FULL PAPER

Simultaneous integrated boost to intraprostatic lesions using different energy levels of intensity-modulated radiotherapy and volumetric-arc therapy

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Objective: This study compared the dosimetry of volumetric-arc therapy (VMAT) and intensity-modulated radiotherapy (IMRT) with a dynamic multileaf collimator using the Monte Carlo algorithm in the treatment of prostate cancer with and without simultaneous integrated boost (SIB) at different energy levels.

Methods: The data of 15 biopsy-proven prostate cancer patients were evaluated. The prescribed dose was 78 Gy to the planning target volume (PTV78) including the prostate and seminal vesicles and 86 Gy (PTV86) in 39 fractions to the intraprostatic lesion, which was delineated by MRI or MR-spectroscopy.

Results: PTV dose homogeneity was better for IMRT than VMAT at all energy levels for both PTV78 and PTV86. Lower rectum doses (V_{30}–V_{50}) were significantly higher with SIB compared with PTV78 plans in both

IMRT and VMAT plans at all energy levels. The bladder doses at high dose level (V_{60}–V_{80}) were significantly higher in IMRT plans with SIB at all energy levels compared with PTV78 plans, but no significant difference was observed in VMAT plans. VMAT plans resulted in a significant decrease in the mean monitor units (MUs) for 6, 10, and 15 MV energy levels both in plans with and those without SIB.

Conclusion: Dose escalation to intraprostatic lesions with 86 Gy is safe without causing serious increase in organs at risk (OARs) doses. VMAT is advantageous in sparing OARs and requiring less MU than IMRT.

Advances in knowledge: VMAT with SIB to intraprostatic lesion is a feasible method in treating prostate cancer. Additionally, no dosimetric advantage of higher energy is observed.

Randomized trials have shown a gain in biochemical relapse-free survival using dose escalation for prostate cancer.[1] However, isolated local failure is still reported in nearly one-third of patients, even with higher radiotherapy (RT) doses.[1] Local recurrence is of clinical importance because a relationship has been suggested between local control, distant metastasis and survival.[2] It has also been demonstrated that intraprostatic failure mainly originates at the initial tumour location as a result of intrinsic resistance of a fraction of the tumour clones, which implies that selective dose escalation to the dominant intraprostatic lesion using simultaneous integrated boost (SIB) might be beneficial.[3]

With new RT techniques, such as intensity-modulated RT (IMRT) and volumetric-arc therapy (VMAT), SIB could be delivered without increasing acute toxicity.[4–7] Several recent studies have performed dosimetric comparison of IMRT and VMAT plans in prostate cancer;[8–10] however, dosimetric evaluation of IMRT and VMAT plans delivering

SIB is rare. In these studies, target volume and organs at risk (OARs) doses may vary with different treatment planning systems. Another aspect not often addressed in these planning studies is the photon energy level.[4,8,9,11] Although higher energy photons have the potential advantage of reduced attenuation with depth, this may in turn increase the risk of secondary malignancies because of the presence of neutrons generated in the accelerator head at treatment energies >8 MV.[12]

Functional imaging techniques can clearly demonstrate tumour within the prostate. MRI, MR spectroscopy (MRS) and positron emission tomography are capable of demonstrating intraprostatic lesions (IPLs).[13] The advent of combined MRI with MRS or dynamic contrast enhanced (DCE)-MRI improves the detection rate of tumours within the prostate.[13–15]

The aim of the present study was to make dosimetric comparisons of VMAT and 7-field IMRT with dynamic

multileaf collimators (MLCs) using the Monte Carlo algorithm with XVMC code in the treatment of prostate cancer with or without SIB, which can provide improved dose calculation accuracy and has been implemented successfully in the clinical setting.[16,17] Additionally, the impact of three photon energies on target volumes, OARs and normal tissue was evaluated in IMRT and VMAT plans.

METHODS AND MATERIALS

The CT and MRI/MRS data of 15 consecutive intermediate risk prostate cancer patients were selected for the present study. The inclusion criterion was the presence of an MRI or MRS detected IPL, which was defined as an MRI- and/or MRS-detected prostate tumour with characteristics suggesting a high probability of malignancy according to the criteria of Cruz et al[18] for MRI and Villeirs et al[13] for MRS.

CT and MRI

All patients had undergone 2.5-mm slice thickness CT with a comfortably full bladder and empty rectum.[19] MRI scans were acquired with the same conditions as CT. Because of the negative effects of androgen deprivation on the metabolism of prostate cancer cells, MRS examinations were performed in the absence of or before hormone therapy.[20] The MRI scans used for image fusion and treatment planning were acquired on a 1.5 T Siemens Avanto® MRI System (Siemens Healthcare, Erlangen, Germany). T_2 weighted (T_2W) diffusion weighted images and DCE-MRI examinations were performed using an eight-element phased array coil during the scans without an endorectal coil. T_1, T_2, MRS, apparent diffusion coefficient (ADC) and DCE images of the prostate were reviewed by an experienced radiologist (GE). The IPLs identified on T_2, ADC, DCE images or MRS were used for SIB planning.[21] The CT and MRI data were digitally transferred to an Eclipse™ (Varian Medical Systems, Palo Alto, CA) workstation and coregistered to delineate the regions of interest. The CT and MRI fusion was done by automated computerized fusion and then checked manually, as described in other IPL boost studies.[14,21,22]

Clinical target volume (CTV) included the prostate and the entire seminal vesicles. The planning target volume for 78 Gy (PTV78) was defined as CTV with a margin of 5 mm posterior and 8 mm in other directions.[19,23] The delineation of IPL was done together with a radiologist (Figure 1). The PTV for 86 Gy (PTV86) was created using a three-dimensional, isotropic, 4-mm margin around the IPL.[6] The OARs included the rectum, sigmoid, bladder and femoral heads. The rectum was delineated

from the anal verge to the recto-sigmoid junction.[24] The femoral heads were contoured to the level of ischial tuberosities.

Treatment plans

The treatment plans were generated using IMRT and VMAT techniques. The IMRT plans consisted of seven coplanar fields, at gantry angles of 0°, 37°, 75°, 135°, 225°, 285° and 327°. The plans were calculated with Monaco treatment planning system (CMS; Elekta, Crawley, UK) using the Monte Carlo algorithm and a sliding window MLC delivery technique. The VMAT plans consisted of a single 360° arc. Gantry speed, MLC leaf position and dose rate varied continuously during VMAT delivery.[25] For each patient, three different plans with 6, 10, and 15 MV energies were generated for both IMRT and VMAT techniques. Additionally, the same plans were made with SIB. All plans were created for delivery on an Elekta linear accelerator (Elekta) equipped with an MLC and designed for dynamic IMRT and VMAT. The leaf width of the Elekta accelerator used in the present study was 0.4 cm, and the leaves did not interdigitate.

Dose prescription

Two plans were generated and each plan was normalized to deliver 99% of CTV and 95% of PTV78 and PTV86 receiving at least 78 and 86 Gy, respectively. All treatments were planned to be delivered in 39 fractions. Dose constraints for the rectum and bladder were based on Radiation Therapy Oncology Group recommendations,[26] where V_{50} and V_{70} for the rectum were 50% and 20% and V_{55} and V_{70} for the bladder were 50% and 30%, respectively. Normal tissue complication probability values for rectum and bladder were <10% and ≤5%, respectively.[27,28] The femoral heads were limited to receive a maximum of 50 Gy.

Plan evaluation

We evaluated the treatment plans by comparing the planning results with the planning and physical indices (Table 1). D_2 and D_{98} were used as surrogates for maximum and minimum doses for target volumes, respectively. Target dose homogeneity index (TDI) was calculated as: $TDI = [(D_2 - D_{98})/D_{50}]$, where D_{50} is the minimal dose to 50% of target volume. Additionally, the heterogeneity index (HI) was defined as $HI = D_1/D_{95}$, where D_1 and D_{95} are minimal dose to 1% and 95% of target volume, respectively. For the rectum, D_{2cc} was defined as the minimum dose value in the 2-cc volume receiving the highest dose. To quantify the dose to normal tissues, relative volumes of the 50% isodose ($V_{50\%}$) was determined.

Dose verification

Dose verification for the treatment plan was performed using a two-dimensional (2D) ion chamber array detector (IMRT

Figure 1. Representative image demonstrating intraprostatic lesion (a) in diffusion weighted MR scan and (b) coregistered MR and CT scans. (c) PTV86 and PTV78 are generated with given margins to intraprostatic lesion and prostate.
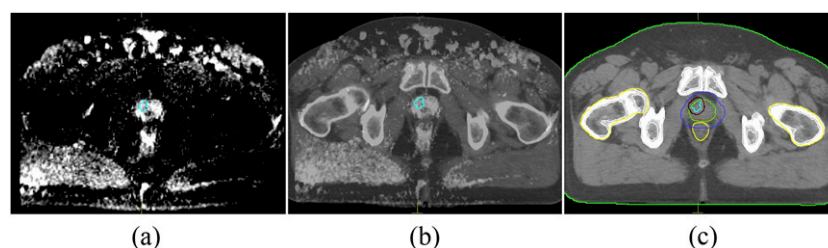

(a) (b) (c)

Table 1. Dosimetric analysis of intensity-modulated radiotherapy (IMRT) and volumetric-arc therapy (VMAT) plans with different energy levels

Parameters	6 MV			10 MV			15 MV		
	IMRT	VMAT	*p*-value	IMRT	VMAT	*p*-value	IMRT	VMAT	*p*-value
CTV									
D_2 (Gy)	81.860 ± 0.600	82.220 ± 0.900	0.020	81.470 ± 0.610	82.150 ± 1.000	0.001	81.520 ± 0.570	81.960 ± 0.900	0.030
D_{98} (Gy)	78.540 ± 0.370	78.580 ± 0.830	0.890	78.470 ± 0.290	78.540 ± 0.800	0.760	78.630 ± 0.310	78.550 ± 0.840	0.680
D_{99} (Gy)	78.320 ± 0.380	78.270 ± 0.900	0.840	78.230 ± 0.350	78.280 ± 0.870	0.860	78.390 ± 0.380	78.240 ± 0.940	0.490
TDI (%)	0.041 ± 0.006	0.045 ± 0.012	0.230	0.0370 ± 0.007	0.045 ± 0.013	0.020	0.036 ± 0.008	0.043 ± 0.013	0.050
D_{mean} (Gy)	80.170 ± 0.530	80.290 ± 0.610	0.500	79.990 ± 0.470	80.230 ± 0.610	0.190	80.190 ± 0.390	80.190 ± 0.700	0.670
PTV (78 Gy)									
D_2 (Gy)	82.420 ± 0.730	82.890 ± 0.590	0.030	82.300 ± 0.610	82.920 ± 0.660	0.010	82.360 ± 0.750	82.770 ± 0.650	0.060
D_{98} (Gy)	77.320 ± 0.280	77.330 ± 0.290	0.920	77.230 ± 0.170	77.260 ± 0.240	0.740	77.130 ± 0.290	77.290 ± 0.260	0.770
D_{99} (Gy)	76.770 ± 0.310	76.770 ± 0.400	0.980	76.640 ± 0.260	76.710 ± 0.300	0.450	76.550 ± 0.300	76.680 ± 0.310	0.340
D_{mean} (Gy)	80.080 ± 0.350	80.400 ± 0.420	0.006	80.020 ± 0.390	80.410 ± 0.480	0.008	80.090 ± 0.350	80.35 ± 0.500	0.080
TDI	0.061 ± 0.008	0.045 ± 0.012	<0.001	0.063 ± 0.009	0.045 ± 0.013	<0.001	0.065 ± 0.012	0.043 ± 0.013	<0.001
HI	1.040 ± 0.007	1.046 ± 0.013	0.080	1.038 ± 0.008	1.046 ± 0.014	0.060	1.037 ± 0.009	1.044 ± 0.014	0.070
MU	624.000 ± 70.000	573.000 ± 54.000	0.002	598.000 ± 73.000	554.000 ± 58.000	0.005	587.000 ± 66.000	544.000 ± 61.000	0.005
PTV (86 Gy)									
D_2 (Gy)	87.980 ± 0.790	88.160 ± 0.900	0.140	87.860 ± 0.680	88.460 ± 0.660	0.130	87.940 ± 0.800	88.020 ± 0.590	0.500
D_{98} (Gy)	78.050 ± 0.700	77.740 ± 0.740	0.100	77.880 ± 0.660	77.610 ± 0.630	0.140	77.760 ± 0.760	77.590 ± 0.610	0.400
D_{99} (Gy)	77.410 ± 0.700	77.010 ± 0.680	0.030	77.240 ± 0.680	76.840 ± 0.600	0.040	77.060 ± 0.790	76.790 ± 0.610	0.240
D_{mean} (Gy)	82.290 ± 0.930	82.580 ± 1.230	0.180	82.240 ± 0.980	82.640 ± 1.000	0.070	82.160 ± 0.880	82.590 ± 1.010	0.030
TDI	0.046 ± 0.008	0.048 ± 0.011	0.001	0.044 ± 0.009	0.045 ± 0.011	0.030	0.041 ± 0.010	0.043 ± 0.011	0.010
HI	1.048 ± 0.009	1.049 ± 0.011	0.001	1.046 ± 0.010	1.047 ± 0.012	0.030	1.042 ± 0.011	1.044 ± 0.011	0.010
MU	604.000 ± 64.000	549.000 ± 47.000	<0.001	554.000 ± 58.000	515.000 ± 53.000	0.003	551.000 ± 63.000	516.000 ± 47.000	0.020

CI, conformity index; CTV, clinical target volume; D_n, minimal dose to n% of target volume; HI, homogeneity index; MU, monitor unit; PTV, planning target volume; TDI, target dose homogeneity index.

Figure 2. Representative axial CT slices showing 50% of prescribed dose distributions for (a) 6 MV, (b) 10 MV, (c)15 MV energy intensity-modulated radiotherapy (IMRT) plans and (d) 6 MV, (e) 10 MV, (f) 15 MV energy volumetric-arc therapy (VMAT) plans.
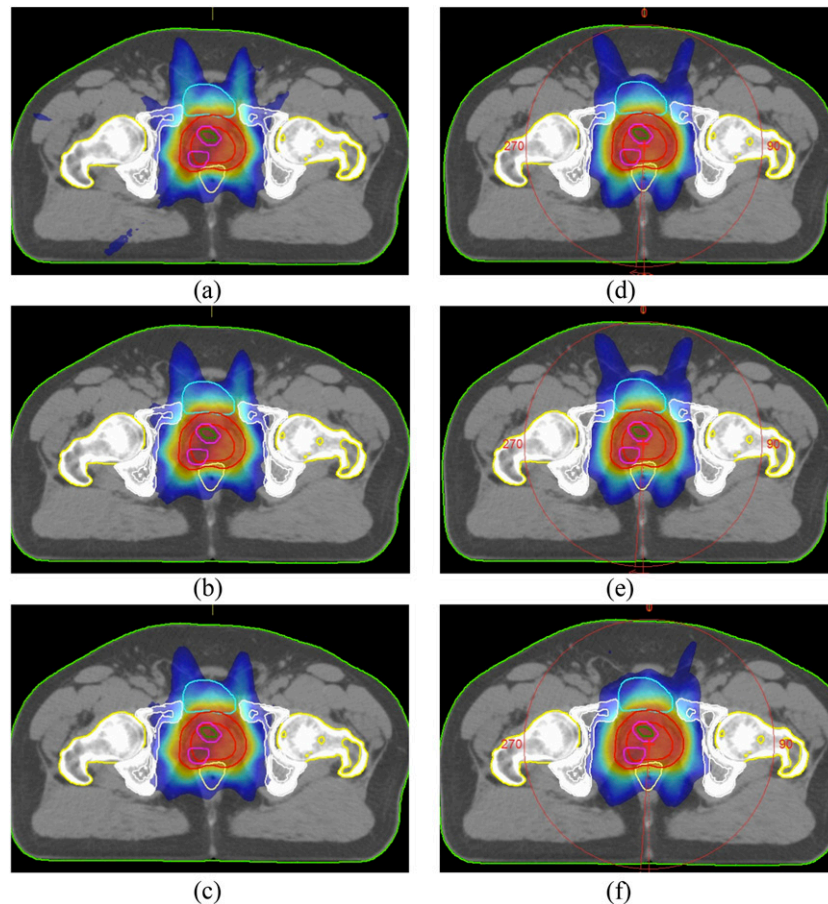
MatriXX™; IBA Dosimetry, GmbH, Germany) that consists of 1020 ion chambers. For dose verification, the MatriXX was inserted into a MULTICube Plastic Water® phantom (CIRS, Norfolk, VA). All IMRT and VMAT plans were recalculated on the MatriXX phantom for each energy level, which was previously scanned and defined as a quality assurance phantom on the planning system. Dose map of the plan at effective 2D array depth was transferred to the dosimetry system. Dose verification used for calculation of 2D γ index, percentage of the $\gamma < 1$ averaged 96.87 ± 1.61 using 3% dose 3-mm distance criteria.

Statistical analysis

Statistical analysis was performed using SPSS® software v. 17.0 (SPSS Inc., Chicago, IL). The Wilcoxon's matched-pairs test was used to determine statistical differences between volumes and doses in IMRT *vs* VMAT plans. The dose–volume parameters of target volumes and OARs for each energy level were also measured and compared across energy levels. The comparison was also made for 78 and 86 Gy plans. The Mann–Whitney U-test was used to compare volumes or dose values in independent patient groups. All p-values reported are two-sided and a $p < 0.05$ was considered significant.

RESULTS

The mean CTV and PTV78 volumes were $34.2 \, \text{cm}^3$ (range, $19.8–74.6 \, \text{cm}^3$) and $148.3 \, \text{cm}^3$ (range, $98.6–225.8 \, \text{cm}^3$), respectively.

The mean IPL and PTV86 volumes were $1.4 \, \text{cm}^3$ (range, $0.4–5.3 \, \text{cm}^3$) and $6.6 \, \text{cm}^3$ (range, $3.3–12.2 \, \text{cm}^3$), respectively. Figure 2 shows representative axial sections depicting dose distributions for IMRT and VMAT plans with different energy levels.

Target volume doses

The dosimetric parameters for target volumes are summarised in Table 1. The average maximum doses for CTV and PTV78 (D_2) were significantly higher in VMAT plans than IMRT plans for all energy levels; however, minimum doses (D_{98}) did not differ significantly. No significant difference was found for D_2 and D_{98} values between IMRT and VMAT plans at all energy levels for PTV86. The mean dose of PTV86 was significantly higher in VMAT plans than in IMRT plans at 15 MV, while the difference was close to the level of significance at 6 and 10 MV.

PTV dose homogeneity was better in IMRT plans than in VMAT plans at all energy levels for both PTV78 and PTV86. For PTV78, the HI had a borderline significance, whereas the HIs of PTV86 were significantly better in IMRT plans than in VMAT plans at all energy levels (Figure 3). No significant difference was observed in normal tissue doses between IMRT and VMAT plans. SIB technique did not cause a significant increase in normal tissue doses both with IMRT and VMAT techniques.

Figure 3. Representative axial CT slices showing 95% of prescribed dose distributions for (a) 6 MV, (b) 10 MV, (c) 15 MV energy intensity-modulated RT (IMRT) plans and (d) 6 MV, (e) 10 MV, (f) 15 MV energy volumetric-arc therapy (VMAT) plans.
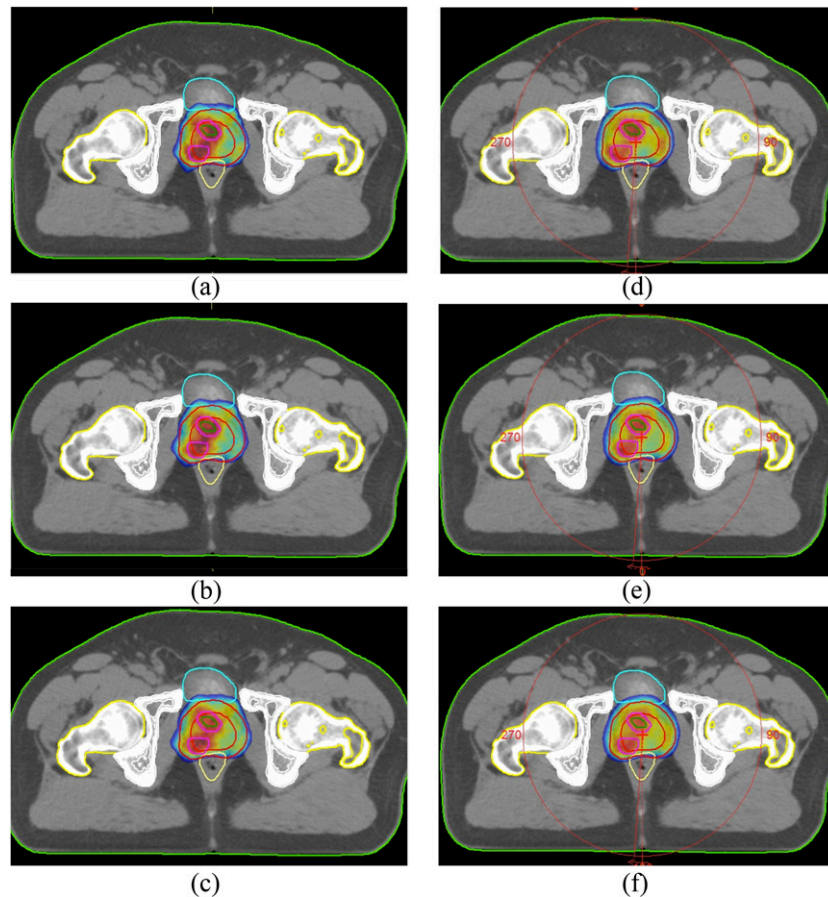
Organ at risk doses

A comparison of the dosimetric parameters of OARs for each of the plan types is listed in Table 2. Compared with IMRT, VMAT plans achieved lower doses for all OARs for nearly all dosimetric end points. Only femur doses were higher in VMAT plans. Although lower rectum doses (V_{30}–V_{50}) were significantly higher in SIB plans than PTV78 plans in both IMRT and VMAT plans at all energy levels; there were no significant differences at high dose levels (Figure 4). The bladder doses at high dose levels (V_{60}–V_{80}) were significantly higher in IMRT plans with SIB at all energy levels compared with PTV78 plans (Figure 5). However, there was no significant difference in bladder doses between SIB plans and PTV78 plans with VMAT at all energy levels.

Compared with IMRT plans, VMAT plans achieved 8.1%, 7.4% and 7.3% relative decreases in the mean number of monitor units (MUs) required for RT delivery in PTV78 plans at 6, 10 and 15 MV energy levels, respectively. VMAT plans with SIB achieved 9.1%, 7.0% and 6.3% decrease in the mean number of MUs at 6, 10 and 15 MV energy levels, respectively.

Dose verification

Dose verification used for calculation of 2D γ index, percentage of the γ <1 using 3% dose and 3-mm distance criteria averaged 97.86 ± 0.98 at 6 MV, 97.42 ± 1.11 at 10 MV and 96.83 ± 1.35 at 15 MV for SIB-IMRT plans. For SIB-VMAT plans, it was 97.89 ± 0.93, 97.73 ± 0.92 and 96.81 ± 0.91 at 6, 10, and 15 MV plans, respectively.

DISCUSSION

This study evaluated the dose distribution of target volumes, and OARs were assessed with two different RT techniques at three energy levels. Moreover, the SIB technique, where higher radiation doses were delivered to the IPL, did not cause any serious increment in OAR doses except for low-dose regions in the rectum and high-dose regions in the bladder. The most prominent advantage of VMAT is a significant decrease in treatment MUs, which means less radiation and shorter treatment time.

Dose escalation for prostate cancer causes improved biochemical control and reduced distant metastasis.[1] However, local failure still occurs in one-third of patients after 78 Gy external RT (ERT).[1] The original IPL is the most frequent location of relapse.[3] Therefore, selectively boosting radiation to these lesions to a very high dose has been hypothesized to be a more effective method to improve the therapeutic ratio than a homogeneous, but more modest, dose escalation to the entire prostate.[29]

The accuracy of MRI and MRS in localizing prostate cancer was 82–85%, and the authors emphasized the importance of incorporating functional imaging techniques such as MRS for prostate cancer RT planning.[30,31] Although MRI with endorectal

Table 2. Dosimetric comparison of organs at risk doses of intensity-modulated radiotherapy (IMRT) and volumetric-modulated arc therapy (VMAT) plans with different energy levels for simultaneous integrated boost plan

Organs at risk	6 MV			10 MV			15 MV		
	IMRT	VMAT	*p*-value	IMRT	VMAT	*p*-value	IMRT	VMAT	*p*-value
Rectum									
V_{30} (%)	75.92 ± 8.05	77.10 ± 8.34	0.470	77.52 ± 6.64	76.28 ± 9.99	0.580	77.25 ± 8.79	76.98 ± 9.79	0.910
V_{40} (%)	60.75 ± 9.96	59.27 ± 11.03	0.450	60.61 ± 8.87	56.78 ± 12.09	0.200	62.05 ± 11.65	59.50 ± 13.00	0.260
V_{50} (%)	38.86 ± 7.85	37.19 ± 8.65	0.150	38.73 ± 7.55	35.96 ± 8.98	0.090	40.40 ± 11.14	37.65 ± 10.13	0.130
V_{60} (%)	25.44 ± 7.29	23.96 ± 7.36	0.040	24.98 ± 6.59	23.52 ± 6.90	0.040	25.76 ± 8.13	24.03 ± 7.18	0.070
V_{65} (%)	20.09 ± 6.09	19.00 ± 5.97	0.050	19.39 ± 5.37	18.48 ± 5.97	0.060	19.75 ± 6.02	18.75 ± 6.02	0.060
V_{70} (%)	14.56 ± 5.08	13.78 ± 4.85	0.020	13.76 ± 4.57	13.50 ± 4.64	0.210	13.68 ± 4.64	13.55 ± 4.88	0.500
V_{75} (%)	8.51 ± 3.24	8.02 ± 2.74	0.110	7.85 ± 2.85	7.94 ± 3.18	0.670	7.57 ± 2.84	7.91 ± 3.21	0.430
V_{80} (%)	1.75 ± 0.34	1.53 ± 0.33	0.340	1.56 ± 0.30	1.77 ± 0.42	0.430	1.48 ± 0.25	1.77 ± 0.40	0.300
D_{2cc} (Gy)	78.08 ± 1.98	77.74 ± 2.14	0.090	77.79 ± 2.17	77.62 ± 2.60	0.570	77.59 ± 2.45	77.87 ± 2.47	0.260
D_{mean} (Gy)	44.70 ± 3.46	44.46 ± 3.66	0.640	44.79 ± 2.60	43.89 ± 4.09	0.240	44.83 ± 3.72	44.55 ± 4.45	0.680
Bladder									
V_{40} (%)	69.03 ± 19.81	64.43 ± 22.92	0.100	68.94 ± 18.71	62.63 ± 23.51	0.030	70.19 ± 19.57	62.68 ± 22.31	0.007
V_{60} (%)	41.50 ± 17.93	36.90 ± 17.16	0.002	40.03 ± 17.20	36.95 ± 18.23	0.040	39.76 ± 16.73	36.85 ± 16.80	0.030
V_{70} (%)	29.56 ± 13.30	27.23 ± 13.48	0.020	28.44 ± 12.64	27.28 ± 14.24	0.270	12.44 ± 3.21	13.07 ± 3.37	0.120
V_{80} (%)	12.74 ± 6.08	10.77 ± 4.71	0.090	10.99 ± 5.17	11.67 ± 6.34	0.580	4.87 ± 1.26	5.16 ± 1.33	0.910
D_{mean} (Gy)	51.16 ± 12.12	48.66 ± 11.21	0.001	50.60 ± 11.72	48.40 ± 11.90	0.004	50.48 ± 11.37	48.47 ± 10.99	0.020
Sigmoid colon									
D_{50} (Gy)	8.56 ± 6.73	8.66 ± 6.03	0.830	8.53 ± 7.04	9.21 ± 7.30	0.250	8.83 ± 7.81	9.59 ± 7.99	0.260
D_{max} (Gy)	28.10 ± 26.16	32.75 ± 29.12	0.290	29.52 ± 26.57	34.58 ± 29.64	0.250	30.99 ± 26.66	35.35 ± 29.59	0.320
Left femur									
D_{50} (Gy)	10.25 ± 4.48	18.38 ± 4.32	<0.001	10.61 ± 4.19	18.77 ± 3.73	<0.001	11.04 ± 4.00	18.90 ± 3.32	<0.001
D_{max} (Gy)	39.84 ± 4.08	38.94 ± 6.07	0.460	40.01 ± 4.51	39.60 ± 5.56	0.710	40.73 ± 3.96	40.21 ± 5.89	0.630
Right femur									
D_{50} (Gy)	12.88 ± 6.35	17.65 ± 4.19	0.010	12.75 ± 5.41	18.46 ± 3.08	0.006	13.44 ± 5.37	18.46 ± 3.08	0.006
D_{max} (Gy)	41.17 ± 3.74	38.72 ± 5.91	0.130	40.38 ± 4.20	39.34 ± 5.59	0.490	41.09 ± 4.05	38.99 ± 5.50	0.190
Normal tissue									
$V\%_{50}$ (cc)	2.88 ± 0.74	2.06 ± 0.65	0.001	2.46 ± 0.60	1.91 ± 0.63	0.001	2.36 ± 0.58	1.88 ± 0.61	0.001

D_n, minimal dose to n% of target volume; V_n, percentage organ volume receiving $\geq n$ Gy.

Figure 4. Rectum doses at different energy levels (a–c) in intensity-modulated RT (IMRT) plans and (d–f) volumetric-arc therapy (VMAT) plans. Solid lines represent plans with simultaneous integrated boost (SIB, PTV86). Dashed lines represent plans without SIB.
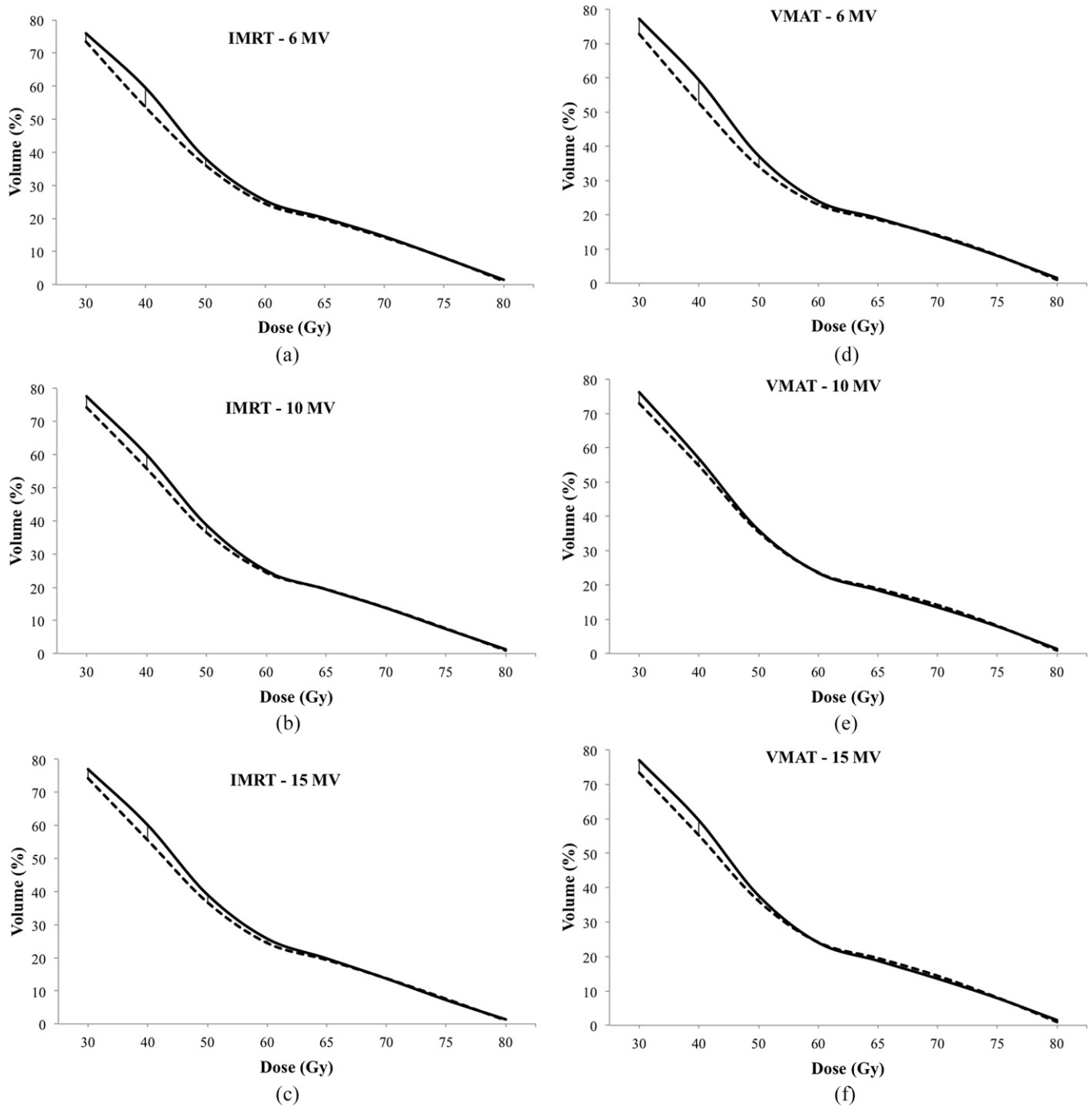
coil has higher sensitivity for staging, this coil can distort the prostate.[32] Therefore, appropriate image fusion was only possible in MRI and CT acquired using the same conditions. In this study, we preferred to use MRI or MRS in detecting the IPL for treatment planning. To obtain adequate images, MRI scans were acquired with the same conditions as CT. Additionally, one experienced radiologist who was aware of detailed histopathological findings contoured the tumour in coregistered CT and MRI images on an Eclipse work station.

Techniques such as VMAT and IMRT are able to generate conformal isodoses, which significantly reduce the OAR doses and normal tissue toxicity. There are numerous dosimetric studies comparing plans with and without SIB. Early results are encouraging, with patients who were treated even up to 94.5 Gy with acceptable early toxicity rates. In these studies, although the delivery techniques for IMRT and VMAT were similar, the results were conflicting. These heterogeneous results may be due to different target definitions and dose constraints. De Meerleer

Figure 5. Bladder doses at different energy levels (a–c) in intensity-modulated RT (IMRT) plans and (d–f) volumetric-arc therapy (VMAT) plans. Solid lines represent plans with simultaneous integrated boost (SIB, PTV86). Dashed lines represent plans without SIB.
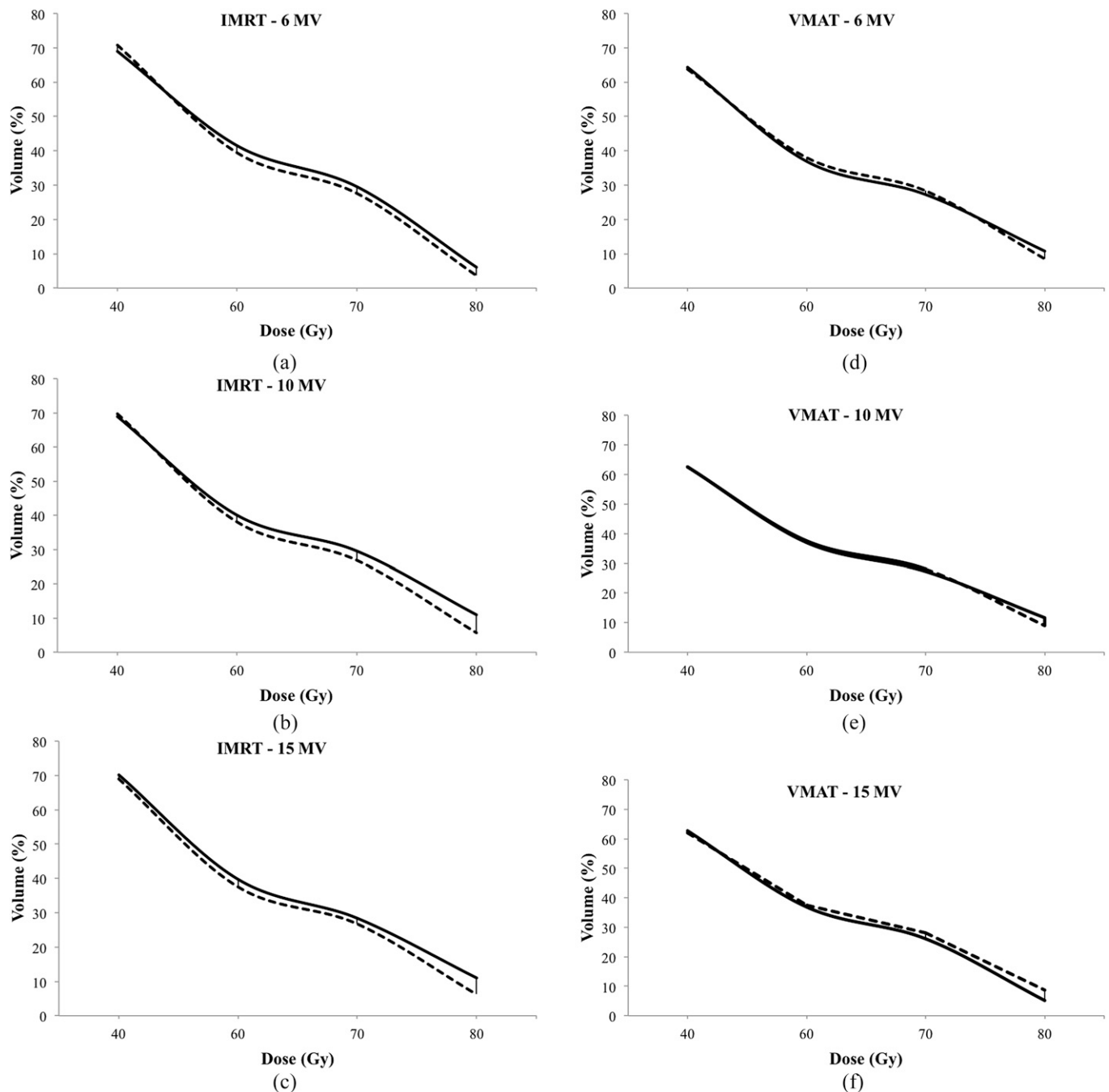
et al[14] compared IMRT plans with 74 Gy prescribed to PTV with or without a simultaneous dose of 80 Gy to the gross tumour volume with no margin detected by MRI and found that the rectum dose levels (V_{70} and D_{max}) were increased with SIB plans. Similarly, Pinkawa et al[6] demonstrated improved dose escalation to the macroscopic tumour with minor rectum and bladder dose changes, similar to our findings. In this study, we escalated the IPL dose to 86 Gy with 78 Gy delivered to prostate and seminal vesicles. For estimated α/β ratios of 1.5 and 3.0, IPL

dose corresponds to a total dose of 89 and 90 Gy, respectively, in conventional fractionation according to the linear-quadratic model.

There are few clinical studies assessing acute toxicity in patients treated with dose escalated SIB plans.[5,29] Fonteyne et al[5] did not find increased severity or incidence of acute toxicity in a group of 118 prostate cancer patients after dose escalation with SIB to an MRI/MRS-detected IPL (76 Gy median dose to PTV and 80 Gy

median dose to gross tumour volume prescribed). In another study by Geier et al,[29] acute side effects and dose–volume histogram data were evaluated in 40 intermediate risk prostate cancer patients treated with a definitive daily image-guided SIB-IMRT protocol *via* helical tomotherapy. The PTV was treated with 70 Gy in 35 fractions. The boost volume containing the prostate and 3-mm safety margins (5 mm craniocaudal) was treated as SIB to a total dose of 76 Gy (2.17 Gy per fraction) without increasing acute toxicity. In this study, we first evaluated the treatment plans dosimetrically. However, the acute toxicity with this escalated dose is a question for an ongoing study.

The techniques of IMRT and VMAT, planning strategies, optimization algorithm and beam angles affect the dosimetric outcome. With different dose calculation algorithms used in these studies, 3–4% deviations in target volume and OAR doses were seen.[5] The Monte Carlo algorithm can improve dose calculation accuracy, which has been implemented successfully in clinical settings. Lafond et al[33] recently compared the Monaco TPS and Pinnacle™ TPS (Philips Medical Systems, Madison, WI) for VMAT plans, and found that the bladder wall, femoral heads and healthy tissue doses were significantly lower in Monaco plans. For PTV doses, Monaco plans had higher conformity than Pinnacle plans. In this study, similar to previous studies, we compared the dose distributions of IMRT and VMAT plans using Monaco 3.2 TPS (CMS; Elekta, Crawley, UK). For normal tissues surrounding the target volume, VMAT is superior to IMRT, as was in our study.[23]

The photon energy may contribute to dose distribution. Recently, Ost et al[4] compared IMRT and VMAT plans at 6 and 18 MV for primary prostate RT with SIB and showed no advantage of high-energy photons over low-energy photons. Pasler et al[8] compared IMRT and VMAT plans with 6, 10 and 15 MV photon beams for prostate cancer involving pelvic lymph nodes and did not show advantages of 15 MV over 6 and 10 MV photon beams in large volume pelvic plans. In this study, we additionally investigated the effect of photon energy levels over dose distributions of IMRT and VMAT plans for only prostate and seminal vesicle, with or without SIB, which was not investigated before. We found no advantage of higher energy levels over lower energy levels both for target volume and OARs doses. Furthermore, we found no difference in low-dose irradiated volume in normal tissue surrounding the target with 6, 10 or 15 MV photons. However, concerning neutron generation for photon energies >8 MV, it was demonstrated that the neutron component is not negligible at 15 MV.[34] Therefore, IMRT or VMAT delivery with low-energy photons may be adequate, since high-energy photons did not result in a significant benefit in terms of target coverage and OAR doses. Additionally, VMAT spares normal tissue surrounding the target volume better than IMRT; thus, rather than IMRT plans with higher energy, VMAT plans with lower energy may be a safe treatment strategy.

This study is not without limitations. First, with its retrospective nature, we only compared the dosimetric parameters of IMRT and VMAT plans in a limited number of patients. To make definitive conclusions, a large number of patients with different planning algorithms are essential. Additionally, the efficacy and toxicity of SIB plans with longer follow-up is required for making clinical decisions. Second, we prefer only single-arc plans in VMAT plans, rather than two or more arcs. Another study addressing the dose distributions of single and double arc VMAT plans with Monaco TPS could be considered.

CONCLUSION

Our study showed that dose escalation to the IPL is a safe technique without any serious increase in OAR doses. Additionally, although IMRT plans resulted in more homogenous dose distribution within the target volumes than VMAT plans, VMAT is better in sparing the rectum and bladder compared with IMRT plans. VMAT also had the added advantage of reducing the MUs required for treatment compared with seven-field IMRT. Moreover, high-energy photons had no advantage over low-energy photons. However, additional studies are needed to evaluate whether SIB plans result in improved biochemical control without increased toxicity and whether long-term follow-up is required to determine the potential effects of dose escalated SIB on local control and survival.

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