

Treatment plan comparison of volumetric-modulated arc therapy to intensity-modulated radiotherapy in lung stereotactic body radiotherapy using either 6- or 10-MV photon energies

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Abstract

Purpose: The aim of this study was to dosimetrically compare volumetric-modulated arc therapy (VMAT) with intensity-modulated radiotherapy (IMRT) techniques using either 6- or 10-MV photon beam energies in lung stereotactic body radiation therapy (SBRT) plans.

Methods: Thirty patients with primary or metastatic lung tumors eligible for SBRT were randomly selected. VMAT and IMRT treatment plans using either 6- or 10-MV photon energies were generated through automatic SBRT planning software in the RayStation treatment planning system.

Results: For planning target volume, there was no difference in $D_{95\%}$ for all plans, whereas $D_{2\%}$ and $D_{50\%}$ were significantly increased by 5.22%–5.98% and 2.47%–2.59%, respectively, using VMAT_{6/10-MV} plans compared to IMRT_{6/10-MV} plans. When comparing the D_{max} of organs at risk (OARs), VMAT_{6/10-MV} was 18.32%–47.95% lower than IMRT_{6/10-MV} for almost all OARs. VMAT_{6/10-MV} obviously decreased D_{mean} , V_{5Gy} , V_{10Gy} , and V_{20Gy} of whole lung by 9.68%–20.92% than IMRT_{6/10-MV}. Similar results were found when comparing VMAT_{6-MV} with IMRT_{10-MV} or VMAT_{10-MV} with IMRT_{6-MV}. The differences in the $D_{2\%}$, heterogeneity index, and conformity index between 6- and 10-MV plans are not statistically significant. Plans using 6-MV performed 4.68%–8.91% lower levels of D_{max} of spinal cord, esophagus, great vessels, and trachea and proximal bronchial tree than those using 10-MV plans. Similarly, D_{mean} , V_{5Gy} , V_{10Gy} , and V_{20Gy} of whole lung were also reduced by 2.79%–5.25% using 6-MV. For dose fall-off analysis, the D_{2cm} and $R_{50\%}$ of VMAT_{6/10-MV} were lower than those of IMRT_{6/10-MV}. Dose fall-off curve based on 10 rings was steeper for VMAT plans than IMRT plans regardless of the energy used.

Conclusions: For lung SBRT plans, VMAT-based plans significantly reduced OARs dose and steepened dose fall-off curves compared to IMRT-based plans. A 6-MV energy level was a better choice than 10-MV for lung SBRT. In addition, the dose differences between different techniques were more obvious than those between different energy levels.

#These authors contributed equally to this work.

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KEYWORDS

intensity-modulated radiotherapy (IMRT), lung cancer, radiotherapy, stereotactic body radiotherapy (SBRT), volumetric-modulated arc therapy (VMAT)

1 | INTRODUCTION

Stereotactic body radiation therapy (SBRT), as an external and noninvasive cancer treatment, uses accurate radiation beams to deliver a high dose of radiation in one to five fractions with 8–30 Gray (Gy) per fraction to treat tumors.^{1,2} SBRT is a standard treatment option for medically inoperable, early-stage non-small cell lung cancer (NSCLC), with a high rate of local control and low treatment-related toxicity.^{3–5} SBRT could also be a promising and comparable radical treatment for operable cases and pulmonary metastases.^{5–8} However, uncertainty still exists regarding the optimal implementation strategy, including the selection of radiation delivery techniques and beam energy levels.

Various irradiation techniques for lung SBRT delivery have been reported, including three-dimensional conformal radiation therapy (3D-CRT), dynamic conformal arc therapy (DCAT), static intensity-modulated radiotherapy (IMRT), and volumetric-modulated arc therapy (VMAT).⁹ Of those, IMRT and VMAT were two common modalities to perform SBRT¹⁰ and both have been demonstrated to be more conformal than 3D-CRT and DCAT.⁹ Several studies revealed that VMAT could provide better delivery accuracy and shorter treatment time compared to IMRT in the SBRT of cervical cancer and spine tumor.^{11,12} For the radiotherapy of early-stage lung cancer using SBRT, coplanar VMAT plan achieved a better plan quality and lower skin dose levels than those with coplanar IMRT plan and decreased delivery time at most by 70%.¹³ However, VMAT usually irradiates the tumor from more incident angles, which may increase the volume of the lung receiving low-dose radiation.¹³ To our knowledge, several studies comparing VMAT and IMRT in lung cancer have yielded conflicting results, such as the V_{5Gy} of whole lung.^{13,14} In practice, considering the diversity of dose and irradiated volume of lung tissue with different techniques, the choice of optimal radiation regimens still be controversial in lung SBRT plans.

Another aspect not often addressed in SBRT plan studies is the photon energy level. Although higher energy photons have the advantage of a lower attenuation with depth, they can also lead to an increased risk of secondary malignancies owing to the presence of neutrons generated in the accelerator head.^{15,16} Protocol-0915 of Radiation Therapy Oncology Group (RTOG) has recommended the use of photons of energy in the range from 4- to 12- MV for NSCLC radiotherapy.¹⁷ However, the issues still existed about the selection of energy levels in lung SBRT plans. Some small lung lesions treated with SBRT are more likely

to be eccentric. Considering the single large dose of SBRT, in order to reduce the dose of locally normal tissues, such as skin, the radiation angle needs to be distributed in a wider range, which would generate some beam angles with longer incident distance. In the circumstances, high energy performs its advantage of stronger penetration. However, low energy has advantage on reducing the dose deposited to the adjacent critical organs because of steep dose fall-off with small penumbra at the field edge.¹⁸ Moreover, the effect of beam energy level on plan quality was related to the number of beams.¹⁹ VMAT has a greater number of beam angles than fixed-field IMRT. Therefore, it needs to be further clarified if the influence of energy on the plan quality of VMAT was less significant than IMRT, making this influence less important.

In addition, rapid dose fall-off gradients beyond the target are very critical for SBRT, because tissues exposed to high fraction doses are prone to significant dysfunction.²⁰ Given the distinction of plan optimization strategies between SBRT and conventional fractionation regimens, it is still unclear about the optimal combination of different techniques and energy levels in lung SBRT. In the present study, in order to demonstrate if an ideal radiation technique may work to best execute SBRT, we used a completely automatic SBRT planning (ASP) system to generate treatment plans, minimizing the impact caused by manual factors, including the experience and clinical preferences, which have been shown to correlate with the quality of the plan.^{21–23} And then, we compared the use of 6-MV photon to 10-MV photon for all techniques. As far as we know, this is the first study to analyze the treatment plan difference between VMAT and IMRT in SBRT based on automatic planning.

2 | MATERIALS AND METHODS

2.1 | Patient selection

Thirty patients with primary or metastatic lung tumors who had received SBRT at our hospital between 2017 and 2019 were selected randomly for analysis. The Clinical Research Committee of the study institute approved the protocol, and the need for written informed consent was waived by the Institutional Review Board.

2.2 | Treatment plans

The localization, simulation, immobilization, targets and organs at risk (OARs) volumes delineation, and

prescription dose constraints were performed according to the RTOG-0915 protocol.¹⁷ We used an ASP system, which has been described and validated previously,²⁴ to generate the planning auxiliary structures, add beams and initial objectives and constraints, and modulate the parameters and optimization on the basis of the RayStation treatment planning system (RaySearch Laboratories, v4.7). There were three steps in the ASP optimization scheme: initial optimization (Step 1), main optimization (Step 2), and final optimization (Step 3). The Step 1, initial optimization was performed automatically. After evaluating the rationality of the initial optimization objectives of auxiliary structures and OARs, the ASP modified the parameters that contradict the target objectives automatically. Assessment criteria: an objective value of less than 0.0001 (equal to the tolerance) for any OAR was considered reasonable. Step 2, the main optimization consisted of repeated multiple optimizations and parameter adjustments. After each optimization, the planning target volume (PTV) dose was scaled to the prescribed dose and the objective values were computed. Then the dose objectives of auxiliary structures and OARs were adjusted to keep the corresponding objective values within the prespecified range. In the final step, the PTV and OARs were checked according to the prescribed dose and the constraints of OARs. If the PTV coverage, dose fall-off beyond the target, and OARs sparing met the dose requirements, ASP automatically saved the plan and exited. Otherwise, the projects that did not meet the standards were adjusted and the plan was re-optimized until all the dose requirements were met or the maximum number of iterations was reached. The SBRT plans of each patient were replanned based on VMAT and IMRT techniques and customized to the accelerator (Elekta Versa HD, Elekta Oncology, UK) with either 6- or 10-MV photon beams. In all, a total of four treatment plans were recreated for each patient: VMAT_{6-MV}, VMAT_{10-MV}, IMRT_{6-MV}, and IMRT_{10-MV}. Collapsed cone algorithm was used to compute the final dose for all plans.

Considering that the higher the number of beams, the longer the treatment time for IMRT, and the fractional displacement increased with the increase of treatment time,²⁵ all IMRT plans were created using seven isometric coplanar static fields and optimized by direct machine parameter optimization. Additional parameters were as follows: the minimum segment area was 4 cm²; the monitor unit of minimum segment was 5; the maximum number of segments was 50. VMAT plans were generated using two coplanar full arcs. Other parameters were in accordance with those of the IMRT plan.

2.3 | Dose prescription and plan acceptance criteria

The prescription dose to PTV was 48 Gy in four fractions. According to the protocol of RTOG-0915, 99% of

TABLE 1 Baseline information of all 30 patients in the present study

Variable	N	%
Age (years)		
Median (range)	53 (36–80)	
Gender		
Male	23	76.7
Female	7	23.3
Histology		
Primary	15	50.0
Metastatic	15	50.0
Site		
Right	13	43.3
Left	17	56.7
PTV Volume (cm ³)		
Median (range)	18.21 (9.48–29)	

Abbreviation: PTV, planning target volume.

the PTV receives a minimum of 90% of the prescribed dose and 95% of the PTV is conformally covered by the prescription isodose surface.

The heterogeneity index (*HI*) was calculated in-line with the International Commission on Radiation Units and Measurements report 83,²⁶ and the conformity index (*CI*) was calculated according to the equation of the Paddick index.²⁷ $D_{2\text{cm}}$ was the maximum dose (in % of dose prescribed) to any point 2 cm away from the PTV in any direction; $R_{50\%}$ was the ratio of 50% prescription isodose volume to PTV. Ten rings (5-mm width for each ring) outside the PTV were created to limit the dose of normal tissue and evaluate the dose fall-off.

2.4 | Statistical analysis

All data were recorded as median value and their interquartile range (25%–75%) for the 30 patients, and dosimetric comparison between plans was performed using the Wilcoxon signed-ranks test of two related samples. The percentage differences were calculated as follows: $(B - A)/A$ (*A* vs. *B*). The Spearman test was used to estimate the correlation between the percentage differences of D_{max} of rings among different plans and the distance away from PTV. Differences were considered significant if a *p* value was <0.05.

3 | RESULTS

For all 30 patients, clinically acceptable plans could be achieved for VMAT_{6-MV}, VMAT_{10-MV}, IMRT_{6-MV}, and IMRT_{10-MV}. Tumor characteristics are summarized in Table 1. The absolute plan parameters are summarized in Table 2.

TABLE 2 Summary of plan parameters

	VMAT _{6-MV} Median (25%–75%)	VMAT _{10-MV} Median (25%–75%)	IMRT _{6-MV} Median (25%–75%)	IMRT _{10-MV} Median (25%–75%)
PTV				
$D_{2\%}$ (Gy)	72.75 (68.48–76.92)	72.72 (70.37–76.14)	68.65 (64.27–71.53)	69.29 (65.91–71.95)
$D_{50\%}$ (Gy)	57.94 (57.23–58.73)	58.14 (57.75–58.81)	56.54 (55.72–57.07)	56.68 (55.84–57.31)
$D_{95\%}$ (Gy)	48.00 (47.99–48.03)	48.00 (47.99–48.01)	48.00 (47.99–48.03)	48.00 (47.99–48.03)
$D_{98\%}$ (Gy)	46.34 (46.04–46.55)	46.24 (46.07–46.40)	46.38 (46.21–46.56)	46.36 (46.10–46.57)
HI	0.45 (0.39–0.53)	0.45 (0.41–0.52)	0.39 (0.32–0.45)	0.40 (0.35–0.45)
CI	0.86 (0.82–0.88)	0.86 (0.83–0.88)	0.85 (0.82–0.88)	0.85 (0.82–0.87)
MUs	2945.18 (2696–3117.35)	3003.34 (2709.75–3274.06)	3020.12 (2823.58–3234.61)	2979.29 (2749.64–3329.84)
Spinal cord				
D_{max} (Gy)	6.16 (4.10–9.74)	6.43 (4.71–9.67)	9.94 (6.60–13.35)	11.37 (6.83–14.26)
$D_{1.2\text{cm}^3}$ (Gy)	4.96 (3.54–8.18)	5.21 (4.01–7.90)	7.33 (1.79–9.83)	7.83 (1.95–10.72)
$D_{0.35\text{cm}^3}$ (Gy)	5.36 (3.72–8.70)	5.56 (4.20–8.44)	8.44 (3.54–10.51)	9.08 (3.74–11.44)
Esophagus				
D_{max} (Gy)	5.61 (4.58–8.33)	5.99 (4.40–9.24)	8.95 (6.85–11.25)	9.54 (7.20–11.87)
$D_{5\text{cm}^3}$ (Gy)	0.69 (0.28–1.59)	0.89 (0.34–2.33)	0.63 (0.36–2.62)	1.01 (0.46–2.48)
Heart				
D_{max} (Gy)	11.23 (7.95–17.79)	11.67 (8.46–19.31)	15.74 (12.92–22.10)	15.60 (13.61–22.38)
$D_{15\text{cm}^3}$ (Gy)	7.80 (4.91–10.37)	8.00 (5.24–11.03)	11.25 (8.42–13.69)	11.86 (9.65–14.88)
Rib				
D_{max} (Gy)	46.97 (24.10–56.94)	47.05 (25.83–57.18)	47.07 (26.16–57.89)	46.71 (28.12–57.45)
$D_{1\text{cm}^3}$ (Gy)	32.44 (16.57–45.54)	31.95 (16.99–45.42)	32.92 (18.87–45.69)	32.50 (20.07–46.14)
$D_{2\text{cm}^3}$ (Gy)	29.45 (15.86–41.85)	29.49 (16.31–41.95)	29.55 (17.99–42.40)	29.30 (19.12–43.06)
$D_{5\text{cm}^3}$ (Gy)	24.27 (13.49–34.32)	25.31 (14.48–34.06)	24.65 (13.83–34.51)	25.32 (14.82–35.09)
$V_{30\text{Gy}}$ (%)	2 (0–8)	2 (0–8)	3 (0–9)	3 (0–9)
Skin				
D_{max} (Gy)	16.63 (12.85–21.65)	16.36 (12.79–21.20)	25.30 (23.34–29.93)	24.02 (21.00–28.13)
$D_{10\text{cm}^3}$ (Gy)	9.72 (7.90–11.37)	9.83 (7.91–11.62)	13.49 (12.08–15.74)	13.07 (12.08–15.00)
Lung (right and left)				
D_{mean} (Gy)	2.24 (1.66–3.92)	2.36 (1.72–4.21)	2.47 (1.95–4.22)	2.60 (2.07–4.51)
$V_{5\text{Gy}}$ (%)	11 (9–19)	12 (9–20)	13 (11–23)	14 (12–24)
$V_{10\text{Gy}}$ (%)	6 (4–11)	6 (4–12)	7 (5–14)	8 (5–14)
$V_{20\text{Gy}}$ (%)	2 (1–5)	2 (1–5)	2 (2–5)	2 (2–6)
Great vessels				
D_{max} (Gy)	10.20 (6.91–15.14)	10.79 (7.22–17.32)	12.71 (10.50–17.94)	13.78 (10.95–19.37)
TPBT				
D_{max} (Gy)	7.38 (2.53–13.60)	7.51 (3.90–14.00)	8.95 (3.36–14.86)	9.92 (4.54–15.82)
$D_{4\text{cm}^3}$ (Gy)	3.76 (0.46–7.22)	3.97 (0.65–7.82)	6.64 (0.56–9.23)	6.85 (0.74–10.17)

Abbreviations: CI , conformity index; D_{max} , maximal dose; D_{mean} , mean dose; $D_{N\text{cm}^3}$, minimum absorbed dose that covers $N\text{cm}^3$ of the volume; D_V , absorbed dose that covers a specified fractional volume V ; HI , homogeneity index; MUs, monitor units; PTV, planning target volume; TPBT, trachea and proximal bronchial tree; V_D , volume that receives at least the absorbed dose D Gy.

3.1 | Comparison of different techniques with the same energy level (IMRT_{6-MV} vs. VMAT_{6-MV} and IMRT_{10-MV} vs. VMAT_{10-MV})

As shown in Table 3, VMAT_{6/10-MV} plans increased $D_{2\%}$, $D_{50\%}$ of PTV by 2.47%–5.98% compared to IMRT_{6/10-MV}

plans, whereas the $D_{98\%}$ of VMAT_{10-MV} was 0.28% lower than that of IMRT_{10-MV}. Regarding the difference between CI and HI , VMAT_{6/10-MV} showed higher CI and HI values compared to IMRT_{6/10-MV}, and the percentage differences were 0.57%–0.75%, 13.09%–15.25%, respectively. When comparing the D_{max} of

TABLE 3 Percentage difference in plan parameters between different techniques with the same energy level

	VMAT _{6-MV} versus IMRT _{6-MV}		VMAT _{10-MV} versus IMRT _{10-MV}	
	Median (25%–75%)	<i>P</i>	Median (25%–75%)	<i>P</i>
PTV				
<i>D</i> _{2%}	−5.98% (−9.61%–2.67%)	0.000	−5.22% (−9.28%–1.84%)	0.000
<i>D</i> _{50%}	−2.59% (−3.63%–1.85%)	0.000	−2.47% (−3.85%–1.53%)	0.000
<i>D</i> _{95%}	0.00% (−0.03%–0.00%)	0.491	0.00% (0.00%–0.02%)	0.271
<i>D</i> _{98%}	0.12% (−0.14%–0.48%)	0.075	0.28% (−0.19%–0.58%)	0.018
<i>HI</i>	−15.25% (−24.43%–7.44%)	0.000	−13.09% (−23.20%–4.05%)	0.000
<i>CI</i>	−0.57% (−0.94%–0.28%)	0.022	−0.75% (−1.10%–0.42%)	0.000
MUs	3.69% (−7.49%–8.32%)	0.766	1.53% (−12.78%–12.40%)	0.586
Spinal cord				
<i>D</i> _{max}	30.57% (5.54%–80.87%)	0.000	33.20% (9.21%–70.90%)	0.000
<i>D</i> _{1.2 cm³}	17.19% (−59.27%–53.48%)	0.090	19.02% (−64.35%–55.42%)	0.075
<i>D</i> _{0.35 cm³}	16.47% (−31.37%–68.34%)	0.012	18.93% (−29.73%–62.35%)	0.012
Esophagus				
<i>D</i> _{max}	34.27% (8.87%–72.79%)	0.000	34.19% (14.38%–73.89%)	0.000
<i>D</i> _{5 cm³}	25.03% (−0.75%–37.70%)	0.006	24.92% (7.60%–46.74%)	0.008
Heart				
<i>D</i> _{max}	34.50% (10.96%–62.75%)	0.000	31.48% (12.79%–56.39%)	0.000
<i>D</i> _{15 cm³}	35.07% (10.49%–59.33%)	0.000	37.58% (12.16%–62.59%)	0.000
Rib				
<i>D</i> _{max}	1.95% (−2.42%–9.41%)	0.229	1.09% (−1.77%–7.88%)	0.141
<i>D</i> _{1 cm³}	4.66% (−0.06%–13.48%)	0.003	2.52% (1.24%–14.63%)	0.000
<i>D</i> _{2 cm³}	2.70% (1.09%–10.80%)	0.001	2.62% (1.40%–13.24%)	0.000
<i>D</i> _{5 cm³}	2.81% (0.64%–7.04%)	0.000	2.53% (0.65%–5.71%)	0.000
<i>V</i> _{30Gy}	6.28% (−3.77%–30.31%)	0.372	6.62% (−0.27%–14.52%)	0.008
Skin				
<i>D</i> _{max}	47.95% (13.37%–99.31%)	0.000	31.86% (14.58%–86.97%)	0.000
<i>D</i> _{10 cm³}	42.23% (30.98%–56.89%)	0.000	36.36% (21.25%–51.26%)	0.000
Lung (right and left)				
<i>D</i> _{mean}	9.68% (6.44%–14.00%)	0.000	9.73% (7.46%–16.59%)	0.000
<i>V</i> _{5Gy}	19.74% (13.78%–30.75%)	0.000	20.92% (12.71%–31.28%)	0.000
<i>V</i> _{10Gy}	18.82% (9.96%–30.02%)	0.000	17.62% (11.20%–31.92%)	0.000
<i>V</i> _{20Gy}	12.98% (7.68%–18.29%)	0.000	12.77% (8.50%–21.95%)	0.000
Great vessels				
<i>D</i> _{max}	29.38% (9.56%–66.65%)	0.000	25.35% (7.18%–60.80%)	0.000
TPBT				
<i>D</i> _{max}	18.32% (9.36%–27.98%)	0.000	22.34% (3.20%–34.95%)	0.000
<i>D</i> _{4 cm³}	28.23% (13.16%–69.54%)	0.000	30.10% (17.86%–73.03%)	0.000

Note: Percentage differences were calculated as (IMRT – VMAT)/VMAT.

Abbreviations: *CI*, conformity index; *D*_{max}, maximal dose; *D*_{mean}, mean dose; *D*_{*N* cm³}, minimum absorbed dose that covers *N* cm³ of the volume; *D*_{*V*}, absorbed dose that covers a specified fractional volume *V*; *HI*, homogeneity index; MUs, monitor units; PTV, planning target volume; TPBT, trachea and proximal bronchial tree; *V*_{*D*}, volume that receives at least the absorbed dose *D* Gy.

OARs, VMAT_{6/10-MV} was lower than IMRT_{6/10-MV} for almost all OARs, including spinal cord, esophagus, heart, skin, great vessels, and trachea and proximal bronchial tree (TPBT) with percentage differences

ranging from 18.32% to 47.95%. VMAT_{6/10-MV} obviously decreased *D*_{mean}, *V*_{5Gy}, *V*_{10Gy}, and *V*_{20Gy} of whole lung by 9.68%–20.92% than IMRT_{6/10-MV}. However, the *D*_{max} comparison of ribs yielded no significant differences.

TABLE 4 Percentage difference in plan parameters between different techniques with different energy levels

	VMAT _{6-MV} versus IMRT _{10-MV}		VMAT _{10-MV} versus IMRT _{6-MV}	
	Median (25%–75%)	<i>P</i>	Median (25%–75%)	<i>P</i>
PTV				
$D_{2\%}$	−4.66% (−11.63%–1.88%)	0.000	−6.09% (−9.30%–2.65%)	0.000
$D_{50\%}$	−2.37% (−3.67%–1.15%)	0.000	−2.84% (−3.97%–1.86%)	0.000
$D_{95\%}$	0.00% (−0.01%–0.02%)	0.861	0.00% (−0.02%–0.00%)	0.734
$D_{98\%}$	0.06% (−0.26%–0.39%)	0.491	0.42% (−0.09%–0.81%)	0.001
<i>HI</i>	−11.75% (−25.09%–3.91%)	0.001	−14.83% (−21.51%–7.39%)	0.000
<i>CI</i>	−0.54% (−0.91%–0.07%)	0.004	−0.81% (−1.21%–0.24%)	0.000
MUs	2.42% (−8.66%–8.78%)	0.894	0.90% (−11.97%–10.36%)	0.673
Spinal cord				
D_{\max}	43.11% (8.30%–102.04%)	0.000	24.83% (6.95%–52.08%)	0.001
$D_{1.2\text{ cm}^3}$	17.17% (−58.49%–68.11%)	0.028	13.18% (−61.32%–47.67%)	0.237
$D_{0.35\text{ cm}^3}$	14.85% (−18.42%–88.71%)	0.004	14.84% (−37.91%–47.62%)	0.039
Esophagus				
D_{\max}	43.33% (20.95%–81.55%)	0.000	23.27% (3.82%–70.38%)	0.000
$D_{5\text{ cm}^3}$	47.07% (26.05%–82.55%)	0.000	7.04% (−26.13%–30.56%)	0.465
Heart				
D_{\max}	35.93% (10.87%–54.87%)	0.000	30.04% (10.03%–62.05%)	0.000
$D_{15\text{ cm}^3}$	48.02% (21.89%–91.48%)	0.000	24.74% (4.86%–43.26%)	0.000
Rib				
D_{\max}	1.29% (−0.30%–12.62%)	0.057	1.06% (−1.53%–4.54%)	0.371
$D_{1\text{ cm}^3}$	4.45% (0.38%–18.22%)	0.000	2.25% (0.26%–7.85%)	0.002
$D_{2\text{ cm}^3}$	4.95% (1.36%–15.84%)	0.000	1.41% (0.31%–7.25%)	0.009
$D_{5\text{ cm}^3}$	5.29% (2.14%–14.56%)	0.000	0.35% (−2.08%–4.22%)	0.371
$V_{30\text{ Gy}}$	14.93% (2.46%–53.93%)	0.006	−2.98% (−8.59%–12.59%)	0.338
Skin				
D_{\max}	35.09% (12.71%–86.14%)	0.000	45.13% (18.64%–100.11%)	0.000
$D_{10\text{ cm}^3}$	39.35% (21.71%–56.94%)	0.000	42.82% (27.19%–53.07%)	0.000
Lung (right and left)				
D_{mean}	16.49% (12.26%–19.96%)	0.000	5.56% (1.97%–10.11%)	0.000
$V_{5\text{ Gy}}$	26.11% (17.42%–37.54%)	0.000	14.28% (8.21%–26.30%)	0.000
$V_{10\text{ Gy}}$	20.86% (15.04%–36.31%)	0.000	13.71% (6.02%–28.12%)	0.000
$V_{20\text{ Gy}}$	17.38% (12.80%–24.86%)	0.000	9.30% (3.22%–16.57%)	0.000
Great vessels				
D_{\max}	32.43% (24.06%–69.41%)	0.000	19.17% (1.98%–64.15%)	0.000
TPBT				
D_{\max}	34.10% (14.96%–62.40%)	0.000	14.09% (−11.83%–19.35%)	0.024
$D_{4\text{ cm}^3}$	44.48% (21.51%–78.42%)	0.000	22.35% (6.01%–65.57%)	0.000

Note: Percentage differences were calculated as (IMRT – VMAT)/VMAT.

Abbreviations: *CI*, conformity index; D_{\max} , maximal dose; D_{mean} , mean dose; $D_{N\text{ cm}^3}$, minimum absorbed dose that covers $N\text{ cm}^3$ of the volume; D_V , absorbed dose that covers a specified fractional volume V ; *HI*, homogeneity index; MUs, monitor units; PTV, planning target volume; TPBT, trachea and proximal bronchial tree; V_D , volume that receives at least the absorbed dose $D\text{ Gy}$.

3.2 | Comparison of different techniques with different energy levels (IMRT_{10-MV} vs. VMAT_{6-MV} and IMRT_{6-MV} vs. VMAT_{10-MV})

Similar results were found when comparing different techniques with different energy levels (Table 4).

VMAT_{6/10-MV} could significantly increase $D_{2\%}$, $D_{50\%}$ by 2.37%–6.09% but was comparable for $D_{95\%}$ compared to IMRT_{10/6-MV}. *CI* and *HI* of PTV were increased by 0.81% and 14.83% using VMAT technique. When comparing OARs, VMAT showed advantages in D_{\max} reduction of spinal cord, esophagus, heart, skin, great

vessels, and TPBT with percentage differences ranging from 14.09% to 45.13%, excepting ribs. Moreover, D_{mean} , $V_{5\text{Gy}}$, $V_{10\text{Gy}}$, and $V_{20\text{Gy}}$ of whole lung for VMAT were significantly decreased by 5.56%–26.11% compared to those parameters for IMRT.

3.3 | Comparison of different energy levels with the same techniques (IMRT_{6-MV} vs. IMRT_{10-MV} and VMAT_{6-MV} vs. VMAT_{10-MV})

As shown in Table 5, the differences in the $D_{2\%}$, $D_{98\%}$, HI , and CI between 6- and 10-MV plans were not statistically significant respectively. Considering the dose sparing of OARs, 6-MV plans performed 4.68%–8.91% lower level of D_{max} of spinal cord, esophagus, great vessels, and TPBT than 10-MV plans. Similarly, D_{mean} , $V_{5\text{Gy}}$, $V_{10\text{Gy}}$, and $V_{20\text{Gy}}$ of whole lung were also reduced by 2.79%–5.25% using 6-MV.

3.4 | Comparison of PTV dose fall-off

Figure 1a,b shows the maximum of $D_{2\text{cm}}$ and $R_{50\%}$ for each of the 30 patients. The maximum of $D_{2\text{cm}}$ of IMRT_{6/10-MV} were obviously higher than those of VMAT_{6/10-MV}. The same trend was visible for the $R_{50\%}$ with IMRT_{6/10-MV} being higher than VMAT_{6/10-MV}. $D_{2\text{cm}}$ and $R_{50\%}$ for almost all patients in VMAT met the requirements of RTOG-0915, whereas IMRT did not. The observed values of both parameters were the lowest for VMAT_{6-MV} and the highest for IMRT_{10-MV}. Dose fall-off curve based on D_{mean} and D_{max} of 10 rings out of PTV are presented in Figure 1c,d. Results showed that the radiation dose fall-off curve was steeper for VMAT plans than IMRT plans regardless of the energy used (6- or 10-MV). Notably, D_{mean} of rings decreased dramatically from Ring 1 to 3 and then moderately from Ring 4 to 10 for all treatment plans. Considering D_{max} of Rings, VMAT plans and IMRT plans showed a similar downward trend until Ring 4, after that, a gap emerged between those two different techniques. The dose fall-off of VMAT plans was sharper than IMRT plans from Ring 4 to 10. In addition, correlation analysis showed the percentage differences of D_{max} of rings between VMAT and IMRT were significantly related to the distance away from PTV (Figure 2). Those differences became more obvious along with the distance further. Moreover, VMAT_{6/10-MV} decreased the integral dose by 1.45–2.77 Gy (median difference) than IMRT_{6/10-MV}.

4 | DISCUSSION

The present study qualified dosimetric differences between delivery techniques with either IMRT- or VMAT-based SBRT using 6- or 10-MV beam energy for lung

tumors. Importantly, we used the fully automated SBRT plan system to avoid any deviations caused by manual adjustment to the most extent. The automatic planning system has been evaluated in a previous study and shown preferable quality than the manual system.²⁴ We found that the differences between different techniques (IMRT vs. VMAT without regard to energy level) were more obvious than those between different energy levels with the same technique (IMRT_{6-MV} vs. IMRT_{10-MV}, VMAT_{6-MV} vs. VMAT_{10-MV}). And then, findings revealed that VMAT showed statistically significant improvement in the protection of OARs and dose fall-off of normal tissues compared to IMRT treatments. Meanwhile, VMAT also performed better conformity but weakening homogeneity. In addition, 6-MV plans performed the ability to reduce dose to OARs when compared with 10-MV plans, whereas this improvement was not pronounced in target coverage.

SBRT for early-stage NSCLC patients delivers higher doses using fewer fractions. Currently, IMRT has been replaced by VMAT in many institutions because of its shorter delivery time.¹⁰ Rossi et al. evaluated the intrafraction motion in SBRT for NSCLC and found that VMAT-based SBRT could reduce intrafraction motion and consequently improve the accuracy of dose delivery due to the significant reduction of delivery time compared with IMRT-based SBRT.¹⁰ Regarding the PTV conformity calculated by 100% prescription dose, Holt et al. reported there was no significant difference between VMAT and IMRT. However, in our study, VMAT_{6/10-MV} brought superior conformity than IMRT_{6/10-MV}. Considering the advantage of automatic planning with minimal bias, we strongly believe that VMAT can improve the conformity of lung SBRT plan. Moreover, we found the PTV HI of VMAT_{6/10-MV} was greater than that of IMRT_{6/10-MV}. However, there was not much difference in absolute values and not much influence on clinical practice.

Lung sparing is regarded as an important factor in lung SBRT plan due to radiation-induced lung toxicity (RILT). Holt et al. analyzed three different SBRT plans of early-stage lung cancer using coplanar and noncoplanar IMRT and coplanar VMAT (using SmartArc). They found that the treatment plan quality for coplanar VMAT using one dual arc was better than that of coplanar IMRT plans using 9 equidistant coplanar beams with a maximum of 18 segments in total, and the $V_{5\text{Gy}}$ of whole lung in VMAT had improved significantly compared to that in coplanar IMRT.¹³ However, Jiang et al. found the opposite results in a conventional fractionation lung cancer study. The higher $V_{5\text{Gy}}$ and $V_{10\text{Gy}}$ were observed in the single-/partial-arc VMAT plans compared to IMRT plans using 5–7 beams with a maximum of 100 segments in total.¹⁴ One possible explanation is that they adopted different VMAT arc numbers and segment numbers. Another reason might be they used manual planning, which may introduce

TABLE 5 Percentage difference in plan parameters between different energy levels with the same techniques

	VMAT _{6-MV} versus VMAT _{10-MV}		IMRT _{6-MV} versus IMRT _{10-MV}	
	Median (25%–75%)	<i>P</i>	Median (25%–75%)	<i>P</i>
PTV				
<i>D</i> _{2%}	0.42% (−1.55%–2.34%)	0.558	0.97% (−1.35%–2.99%)	0.382
<i>D</i> _{50%}	0.15% (−0.14%–1.09%)	0.047	0.16% (−0.27%–0.65%)	0.199
<i>D</i> _{95%}	0.00% (−0.02%–0.00%)	0.185	0.00% (0.00%–0.04%)	0.530
<i>D</i> _{98%}	−0.27% (−0.52%–0.15%)	0.090	−0.14% (−0.35%–0.13%)	0.090
<i>HI</i>	1.30% (−5.01%–5.92%)	0.600	3.26% (−4.10%–10.85%)	0.393
<i>CI</i>	0.10% (−0.21%–0.62%)	0.102	0.02% (−0.67%–0.45%)	0.704
MUs	0.88% (−2.16%–4.27%)	0.329	−0.39% (−3.27%–2.35%)	0.491
Spinal cord				
<i>D</i> _{max}	6.93% (2.33%–17.84%)	0.000	4.68% (0.47%–12.14%)	0.000
<i>D</i> _{1.2 cm³}	7.58% (−1.61%–18.35%)	0.009	7.21% (3.72%–11.36%)	0.000
<i>D</i> _{0.35 cm³}	8.63% (−1.01%–18.08%)	0.008	5.92% (−0.01%–12.22%)	0.002
Esophagus				
<i>D</i> _{max}	5.41% (−0.59%–11.59%)	0.006	6.17% (−0.16%–10.80%)	0.001
<i>D</i> _{5 cm³}	19.28% (7.41%–38.85%)	0.000	23.05% (6.90%–40.72%)	0.000
Heart				
<i>D</i> _{max}	0.39% (−2.22%–7.95%)	0.280	0.05% (−3.89%–5.48%)	0.926
<i>D</i> _{15 cm³}	5.97% (2.13%–9.91%)	0.001	8.46% (3.70%–11.37%)	0.000
Rib				
<i>D</i> _{max}	1.11% (−1.17%–5.23%)	0.098	1.42% (−0.59%–3.73%)	0.045
<i>D</i> _{1 cm³}	1.76% (−0.81%–4.79%)	0.066	1.66% (0.21%–3.81%)	0.000
<i>D</i> _{2 cm³}	1.30% (−0.57%–4.53%)	0.032	1.73% (0.29%–4.28%)	0.000
<i>D</i> _{5 cm³}	3.30% (−0.77%–7.23%)	0.007	2.15% (0.08%–4.85%)	0.000
<i>V</i> _{30Gy}	4.03% (−2.30%–27.98%)	0.123	8.56% (0.65%–16.69%)	0.001
Skin				
<i>D</i> _{max}	−0.64% (−2.56%–3.68%)	0.658	−6.25% (−13.39%–1.20%)	0.000
<i>D</i> _{10 cm³}	2.53% (−0.46%–5.89%)	0.005	−1.99% (−6.77%–1.34%)	0.012
Lung (right and left)				
<i>D</i> _{mean}	4.52% (3.17%–5.92%)	0.000	5.25% (3.76%–7.09%)	0.000
<i>V</i> _{5Gy}	4.02% (1.92%–6.11%)	0.000	3.99% (3.15%–5.91%)	0.000
<i>V</i> _{10Gy}	2.79% (0.00%–6.96%)	0.002	4.71% (2.33%–5.99%)	0.000
<i>V</i> _{20Gy}	3.18% (−1.03%–5.42%)	0.003	4.06% (0.88%–7.40%)	0.000
Great vessels				
<i>D</i> _{max}	4.82% (−0.24%–13.04%)	0.005	6.26% (−0.23%–9.38%)	0.001
TPBT				
<i>D</i> _{max}	8.91% (−1.77%–39.86%)	0.028	7.04% (3.52%–32.70%)	0.000
<i>D</i> _{4 cm³}	6.91% (2.77%–18.59%)	0.000	7.13% (2.45%–14.17%)	0.000

Note: Percentage differences were calculated as (10-MV − 6-MV)/6-MV.

Abbreviations: *CI*, conformity index; *D*_{max}, maximal dose; *D*_{mean}, mean dose; *D*_{*N* cm³}, minimum absorbed dose that covers *N* cm³ of the volume; *D*_{*V*}, absorbed dose that covers a specified fractional volume *V*; *HI*, homogeneity index; MUs, monitor units; PTV, planning target volume; TPBT, trachea and proximal bronchial tree; *V*_{*D*}, volume that receives at least the absorbed dose *D* Gy.

subjective error and affect the results of comparison. In our study, the parameters, including *MLD*, *V*_{5Gy}, *V*_{10Gy}, and *V*_{20Gy} of IMRT, were significantly higher than those of VMAT no matter using 6- or 10-MV. Our results may help resolve the confusion caused by the conflicting

results of previous studies because all those comparisons were performed based on unbiased ASP and we believed our conclusion was stable. As reported previously, dosimetric parameters, including *MLD*, *V*_{5Gy}, and *V*_{20Gy}, were related to RILT,^{28–30} which caused by

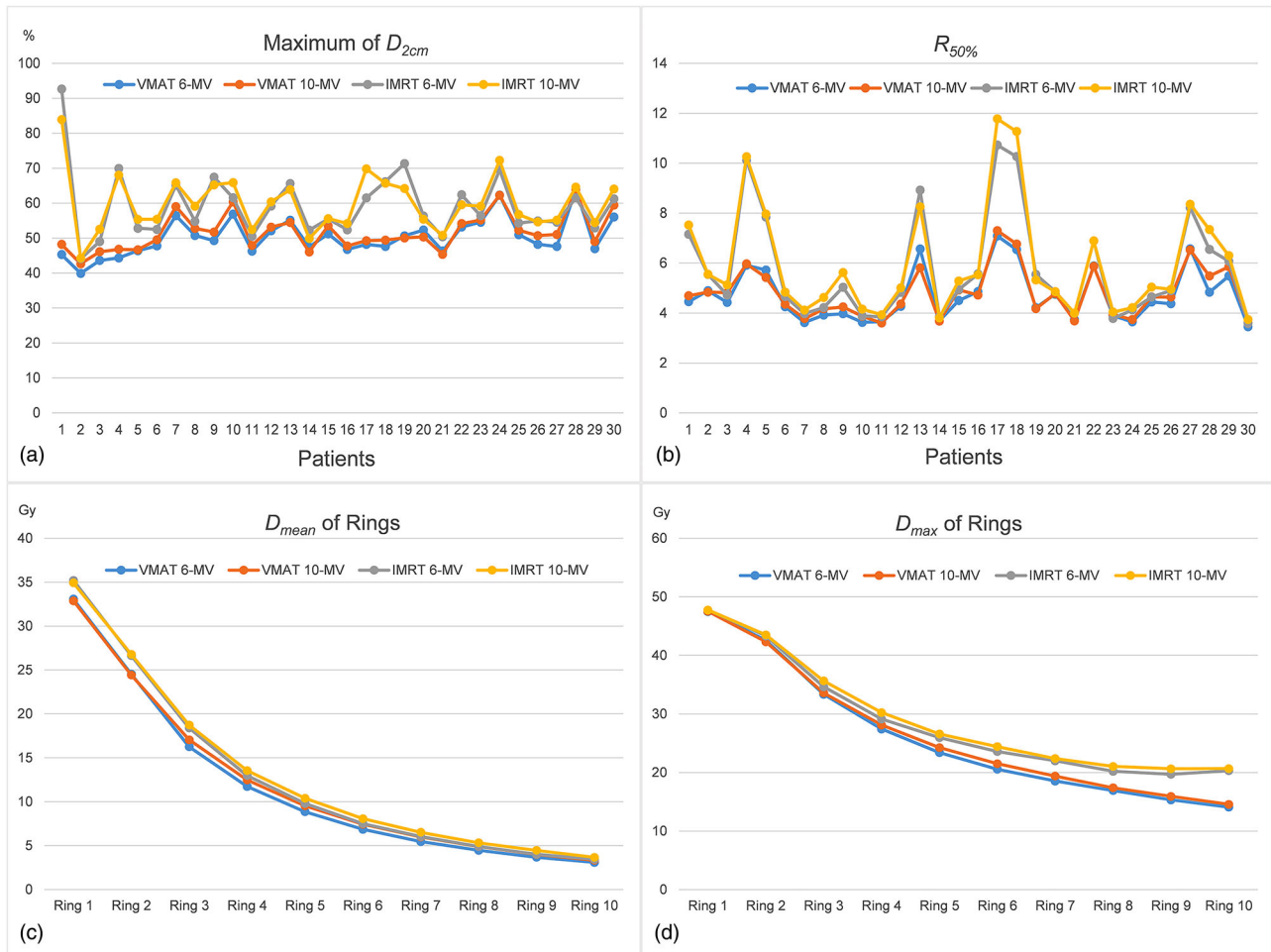


FIGURE 1 Dose fall-off analysis among four stereotactic body radiation therapy (SBRT) treatment plans: (a) the maximum of D_{2cm} of all 30 patients; (b) $R_{50\%}$ of all 30 patients; (c) D_{mean} (median value) of 10 rings; and (d) D_{max} (median value) of 10 rings

excessive radiation dose to the normal lung tissue and should be noticed in lung SBRT performance.³¹ Therefore, our study robustly and comprehensively confirmed the advantage of VMAT in reducing pulmonary toxicity for lung tumor SBRT.

In addition to whole lung, it is important to reduce the dose to other OARs to minimize the side effects of lung SBRT, including central airways, esophagus, great vessels, heart, skin, and spinal cord. The previous study demonstrated that, when comparing the coplanar VMAT and the coplanar IMRT, the maximal doses to the OARs, including heart, esophagus, and skin, were significantly lower for VMAT while there was no difference in the D_{max} of spinal cord and V_{5Gy} of chest wall.¹³ However, in our study, the VMAT_{6/10-MV} were superior to the IMRT_{6/10-MV} for almost all OARs dose indices, except for the D_{max} of rib, and the absolute dose improvement was mostly greater than that in the study of Holt et al.¹³ Considering the comparisons were based on unbiased ASP, we believed our results were stable. Moreover, the D_{max} of rib in VMAT was higher than that in IMRT. One possible

explanation was that the distance between lesions and chest wall was shorter in peripheral lung tumors, which was mainly discussed in the present study, resulting in the D_{max} of ribs approximating the maximum dose of targets.

Previous studies revealed that lateral scatter of high-energy electrons leads to an extended path in low-density tissues such as the lung, resulting in the augment of beam penumbra, larger volumes of lung irradiated, and reduced target dose.³² Hence, low-energy photons were suggested for lung tumor radiotherapy to minimize lateral electronic disequilibrium and to decrease the irradiated volume of the normal lung tissue.³³ Commonly, 6-MV photon beams are typically used for SBRT due to the small beam penumbra of an open-field beam compared to other higher photon energies in conventional linear accelerators.³⁴ However, with the use of IMRT or VMAT, the effective penumbra realized in the treatment plan may not be so clear due to the impact of beam fluence optimization.³⁵ Henry et al. found that in liver SBRT, 10-MV photon energy

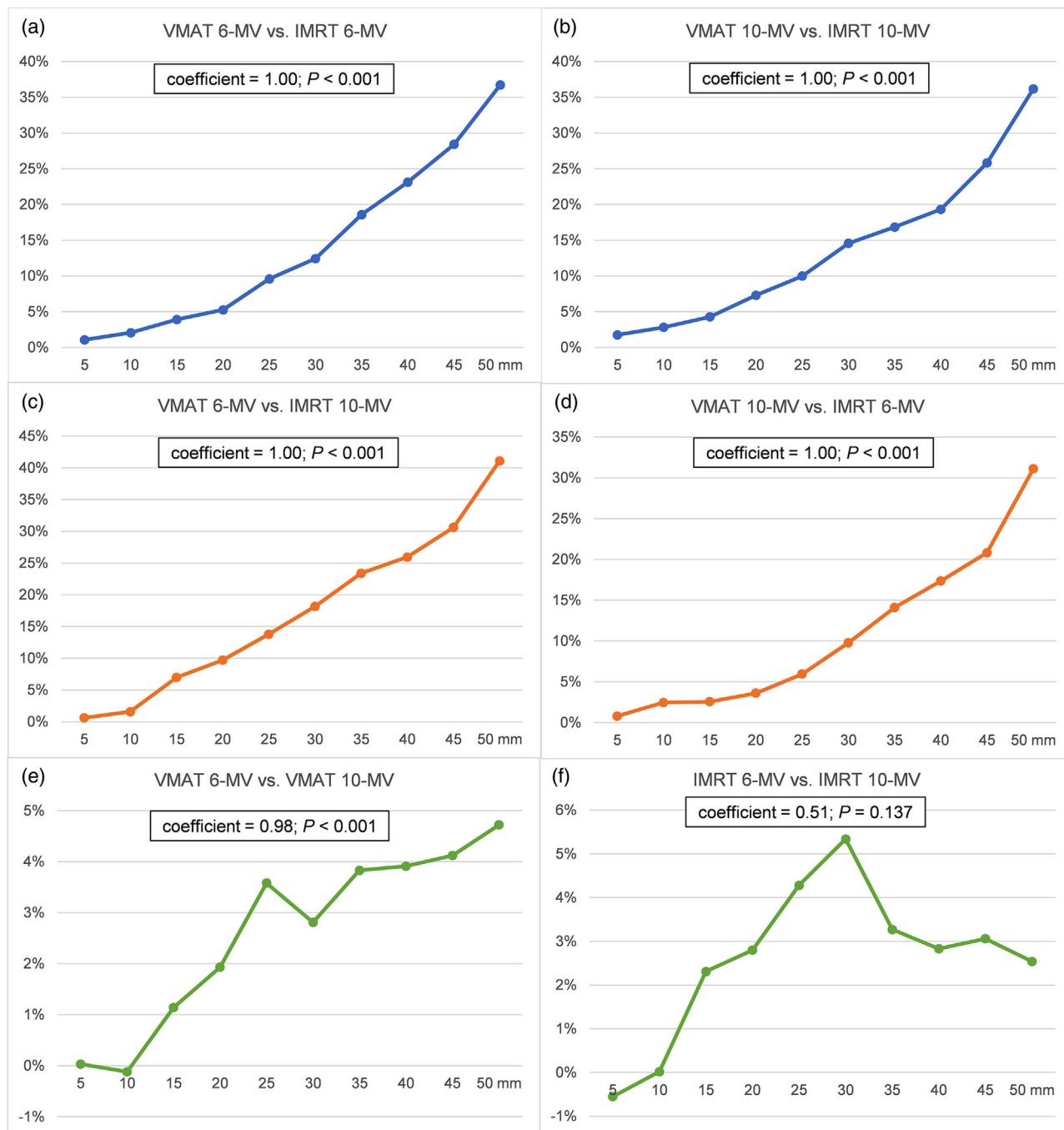


FIGURE 2 Correlation analysis of percentage differences of D_{max} of rings and distance away from planning target volume (PTV): (a) volumetric-modulated arc therapy (VMAT)_{6-MV} versus intensity-modulated radiotherapy (IMRT)_{6-MV}; (b) VMAT_{10-MV} versus IMRT_{10-MV}; (c) VMAT_{6-MV} versus IMRT_{10-MV}; (d) VMAT_{10-MV} versus IMRT_{6-MV}

using noncoplanar, fixed-field IMRT delivery technique approach showed a faster dose fall-off and improved up to 18.5% in the $R_{30\%}$ parameter compared to 6-MV, but no difference was noted in the $R_{50\%}$.³⁴ However, the variation of tissue density in lung and liver limited the extension of the conclusion. There were few studies performing dosimetric comparing of SBRT using different energy levels. In the present study, we found that the dose differences of the same technique with dif-

ferent energy levels were slighter. The target coverage was comparable between 6- and 10-MV regardless of techniques.

Because of the high ablative doses used in SBRT, high-quality SBRT treatment plans should ensure fast dose fall-off and compact dose distributions. Any improvements in SBRT treatment plan quality by improving the dose fall-off may have implications for SBRT treatments. A fast dose fall-off is essential and beneficial

to protect normal tissue in lung SBRT. RTOG-0813 and 0915 recommend using $D_{2\text{cm}}$ and $R_{50\%}$ as plan quality metrics for evaluation of normal tissue sparing and dose fall-off in SBRT of lung lesion. Clearly, the improved compactness from the faster dose fall-off translates into a reduction of dose in involved and adjacent normal tissues. In the setting of the RTOG-0915 trial, an $R_{50\%}$ value was stipulated to be $<2.9\text{--}7.5$; the maximum $D_{2\text{cm}}$ in any direction criterion was stipulated to be $<50.0\%\text{--}94.0\%$ of the prescription dose. Delgado et al. evaluated the target dose fall-off in IMRT and VMAT planning techniques for cervical SBRT through analyzing $R_{50\%}$ and found that VMAT_{3-arc} 10-MV appears to provide the best dose fall-off than IMRT.¹¹ However, there have been few research studies comparing the dose fall-off using VMAT and IMRT treatment plans for lung tumors. In the present study, VMAT offered an obvious reduction of $R_{50\%}$ compared to IMRT technique, whereas the values of $R_{50\%}$ using 6-MV were significantly lower than those using 10-MV. Similarly, the comparison of $D_{2\text{cm}}$ also showed the same trend except that the difference between IMRT_{6-MV} and IMRT_{10-MV} was not significant. That is, VMAT_{6-MV} provided a steeper dose fall-off outside of the target volume in lung SBRT. Notably, the dose fall-off advantage of VMAT over IMRT is greater than that of 6-MV over 10-MV, both in terms of absolute dose and the number of patients meeting the RTOG-0915 criterion. Therefore, VMAT and 6-MV are more suitable for lung tumor SBRT than IMRT and 10-MV.

Normal tissue sparing could be also analyzed using multiple concentric rings outside the PTV, which has been studied among stereotactic radiosurgery plans.³⁶ In the present study, we conducted 10 concentric rings evaluating the dose fall-off of normal tissues and compared the dosimetric parameters inside every ring. As far as we know, this is the study using the most rings in SBRT to date. Consistent with the results for $R_{50\%}$ and $D_{2\text{cm}}$, the analysis based on D_{max} of rings concluded that VMAT could perform a faster dose fall-off than IMRT, which further revealed the advantage of VMAT in involved and adjacent normal tissue sparing when treating lung tumors using SBRT. The potential gains in dose fall-off may allow for a potential dose escalation to the target volume, and more aggressive dose may be associated with higher local control rates of disease.³⁷ Moreover, the dose fall-off curve based D_{mean} of rings was steeper from Ring 1 to 4 and then became mild from Ring 4 to 10, although the automatic optimization strategy did not favor either ring. This trend suggested that the dose fall-off gradient of normal tissues close to PTV was sharper compared to tissues far away from PTV, with an inflection point at 1.5–2.0 cm away from PTV. A discrepant trend was found in the curve of D_{max} of rings. There was an obvious separation between VMAT plans and IMRT plans since Ring 4, indicating VMAT techniques provided better protection for normal tissues 2 cm or greater away from PTV.

This kind of advantage was enhanced along with the distance further. Moreover, the integral dose is important in assessing SBRT plans because it is able to detect unsuspected regions of a high absorbed dose beyond PTV. We found VMAT_{6/10-MV} decreased the integral dose compared to IMRT_{6/10-MV}, which could reduce the risk of late effects, such as carcinogenesis.

The limitations of our study should also be aware of. First, it was a retrospective design from a single center, and the risk of selection bias may exist. And then, we compared the OARs sparing that had influences on radiation-related normal tissue toxicities. However, clinical outcomes, especially SBRT adverse events of patients, were not analyzed in the present study. Definitely, prospective studies exploring optimal choice were needed for the SBRT plans in the future. Despite these limitations, we believe that our report can serve as a hypothesis-generating study.

5 | CONCLUSIONS

In the present study, using an automatic planning system, we performed a comprehensive plan comparison of VMAT to IMRT in lung SBRT using either 6- or 10-MV photon energies. The differences between different techniques were more obvious than those between different energy levels with the same technique. VMAT showed prominent benefits in the protection of OARs and provided sharper dose fall-off of normal tissues than IMRT treatments. For lung SBRT plans, VMAT techniques may be superior to IMRT techniques and 6-MV energy level was a better choice than 10-MV.

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CONFLICT OF INTEREST

The authors report no conflict of interest with this study. We declare that we do not have any commercial or associative interest that represents a conflict of interest in connection with this work.

AUTHOR CONTRIBUTIONS

(I) Conception and design: Jianghong Xiao and Xingchen Peng; (II) administrative support: Jianghong Xiao; (III) provision of study materials or patients: Zhigong Wei and Xingchen Peng; (IV) collection and assembly of data: Zhigong Wei, Xingchen Peng, Ling He, and Zheran Liu; (V) data analysis and interpretation: Zhigong Wei, Xingchen Peng, and Jingjing Wang; (VI) manuscript writing: all authors; and (VII) final approval of manuscript: all authors.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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