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Original Article

Dosimetric Evaluation of Intensity Modulated Radiotherapy and 4-Field 3-D Conformal Radiotherapy in Prostate Cancer Treatment

Bora Uysal, Murat Beyzadeoğlu, Ömer Sager, Ferrat Dinçoğlan, Selçuk Demiral, Hakan Gamsız, Serdar Sürenkök, Kaan Oysul

Department of Radiation Oncology, Gülhane Military Medical Academy, Ankara, Turkey

ABSTRACT

Objective: The purpose of this dosimetric study is the targeted dose homogeneity and critical organ dose comparison of 7-field Intensity Modulated Radiotherapy (IMRT) and 3-D 4-field conformal radiotherapy.

Study Design: Cross sectional study.

Material and Methods: Twenty patients with low and moderate risk prostate cancer treated at Gülhane Military Medical School Radiation Oncology Department between January 2009 and December 2009 are included in this study. Two seperate dosimetric plans both for 7-field IMRT and 3D-CRT have been generated for each patient to comparatively evaluate the dosimetric status of both techniques and all the patients received 7-field IMRT.

Results: Dose-comparative evaluation of two techniques revealed the superiority of IMRT technique with statistically significantly lower femoral head doses along with reduced critical organ dose-volume parameters of bladder V60 (the volume receiving 60 Gy) and rectal V40 (the volume receiving 40 Gy) and V60.

Conclusion: It can be concluded that IMRT is an effective definitive management tool for prostate cancer with improved critical organ sparing and excellent dose homogenization in target organs of prostate and seminal vesicles.

Key Words: Intensity-modulated radiotherapy, prostate cancer, three-dimensional conformal radiotherapy

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Introduction

Prostate cancer is the most common cancer and second most common cause of cancer-related mortality in men (1). Radiotherapy (RT), either used alone or in combination with surgery and /or hormonotherapy, plays a central role in the treatment of low, intermediate and high-risk prostate cancer. Prostate RT can be delivered either externally through Intensity Modulated RT (IMRT) and Three-Dimensional Conformal RT (3D-CRT), or internally in the form of brachytherapy which can be used alone or as adjunct to external RT in the boost form. A 4-field box technique had been utilized for the definitive RT for prostate cancer until mid-1990's (2, 3). The 3D-CRT was shown to be superior to 4-field box therapy in late 1990's (4-8). IMRT is a highly conformal treatment planning and delivery method for RT, providing improved dose distribution via the implementation of non-uniform beam patterns. IMRT was first used in the treatment of head and neck cancers. With growing experience, clinical practice of IMRT has gained widespread acceptance in the treatment of various tumor sites (9). For prostate cancer, the toxicity rates of IMRT to total dose of up to 80 Gray (Gy) has been shown to be comparable with the toxicity rates of 70 Gy 3D-CRT (10).

We hypothesised that IMRT may have superiority over the 3D-CRT in terms of critical organ sparing and dose homogeneity. Therefore we aimed to compare these two techniques based on dosimetric manner in low and intermediate risk prostate cancer patients, retrospectively. This article will help on decision about curative radiotherapy of prostate cancer.

Material and Methods

Twenty patients with histopathologically confirmed prostate cancer treated with IMRT at Radiation Oncology Department of Gulhane Military Medical Academy between January 2009 and December 2009 were enrolled in this study. A standard dose of 68 Gy in 2 Gy fractions was delivered to treat the prostate and/or seminal vesicles using IMRT technique. In order to make a dosimetric comparison, 4-field 3D-CRT treatment plans were generated for the same patient group. Critical organ doses and target volume dose homogenization were comparatively evaluated. Acute and late effects and potential complications of treatment were explained clearly to every patient, and a patient-signed informed consent was obtained from each patient prior to the study enrollment. The study was approved by the institutional ethics

Address for Correspondence: *Dr. Bora Uysal, Department of Radiation Oncology, Gulhane Military Medical Academy, Ankara, Turkey*
Phone: +90 312 304 46 85 e-mail: drborauysal@windowslive.com

committee. Fleet enema was used before CT simulation. The patients were instructed to drink water and CT images with 2.5 mm slice thickness were acquired in our CT planning unit (GE Lightspeed GE Healthcare, Chalfont St. Giles, UK) as soon as they started to have urgency. All the patients were immobilized with knee and ankle support in the supine position. Three fiducials were aligned on patient skin with laser. Scout views were taken, and then intravenous contrast medium of 100 cc was infused before image acquisition. These images were sent to the contouring workstation via network. ELEKTA UK Precise planning system Release 2.16 was used as an algorithm for planning (Figure 1). Body was contoured automatically and surrounding critical structures were contoured manually. Clinical Target Volume (CTV) included only prostate in low-risk and prostate+seminal vesicle in intermediate-risk patients. Planning Target Volume (PTV) was created by a 8 mm expansion around CTV in all directions except 5 mm posterior margin. Target and critical organ delineations were performed by the same radiation oncologist using ELEKTA SimMD software. Likewise, the same medical physicist did the dosimetric planning. Treatment set-up was done with X-Ray Volumetric Imaging (XVI) and electronical portal imaging system. PTV was planned in the constraints of 95-105% and the following critical tolerance dose criteria were used; V65 (the volume receiving 65 Gy) of rectum ≤17% of all volume, V65 of bladder ≤25% of all volume, the volume receiving 50 Gy (V50) of femoral heads ≤10% of all volume, the maximum dose of small bowel ≤50 Gy. 4-field 3DCRT plans were generated for 20 patients treated with IMRT. Consequently, 2 separate plans for each patient were generated to compare CTV, PTV and critical structures dosimetrically by using Dose Volume Histograms (DVH). The dosimetric comparison groups were as follows;

First group: 7-field IMRT; The dosimetric planning was done for the treatment angles of 0, 51, 102, 153, 204, 255 and 306 degrees.

Second group: 4-field 3DCRT; The dosimetric planning was done for the treatment angles of 0, 90, 180 and 270 degrees.

Values of PTV maximum, PTV minimum, CTV maximum, CTV minimum, V25 (the volume receiving 25 Gy), V40 and V60 of rectum, bladder and mean doses of femoral heads were analyzed. The endpoint of this study was to treat the cancer with less critical organ irradiation and best possible target volume dose homogeneity. For this purpose, maximum and minimum values of CTV, PTV, mean values of V25, V40 and V60 of rectum and bladder and mean doses of femoral heads were computed for 2 separate techniques and the data extracted from DVH's were statistically analyzed. Dependent-t test was used for eligible group and Wilcoxon test for ineligible group whilst p value was set at $p<0.05$ for statistical significance.

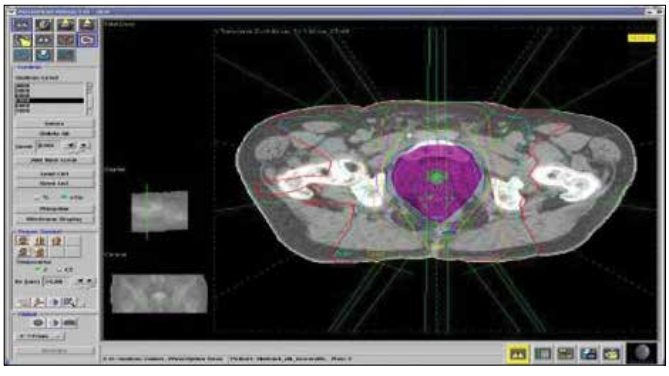

Figure 1. Axial IMRT planning slice of the patient who was included in our study

Results

Age, staging, PSA level and Gleason scores of all patients were saved and analyzed statistically. The patient characteristics are shown in Table 1. The mean age was 70 (55-80). Mean initial PSA at presentation was 4.61 (0.64-9.12). Mean Gleason score was 6 (6-9). Mean age, initial PSA and Gleason score are shown in Table 2.

Optimal dose distribution and target coverage are one of the major goals of radiotherapy. For this reason, we compared PTV, CTV minimum and maximum doses of both IMRT and 3DCRT arms statistically. Comparative mean PTV-CTV minimum and mean PTV-CTV maximum doses of target organ for IMRT and 3DCRT arms were statistically significant and revealed a better dose homogeneity for IMRT arm ($p<0.05$) (Table 3).

Table 1. Patient characteristics

Number of patient	Age	Staging	PSA (ng/mL)	Gleason score
1	80	T1CN0M0	4.23	6
2	72	T2BN0M0	5.44	7
3	59	T2AN0M0	8.44	6
4	75	T2BN0M0	5.3	6
5	72	T2BN0M0	3.16	6
6	74	T2AN0M0	3.0	6
7	66	T2BN0M0	6.68	8
8	69	T2BN0M0	5.0	7
9	61	T1CN0M0	1.08	7
10	65	T2AN0M0	2.87	6
11	64	T1CN0M0	9.12	7
12	72	T2BN0M0	4.0	6
13	64	T1CN0M0	7.02	6
14	75	T1CN0M0	5.48	7
15	75	T1CN0M0	1.9	9
16	78	T2BN0M0	2.0	6
17	55	T2BN0M0	8.76	6
18	70	T2BN0M0	0.64	6
19	65	T1CN0M0	4.0	6
20	70	T1CN0M0	5.0	7

Table 2. Minimum, maximum and mean values of age, PSA and Gleason scores

	Age	PSA (ng/mL)	Gleason score
Minimum	55	0.64	6
Maximum	80	9.12	9
Mean	70	4.615	6

Major critical structures that needed to be spared in prostate cancer radiotherapy are rectum, bladder and femoral heads. We analyzed mean V25, V40 and V60 of rectum and bladder and mean right and left femoral heads. Mean rectum V25, rectum V40 and rectum V60 percentage values were compared and only V40 and V60 rectal DVH percentage values revealed to be statistically significant ($p<0.05$) in favor of IMRT group compared to 3DCRT whilst V25 percentage values for both techniques were statistically insignificant ($p>0.05$) (Table 4).

Only mean bladder V60 percentage DVH values comparing IMRT and 3DCRT arms revealed to be statistically significant ($p<0.05$) whereas comparative mean V25 and V40 values were statistically insignificant ($p>0.05$) (Table 5).

Both mean right and left femoral head dose values were significantly lower in IMRT arm compared to 3D-CRT arm ($p<0.05$) (Table 6).

Discussion

In this study, the plans of IMRT and 3D-CRT were compared in terms of dose distribution and doses to critical structures in patients with low- and intermediate-risk prostate cancer, and we found that IMRT was superior over 3D-CRT by better dose homogeneity and lower critical organ doses. IMRT has long been standard of care in the treatment of patients with prostate cancer as a viable alternative to surgery. Zelefsky et al. (11) in a similar comparative study of IMRT and 3D-CRT showed that IMRT was therapeutically superior to 3D-CRT in prostate cancer treatment. IMRT dose homogeneity was better with lower critical structures doses. Accumulative dose to femoral heads in that study was 30 Gy in IMRT and 45 Gy in 3D-CRT arm. Likewise, respective V60 doses with IMRT and 3D-CRT were 20 Gy and 40 Gy for rectum, and 35 Gy and 42 Gy for bladder. Our results are consistent with the study by Zelefsky et al. (11) and 2 other similar studies by Lee et al. (12) and Zhu et al. (13) regarding dose homogeneity and critical organ doses.

In an article by Wolff et al. (14), V40 of rectum was 35% in IMRT and 80% in 3D-CRT consistent with our results. In another article by Vaarkamp et al. (15), V60 of rectum was 12.8% in IMRT and 22.6% in 3D-CRT along with the beneficial effect of the increasing beam numbers to have better dose homogenization and critical organ dose reduction. The dose delivered in the study by Vaarkamp et al. (15) study was 86.4 Gy for IMRT where 40 patients were treated succesfully with no increase in acute toxicity.

In an another article by Fenoglietto et al. (16), mean V25 of rectum was 52% in IMRT and 85% in 3D-CRT, V40 of rectum was 40% in IMRT and 60% in 3D-CRT, V25 of bladder was 50% in IMRT and 80% in 3D-CRT, V40 of bladder was 40% in IMRT and 50% in 3D-CRT, V60 of bladder was 30% in IMRT and 35% in 3D-CRT all of which percentage values in line with our study except for V25 of rectum. The insignificance of V25 for rectum in our study may be due to the IMRT technique that includes multipl fields or the lack of rectum dose tolerance limitation. We kept the volume of rectum which received more than or equal to 65 Gy at less than or equal to 17% and did not give specific dose constraint for 25 Gy.

Table 3. Mean PTV-CTV minimum and maximum values of IMRT and 3DCRT

	IMRT (Gy) (mean±SD)	3DCRT (Gy) (mean±SD)	p
PTV minimum	65±3.1	63±1.7	0.001
PTV maximum	74.57±3.52	69.42±0.87	0.001
CTV minimum	67±5.1	65±2.8	0.001
CTV maximum	73.17±3.38	69.29±0.73	0.001

PTV: Planning target volume, CTV: Clinical target volume, IMRT: Intensity-modulated radiotherapy, Gy: Gray, SD: Standart deviation, 3DCRT: 3-dimensional conformal radiotherapy

Table 4. Mean % V25, V40 and V60 values of rectum in IMRT and 3DCRT

	IMRT (%) (mean±SD)	3DCRT (%) (mean±SD)	p
RectumV25	79±8.47	78.45±12.27	0.084
Rectum V40	50.9±7.98	45.55±10.04	0.028
Rectum V60	4.55±6.3	25.70±11.53	0.001

IMRT: Intensity-modulated radiotherapy, SD: Standart deviation, 3DCRT: 3-dimensional conformal radiotherapy

Table 5. Mean % V25, V40 and V60 values of bladder in IMRT and 3DCRT

	IMRT (%) (mean±SD)	3DCRT (%) (mean±SD)	p
Bladder V25	54.4±20.38	67.9±22.96	0.131
Bladder V40	37.1±14.26	49.3±22.2	0.185
Bladder V60	7.45±4.5	32.4±17.7	0.001

IMRT: Intensity-modulated radiotherapy, SD: Standart deviation, 3DCRT: 3-dimensional conformal radiotherapy

Table 6. Mean values of femur heads in IMRT and 3DCRT

	IMRT (Gy) (mean±SD)	3DCRT (Gy) (mean±SD)	p
Left femur	18.79±5.67	31.5±4.11	0.001
Right femur	17.98±4.51	31.95±3.47	0.001

IMRT: Intensity-modulated radiotherapy, Gy: Gray, SD: Standart deviation, 3DCRT: 3-dimensional conformal radiotherapy

One of the challenges to be solved in RT for prostate cancer is the prostate immobilization. The unfavorable factors of definitive prostate cancer therapy are full rectum, respiratory movement, inter- and intra-fractional prostate motion combined with anatomic mobility of prostate gland itself. One way to overcome intra-fractional prostate motion is to use rectal balloon. In our study, knee and ankle support were used for the purpose of immobilization but rectal balloon immobilization could not be routinized due to patient resistance. However, as pointed out by Wachter et al. (17), complete prevention

of the prostate movement could not even be maintained with rectal balloon application with 20% rectal balloon failure (17).

The first advantage of our study is that the planning was done for all patients by the same radiation oncologist and same physicist minimizing the inter-observer variability commonly experienced at RT practice. The second one is its one of the rare dosimetric studies comparing IMRT and 3D-CRT in prostate cancer radiotherapy.

In our study, gold-seed implantation or Magnetic Resonance-Computerized Tomography (MR-CT) fusion were not used. Additionally, total dose of 68 Gy was lower for IMRT compared to the literature. These may be the limitations of our study. In literature, 3D-CRT and IMRT plans were compared dosimetrically and 3D-CRT plans were suitable for Radiation Therapy and Oncology Group (RTOG) criteria for Planning Target Volume (PTV) coverage and dose criteria for organs at risk. PTV coverage was better for IMRT plans compared to 3D-CRT plans but not statistically significant in contrast to our study (18). The impact of 3D-CRT and IMRT for radiation-induced second cancers was analyzed and resulted as an increased incidence for IMRT compared to 3D-CRT due to the larger volume irradiated to lower doses, dose distribution and increase in monitor units (19). In this study, target dose distribution and lower doses of critical organs were shown to be statistically significant.

This study is based on dosimetric comparison of IMRT and 3D-CRT in prostate cancer treatment regarding target dose homogeneity and critical structure sparing. We showed the clear dosimetric target homogeneity and critical structure dose reduction effect of IMRT compared to 3D-CRT ($p<0.05$). We believe that future studies of tumoral area dose-painting and escalated target doses with IMRT will be resulting in promising improved therapeutic outcome.

Ethics Committee Approval: *Ethics committee approval was received for this study.*

Informed Consent: *Written informed consent was obtained from patients who participated in this study.*

Peer-review: *Externally peer-reviewed.*

Author contributions: *Concept - B.U.; Design - M.B.; Supervision - Ö.S.; Resource - S.D.; Materials - F.D.; Data Collection&/or Processing - H.G.; Analysis&/or Interpretation - S.S.; Literature Search - B.U.; Writing - B.U., M.B., Ö.S., F.D.; Critical Reviews - S.D., H.G., S.S., K.O.*

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