) of dosimetric parameters for bladder for all three treatment techniques.

Parameters	IMRT (15 MV)	IMRT (6 MV)	3DCRT
	Mean Value $\pm$ SD Global (n = 24)	Mean Value $\pm$ SD Global (n = 24)	Mean Value $\pm$ SD Global (n = 24)
Volume (cc)	215.74 $\pm$ 75.49	215.74 $\pm$ 75.49	215.74 $\pm$ 75.49
Dmean (Gy)	35.08 $\pm$ 5.48	35.48 $\pm$ 5.23	37.10 $\pm$ 6.56
Dmedian (Gy)	32.95 $\pm$ 6.09	33.52 $\pm$ 5.72	35.90 $\pm$ 5.69
Dmaximum (Gy)	75.65 $\pm$ 0.20	75.18 $\pm$ 0.30	74.21 $\pm$ 0.26
V45 (%)	34.10 $\pm$ 6.58	34.55 $\pm$ 6.28	37.80 $\pm$ 8.74
V50 (%)	28.60 $\pm$ 5.51	28.64 $\pm$ 5.24	32.79 $\pm$ 7.67
V55 (%)	23.87 $\pm$ 4.72	23.74 $\pm$ 4.47	28.51 $\pm$ 7.18
V60 (%)	19.75 $\pm$ 4.14	19.61 $\pm$ 3.99	24.33 $\pm$ 6.72
V70 (%)	11.34 $\pm$ 2.52	11.18 $\pm$ 2.46	14.81 $\pm$ 5.47
NTCP	0.00071 $\pm$ 0.0013	0.00065 $\pm$ 0.002	0.0012 $\pm$ 0.001

Table 2. Mean value and standard deviation (SD) of dosimetric parameters for rectum for all three treatment techniques.

Parameters	IMRT (15 MV)	IMRT (6 MV)	3DCRT
	Mean Value $\pm$ SD Global (n = 24)	Mean Value $\pm$ SD Global (n = 24)	Mean Value $\pm$ SD Global (n = 24)
Volume (cc)	66.66 $\pm$ 19.68	66.66 $\pm$ 19.68	66.66 $\pm$ 19.68
Dmean (Gy)	33.25 $\pm$ 3.45	33.88 $\pm$ 3.79	36.99 $\pm$ 5.48
Dmedian (Gy)	35.25 $\pm$ 1.01	36.35 $\pm$ 1.51	40.73 $\pm$ 4.02
Dmaximum (Gy)	75.02 $\pm$ 0.69	74.37 $\pm$ 0.92	71.96 $\pm$ 0.55
V45 (%)	23.81 $\pm$ 3.04	24.13 $\pm$ 3.27	34.12 $\pm$ 12.06
V50 (%)	18.43 $\pm$ 2.40	18.33 $\pm$ 2.43	28.52 $\pm$ 10.32
V55 (%)	14.34 $\pm$ 1.75	14.22 $\pm$ 1.75	22.79 $\pm$ 7.46
V60 (%)	10.90 $\pm$ 1.25	10.79 $\pm$ 1.24	17.66 $\pm$ 5.11
V70 (%)	4.98 $\pm$ 1.52	4.33 $\pm$ 1.42	6.39 $\pm$ 2.58
NTCP	0.021 $\pm$ 0.015	0.018 $\pm$ 0.02	0.039 $\pm$ 0.04

Dosimetric Analysis

Tables 1-4 summarize the quantitative dosimetric comparison for bladder, rectum, PTV1, PTV2, and healthy tissue for three treatment techniques. In all the three techniques, planning objectives were achieved in terms of target conformity, and global dose maximum was lesser than 107%. The overall highest mean conformity index

(CI) were 0.983 and 0.99 observed with IMRT 15 MV technique for PTV1 and PTV2 respectively. Over dose index (ODI) was zero with 3DCRT for both PTV1 and PTV2 as compare to IMRT techniques. ODI was greater than zero for only one patient (patient 3) for IMRT 6 MV whose PTV1 volume was maximum (266.8 cc). For PTV2, ODI was zero for IMRT 6 MV and 3DCRT techniques for all patients and only two patients had ODI greater than zero with IMRT 15 MV. The CI was higher for IMRT 15 MV for each individual patient, followed by IMRT 6 MV. CI depends on the target volume and the volume of surrounding normal structures. For a set of same dose constraints and smaller bladder and rectal volumes, the plan complexity increases with both IMRT techniques and CI decreases and ODI increases.

While considering the dose to healthy tissue the mean dose was highest in case of IMRT 6 MV. IMRT 15 MV and 3DCRT techniques have similar mean doses as shown in table 3. The body healthy tissue exposed to low radiation doses was also higher with IMRT 6 MV. Although the IrV10 and IrV20 were lesser for 3DCRT

but IrV36 was almost double compared to both IMRT techniques. Treated healthy tissue volume IrV90 was higher for 3DCRT techniques showing greater dose spillage out side PTV. From tables 1 and 2 it is evident that both IMRT techniques are able to spare surrounding critical structures as compare to 3DCRT.

Table 3. Mean value and standard deviation (SD) of dosimetric parameters for body for all three treatment techniques.

Parameters	IMRT (15 MV)	IMRT (6 MV)	3DCRT
	Mean Value $\pm$ SD Global (n = 24)	Mean Value $\pm$ SD Global (n = 24)	Mean Value $\pm$ SD Global (n = 24)
Dmean (Gy)	7.79 $\pm$ 3.03	8.27 $\pm$ 3.15	7.69 $\pm$ 3.01
Dmedian (Gy)	0.96 $\pm$ 0.62	1.36 $\pm$ 0.78	0.65 $\pm$ 0.30
IrV10 (cc)	3474 $\pm$ 319	3512 $\pm$ 330	2775 $\pm$ 259
IrV20 (cc)	2309 $\pm$ 236	2592 $\pm$ 249	2347 $\pm$ 302
IrV36 (cc)	697.8 $\pm$ 108.6	752.6 $\pm$ 125	1468 $\pm$ 164
IrV90 (cc)	52.24 $\pm$ 13.04	50.09 $\pm$ 13.52	73.75 $\pm$ 21.6

Table 4. Mean value and standard deviation (SD) of dosimetric parameters for PTV1 and PTV2. TCP is calculated over a range of hypothetical value (s) related with tumor sensitivity.

Parameters	IMRT (15 MV)	IMRT (6 MV)	3DCRT
	Mean Value $\pm$ SD Global (n = 24)	Mean Value $\pm$ SD Global (n = 24)	Mean Value $\pm$ SD Global (n = 24)
PTV1			
Volume (cc)	195.28 $\pm$ 39.10	195.28 $\pm$ 39.10	195.28 $\pm$ 39.10
Dmean (Gy)	54.47 $\pm$ 0.13	54.22 $\pm$ 0.12	54.10 $\pm$ 0.16
Dmedian (Gy)	54.60 $\pm$ 0.12	54.39 $\pm$ 0.12	54.27 $\pm$ 0.18
Dmaximum (Gy)	57.04 $\pm$ 0.19	56.67 $\pm$ 0.26	55.96 $\pm$ 0.20
V95 (%)	98.28 $\pm$ 0.59	98.18 $\pm$ 0.87	97.44 $\pm$ 0.22
V90 (%)	99.85 $\pm$ 0.18	99.66 $\pm$ 0.16	99.62 $\pm$ 0.32
CI	0.983 $\pm$ 0.59	0.982 $\pm$ 0.87	0.974 $\pm$ 0.22
ODI	0.022 $\pm$ 0.02	0.002 $\pm$ 0.004	0.00 $\pm$ 0.00
PTV2			
Volume (cc)	157.40 $\pm$ 36.26	157.40 $\pm$ 36.26	157.40 $\pm$ 36.26
Dmean (Gy)	72.79 $\pm$ 0.18	72.48 $\pm$ 0.19	72.16 $\pm$ 0.27
Dmedian (Gy)	72.95 $\pm$ 0.17	72.65 $\pm$ 0.18	72.29 $\pm$ 0.25
Dmaximum (Gy)	75.86 $\pm$ 0.17	75.20 $\pm$ 0.29	74.70 $\pm$ 0.27
V95 (%)	99.00 $\pm$ 0.56	98.80 $\pm$ 0.64	97.46 $\pm$ 0.93
V90 (%)	99.87 $\pm$ 0.16	99.81 $\pm$ 0.17	99.53 $\pm$ 0.48
CI	0.990 $\pm$ 0.56	0.988 $\pm$ 0.64	0.975 $\pm$ 0.93
ODI	0.008 $\pm$ 0.01	0.00 $\pm$ 00	0.00 $\pm$ 0.00
TCP (s = 0.1)	99.32 $\pm$ 0.40	99.19 $\pm$ 0.1	99.04 $\pm$ 0.10
TCP (s = 0.5)	96.64 $\pm$ 1.80	95.99 $\pm$ 0.4	95.29 $\pm$ 0.40
TCP (s = 1.0)	93.42 $\pm$ 1.60	92.15 $\pm$ 0.08	90.82 $\pm$ 0.70

Radiobiological Analysis

Tumor control probability was calculated for 3DCRT and both IMRT techniques for a cohort of twenty four patients over a range of hypothetical possible tumor sensitivity ($0.1 \leq s \leq 1$). Although the initial planning dose per fraction (2 Gy) was same for all techniques, but TCP values were higher for IMRT techniques because of higher mean dose and thus higher dose per fraction. TCP was highest for IMRT 15 MV. IMRT 6 MV has greater TCP than 3DCRT but the TCP values were comparable for all techniques for higher tumor sensitivity. TCP value decreases for all three techniques as the tumor sensitivity decreases. For femoral head, the calculated NTCP was zero for all three techniques. NTCP for bladder was higher for 3DCRT than IMRT techniques but difference was not statistically significant ($p = 0.12$, paired *t*-test). A statistically significance difference ($p = 0.0015$, paired *t* test) was found in NTCP for rectum when 3DCRT technique was compared with IMRT 6MV and $p = 0.0029$ with IMRT 15 MV. But there was no significant difference found between two IMRT techniques.

DISCUSSION

It is always desirable in conformal radiation treatment to shape the prescribed isodose volume perfectly around the PTV to achieve the CI of 1.0, but because of irregular shapes of PTV, close proximity of critical

organs and inadequacy of field shaping devices such as MLC leaf width and MLC transmission, make it difficult to be achieved practically.

In the present study our aim was to assess the potential benefits that could arise from the introduction of different modern techniques with increased plan and delivery complexity for prostate cancer patients. Both IMRT techniques showed a systematic and significantly improvement over 3DCRT in terms of target coverage and simultaneously reducing dose to bladder and rectum.

In a study by Lee *et al.* ⁽¹⁷⁾ grade 2-3 rectal morbidity developed in 18% patients and majority of cases consisted of rectal bleeding but no patient has developed grade 4 or 5 rectal morbidity in median time of 15 months with 3DCRT in dose ranges of 71-75 Gy. But use of rectal block significantly reduced (22%) the incidence of Grade 2-3 toxicity ($p = 0.003$). They also suggested for the dose escalation above 76 Gy with treatment techniques that can limit the total dose to the anterior rectal wall.

Zelevsky *et al.* ⁽¹⁸⁾ also compared the IMRT and 3-DCRT techniques with prescription dose 81 Gy, for urinary and rectal complications and showed the improved conformality with IMRT. They found 2-year actuarial risk of grade 2 bleeding was 2% for IMRT and 10% for conventional 3DCRT ($p = 0.001$) according to the RTOG morbidity scale ⁽¹⁹⁾. In another study by Zelevsky *et al.* ⁽²⁰⁾ have shown the evidence that prostate radiotherapy may be associated with radiation-induced damage to the urethra rather than the bladder and it is unknown that whether IMRT can restrict the dose to the urethra without creating unacceptable cold spots in the PTV.

In a preliminary study of acute complications for bladder and rectum treated with IMRT and 3DCRT by Hancock *et al.* ⁽²¹⁾, they also found lower grade 2 rectal complications rate in IMRT patients compared to 3DCRT. For grade 2 urinary complications (RTOG morbidity scale), there was not significant difference between two techniques. The results of similar previous

studies by Luxton *et al.* ⁽²²⁾ are in qualitative agreement with our present study. We observed reduction in rectal toxicity in terms of NTCP but we did not observe reduced urinary toxicity with IMRT. This may be because of larger PTV overlap with bladder and soft constraints used in the inverse planning optimization program for the dose to the bladder and higher bladder volumes.

All dosimetric parameters were highest for 3DCRT technique when considering dose to bladder and rectum. In case of bladder and rectum doses when comparing only two IMRT techniques, mean dose is slightly higher for IMRT 6 MV. Bladder and rectum are better spared for higher dose regions with IMRT 6 MV compared to IMRT 15 MV. This may be because of higher percentage depth dose with 15 MV photons. Global dose maximum and D_{median} were higher for IMRT 15 MV but difference was not significantly higher compare to other two techniques.

In terms of normal healthy tissue irradiation, the percentage tissue volume receiving lower radiation doses as IrV10 was lesser with 3DCRT as compare to IMRT techniques but IrV20 was almost equal in all techniques. The irradiated normal tissue volume IrV36 was more than double for 3DCRT technique. It is well known fact that the monitor units required for IMRT is much more as compare to 3DCRT. The amount of radiation transmitted and scattered dose through MLC and neutron dose increases with beam energy and number of monitor units. However risk of secondary radiation induced malignancies has been accepted to take advantage of benefits of local tumor control. The rate of local control with acceptable complications found with high energy photons for deep seated tumors has led to common practice of high energy photons for these tumors. The important result derived from this analysis is that, when considering lower dose to normal healthy tissue, different spatial distributions do not necessarily reflect drawbacks of IMRT technique, and this should not be considered as an obstacle to IMRT

CONCLUSION

Comparison of dosimetric and radio biological parameters between and 3DCRT and IMRT techniques, presented in this study for a cohort of twenty four patients with localized prostate cancer yields some useful indications for future studies. Target coverage and TCP with 3DCRT is comparable with IMRT techniques but in terms of late rectal complications IMRT has definitively upper edge. Yielding the same tumor control with reduced complications is also desirable in radiotherapy. May be, the more advances in IMRT as simultaneous integrated boost technique; result with better tumor control and at the same time with acceptable tissue complications. No significant difference was found in terms of target coverage and normal tissue complications when IMRT 6 MV and IMRT 15 MV techniques are compared. Because of lesser transmission dose through MLC and neutron dose, IMRT 6 MV technique should be preferred over IMRT 15 MV technique when user has both options.

REFERENCES

1. Powlis WD, Smith AR, Cheng E, et al. (1993) Initiation of multileaf collimator conformal radiation therapy. *Int J Radiat Oncol Biol Phys*, **25**: 171-179.
2. LoSasso T, Chui CS, Kutcher GJ, Leibel SA, Fuks Z, Ling C (1993) The use of multileaf collimator for conformal radiotherapy of carcinomas of the prostate and nasopharynx. *Int J Radiat Oncol Biol Phys*, **25**: 161-170.
3. Boyer AL, Biggs P, Galvin J, et al. (2001) Basic applications of multileaf collimators. Report of the AAPM Radiation Therapy Committee Task Group No. 50, Med Phys.
4. Boyer AL and Yu CX (1999) Intensity modulated radiation therapy with dynamic multileaf collimator. *Semin Radiat Oncol*, **9**: 48-59.
5. Wu VW, Kwong DL, Sham JS (2004) Target dose conformity in 3-dimensional conformal radiotherapy and intensity modulated radiotherapy. *Radiother Oncol*, **71**: 201-206.
6. Boethmer D, Bohsung J, Eichwurz I, Moys A, Budach V (2004) Clinical and physical quality assurance for intensity modulated radiotherapy of prostate cancer. *Radiother Oncol*, **71**: 319-325.
7. Boyer AL and Yu CX (1999) Intensity-modulated radiation therapy with dynamic multileaf collimators. *Semin Radiat Oncol*, **9**: 48-59.
8. Burman C, Chui CS, Kutcher G, et al. (1997) planning, delivery, and quality assurance of intensity-modulated radiotherapy using dynamic multileaf collimator: A strategy for large-scale implementation for the treatment of carcinoma of the prostate. *Int J Radiat Oncol Biol Phys*, **39**: 863-873.
9. Klein EE, Low DA, Sohn JW, Purdy JA (2000) Differential dosing of prostate and seminal vesicles using dynamic multileaf collimation. *Int J Radiat Oncol Biol Phys*, **48**: 1447-1456.
10. Storey MR, Pollack A, Zagars G, Smith L, Antolak J, Rosen I (2000) Complications from radiotherapy dose escalation in prostate cancer: preliminary results of a randomized trial. *Int J Radiat Oncol Biol Phys*, **48**: 635-642.
11. International Commission on Radiation Units and Measurements (1993) ICRU report 50: prescribing, recording, and reporting photon beam therapy. Bethesda: ICRU.
12. International Commission on Radiation Units and Measurements (1999) ICRU report 62: prescribing, recording, and reporting photon beam therapy (supplement to ICRU report 50). Bethesda: ICRU.
13. Lyman JT (1985) Complication probability as assessed from dose-volume histograms. *Radiat Res*, **104**: S13-19.
14. Burman C, Kutcher GJ, Emami B, Goitein M (1991) Fitting of normal tissue tolerance data to an analytic function. *Int J Radiat Oncol Biol Phys*, **21**: 123-135.
15. Emami B, Lyman J, Brown A, Coia L, Goitein M, Munzenrider JE, et al. (1991) Tolerance of normal tissue to therapeutic irradiation. *Int J Radiat Oncol Biol Phys*, **21**: 109-122.
16. Kutcher GJ, Burman C, Brewster L, et al. (1991) Histogram reduction method for calculating complication probabilities for three dimensional treatment planning evaluations. *Int J Radiat Oncol Biol Phys*, **21**: 137-146.
17. Lee WR, Hanks GE, Hanlon AL, Schltheiss TE, Hunt MA (1996) Lateral rectal shielding reduces late rectal morbidity following high dose three-dimensional conformal radiation therapy for clinically localized prostate cancer: further evidence for a significant dose effect. *Int J Radiat Oncol Biol Phys*, **35**: 251-257.
18. Zelefsky MJ, Fuks Z, Happersett L, et al. (2000) Clinical experience with intensity modulation radiotherapy (IMRT) in prostate cancer. *Radiother Oncol*, **55**: 241-249.
19. Lawton CA, Won M, Pilepich MV, et al. (1991) Long term treatment sequelae following external beam irradiation for adenocarcinoma of the prostate: Analysis of RTOG studies 7506 and 7706. *Int J Radiat Oncol Biol Phys*, **21**: 935-939.
20. Zelefsky MJ, Aschkenasy E, Leibel SA, Kelson S, Fuks Z (1997) Tolerance and early outcome results of post-prostatectomy three dimensional conformal radiation therapies. *Int J Radiat Oncol Biol Phys*, **39**: 327-333.
21. Hancock SL, Luxton G, Chen Y, et al. (2000) Intensity modulated radiotherapy for localized or regional treatment of prostatic cancer: Clinical implementation and improvement in acute tolerance [abstract]. *Int J Radiat Oncol Biol Phys*, **48**: 252-253.
22. Luxton G, Hancock SL, Boyar AL (2004) Dosimetric and radiobiologic model comparison of IMRT and 3D conformal radiotherapy in treatment of carcinoma of the prostate. *Int J Radiat Oncol Biol Phys*, **59**: 267-284.