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Comparison of conformal radiotherapy, intensity-modulated radiotherapy and tomotherapy irradiation techniques in prostate cancers

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Original Article

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Abstract

Aim: The aim of this study is to compare three-dimensional conformal radiotherapy (3D-CRT), intensity-modulated radiotherapy (IMRT) and tomotherapy techniques used in the treatment of prostate cancer with target and critical organ doses to be included. *Materials and Methods:* The target dose was studied with 4-and 6-field 3D-CRT, 7-field IMRT and tomotherapy techniques used to treat ten patients for prostate cancer and the dose volume histograms of critical organs were analyzed. The same target volumes, critical organs doses prescribed and treatment times for the three techniques were compared. Total dose of 76 Gy was given using 6 MV and 18 MV for 3D-CRT, 6 MV for IMRT and tomotherapy techniques. *Results:* When we compare the three techniques, for rectum V_{35}(p:0·001), V_{65}(p:0·001), D_{50}(p:0·020) and D_{25}(p:0·002), for bladder V_{50}(p:0·027), V_{65}(p:0·006), V_{100}(p:0·006) and for femoral head, the V_{50}(p:0·001) dose was found to be significantly different and more favourable in the tomotherapy technique. Significant differences were found with IMRT planning in 50% of bladder volume (p:0·002). There is no significant difference between the three techniques for doses of 100% volume of rectum and 25% of volume of bladder. The minimum dose that healthy tissue received which was outside the tumour volume was investigated. *Findings:* Doses to critical organs were lower using the tomotherapy technique. However, the minimum doses that healthy tissue received were higher for the tomotherapy technique. When the beam on times were compared for all three techniques, a significant difference was found in favor of tomotherapy.

Introduction

Prostate cancer is one of the most common health problems occurring in men. It is the second most common cause of cancer mortality after lung cancer. A radiation dose of above 70 Gy is preferred to ensure local control of prostate cancer.[1] Three-dimensional conformal radiotherapy (3D-CRT) delivers a more homogeneous dose distribution in the target volume and gives lower doses to normal tissues than conventional radiotherapy. Several treatment fields are used in conformal treatment of prostate cancer, usually six or seven are used. Multi-leaf collimators, dose loadings and wedge angles are altered to achieve an adequate dose distribution.[2] Intensity-modulated radiation therapy (IMRT) treatment technique is an advanced form of 3D-CRT. In addition to the main photon beam, small fields (segments) of radiation are adjusted to create different dose intensities.[3] Using these properties, IMRT increases tumour control and reduces side effects associated with radiation therapy, thereby enhancing quality of life.[4] Two types of IMRT technique are used at present, these are static IMRT (step and shoot) and dynamic IMRT techniques.[4]

Tomotherapy is delivered by an external beam radiotherapy machine with the capability to provide helical beams of radiation. The latest advanced form of tomotherapy is known as helical tomotherapy (HT), which operates by movement of the gantry and the treatment table. HT is a type of radiation therapy in which the radiation is delivered slice-by-slice and is a form of computed tomography guided IMRT. HT machines are purposely built for IMRT and delivery differs from IMRT delivered by conventional medical linear accelerators in a number of ways. The main difference is that in HT a narrow intensity modulated pencil beam is delivered from a rotating gantry while the patient is simultaneously moved through the bore of the machine, compared to the much wider intensity modulated beam and static patient in conventional IMRT. Unlike a conventional linear accelerator, HT has a 85 cm source to skin distance (SSD) instead of 100 cm.[5] HT produces a 6 MV photon beam and the radiation source is placed on an annular gantry. Pitch (or pitch ratio) is an important concept in tomotherapy which is defined as the motion distance per rotation of the gantry table.[6,7]

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Table 1. Mean dose and volumes for critical organs and beam on time for three irradiation techniques

		D100 (cGy)	D50 (cGy)	D25 (cGy)	V50 (%)	V65 (%)	V35 (%)
Bladder	3DCRT	325	2,775	5,506	31·4	19·9	
	IMRT	388	2,227	4,887	26·5	17·1	
	Tomotherapy	300	3,083	5,650	23·8	15·1	
Rectum	3DCRT	568	4,336	6,338		20·6	56·1
	IMRT	555	4,196	5,783		15·2	54·4
	Tomotherapy	562	2,462	4,907		13·5	41·9
Femoral head	3DCRT				8·1		
	IMRT				4·2		
	Tomotherapy				2·4		
Beam on time (sec)	3DCRT	472·2					
	IMRT	386·5					
	Tomotherapy	219·7					

Modulation factor is a factor that affects the opening and closing speed of the multi-leaf collimators. A smoothing filter, which is used for providing a homogenous dose distribution in a conventional linear accelerator, does not exist in the HT machine, which is designed for just performing IMRT and this appears to be an advantage.[8]

The aim of this study is to compare 3D-CRT, IMRT and tomotherapy techniques in terms of target surrounding, critical organ dose and duration of treatment. In addition, this study was performed to determine the most effective technique on dose reduction to critical organ and overall treatment time for the delivery.

Material and Methods

This study included ten prostate cancer patients selected at random. The prostate and seminal vesicles were identified as the intended treatment target volume. Localisation images were obtained for each patient via Siemens Biograph Truepoint PET-CT (Siemens AG, Munich, GERMANY) system with a thickness of 5 mm. The rectum, bladder and femoral heads were identified as critical organs. We used Precise Plan Treatment Planning System (TPS), Elekta Software, for the 3D-CRT and IMRT planning. The pencil beam algorithm was used for 3D-CRT plans and IMRT plans. We used Tomotherapy Hi-Art Treatment Planning System for Tomotherapy planning and the convolution/superposition algorithm was used for tomotherapy plans. We used the beam parameters of the linear accelerator (Elekta Synergy Platform) with 80 leaves MLC for 3D-CRT and IMRT plans.

A four-field box technique with 6MV and 18 MV photon energies up to 40 Gy was used in the 3D-CRT plan for the treatment plan. Between 40 Gy and 76 Gy; 6 fields and 6 MV photon energy was used with gantry angles of 45°, 90°, 135°, 225°, 270° and 315° (Figure 1). Seven non-coplanar fields were used in IMRT with gantry angles of 210°, 260°, 310°, 0°, 50°, 100° and 150°. The energy of the beam was selected as 6 MV and the inverse planning technique was used.

The PTV and organs at risk were outlined and planning undertaken for all three techniques. In the planning of the IMRT delivered by tomotherapy, this required determination of the Pitch value, this was determined as 0·287 and modulation factor was 2·5. Doses for 100%, 50% and 25% of the volumes of rectum and bladder (D_{100}, D_{50}, D_{25}) and volumes of femoral head for 50 Gy dose (V_{50Gy}) were assessed in the comparison of 3D-CRT, IMRT and tomotherapy plans (Figure 2). We also compared for all treatment plans (total 30 plans) conformity index (CI) and homogeneity index (HI) (Equations (1) and (2)).

$$\mathbf{CI}: \mathbf{V_{RI}} / \mathbf{TV} \quad (1)$$

$$\mathbf{HI}: \mathbf{I_{max}} / \mathbf{RI} \quad (2)$$

V_{RI} defines PTV volume that the dose covers, TV defines the total PTV volume, I_{max} defines the highest dose in PTV volume and RI defines the dose described for PTV volume in here. For 3D-CRT, four and six fields were used to plan the treatment and for IMRT, seven fields were used. For IMRT, seven fields were used. Planning target volume (PTV) and dose volume histograms (DVH) of rectum, bladder and femoral heads were obtained to decide whether treatment is carried out in an appropriate manner. Clinical target volume (CTV) was placed in 0·6 cm posterior and 1 cm away from all directions of gross tumour volume (GTV). PTV was placed at a distance of 0·5 cm from the CTV to avoid installation errors and reduction caused by the penumbra of the radiation beam. A total dose of 76 Gy was planned to be administered in PTV with a daily fraction dose of 2 Gy in 38 fractions.

Target and critical organ doses were assessed by DVH in all three techniques.

Results

Rectum, bladder, femoral heads and PTV doses were compared with the use of DVH as well as CI and HI values for all three techniques (Figure 3).

Mean dose and volumes for critical organs were compared between the three techniques and are displayed in Table 1. Mean

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doses for 100%, 50% and 25% of the volume of the bladder were compared between 3D-CRT, IMRT and tomotherapy. There was a significant difference in the mean dose in 100% of the volume of bladder in tomotherapy plans and 50% of the volume of bladder in IMRT plans. About 25% of the bladder volumes of all three planned techniques did not differ significantly. Mean volumes of 50 Gy and 65 Gy for bladder were compared between 3D-CRT, IMRT and tomotherapy.

There was a significant difference in the volumes of 50 Gy and 65 Gy for bladder in tomotherapy plans and bladder dose was lower, these data are presented in Table 1. There was a significant difference in 50%, 25% of the volume of bladder in tomotherapy plans. About 100% of the volumes of all three plans did not differ significantly

Mean volumes receiving 35 Gy and 65 Gy for rectum were compared between 3D-CRT, IMRT and tomotherapy. Mean doses for 100%, 50% and 25% of the volume of rectum were compared between 3D-CRT, IMRT and tomotherapy. There was a significant difference of dose received in the volumes of 35 Gy and 65 Gy for rectum in tomotherapy plans and rectum was better spared.

Mean volumes of 50 Gy for femoral head were compared between 3D-CRT, IMRT and tomotherapy. There was a significant difference in the volumes of 50 Gy for femoral head in tomotherapy plans.

There was a significant difference in terms of CI between all three planned techniques favoring tomotherapy and PTV coverage was better. There was a significant difference in terms of HI between all three plans favoring tomotherapy, the dose distributed was more homogenous in the PTV than in the other planning techniques.

Beam on time was counted in seconds for all three planning techniques and a significant difference was found in treatment delivery time, in favour of the tomotherapy technique. Time to deliver treatment with the tomotherapy technique was much shorter time than for the other techniques.

Discussion

The main goal of radiotherapy is to adequately treat the tumour volume while keeping the dose to critical organs as low as possible, to ensure tumour control and to reduce the risks of long-term side effects. Parallel to the developments in computer technology, radiotherapy treatment planning and application systems are rapidly developing. In recent years, the development of IMRT has enhanced treatment accuracy, based on the use of different intensities of radiation, which is an improved form of 3D-CRT and allows a minimum dose to be delivered to normal surrounding tissues.

The use of IMRT is increasing due to the ability to protect critical normal tissues and dose distribution correction. Plan comparisons using IMRT and 3DCRT techniques indicate that IMRT is superior because of the reduction of doses of organs to risk and uniform dose distribution in a number of treatment sites. Unlike conventional RT and 3DCRT in IMRT, dose intensity varies with the action of MLCs. The tomotherapy machine delivers radiation differently from classical linear accelerator.

In a conventional linear accelerator, only MLC leaves and gantry movements occur during irradiation. In the tomotherapy machine, the MLC leaves, gantry and table are on the move during irradiation. HT, with its dynamic IMRT technique, can produce excellent results in both tumour control and protection of organs at risk.

In a study by Zelefsky et al., they used V50Gy <65%, V60Gy <50%, V70Gy <30% for the rectum, V65Gy <100%, V78Gy <2·9% for the bladder and V50Gy <10% for femur heads in the plan evaluation.[9] According to RTOG (Radiation Therapy Oncology Group), 0126 dose limits were given as V70Gy <35%, V65Gy <50% for the bladder, V70Gy <25%, V65Gy <35% for the rectum and maximum dose V52Gy <5% for the femur head.[10] In this study, 50 Gy and 65 Gy for the bladder; 35 Gy and 65 Gy for the rectum and 50 Gy for the femur were evaluated.

In a study conducted Wolff et al., 3D-CRT, IMRT, and tomotherapy techniques were examined in terms of the doses, CI and HI of critical organs.[5] They observed sharper dose reductions in tomotherapy and IMRT planning than in 3D-CRT. Mean doses posterior to the rectum were 31·85 Gy in the tomotherapy plan, 34·89 Gy in the IMRT and 55·43 Gy in the 3D-CRT while the mean doses in anterior to the rectum were 50·69 Gy in the tomotherapy plan, 53·99 Gy in the IMRT plan and 66·33 Gy in the 3D-CRT plan. They found that the rectum doses for tomotherapy planning were much lower than for 3D-CRT and IMRT planning.

In our study, the rectum 65 Gy and 35 Gy dose volumes were lower in tomotherapy planning. The mean volume of the 35 Gy dose of the rectum was determined as 41·9% in the tomotherapy plan, 54·4% in the IMRT plan and 56·1% in the 3D-CRT plan. When all three planning techniques were statistically analysed, a significant difference was found in favour of tomotherapy ($p = 0·001$) for the volume of 35 Gy dose of the rectum. The dose of 65 Gy of the rectum was found to be 13·5% for tomotherapy, 15·2% for IMRT and 20·6% for 3D-CRT. When statistically examined, a significant difference was found in favor of tomotherapy planning ($p = 0·001$) in the volume of the rectum with a dose of 65 Gy. Also the best tumour coverage has been in tomotherapy plans. The doses of 100%, 50% and 25% of the rectum were also examined. The average dose of 100% volume of the rectum was found to be 5·62 Gy for tomotherapy, 5·55 Gy for IMRT and 5·68 Gy for 3D-CRT. Doses with 50% volume; 24·62 Gy for tomotherapy, 41·96 Gy for IMRT and 43·36 Gy for 3D-CRT, while the 25% volume of doses is 49·07 Gy for tomotherapy, 57·83 Gy for IMRT and 63·38 Gy for 3D-CRT, respectively. When all three planning techniques were compared, there was a significant difference in favor of tomotherapy plans for 50% ($p = 0·020$) and 25% ($p = 0·002$) volumes of the rectum. No significant difference was found between the three planning techniques in the 100% volume.

The average volume of 50 Gy dose for bladder was found to be 31% for 3D-CRT, 27% for IMRT plans and 24% for tomotherapy plans. When all three planning techniques were compared, a significant difference was found in favor of tomotherapy plans ($p = 0·027$) for the volume of 50 Gy dose of bladder. The volume of bladder was found to be 20% for 3D-CRT, 17% for IMRT and 15% for tomotherapy.

According to these results, the bladder received less dose in tomotherapy plans than other plans. When we compared all three planning methods statistically, the plans for tomotherapy resulted in a significant difference for the volume of bladder receiving a dose of 65 Gy ($p = 0·006$). In addition, 100%, 50% and 25% of the bladder volumes were also evaluated for the doses they received. The dose that the patient has received a 25% dose of bladder is 56·50 Gy in the tomotherapy plan, 48·87 Gy in the IMRT plan, 55·06 Gy in the 3D-CRT plan and 50% dose of bladder is 30·83 Gy in the tomotherapy plan, 22·27 Gy in IMRT plans and 27·75 Gy in

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3D-CRT plans. The mean doses at which 100% volume was taken; 3·00 Gy for tomotherapy, 3·88 Gy for IMRT and 3·25 Gy for 3D-CRT. Compared with tomotherapy, 3D-CRT and IMRT plans; tomotherapy caused a significant difference in 100% volume of bladder ($p = 0·006$) and IMRT plans in 50% volume ($p = 0·002$) of bladder. No significant difference was found between the three techniques for the 25% volume.

In the study by Wolff et al., the dose that 95% of the tumour received was 69·79 Gy for tomotherapy, 70·51 Gy for IMRT and 73·42 Gy for 3D-CRT. In our study, the dose that the 95% volume of the tumour had received was found to be 76·01 Gy in the tomotherapy, 75·35 Gy in the IMRT and 75·56 Gy in the 3D-CRT plan.[5] When three planning techniques were compared, a significant difference was found in favor of the tomotherapy plans ($p = 0·006$). In our study, femur head doses were also checked for all three planning methods. Femur head volumes receiving 50 Gy; 8·1% for 3D-CRT, 4·2% for IMRT and 2·4% for tomotherapy. When three planning techniques were compared, a significant difference was found in favor of the tomotherapy plans ($p = 0·001$).

Doses to healthy tissues other than PTV were examined. In the region of the tumour, the minimum dose received by the healthy tissues other than the tumour was lower in 3D-CRT and IMRT planning. About 100% of the healthy tissues in this region received a mean dose of 5·08 Gy in the tomotherapy plan, 0·4 Gy for 3D-CRT and 0·42 Gy for IMRT. It has been determined that more doses are given to healthy tissues other than tumours in tomotherapy plans.

In addition, the CI and HI were compared for all three planning techniques. The average CI was found to be 0·943 for 3D-CRT, 0·934 for IMRT and 0·952 for tomotherapy. The homogeneity index was determined as 1·071 for 3D-CRT, 1·068 for IMRT and 1·047 for tomotherapy. In the light of these results, it has been found that tomotherapy provides a better homogeneous dose distribution and better coverage of the tumour.

In the study of Ramsey et al., mean HT treatment duration was determined to be approximately 5 minutes.[11] In our study, the average beam on times were set to 220 seconds for tomotherapy, 386 seconds for IMRT and 472 seconds for 3D-CRT. When the beam on times were compared for all three techniques, a significant difference was found in favor of tomotherapy ($p < 0·05$).

Conclusion

In conclusion, experiencing a sharp decline in dose, better PTV covering, being less than the expected treatment period, reducing significant doses to critical organs such as bladder, rectum and femoral heads were observed in tomotherapy planning than the seven fields in IMRT planning and 4–6 fields used in 3D-CRT planning. Intact tissues except the tumour expose to integral doses and this increases the risk of secondary cancer development. The data in this study were limited to ten patients but the results were consistent for all patient plans for each of the techniques.

For individual patients, the critical organ doses, the dose for PTV and the overall integral doses should be rigorously evaluated and the appropriate planning technique should be selected by clinicians.

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Conflicts of Interest. None.

Ethical Standards. The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national guidelines on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008, and has been approved by the institutional committees (Yüzüncü yıl University) and the authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national guides on the care and use of laboratory animals (Taylan Tuğrul) and has been approved by the institutional committee (Yüzüncü yıl University).

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