A Dosimetric Comparison of 7 Field IMRT, 9 Field IMRT, VMAT and 3-D Conformal Radiotherapy for the Treatment of Localized Intermediate Risk Prostate Cancer

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ABSTRACT

The objective of this study was to invastigate the potential role of various radiotherapy planning methods for localised intermediate risk prostate cancer. We compare Linac-based 7 field intensity modulated radiation therapy (IMRT), 9 field IMRT, volumetric modulated arc therapy (VMAT) and 3-D conformal radiotherapy (3D-CRT) techniques for localised prostate cancer. Forty plans with localised prostate cancer treated at our institution were randomly selected for this study. Ten radiotherapy treatment plans have been created for all 10 patients, including 7 field IMRT, 9 field IMRT, VMAT and 3D-CRT. All plans were designed to deliver 76 Gy in 38 fractions to the planning target volume (PTV). The HI and CI for 7-IMRT, 9-IMRT and VMAT modalities were better than 3D-CRT. For the CI, VMAT was better than 9-IMRT and 3D-CRT, but no significant difference was found with 7-IMRT modality. PTVDmax was found to be lower in 3D-CRT compared to other three treatment methods. VMAT was better than 3D-CRT in femoral head V30, but there was no difference between other modalities. In the number of monitor units(MU) 3D-CRT was found to be lower than the other modalities, in VMAT the number of MU's was found to be lower than 7 and 9-IMRT modalities. It was observed that the three IMRT modalities studied showed superior target coverage with less variation between each plan in comparison to 3D-CRT. VMAT treatment duration and femoral head V30 dose were superior to IMRT techniques.

Keywords: Prostate cancer, Radiotherapy, Dosimetric comparison, Treatment planning

INTRODUCTION

Prostate cancer is the most common malignant disease in men, except for skin cancers. The risk of developing prostate cancer is closely related to aging: about 14% at 50 years old and 50% from 80 years old upward.[1] External beam radiotherapy (EBRT) is one of the potential curative treatment options for clinically localized prostate cancer. Over the past few decades radiotherapy techniques have evolved from conventional two dimensional planning in early 1990's to three dimensional (3D) planning in late 1990's. In past few years, there have been significant refinements in IMRT technology. Linac based- IMRT and volumetric arc therapy (VMAT) planning and delivery has been implemented successfully in clinical practice.[2]

In IMRT, multiple beam angles are used and the intensity of each beam can be modulated by using multileaf collimators (MLCs), enabling the creation of complex yet highly conformal dose profiles. Volumetric modulated arc therapy (VMAT) has attracted increasing attention because of its greatly improved delivery efficiency over fixed-field IMRT.

Unlike IMRT, which typically includes less than 10 fixed-field beam angles, VMAT includes a large number of beam directions from an arc trajectory and delivers doses dynamically during rotation of the gantry. From each direction, however, there is no beam modulation by the MLCs so the intensity from each beam direction is uniform in VMAT.[3,4]

IMRT is a highly conformal treatment plan¬ning and delivery method for radiotherapy, 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 vari¬ous tumor sites.[5] There is a growing body of literature supporting that VMAT is capable of delivering treatment to the prostate with a similar or better dose distribution compared to fixed-field IMRT, yet requires significantly fewer MUs and reduced treatment time than IMRT.[6]

VMAT has been previously compared with IMRT for various types of cancer at different sites. Although it has been well established that VMAT results in improved delivery efficiency over IMRT, it is still unclear whether VMAT also generates a better plan quality than IMRT for prostate cancer treatment planning.4 Several recent studies have compared VMAT with IMRT for prostate radiotherapy. Although shortened treatment time is a common finding, there are inconsistencies in the dosimetric outcome. Some of these studies found largely equivalent sparing of organs at risk (OARs) between VMAT and IMRT. However, other planning studies have reported contradictory results.[7]

Ren et. al, was comprised 10 studies of VMAT and IMRT comparisons in a meta-analysis. For the radiation dose to rectum and bladder, V40, V60, and V70 of rectum were significantly decreased in VMAT than in IMRT. However, V50 of rectum and V40, V50, V60, V70 of bladder had no statistical differences between IMRT and VMAT plans. Compared with IMRT, the treatment time and MUs of VMAT were significantly lower.[8]

In the present study, we compare the performance of 7-field IMRT, 9-field IMRT, VMAT and 3-D Conformal radiotherapy for patients with intermediate-risk prostate cancer. This study focused on the evaluation of the dosimetric results and treatment delivery efficiency.

MATERIALS AND METHODS

CT data sets of 10 consecutive intermediate-risk prostate cancer patients who were treated with RapidArc in our institution between January 2019 and February 2021 were included in this study. For all patients neoadjuvant androgen deprivation was used for prostate volume reduction before radiotherapy. Based on our departmental policy, all patients were first prescribed neoadjuvant androgen deprivation containing goserelin and bicalutamide for 3 months before undergoing radiotherapy. A dose of 76 Gy was delivered to a clinical target volume (CTV) encompassing the prostate and proximal seminal vesicles in 38 fractions of 2 Gy. Fleet enema was used before Computed Tomography (CT) simulation. Patients were instructed to have a full bladder at time of simulation and treatment. For the full bladder preparation protocol, the advice was to void the bowel and bladder and then drink 300 ml of water within the next 15 min and 30 min later proceed with the RT planning scan. This process would then be repeated daily prior to each treatment. CT images with 3 mm slice thickness were acquired in our CT planning unit (Siemens, Biograph, Germany) 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. Eclipse (Varian medical system, version 15.1.51) planning system was used as an algorithm for planning. Body was contoured auto¬matically and surrounding critical structures were contoured manually. Magnetic Resonance Imaging (MRI) and CT fusion were used for counturing. Clinical Target Volume (CTV) included prostate and proximal seminal vesicle in intermediate-risk patients. Planning Target Volume (PTV) was created by a 8 mm expansion around CTV in all directions except 6 mm posterior margin. Contouring of OARs, including the rectum, bladder, femoral heads and bowel bag,

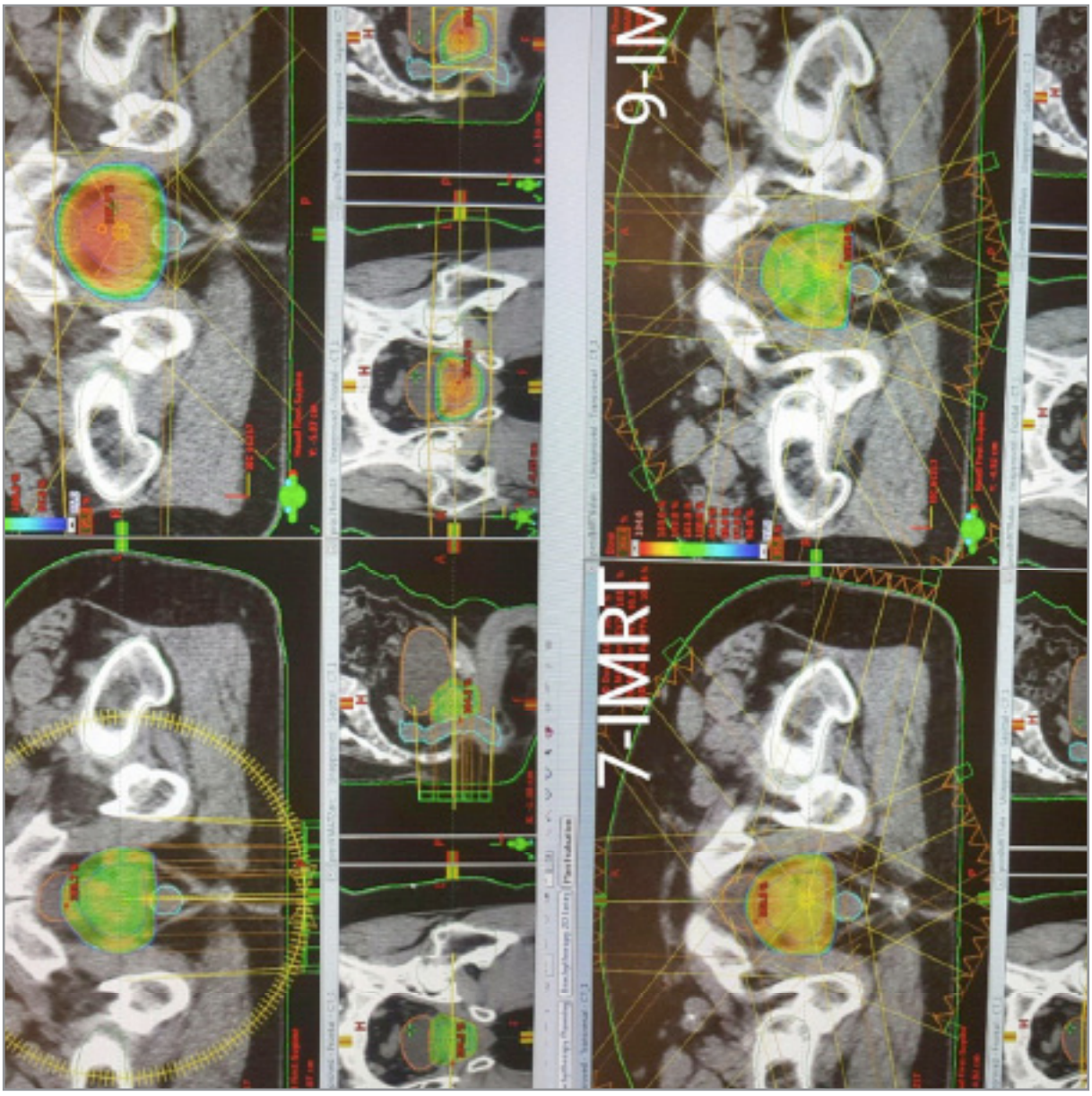

Figure 1. Dose distributions and dose volume histograms of four planning techniques
a) 3D-CRT **b)** 7-IMRT **c)** 9-IMRT **d)** VMAT

were defined according to the RTOG pelvic normal tissue contouring guidelines.[9] The OARs were contoured and considered as solid organs. The rectum was segmented starting at the level of ischial tuberosities to the rectosigmoid flexure, and the bladder was contoured from its base to the dome. The femoral heads were delineated to the level of the ischial tuberosities. The bowel bag was defined as the entire volume of peritoneal space in which the small bowel can move.

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.

The 3D-CRT plans used the traditional opposing 7-field lateral coplanar beams. Beams were individually optimally weighted to provide adequate

PTV coverage. Equally spaced 7-f and 9-f dynamic MLC-based IMRT plans were generated. All IMRT plans used a fixed-dose rate of 600 MU min-1. VMAT treatment plans used 2 partial arcs for treatment. All plans were generated with 6-MV photons using a multileaf collimator. In general, two-arc VMAT can achieve higher conformity and homogeneity compared with a one-arc plan. We used two arcs in all the RapidArc plans generated in this study because one-arc plan was not dosimetrically feasible given the complexity of the dose distribution6. An example of typical patient plans with the 4 treatment modalities is shown in the Figure 1.

Various methods were employed to minimize bias in the present study. Overall, 10 consecutive patients who required replanning were included in this study to minimize sampling bias. All contours were performed by a single radiation oncologist (C.S.) and approved by at least 2 additional radiation oncologist. A standard treatment planning optimization strategy was used for all plans. Conformity indexes, homogeneity indexes, and DVHs were assessed to ensure comparable PTV coverage between plans to minimize any bias when comparing normal tissue dosimetry between plans.

Treatment plans for the 4 different treatment techniques were compared using DVHs parameters. Minimum, mean, and maximum dose (Dmin, Dmean, and Dmax); HI; and CI were compared for the PTV between all 4 treatment modalities. HI was used to evaluate dose homogeneity within target volume. HI is calculated from the following formula:

HI = (D2-D98/Dp) x100%

where D2, D98, and Dp represent the doses to 2%, 98%, and prescribed dose to the PTV, respectively, and where[10] HI formula shows that lower HI values indicate a more homogeneous target dose (0 is the ideal value).

We used a CI value that was previously proposed by Van't Riet et al.[11] This CI simultaneously takes into account irradiation of the target volume and irradiation of the healthy tissues. CI is calculated from the following formula:

CI = (TVRI/TV)(TVRI/VRI)

where TVRI is the target volume covered by the reference isodose (95% of the prescribed dose), TV is the target volume, and VRI is the volume of the reference isodose. The CI ranges from 0 to 1, where 1 is the ideal value.

For OAR, the values of Dmean, V5, V10, V15, V20, V30, V40, V50, V60, V65, V70 and V75 for bladder; Dmean, V5, V10, V15, V20, V30, V40, V50, V60, V65, V70 and V75 for rectum; Dmean for penil bulb; Dmean for femoral heads and Dmax for small bowel were evaluated and compared. For this analysis, Vx was defined as the percentage of a given tissue volume receiving at least x Gy. Additionally, for all treatment plans, the DVH of the normal tissue sparing (body-PTV) and monitor unit settings required for each plan were calculated and compared. Statistical analyses were conducted using the IBM SPSS Statistic 19.0 software package. The data were analysed first to test for normality, and if it passed it was analysed for statistical difference with the parametric paired t-test and repeated measures analysis of variance (RM ANOVA). In comparing the data, if parametric conditions were provided, analysis of variance post hoc was used, otherwise, the Kruskal-Wallis test was used. In the paired group comparisons of quantifiable data, if parametric conditions were provided the Bonferroni modified test was applied, otherwise the Mann-Whitney U test was used. All statistical tests were 2 sided, with a threshold for statistical significance of $p< 0.05$.

RESULTS

The mean volume of the PTV was 128,1±42,3. Average mean doses for PTV were 78.81, 77.20, 77.07, and 77.11 Gy for 3-DCRT, 7-IMRT, 9-IMRT and VMAT plans, respectively. In all cases, 95% of the prescription dose covered at least 95% of each PTV. No point dose outside PTV's was 105% of the prescribed dose, and no point dose within PTV's was 110% of the prescribed dose. The average maximum and minimum PTV doses were 81.00 and 72.92 Gy for 3D-CRT, 79.10 and 68.84 Gy for 7-IMRT, 79.37 and 69.49 Gy for 9-IMRT, and 79.40 and 69.38 Gy for VMAT plans, respectively. In HI and CI; 7-IMRT, 9-IMRT and VMAT modalities were better than 3D-CRT. Fort he CI VMAT was better than 9-IMRT and 3D-CRT, but

Table 1. Dose statistics comparison for planning target volumes

Parameter	3D-CRT	7-IMRT	9-IMRT	VMAT	3D-CRT vs VMAT	7-IMRT vs VMAT	9-IMRT VMAT	3D-CRT 7-IMRT	3D-CRT vs 9-IMRT
Dmax(Gy)	81.10±0.40	79.10±1.13	79.38±1.01	79.40±1.12	0.004	n	n	0.001	0.003
Dmean(Gy)	78.82±0.18	77.20±0.35	77.07±0.31	77.12±0.33	0.000	n	n	0.000	0.000
Dmin(Gy)	72.93±0.44	68.85±4.35	69.49±5.00	69.39±5.09	n	n	n	n	n
D98(%)	75.13±0.13	75.20±0.29	75.20±0.40	75.45±1.20	n	n	n	n	n
D2(%)	80.78±0.39	78.17±0.64	78.02±0.50	78.25±0.54	n	n	n	n	n
HI	1.07±0.00	1.04±0.01	1.04±0.01	1.04±0.02	0.000	n	n	0.000	0.000
CI	0.62±0.02	0.81±0.046	0.79±0.05	0.84±0.02	0.000	n	0.021	0.000	0.000

n: statistically not significant, 3D-CRT:3 dimensional radiotherapy, IMRT: intensity modulated radiotherapy, VMAT: volumetric modulated arc therapy

no significant differecence was found with 7-IMRT modality. In the HI no significant difference was found between the other three treatment modalities. PTVDmax was found to be lower in 3D-CRT compared to other three treatment methods. The dose statistical dosimetric evaluation and comparison of the 4 planning techniques for PTV were listed in Table 1.

In the number of monitor units(MU) 3D-CRT was found to be lower than the other modalities, in VMAT the number of MU's was found to be lower than 7 and 9-IMRT modalities.

The average mean doses to the rectum were 33.96, 25.43, 25.43, and 24.94 Gy for 3D-CRT, 7-IMRT, 9-IMRT and VMAT plans, respectively. There was no significant difference in the doses of rectum mean, V30, V40, V50, V60 and V75 doses between 7-IMRT, 9-IMRT, and VMAT, but three treatment methods were found to be better than 3D-CRT.

The average mean doses to the bladder were 30.08, 26.81, 26.93, and 25.43 Gy for 3D-CRT, 7-IMRT, 9-IMRT and VMAT plans, respectively. No significant differences were found between 3D-CRT vs 7-IMRT, 3D-CRT vs 9-IMRT, 3D-CRT vsVMAT, 7-IMRT vs 9-IMRT, VMAT vs 7-IMRT and VMAT vs 9-IMRT plans for bladder mean doses and volume-based criteria(V5, V15, V20, V30, V40, V50, V60, V65, V70, V75).

There was no significant difference in the femoral head mean doses between 7-IMRT, 9-IMRT, and VMAT, but three treatment methods were found to be better than 3D-CRT. VMAT was better than 3D-CRT in femoral head V30, but there was no difference between other modalities.

The average mean doses to the penil bulb were 21.69, 15.47, 15.39, and 12.70 Gy for 3D-CRT, 7-IMRT, 9-IMRT and VMAT plans, respectively. The average maximum doses to the small bowel bag were 18.50, 18.91, 18.66, and 15.70 Gy for 3D-CRT, 7-IMRT, 9-IMRT and VMAT plans, respectively. There was no significant difference in the penil bulb mean doses and small bowel Dmax doses between 7-IMRT, 9-IMRT, and VMAT. The statistical dosimetric of doses and comparison of OARs were listed in Table 2.

DISCUSSION

Prostate cancer is the second tumor most commonly diagnosed among men around the World.[1] Indeed, about 1 million men are diagnosed with prostate cancer each year and this number is expected to increase due to general improvement in living conditions and therefore the world population aging. Nowadays, it is possible to detect such malignancy in its early stages and intervene promptly, by allowing low mortality rate, thanks to screening campaigns, early diagnoses and technological progress.[12,13]

Technological advancements continue to provide us with new treatment approaches that result in dose reduction to uninvolved nontarget tissues. In this study, we compared 4 common radiotherapy modalities for localised intermediate-risk prostate

Table 2. Dose statistics comparison for organs at risk

Parameter	3D-CRT	7-IMRT	9-IMRT	VMAT	3D-CRT vs VMAT	7-IMRT vs VMAT	9-IMRT vs VMAT	3D-CRT vs 7-IMRT	3D-CRT vs 9-IMRT
Rectum									
Mean (Gy)	34.0±5.9	25.4±4.5	25.4±5.5	24.9±3.6	0.001	n	n	0.003	0.003
V5(%)	76.8±10.4	73.6±11.6	74.8±11.8	74.1±9.6	n	n	n	n	n
V15(%)	63.0±10.1	57.5±10.4	57.0±12.8	56.5±8.9	n	n	n	n	n
V20(%)	58.6±10.0	52.6±10.4	52.3±14.5	52.7±7.9	n	n	n	n	n
V30(%)	51.7±10.19	38.2±9.1	38.8±12.2	37.6±6.4	0.015	n	n	0.022	0.031
V40(%)	43.2±9.5	22.9±7.8	21.0±6.3	20.5±4.4	0.000	n	n	0.000	0.000
V50(%)	34.3±9.0	14.9±5.3	15.5±6.6	13.7±3.6	0.000	n	n	0.000	0.000
V60(%)	21.8±5.6	10.6±4.0	10.7±3.6	9.6±3.0	0.000	n	n	0.000	0.000
V65(%)	16.8±4.7	8.8±3.3	8.8±3.4	7.8±2.8	n	n	n	n	n
V70(%)	13.1±3.5	6.5±2.6	6.8±2.9	6.1±2.4	n	n	n	n	n
V75(%)	7.4±2.7	4.1±1.9	4.5±2.4	3.4±2.0	0.002	n	n	0.015	0.041
Bladder									
Mean (Gy)	30.1±15.0	26.8±10.2	26.9±10.3	25.4±10.2	n	n	n	n	n
V5(%)	70.4±21.2	71.2±20.6	71.4±20.8	72.2±19.7	n	n	n	n	n
V15(%)	56.2±25.0	50.8±20.6	52.0±21.6	49.0±20.4	n	n	n	n	n
V20(%)	51.3±24.5	46.2±18.5	46.9±19.8	43.7±18.7	n	n	n	n	n
V30(%)	40.3±23.2	37.2±16.7	37.5±16.5	34.8±17.0	n	n	n	n	n
V40(%)	32.8±20.2	28.6±15.0	28.9±14.5	26.3±14.8	n	n	n	n	n
V50(%)	26.3±16.9	21.6±11.6	21.8±11.5	19.4±11.3	n	n	n	n	n
V60(%)	21.5±14.4	16.3±8.9	16.3±8.4	14.6±8.6	n	n	n	n	n
V65(%)	18.8±12.3	13.8±7.7	13.8±7.5	12.2±7.2	n	n	n	n	n
V70(%)	14.9±9.7	11.3±6.2	11.7±6.2	10.4±6.0	n	n	n	n	n
V75(%)	10.2±7.2	8.2±4.4	8.3±4.5	7.8±4.6	n	n	n	n	n
Femoral head									
Mean (Gy)	21.93±4.4	16.29±4.93	16.0±2.83	16.00±3.54	0.013	n	n	0.02	0.01
V30(%)	17.0±8.1	11.3±13.5	13.7±9.2	4.4±5.4	0.033	n	n	n	n
Penil bulb									
Mean (Gy)	21.7±18.55	15.47±9.84	15.39±9.6	12.7±7.5	n	n	n	n	n
Small bowel									
Dmax (Gy)	18.5±19.3	18.9.50±19.29	18.7±19.2	15.7±15.6	n	n	n	n	n

n: statistically not significant, 3D-CRT:3 dimensional radiotherapy, IMRT: intensity modulated radiotherapy, VMAT: volumetric modulated arc therapy

cancer for a randomly selected cohort of 10 patients. Our primary objective was to determine the capability of each modality to provide PTV coverage and simultaneously evaluate nontarget organ dose limitations.

IMRT has long been standard of care in the treatment of patients with prostate cancer as a viable alternative to surgery. Zelefsky et al, 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.[14] In our study, the plans of IMRT and 3D-CRT were compared

in terms of dose distribution and doses to critical structures in patients with intermediate-risk prostate cancer, and we found that IMRT techniques were superior over 3D-CRT by better dose homogeneity and lower critical organ doses.

Generally, better quality IMRT plans can be obtained with a larger number of fields at the expense of higher MUs and longer treatment times. In this study, we decided to use 7-f IMRT and 9-f IMRT, which are the irradiation techniques used in actual clinical practice. We set the IMRT dose rate at 600 MU min-1, which is currently used for patient treatment in our institution. During the optimisation process of each subject, special care was taken to match the PTV coverage among RapidArc plans and the two IMRT plans, with the aim of avoiding a trade-off between PTV coverage and OAR sparing.

VMAT was demonstrated to produce dose distributions that had a better conformity to the PTV than IMRT. This outcome supports the findings from previous published research. The improved conformity observed using VMAT is a consequence of arc delivery that delivers dose from 360^0.[6,15,16] In our study, the CI for VMAT was better than 9-IMRT and 3D-CRT, but no significant differecence was found with 7-IMRT modality.

There is a growing body of evidence supporting that VMAT treatment of prostate cancer is significantly faster and requires fewer MUs compared to IMRT.[17,18] As expected, our results demonstrate that the treatment time using the VMAT technique was significantly faster than using IMRT. In VMAT the number of MU's was found to be lower than 7 and 9-IMRT modalities. The reduction in treatment time could reduce the intrafractional pelvic and prostate motion. Moreover, this time saving could be used to increase patient throughput on a treatment unit that provides additional time for online image guidance without increasing the overall treatment time. Meanwhile, the decrease in MUs required with VMAT reduces whole-body exposure of the patient owing to leakage radiation, which is a concern regarding the development of secondary malignancies.[19]

In our study, there was no significant difference in the doses of rectum mean, V30, V40, V50, V60, V75 and femoral head mean doses between 7-IMRT, 9-IMRT, and VMAT, but three treatment methods were found to be better than 3D-CRT. Also, there was no significant difference in the bladder mean doses and volume-based doses between four modalities. VMAT was better than 3D-CRT in femoral head V30, but there was no difference between other modalities.

There are several limitations to the current study. This is a dosimetric study, and it does not consider vital aspects required for clinical use. The treatment modalities studied other than 3D- CRT radiotherapy have the potential to improve, or at least not compromise PTV dose coverage, then they are of potential clinical benefit. The number of patients used for comparison in this study was limited to 10, this may be improved in the future to obtain a better sample. To expand the sample of population for our recommendations, we attempted to select both patients with normal anatomy and those with intermediate risk prostate cancer patients. The effect of organ motion was not assessed in this study. Clearly there is some degree of organ motion when treating the prostate, and the typical boundaries with conventional techniques account for this motion.

From another perspective, our results demonstrate that the difference in the plan quality of VMAT and IMRT is due to the difference in the number of beam angles and the level of modulation from each angle used in the two modalities. Our results show that having a large number of beam angles but few modulations (control points) from each angle is superior (in terms of plan quality) to having many modulations from each angle but a small number of beam angles. However, a large number of modulations from many beam angles in IMRT may compensate for the insufficient number of beams and produce a plan quality similar to that of VMAT, when the number of beams in IMRT is sufficiently large.

Based on the dosimetric findings in this study, there is a potential clinical advantage for 7-IMRT, 9-IMRT, or VMAT treatment modalities compared with 3D-CRT for the treatment of localised prostate cancer. VMAT treatment duration and femoral head V30 dose were superior to IMRT techniques. All these 3 modalities showed superiority with less

variation among themselves compared with 3D-CRT plans, with the exception of treatment time. Clinical investigation is warranted to determine if these treatment approaches will translate into a reduction in radiation therapy-induced toxicities.

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