

Radiotherapy of Prostate Cancer Using RapidArc: Dosimetric Study of Military Teaching Hospital Mohamed V, Morocco

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Abstract

Background: RapidArc®, the Varian solution of Volumetric-modulated arc therapy (VMAT) is currently used in the curative treatment of localized prostate cancer. The aim of this study was to evaluate the dosimetric parameters (effectiveness and efficiency) of the arc dynamic therapy at the Teaching Hospital Mohamed V.

Materials and methods: Thirty two patients were treated with curative intent, between June 2013 and December 2014, for localized prostate cancer with RapidArc. Computed tomography (CT) based treatment planning was performed in the supine position with immobilization devices. The patients were instructed to have a comfortably full bladder and an empty rectum at CT acquisition and before each treatment. Delineation of target volume and organs at risk (OARs) was based on the consensus recommendations of the RTOG. The dose prescription was performed with simultaneous integrated boost (SIB) method. Data was collected from dose-volume histograms (DVH) either for planning target volumes (PTV2) or OARs. We calculated the homogeneity index (HI) and the conformity index (CI). We also reported acute and late toxicity related to radiation therapy.

Results: The mean age was 66.63 ± 7.24 years old. Of the 32 patients, 24(75%) defined as high-risk. All PTV received dose ranging from 95% to 107% of the prescribed dose. The homogeneity and conformity index was very close to 1 of all treatment plans. The dose limits were respected in all OARs as recommended in QUANTEC reviews 2010. Respectively, the analysis of the HDV in the rectum and the bladder found a V70 at 7.15 ± 5.63% and 16.88 ± 8.62% and a V60 at 16.32 ± 7.97% and 27.68 ± 10.32%. The V50 in the femoral heads was 0.39 ± 0.57% on the right and 0.71 ± 1.35% on the left. The V50, V40 and V30 in the bowel bag were 38.76 ± 39.73 cc, 155.38 ± 85.60 cc and 320.09 ± 180.41 cc, respectively. The mean MU was 555.94 ± 86.34 and delivery treatment time (min) was 1.99 ± 0.47. After three months of radiation therapy, no grade 3 or 4 toxicity was reported. The median control PSA was very low at 0,052 [0.012, 0.417] ng/ml.

Conclusion: This present study demonstrated that RapidArc showed optimal PTV coverage and the best OARs sparing with less number of MUs and short treatment time. Acute GI and GU toxicities were very low. Further studies are needed to evaluate late toxicities and tumor control.

Keywords: RapidArc radiotherapy; Prostate cancer; Dosimetric study

Abbreviations: EBRT: External Beam Radiation Therapy; 3D-CRT: Three-Dimensional Conformal Radiotherapy; VMAT: Volumetric Modulated Arc Therapy; IMRT: Intensity Modulated Radiation Therapy; MLC: Multi Leaf Collimator; PRO: Progressive Resolution Optimization; CT: Computed Tomography; CTV: Clinical Target Volume; PTV: Planning Target Volume; OAR: Organs at Risk; SIB: Simultaneous Integrated Boost; DVH: Dose Volume Histograms; CI: Conformity Index; HI: Homogeneity Index; GI: Gastrointestinal; GU: Genitourinary; CTCAE: Common Terminology Criteria for Adverse Events; IQR: Interquartile Range; SD: Standard Deviation; ADT: Androgen Deprivation Therapy; AJCC: American Joint Committee On Cancer; PSA: Prostate-Specific Antigen; QUANTEC: Quantitative Analyses of Normal Tissue Effects in the Clinic; IGRT: Image-Guided Radiation Therapy; CBCT: Cone Beam CT; RT: Radiation Therapy; RTOG: Radiation Therapy Oncology Group; MU: Monitor Units

Introduction

Prostate cancer is the second most common cancer in men worldwide, with an estimated 1,100,000 cases and 307,000 deaths in 2012 [1]. External beam radiation therapy (EBRT) with three-dimensional conformal radiotherapy (3D-CRT) is frequently used in the curative treatment of localized prostate cancer, and dose-escalation has been shown in multiple randomized, controlled trials to improve

biochemical disease-free survival but at the cost of increased toxicity [2]. Due to current advances in the technology of EBRT such as volumetric modulated arc therapy (VMAT) and intensity modulated radiation therapy (IMRT), it is possible to deliver conformal dose to the target while the dose to surrounding normal tissue can be significantly reduced [3,4]. Due to these improved outcomes, classic IMRT and VMAT techniques are becoming the new standard for curative EBRT. Despite several dosimetric differences among planning studies, the greatest advantage of VMAT is requiring less number of MUs and shorter delivery treatment time when compared to classic IMRT with fixed field [5,6].

VMAT can deliver modulated radiation beam with simultaneous

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adjustment of dose rate, gantry speed, and multi leaf collimator (MLC) field aperture, facilitating highly conformal treatment and optimal sparing of the normal tissue near the target [7]. RapidArc® uses the Progressive Resolution Optimization (PRO) algorithm in the Eclipse planning system developed by Varian Medical System (Palo Alto, California, USA). The optimisation process is based on an iterative inverse planning process aiming to simultaneously optimise the instantaneous multi leaf collimator (MLC) positions, the dose rate, and the gantry rotation speed to achieve the desired dose distribution [8,9].

The aim of our study was to evaluate the dosimetric parameters (effectiveness and efficiency) of the arc dynamic therapy at the Military Teaching Hospital Mohamed V.

Material and Method

Study population

This is a retrospective study of localized prostate cancer patients treated with RapidArc at the radiotherapy department of Military Teaching Hospital Mohamed V of Rabat in Morocco, between Jun 2013 and December 2014. There were three plans of treatment according to the stratification risk: prostate ± seminal vesicles, whole pelvic, and prostate bed in the post-operative sitting.

Treatment planning

Computed tomography (CT) based treatment planning was performed in the supine position, with 2.5-mm thick slices from upper abdomen to 5 cm below the ischial tuberosities with their legs and pelvis immobilized by a custom vacuum immobilization device. The patients were instructed to have a comfortably full bladder and an empty rectum at CT acquisition and before each treatment. The CT data set was transferred to the Eclipse ver. 10.0 treatment planning system (Varian Medical Systems, Palo Alto, CA).

The prostate clinical target volume (CTV) was defined as the entire prostate and proximal 2.0 cm of seminal vesicles. The prostate planning target volume (PTV) was generated by adding a 10 mm isotropic margin around to the prostate CTV in all dimensions, except posteriorly, where a 5 mm margin was used. The nodal CTV begin at the L5/S1 interspace, with the external iliac nodal contours stop at the top of the femoral head and the obturator nodal contours extend inferiorly to the top of symphysis pubis, based on the consensus recommendations of the RTOG. The nodal PTV consisted of a 0.7 cm expansion of the nodal CTV. Target volumes were defined as PTV1, which included the prostate or prostate bed, and PTV2, which included the seminal vesicles or lymph nodes. Organs at risk (OARs) contoured on the treatment planning CT include the left and right femoral heads to the level of the ischial tuberosity, the bowel bag, the bladder, and the rectum from the superior rectosigmoid flexure to the inferior level of the ischial tuberosities.

The prescribed doses to PTV1 and PTV2 were 56Gy in 37 fractions and 74Gy in 37 fractions, respectively, using single-arc or double-arc with simultaneous integrated boost (SIB) plans to cover 95% of the PTV, with the maximum dose in the PTV no more than 107% of the prescription dose. However, the prostate bed received 66Gy in 33 fractions.

Evaluation planning

Dose volume histograms (DVHs) were constructed for the PTV2, rectum, bladder, femoral heads, and bowel bag. Parameters chosen for evaluation of the PTV2 in each plan were D2% (%), D5% (%),

D95% (%), D98% (%), V95% (%), V107% (%), we also calculated the conformity index (CI) and the homogeneity index (HI) using following formulas:

$$CI = V95\%/V100\%$$

$$HI2\% = D2\%/D95\%$$

$$HI5\% = D5\%/D95\%$$

The analysis included V74Gy (%), V70Gy (%) and V60Gy (%) for the rectum and bladder. The mean dose (Gy) and V50Gy (%) of each femoral head. The mean dose (Gy), D2% (Gy), V50Gy (cc), V40Gy (cc) and V30Gy (cc) of bowel bag were also notified. The total number of monitor units (MUs) per fraction and the treatment time were also used to evaluate the efficiency of treatment delivery.

Acute toxicities such as gastrointestinal (GI) and genitourinary (GU) toxicities were notified for all patients, using the Common Terminology Criteria for Adverse Events (CTCAE) version 4.0 adverse event scoring system. The response to treatment was evaluated by PSA 3 months after the end of radiation therapy.

Statistical analysis

Statistical analysis was performed using SPSS (version 20.0.0; SPSS, Chicago, IL). Qualitative variables were presented as number and percentages. Quantitative variables were presented as mean ± standard deviation for variables with normal distribution, and as median and interquartile range (IQR) for variables with skewed distributions.

Result

Patient characteristics

Patient characteristics are summarized in Table 1. The mean age was 66.63 ± 7.24 years old. Of the 32 patients, 24 (75%) defined as high-

Characteristic(n=32)	
Age (years)	66.63 ± 7.24
Pretreatment PSA (ng/ml) §	16.5 [6.9 ; 25.7]
Gleason score*	
5	1 (3.1%)
6	13 (40.6%)
7	10 (31.3%)
8	7 (21.9%)
9	1 (3.1%)
AJCC T-stage*	
T2a	3 (9.4%)
T2b	2 (6.3%)
T2c	11 (34.4%)
T3a	6 (18.8%)
T3b	9 (28.1%)
T4	1 (3.1%)
D'Amico risk stratification*	
Low risk	2 (6.3%)
Intermediate risk	6 (18.8%)
High risk	24 (75%)
Androgen deprivation therapy (ADT)*	30 (93.9%)
Radical prostatectomy *	4 (12.5%)

*Qualitative variables presented as number and percentages n (%)
 †Quantitative variables presented as mean ± standard deviation (SD)
 §Quantitative variables presented as median and interquartile range (IQR)
 Abbreviation: AJCC, American Joint Committee on Cancer; PSA, prostate-specific antigen

Table 1: Patients characteristics.

risk, 6 (18.8%) as intermediate-risk and 2 (6.3%) as low-risk. Androgen deprivation therapy (ADT) was indicated to 30 (93.9%) patients.

Target coverage, homogeneity and conformity index

All PTV received dose ranging from 95% to 107% of the prescribed dose. The D98%, also called near-minimum absorbed dose, for PTV prostate ± seminal vesicles, whole pelvic and prostate bed, was respectively 94.47 ± 3.64 , 92.96 ± 9.85 and 97.08 ± 0.58 . The D95% was 97.51 ± 2.78 , 97.49 ± 3.87 and 99.67 ± 0.26 respectively. The D2%, also called near-maximum absorbed dose, was respectively 103.75 ± 1.43 , 103.46 ± 1.51 and 104.59 ± 1.03 . The homogeneity and conformity index was very close to 1 of all treatment plans. Coverage Parameters of PTV2 was summarized in Table 2. Figures 1 and 2 shows respectively isodoses distributions of PTV1 and PTV2 using RapidArc technique for 1 patient.

Parameter	Objective	Plan of treatment		
		Prostate ± vesicles N=17	Whole pelvic n=11	Prostate bed* n=4
PTV2 volume (cc)		157.20 ± 33.32	158.26 ± 84.07	185.07 ± 53.89
D2% (%)		103.75 ± 1.43	103.46 ± 1.51	104.59 ± 1.03
D5% (%)		103.24 ± 1.33	102.98 ± 1.41	104.14 ± 1.01
D95% (%)		95.25 ± 5.76	95.81 ± 4.55	98.15 ± 0.42
D98% (%)		94.47 ± 3.64	92.96 ± 9.85	97.08 ± 0.58
V95% (%)		97.51 ± 2.78	97.49 ± 3.87	99.67 ± 0.26
V107% (%)		0.05 ± 0.12	0.04 ± 0.08	0.01 ± 0.01
CI	1	0.97 ± 0.02	0.97 ± 0.03	0.99 ± 0.002
HI2%	1	1.09 ± 0.08	1.08 ± 0.05	1.06 ± 0.01
HI5%	1	1.08 ± 0.08	1.07 ± 0.05	1.06 ± 0.01

*In the post-operative sitting
Quantitative variables presented as mean ± standard deviation (SD)
Abbreviation: CI, conformity index; HI, homogeneity index

Table 2: Summary of dose coverage of the PTV2 according to plan of treatment.

Organs at risk DVH Analysis

Results concerning OAR doses were reported in Table 3. The dose limits was respected in all structures as recommended in QUANTEC reviews 2010. Respectively, the analysis of the HDV in the rectum and the bladder found a V70 in $7.15 \pm 5.63\%$ and $16.88 \pm 8.62\%$ and a V60 in $16.32 \pm 7.97\%$ and $27.68 \pm 10.32\%$. The V50 in the femoral heads was $0.39 \pm 0.57\%$ on the right and $0.71 \pm 1.35\%$ on the left. The V50, V40 and V30 in the bowel bag was 38.76 ± 39.73 cc, 155.38 ± 85.60 cc and 320.09 ± 180.41 cc, respectively.

OAR	Parameter	Dose constraints*	Mean ± SD
Rectum	Volume (cc)		67.85 ± 35.73
	V74Gy (%)	V75<15%	1.32 ± 1.43
	V70Gy (%)	V70<20%	7.15 ± 5.63
	V60Gy (%)	V60<35%	16.32 ± 7.97
Bladder	Volume (cc)		122.28 ± 46.35
	V74Gy (%)	V75 ≤ 25%	6.39 ± 7.01
	V70Gy (%)	V70 ≤ 35%	16.88 ± 8.62
	V60Gy (%)	V65 ≤ 50%	27.68 ± 10.32
Right femoral head	Volume (cc)		150.56 ± 29.80
	D mean (Gy)		21.39 ± 3.53
	V50Gy (%)	V50 ≤ 10%	0.39 ± 0.57
Left femoral head	Volume (cc)		154.56 ± 26.15
	D mean (Gy)		20.13 ± 2.98
	V50Gy (%)	V50 ≤ 10%	0.71 ± 1.35
Bowel bag	Volume (cc)		709.06 ± 250.90
	D mean (Gy)		29.03 ± 10.023
	D 2% (Gy)		47.37 ± 13.15
	V50Gy (cc)	V45 to V50<195mL	38.76 ± 39.73
	V40Gy (cc)		155.38 ± 85.60
	V30Gy (cc)		320.09 ± 180.41

*QUANTEC Summary

Table 3: Summary of organs at risk (OARs) dose volume.

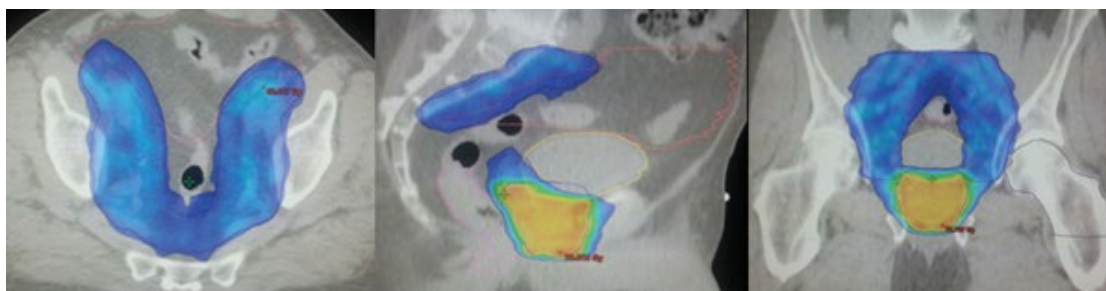


Figure 1: Isodose distribution of PTV1. Axial (left), sagittal (middle) and coronal (right) views of 1 patient.

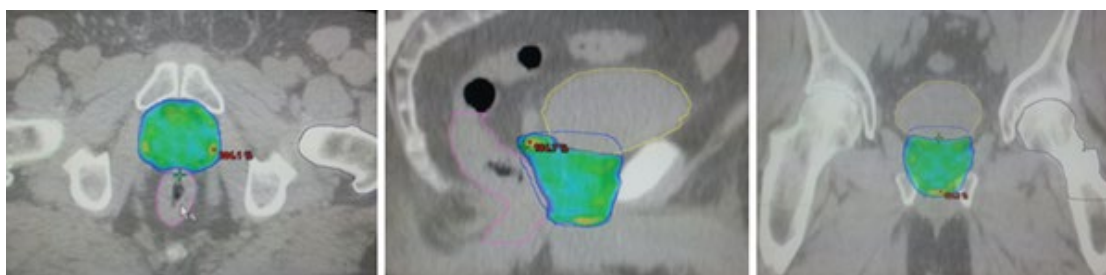


Figure 2: Isodose distribution of PTV2. Axial (left), sagittal (middle) and coronal (right), views of 1 Patient.

	Prostate ± vesicles	Whole pelvic	Prostate bed*
Monitor units (MUs)	586.24 ± 97.554	520 ± 65.32	526.00 ± 32.40
Delivery treatment time (min)	1.96 ± 0.49	2.18 ± 0.31	1.62 ± 0.57

*In the post-operative sitting
Quantitative variables presented as mean ± standard deviation (SD)

Table 4: Treatment efficiency.

	Prostate ± vesicles	Whole pelvic	Prostate bed*
GI toxicities (Grade 3-4)	0	0	0
GU toxicities (Grade 3-4)	0	0	0
PSA after three months	0.12 [0.024,2.39]	0.08 [0.01,0.48]	0.024 [0.002,0.047]

*In the post-operative sitting
Quantitative variables presented as median and interquartile range (IQR)
Abbreviation: GI, Gastrointestinal; GU, Genitourinary

Table 5: Acute toxicity and response to treatment.

Acute toxicity and treatment efficiency

Results about delivery treatment time and MU are summarized in Table 4. The mean MU was 555.94 ± 86.34 and delivery treatment time (min) was 1.99 ± 0.47. After three months of radiation therapy, no grade 3 or 4 toxicity was reported. The median control PSA was very low at 0,052 [0.012, 0.417]. This result was summarized in Table 5.

Discussion

Previous studies comparing VMAT to IMRT for prostate treatment have highlighted the fact that VMAT delivery is more efficient than that of IMRT [10-14]. VMAT is an arc-based approach of IMRT that allows modulated radiation beam with simultaneous adjustment of dose rate, gantry speed, and multi leaf collimator (MLC) field aperture, facilitating highly conformal treatment and optimal sparing of the normal tissue near the target [7]. In our study, all dose constraints were met satisfactorily for all treatment plans with a little treatment time. Clinical outcomes were also promising, showed low rates of acute GI and GU toxicity.

In the last few years, IMRT and VMAT have been increasingly utilized to treat prostate cancer to permit more conformal dose distribution and dose escalation. Both of these techniques have the potential to generate concave dose distributions with radical doses to the pelvic nodes and prostate gland while reducing the dose to surrounding adjacent normal tissues. Several authors have showed that IMRT provides improved OAR sparing and target coverage over 3D-CRT [3,4]. To evaluate target volumes coverage, there are many parameters such as D2%, D98%, and homogeneity, conformity index, which are recommended by ICRU report 83. However, there is no standardized formula to calculate CI and HI. This issue makes difficult any comparison between series especially for CI. The DVH data in the present study showed that RapidArc can generate highly conformal treatment with very close homogeneity and conformity index of all treatment plans when compared with IMRT and VMAT as found in other series [15,16]. A major feature of VMAT is its excellent dose conformity, which is inherited from the arc therapy nature. The DVH of normal tissue surrounding the PTV indicates that VMAT plans are more conformal regarding to the amount of normal tissue with respect the Quantitative Analyses of Normal Tissue Effects in the Clinic (QUANTEC) dose recommendations, in which the bowel bag volume receiving 45 to 50 Gy should be <195 ml, the rectum V50, V60,

V65, V70, and V75 should be less than 50%, 35%, 25%, 20%, and 15%, respectively [17].

A significant advantage of VMAT over IMRT originates from the superior radiotherapy delivery efficiency. With RapidArc in our study, the mean delivery treatment time was 1.99 ± 0.47 minutes. These are considerably shorter times than it takes to deliver the IMRT plans, which take approximately 4 to 5 minutes to deliver. Thus, the risk of intra fractional prostate motion is reduced [18,19]. Moreover, this time saving could be used to improve patient throughput on a treatment unit, which then provides additional time for on-line image guidance without increasing the overall treatment time. In this study, the mean MUs required by RapidArc were 555.94 ± 86.34 units. While several studies have found that the number of required MUs is less with VMAT than with IMRT [6,20-22], the number of MUs delivered by VMAT or IMRT varies significantly depending upon the planning algorithm. However, the VMAT treatment planning software with Eclipse RapidArc (Varian Medical Systems, Inc, Palo Alto, CA) reduced MUs by 32% compared with Pinnacle SmartArc (Philips Healthcare, Andover, MA) [23]. Palma et al. [24] compared 3D-CRT, Dynamic IMRT and arc therapy using Varian's Rapid Arc. They reported better treatment efficiency for the arc therapy (491.6 and 454.2 MUs for constant and variable dose rate respectively) vs.788.8 MUs for Dynamic IMRT. Also, 2-arc, SmartArc VMAT plans delivered statistically significantly more MUs than 1-arc plans [24].

All studied intensity modulated techniques yield treatment plans of significantly improved quality and higher MUs when compared to 3D-CRT. But, there are limited data showing the acute toxicity of IMRT in the setting of the prostate cancer. In our study, no grade 3 or 4 GI or GU toxicities was reported. Therefore, it seems reasonable to declare that RapidArc is a useful and valuable technique to treat patients with prostate cancer. Additionally, despite a number of favorable dosimetric studies [12,21,22], clinical outcome data studying toxicity in prostate cancer patients treated with RapidArc in the literature are lacking. Further, image-guided RT (IGRT) has been shown to be associated with reductions in toxicity [24]. Daily image guidance with cone beam CT (CBCT) was practiced in all our patients. The small amount of patients and incoherent population were principal limitations to this study [25].

Conclusion

In conclusion, the present study demonstrated that RapidArc provided feasible PTV coverage and OARs sparing with less number of MUs and short treatment time. Acute GI and GU toxicities were acceptably low with no grade 3 or 4, supporting the use of VMAT with frequently CBCT. Further study is needed to study late toxicity and tumor control.

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Conflict of Interest

Author Issam Lalya declares that he has no conflict of interest. Author Abdelhak Maghous declares that he has no conflict of interest. Author El Amin Marnouche declares that he has no conflict of interest. Author Noha Zaghba declares that she has no conflict of interest. Author Khalid Andaloussi declares that he has no conflict of interest. Author Mohamed Elmarjany declares that he has no conflict of interest. Author Khalid Hadadi declares that he has no conflict of interest. Author Hassan Sifat declares that he has no conflict of interest. Author Hamid Mansouri declares that he has no conflict of interest.

Ethical Approval

This article does not contain any studies with human participants or animals performed by any of the authors.

Informed Consent

For this type of study, formal consent is not required.

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