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Partial and Full Arc Volumetric Modulated Arc Therapy in Lung Cancer Stereotactic Body Radiotherapy with Different Definitions of Internal Target Volume Based on 4D CT

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Abstract

Purpose: To investigate the feasibility of partial arc volumetric modulated arc therapy (VMAT) in lung cancer stereotactic body radiotherapy (SBRT), as well the volumetric and dosimetric effects of different internal target volume (ITV) definitions with 4D CT. **Methods:** Fourteen patients with primary and metastatic lung cancer underwent SBRT were enrolled. Full and partial arc VMAT plans were generated with four different ITVs: ITV_{all}, ITV_{MIP}, ITV_{AIP} and $ITV_{2phases}$, representing ITVs generated from all 10 respiratory phases, maximum intensity projection (MIP), average intensity projection (AIP), and 2 extreme respiratory phases. Volumetric and dosimetric differences, as well as MU and delivery time were investigated. **Results:** Partial arc VMAT irradiated more dose at 2 cm away from planning target volume (PTV) (P = 0.002), however, it achieved better protection on mean lung dose , lung V5, spinal cord, heart and esophagus compared with full arc VMAT. The average MU and delivery time of partial arc VMAT were 240 and 1.6 min less than those of full arc VMAT. There were no significant differences on target coverage and organ at risks (OARs) sparing among four ITVs. The average percent volume differences of ITV_{MIP}, ITV_{AIP} and $ITV_{2phases}$ to ITV_{all} were 8.6%, 13.4%, and 25.2%, respectively. **Conclusions:** Although partial arc VMAT delivered more dose 2 cm out of PTV, it decreases the dose to lung, spinal cord, and esophagus, as well decreased the total MU and delivery time compared with full arc VMAT without sacrificing target coverage. Partial arc VMAT was feasible and more efficient for lung SBRT.

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Keywords

Lung Cancer, Stereotactic Body Radiotherapy, Four Dimensional Computed Tomography, Internal Target Volume, Volumetric Modulated Arc Therapy

1. Introduction

Lung cancer remains the leading cause of cancer death in both men and women in the United States [1], Asian countries [2], and the world [3]. Currently, stereotactic body radiotherapy (SBRT) has been widely applied to treat patients with medically inoperable non-small-cell lung carcinoma (NSCLC) [4] and oligometastatic lung cancers [5] [6]. Three dimensional conformal radiation therapy (3DCRT) with 10 - 15 static fields is the most common technique used to create the desired conformal dose distribution for SBRT. The main drawback of 3DCRT planning is the lengthy treatment time relating to patient setup and radiation delivery resulted from many fields needed to create an acceptable treatment plan [7]. Depending on equipment and dose rate utilised, patient setup time can take up to 22 min and 100 min for treatment delivery [8] [9]. Longer treatment time significantly increases the chances of intrafraction motion and error [10]. Many conformal SBRT studies have reported frequently occurring and clinically significant treatment related toxicity complications [11].

Recently there has been much interest in mitigating the risks associated with SBRT by delivering stereotactic doses through different techniques other than static noncoplanar/planer 3DCRT beams, such as intensity modulated therapy (IMRT) [12], volumetric modulated arc therapy (VMAT) [13]. VMAT is an extended form of IMRT with variable dose rate, gantry speed, and dynamic multileaf collimator movement [14]. The capability of VMAT to increase the sparing of organs at risk (OARs) without compromising conformal dose distributions in a shorter treatment time compared with IMRT and 3DCRT has been demonstrated for both conventional fractional radiotherapy and SBRT in the treatment of lung cancer [15] [16].

SBRT allows delivery of very high fraction dose in a few fractions, and it requires both a precise target definition with a relatively tight margin around gross tumor volume (GTV) and a careful target motion management with precise daily set-up verification prior to achieve conformal planning. An individual internal target volume (ITV) for each patient will usually generate from GTV with four dimensional computed tomography (4D CT) by considering the tumor motion induced by respiratory to achieve adequate tumor coverage and spare surrounding normal tissues [17] [18]. Ideally, the most accurate way to determine ITV is to contour GTVs in a 4D CT set with 10 breath phases, but this is very time-consuming and labor-intensive. To reduce the workload of contouring multiple GTVs, maximum intensity projection (MIP) technique [19], average intensity projection (AIP) [20], and contouring with reduced breath phases im-

age sets [21], have been suggested to form the ITV.

It is of interesting to investigate whether the application of 4D CT with different target delineations will benefit from partial arc VMAT treatment with an intend to further increase the treatment efficiency. The purpose of this study is to investigate the feasibility of partial arc VMAT SBRT, as well the volumetric and dosimetric differences of different 4D CT target delineations for lung cancers SBRT.

2. Materials and Methods

2.1. Patients and 4DCT Simulation

Patients with stage I primary NSCLC and less than two metastatic lung tumors were included in the study. Patients with more than three metastatic lung tumors and large primary unsuitable for SBRT were excluded. Eight patients with Stage 1 NSCLC and six with metastatic lung cancer treated by SBRT were enrolled. The average age of these patients was 60 years (range 45 - 81) at the time of treatment. BodyFix system (Elekta, Crawley, UK) was applied to immobilize the patients with their arms on the forehead to reduce the target motion and setup uncertainties. 4D CT images were acquired using a 16-slice Brilliance Big Bore CT scanner (Philips Healthcare, Cleveland, OH.) with Bellows system. Bellows is a deformable rubber belt that can measure lung volume changes when placed across the patient's chest/waist to generate a breathing signal accordingly. 4D CT images were sorted into 10 respiratory phases after reconstruction with each representing 10% of the respiratory cycle. Two extreme inhale and exhale phases were 0% and 50% of the respiratory cycle.

2.2. Target Delineation and Planning

A senior radiotherapy oncologist delineated the GTV in the 10 CT data sets with different respiratory phases. Four ITVs were generated: 1) ITV_{all}: ITV generated by combining ten GTVs from the 10 4D CT data sets with different respiratory phases; 2) ITV_{MIP}: ITV generated with MIP post-processing; 3) ITV_{AIP}: ITV generated with AIP post-processing; 4) $ITV_{2phases}$: combining GTVs on CTs of the peak inhale (0% phase) and exhale phases (50%). A PTV were generated by adding a uniform 3 mm margin to the ITVs.

Plans were generated on a free breathing CT with Monaco treatment planning system (TPS) (Monaco 5.1.1; Elekta, Crawley, UK). Monte Carlo algorithm was applied to optimized VMAT plans using identical objective functions and optimization parameters with a leaf motion of 0.46 cm/deg and a final arc space degree of 4. Full and partial arc VMAT plans were generated with a gantry rotational angle of 360 degree (from −179˚ to 180˚) and 180 degree (from −179˚ to 0˚), respectively. The effects of different ITV definitions on dosimetric distributions and the feasibility of partial arc VMAT in the lung cancer SBRT was investigated. The prescription dose for all these VMAT plans were 11 Gy per fraction for 5 fractions to achieve a biological equivalent dose (BED) of 115.5 Gy for an

α/β of 10.

During planning optimization, following dosimetric constraints were followed according to RTOG 236 protocol: 95% volume of the PTV was covered by the prescribed dose; 99% volume of the PTV was covered by 90% prescribed isodose, parameters of conformal index (CI), defined as the ratio between the volume of 100% prescribed isodose and the PTV volume, the percent of maximum dose at 2 cm away from PTV (D_{2cm}) to prescription dose in any direction, and the ratio of the volume of prescribed 50% isodose to the PTV volume (R50%) [22]. VMAT optimization physical constraints included a 0.30 cm grid, a 1% statistical uncertainty per calculation for Monte Carlo photon algorithm, a maximum number of control points per arc of 180 with a minimum segment width of 0.5 cm.

2.3. Volumetric and Dosimetric Evaluation

ITV volumes were measured and compared with ITV_{all} by percent volume difference (PVD), which was defined as ((Va − Vb)/Va). Dose-volume histogram (DVH) were analyzed to investigate the dosimetric differences caused by volumetric differences. The target coverage (V95), CI, D_{2cm} and $R_{50\%}$ were evaluated for PTV. For OAR evaluation, the mean lung dose (MLD), the percent lung volume irradiated by 5, 12, 20 Gy (V5, V12, V20), the D_{1cc} of spinal cord, Dmean and D_{15cc} of heart, Dmax and D_{5cc} of esophagus were compared.

2.4. Statistics

One way ANOVA method was applied to compare the volumetric and dosimetric results among different ITV methods presenting as mean ± standard deviation (SD)., The post hoc Turkey's test was applied when an overall significant difference observed to determine the differed pair-wise comparisons. Statistical analysis was performed using SPSS 17.0. $p < 0.05$ was considered statistically significant.

3. Results

Table 1 presents the detailed characteristics of the 14 lung cancer patients involved. There were two patients with tumor location in left middle lobe (LML), seven in right middle lobe (RML), three in right lower lobe (RLL), one in left upper lobe (LUL) and one in right upper lobe (RUL). Figure 1 shows one typical contours of different ITV definitions for one patient. Detailed ITV volumes and PVD of these volumes to ITV_{all} were also presented in Table 1. The average PVD of ITV_{MIP}, ITV_{AIP} and $ITV_{2phases}$ to ITV_{all} were 8.6%, 13.4%, and 25.2%, respectively.

A typical dose distribution and DVH comparison between full arc and partial arc VMAT plans were presented in Figure 2 and Figure 3. Table 2 shows the detailed dosimetric comparisons between full arc and partial arc VMAT plans. Full arc VMAT irradiated less dose 2 cm away from the PTV compared with

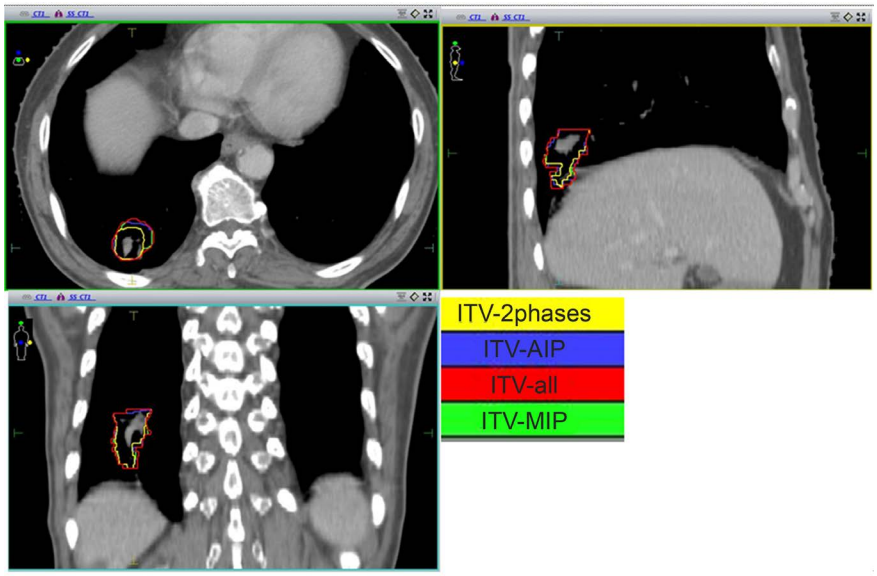

Figure 1. Typical internal target volume (ITV) definitions based on gross tumor volume from all ten respiratory phases (ITV_{all}), maximum intensity projection (ITV_{MIP}), average intensity projection (ITV_{AIP}), and 2 extreme respiratory phases ($ITV_{2phases}$).

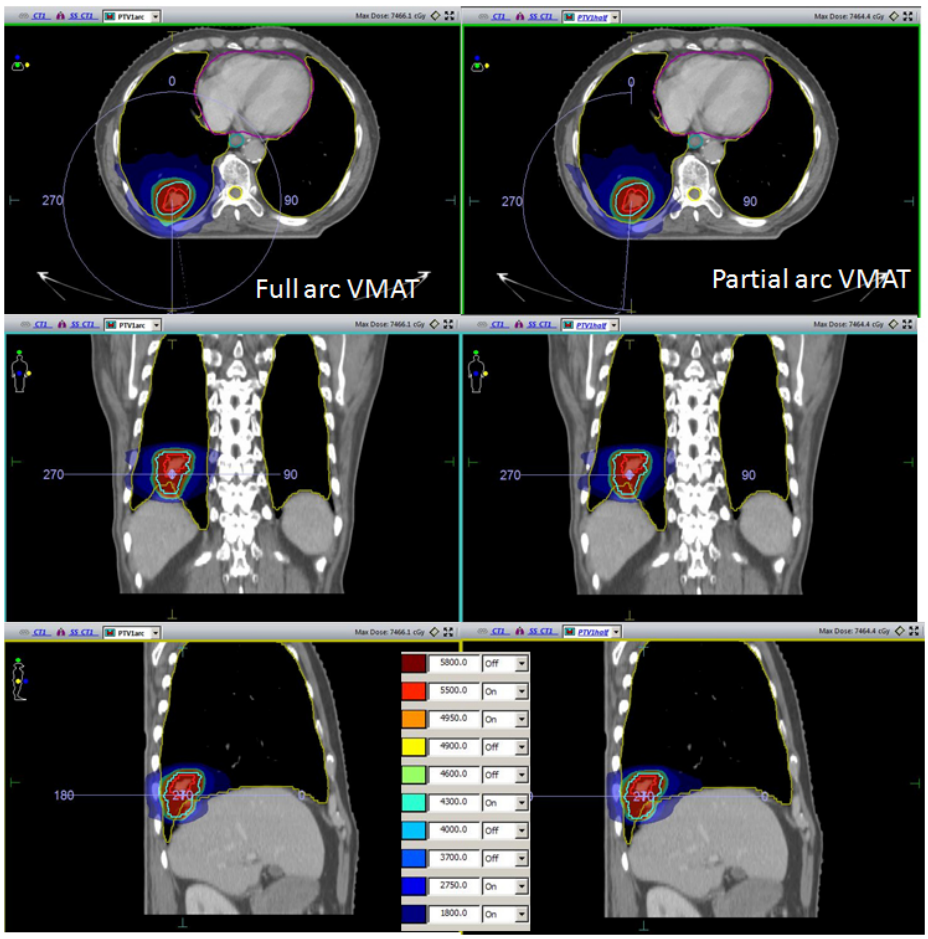

Figure 2. A typical dosimetric distribution comparison between partial and full arc VMAT plans for one patient.

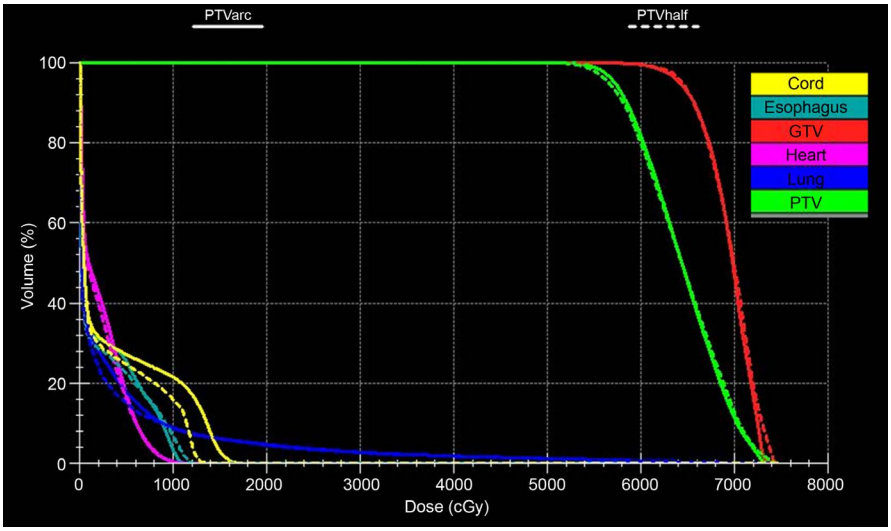

Figure 3. A typical dose volume histogram comparison between partial and full arc VMAT plans for one patient.

Table 1. Patient characteristics and volumetric differences for different internal target definition.

Patients	Age (yr)	Gender	Tumor Location	GTV (cm^3)	ITV_{all} (cm^3)	ITV_{MIP} (cm^3)	ITV_{AIP} (cm^3)	$ITV_{2phases}$ (cm^3)	PVD_{MIP}	PVD_{AIP}	PVD_{2phase}
1	81	male	LML	4.82	9.23	8.49	6.81	7.55	−0.08	−0.26	−0.18
2	73	male	RML	4.05	9.61	8.67	6.49	4.60	−0.10	−0.32	−0.52
3	75	female	RML	2.52	7.11	6.18	6.26	4.52	−0.13	−0.12	−0.36
4	58	female	RLL	7.26	18.09	16.23	16.33	13.49	−0.10	−0.10	−0.25
5	78	male	RML	7.84	17.59	15.08	15.74	13.09	−0.14	−0.10	−0.26
6	65	male	RML	7.05	15.01	14.00	13.48	11.76	−0.07	−0.10	−0.22
7	52	female	RLL	7.11	25.53	22.81	22.18	19.42	−0.11	−0.13	−0.24
8	59	female	RML	10.91	23.93	22.63	20.45	17.79	−0.05	−0.15	−0.26
9	55	female	RML	2.59	7.26	6.75	5.88	4.89	−0.07	−0.19	−0.33
10	60	male	LML	4.11	13.30	12.61	11.95	11.23	−0.05	−0.10	−0.16
11	83	male	RLL	4.80	18.46	16.51	16.85	14.87	−0.11	−0.09	−0.19
12	52	male	LUL	6.94	21.62	20.58	19.89	17.99	−0.05	−0.08	−0.17
13	47	female	RUL	3.71	9.43	8.76	8.85	7.77	−0.07	−0.06	−0.18
14	75	male	RML	12.78	37.16	34.40	34.59	28.83	−0.07	−0.07	−0.22

Notes: LML: left middle lobe; RML: right middle lobe; RLL: right low lobe; LUL; left upper lobe; RUL: right upper lobe; GTV: gross target volume; ITV: internal target volume; MIP: maximum intensity projection; AIP: average intensity projection; PVD: percent volume difference.

Table 2. dosimetric differences with full arc VMAT plans for different ITV definitions.

	ITV_{all}	TIV_{MIP}	ITV_{AIP}	ITV_{2phase}	p
PTV					
D_{2cm} (%)	59.83 ± 7.47	58.28 ± 5.51	58.00 ± 5.46	59.36 ± 6.43	0.85
CI	1.13 ± 0.06	1.16 ± 0.06	1.16 ± 0.08	1.17 ± 0.09	0.59

Continued

$R_{50\%}$	5.23 ± 0.42	5.23 ± 0.33	5.30 ± 0.38	5.40 ± 0.38	0.59
V_{95} (%)	99.45 ± 0.41	99.48 ± 0.40	99.42 ± 0.53	99.33 ± 0.38	0.82
Lung					
MLD (cGy)	478.92 ± 98.08	449.07 ± 94.49	444.50 ± 105.04	424.25 ± 97.67	0.54
V5 (%)	23.22 ± 4.90	21.14 ± 4.57	21.60 ± 5.43	20.38 ± 4.68	0.48
V12 (%)	10.80 ± 2.99	10.01 ± 2.74	9.88 ± 2.82	9.23 ± 2.51	0.52
V20 (%)	6.48 ± 1.87	5.84 ± 1.61	5.70 ± 1.60	5.42 ± 1.75	0.42
Spinal cord					
D_1 (cGy)	1286.79 ± 343.82	1346.50 ± 349.61	1321.21 ± 390.59	1254.21 ± 443.65	0.93
Heart					
Dmean (cGy)	312.30 ± 202.47	289.68 ± 198.89	291.04 ± 210.27	259.11 ± 171.31	0.91
D_{15cc} (cGy)	1290.21 ± 799.96	1225.43 ± 800.22	1266.9 ± 883.39	1033.57 ± 687.49	0.82
Esophagus					
Dmax (cGy)	1246.86 ± 505.03	1319.07 ± 466.58	2098.64 ± 1653.93	1210.29 ± 422.03	0.04
D_{5cc} (cGy)	740.04 ± 408.64	747.21 ± 416.30	738.50 ± 318.21	646.64 ± 301.18	0.87

Notes: PTV: planning target volume; ITV: internal target volume; MIP: maximum intensity projection; AIP: average intensity projection; MLD: mean lung dose.

partial arc VMAT (P = 0.002). However, partial arc VMAT irradiated less MLD and V5 compared with full arc VMAT. Partial arc VMAT also achieved better protection on spinal cord, heart and esophagus compared with full arc VMAT. The average MU and delivery time of full arc VMAT plans were 240 and 1.6 min more than those of partial arc VMAT. No other significant difference was observed between these two planning schemes.

The dosimetric variations resulting from different ITVs according to full arc VMAT plans were presented in Table 3. The CI of ITV_{all}, ITV_{MIP}, ITV_{AIP} and $ITV_{2phases}$ were 1.13 ± 0.06, 1.16 ± 0.06, 1.16 ± 0.08 and 1.17 ± 0.09, respectively. The $R_{50\%}$ of ITV_{all}, ITV_{MIP}, ITV_{AIP} and $ITV_{2phases}$ were 5.23 ± 0.42, 5.23 ± 0.33, 5.30 ± 0.38, and 5.40 ± 0.38, respectively. The target coverage were more than 99% for all four PTVs and no significant difference on PTV coverage was observed. There were also no significant differences on OARs sparing among these four ITVs. VMAT plans for ITV_{MIP}, ITV_{AIP} and $ITV_{2phases}$ irradiated less lung volume compared to those for ITV_{all}, but the differences were not statistically significant. Except for ITV_{AIP} irradiated a significant higher maximum dose to esophagus compared with plans for other three, there were no significant differences among these four ITVs on sparing of spinal cord, heart and esophagus.

4. Discussion

Tumor motion caused by respiration and the effects on treatment delivering and target definition were major concerns in lung cancer SBRT. The feasibility of partial arc VMAT in lung cancer SBRT treatment, as well the volume changes

Table 3. Dosimetric comparison between full arc and partial arc VMAT plans.

	Full arc VMAT	Partial arc VMAT	p
PTV			
D_{2cm} (%)	58.87 ± 6.14	61.16 ± 6.67	0.002
CI	1.15 ± 0.07	1.14 ± 0.08	0.13
$R_{50\%}$	5.29 ± 0.37	5.28 ± 0.37	0.44
V95 (%)	99.42 ± 0.42	99.46 ± 0.40	0.46
Lung			
MLD (cGy)	449.19 ± 98.16	430.60 ± 99.30	<0.001
V5 (%)	21.59 ± 4.88	18.50 ± 4.99	<0.001
V12 (%)	9.98 ± 2.75	9.88 ± 2.73	0.59
V20 (%)	5.86 ± 1.71	5.89 ± 1.60	0.72
Spinal cord			
D_1 (cGy)	1302.18 ± 375.03	1043.32 ± 488.18	<0.001
Heart			
Dmean (cGy)	288.03 ± 191.81	239.50 ± 174.12	<0.001
D_{15cc} (cGy)	1204.04 ± 780.51	1064.21 ± 781.51	0.001
Esophagus			
Dmax (cGy)	1468.71 ± 967.80	1115.36 ± 479.74	0.006
D_{5cc} (cGy)	718.10 ± 357.14	630.89 ± 268.58	0.01

and dosimetric variation of different ITVs with 4D CT were investigated in this study.

The long delivery time required by 3DCRT SBRT is a crucial drawback due to significant changes in tumor volume and/or position resulted from respiratory motion for lung cancer patients [23]. Single arc VMAT planning had been reported to reduce the treatment time by 37% - 63% and reduce substantially the dose to surrounding normal tissue without comprise the target coverage compared to 3DCRT [24]. In this study, partial arc VMAT was applied to further reduce the required MU and treatment time.

As shown in **Table 2**, there was no significantly difference between full arc and partial arc VMAT in target coverage except for that partial arc VMAT irradiated more dose at 2 cm away from the PTV (P = 0.002). As for normal tissue sparing, partial arc VMAT irradiated less MLD, V5, and achieved better protection on spinal cord, heart and esophagus compared with full arc VMAT. Although the magnitudes of these reductions were small, partial arc VMAT decreased the average MU by 240 and the treatment time by 1.6 min compared with full arc VMAT. This improved treatment efficiency will reduce the patient's time on the table and lead to enhance patient satisfaction and comfort, reduce intrafraction variation, increase time for image-guided positioning and correction, and potentially lead to further reduction in target margin requirements

[25].

Target motion of lung cancer caused by respiration is often unpredictable and a generous isocentric expansion of GTV based on 3D CT images is usually can not fully cover it [26]. Individualized target volume including tumor motion is believed achievable with 4D CT. However, it is still uncertain how can we utilize the information of 4D CT best to generate ITV [27] [28]. In this study, the average PVD of ITV_{MIP}, ITV_{AIP} and $ITV_{2phases}$ to ITV_{all} were 8.6%, 13.4%, and 25.2%, respectively. The MIP-based ITVs showed best agreement with ITV_{all}. This was consistent with previous studies in which it reported that MIP-based ITV was widely adapted due to its excellent correlation with ITV_{all} and significantly reduced clinical workload associated with treatment planning [23].

MIP projections reflect the highest data value encountered along the viewing ray for each pixel of volumetric data, giving rise to a full intensity display of the brightest object along each ray on the projection image. As such, these projections represent composite images with phase summation of tumor positions during all phases of respiration, thereby allowing for direct generation of ITVs. However, when a tumor was located adjacent to high intensity tissues, MIP images may fail to visualize the full extent of the ITV_{all} as a result of ITV_{all} overlapping with tissues due to respiratory motion, leading to significant underestimation of ITV_{all} by ITV_{MIP} [29]. The small PVD between ITV_{all} and ITV_{MIP} in this study may partially due to contour deviations and due to the vicinity of some tumor location to lower and upper lobes.

The ITV_{AIP} and $ITV_{2phases}$ were much less than those of ITV_{all}. The $ITV_{2phases}$ in this study was nearly 25% less than ITV_{all}. This is not a minor deviation considered the small tumor volume of SBRT lung patients as declared in other study [30]. A percent volume difference of 15.3% ± 6.6% between $ITV_{2phases}$ and ITV_{all} had also been reported [31]. However, these volumetric differences did not result in significant dosimetric deviations.

As shown in **Table 2**, the dose differences were small among different ITVs. No significant difference on CI and target coverage was observed. The MLD and the percent lung volume irradiated by certain dose of $ITV_{2phases}$ were smaller than those of ITV_{all} resulted from the significant volumetric differences. The doses delivered to the normal tissues were similar among ITV_{all}, ITV_{MIP} and ITV_{AIP}. Contrary, a previous study reported significant decreases in MLD, lung percent volumes with the decrease of ITV volumes [30]. This inconsistency could be resulted from different normal lung delineations and different window/level settings were applied.

5. Conclusion

Although partial arc VMAT delivered more dose 2 cm out of PTV, it decreases the dose to lung, spinal cord, and esophagus compared with full arc VMAT without sacrificing target coverage. Partial arc VMAT also decreased the total MU and delivery time. Although ITV volumes based on MIP, AIP and 2 extreme

phases of 4D CT were smaller than ITV generated from all ten respiratory phases, there were no significant dosimetric differences resulted due to a relative small GTV of lung SBRT patients.

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Conflicts of Interest

The authors declare that they have no competing interests.

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