Journal of the Korean Physical Society, Vol. 67, No. 9, November 2015, pp. 1672∼1678

Dosimetric Comparison of a 6-MV Flattening-filter and a Flattening-filter-free Beam for Lung Stereotactic Ablative Radiotherapy Treatment

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(Received 26 March 2015, in final form 7 September 2015)

The purpose of this study was to test the feasibility of clinical usage of a flattening-filter-free (FFF) beam for treatment with lung stereotactic ablative radiotherapy (SABR). Ten patients were treated with SABR and a 6-MV FFF beam for this study. All plans using volumetric modulated arc therapy (VMAT) were optimized in the Eclipse treatment planning system (TPS) by using the Acuros XB (AXB) dose calculation algorithm and were delivered by using a Varian TrueBeam^{TM} linear accelerator equipped with a high-definition (HD) multi-leaf collimator. The prescription dose used was 48 Gy in 4 fractions. In order to compare the plan using a conventional 6-MV flattening-filter (FF) beam, the SABR plan was recalculated under the condition of the same beam settings used in the plan employing the 6-MV FFF beam. All dose distributions were calculated by using Acuros XB (AXB, version 11) and a 2.5-mm isotropic dose grid. The cumulative dose-volume histograms (DVH) for the planning target volume (PTV) and all organs at risk (OARs) were analyzed. Technical parameters, such as total monitor units (MUs) and the delivery time, were also recorded and assessed. All plans for target volumes met the planning objectives for the PTV (*i.e.*, $V_{95\%} > 95\%$) and the maximum dose (*i.e.*, $D_{max} < 110\%$) revealing adequate target coverage for the 6-MV FF and FFF beams. Differences in DVH for target volumes (PTV and clinical target volume (CTV)) and OARs on the lung SABR plans from the interchange of the treatment beams were small, but showed a marked reduction (52.97%) in the treatment delivery time. The SABR plan with a FFF beam required a larger number of MUs than the plan with the FF beam, and the mean difference in MUs was 4.65%. This study demonstrated that the use of the FFF beam for lung SABR plan provided better treatment efficiency relative to 6-MV FF beam. This strategy should be particularly beneficial for high dose conformity to the lung and decreased intra-fraction movements because of the shorter treatment delivery time. Future studies are necessary to assess the clinical outcome and the toxicity.

PACS numbers: 87.53.Ly, 87.53.Tf
Keywords: Stereotactic ablative radiotherapy (SABR), Flattening-filter-free (FFF) beam, Lung cancer
DOI: 10.3938/jkps.67.1672

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I. INTRODUCTION

Stereotactic ablative radiation therapy (SABR) uses ultra-hypofractionation to deliver escalated doses in a small number of treatments. In the early stages of lung cancer, this technique has become a standard treatment with an innovative radio-therapeutic technique [1]. Various recent studies oN SABR have reported promising clinical results. Onishi *et al.* evaluated a large number of SABR treatments from a Japanese multi-institutional database [2]. The study showed that SABR was promising as a radical treatment for operable-stage non-small-cell lung cancer (NSCLC). In the Radiation Therapy Oncology Group (RTOG) 0236 trial, a phase II trial of SABR for medically inoperable stage I/II NSCLC, the 3-year local control and overall survival rates were 98 and 56%, respectively [3].

Recently, Truebeam^{TM} linear accelerators with a flattening-filter-free (FFF) beam were introduced into clinical operations. With removal of the flattening filter, two benefits can be expected in radiation therapy: The first is a reduction in the out-of-field dose due to reduced head scatter and leakage. This leads to reduced exposure of normal tissue to scattered doses outside the field. The second benefit is a quicker delivery time with high dose rates. This implies the possibility of fast beam delivery for SABR [4,5].

On the other hand, a profile of the FF beam is not required for volumetric modulated arc therapy (VMAT) because of the superposition of multiple intensity patterns. FFF beams are frequently used for treatment where higher fraction doses need to be delivered, especially hypo- fractionated SABR of the lung, liver, and other sites [6–11]. The feasibility of using the FFF beam for SABR and three dimensions conformal radiotherapy (3DCRT) has been shown in recent studies [7]. 3DCRT and SABR plans using small- and medium-sized beams are, in general, not very different for the FF and the FFF beams. Compared to 3DCRT, SABR use a larger number of treatment fields to achieve a higher conformal dose distribution around the target volumes.

In this study, we accessed the feasibility of clinical usage of a 6-MV FFF beam, compared to conventional 6-MV FF beam for lung SABR using the VMAT technique. The cumulative dose-volume histograms (DVH) for target volumes and organs at risk (OARs) between the plans using the FF and the FFF beam were analyzed for dosimetric quantification. Additional, technical parameters, such as total monitor units (MUs) and delivery times, were investigated.

II. MATERIALS AND METHODS

1. Patient Selection

Ten patients who had been treated with lung SBAR at our clinic between May 2013 and January 2014 were selected at random for the current planning study, which was approved by our institutional review board (IRB). Six and four patients had tumors in the left and the right lungs, respectively. The average clinical target volume (CTV) and planning target volume (PTV) were 5.54 (range: $0.42 - 12.55$ cm^3) and 18.44 cm^3 (range: $6.10 - 38.70$ cm^3), respectively.

2. Treatment Planning

All patients were treated in the supine position with their arms crossed above their heads during free breathing. The SABR immobilization platform (Body Pro-Lok, CIVCO, Orange City, IA, USA) was used to fix the thoracic and abdominal regions and reduce residual body motion. Four-dimensional computed tomography (4DCT) data for these patients with lung tumors who underwent SABR were used, and the scans were acquired with 2-mm slice spacing on the flat table top of a Philips Big-bore CT scanner. The Digital Imaging and Communications in Medicine (DICOM) CT data were electronically transferred to the Eclipse TPS for contouring and planning. The gross tumor volume (GTV) was contoured in each of the 10 4DCT data and the CTV was generated by combining the GTVs from all respiratory phases ($0 - 90\%$) of 4DCT. PTVs were created by adding 5-mm margins to the CTV in all directions. The OARs considered were the lungs, heart, and spinal cord. The lung volume was divided into ipsilateral and contralateral lung volumes. Both lung volumes were defined as the bilateral lung outside the PTV.

The beam parameters of the clinical treatment plan were set up in the Eclipse TPS, and the plans for each beam were calculated by using the VMAT (RadpidArc®, Varian Medical Systems) technique with two partial arcs allowing maximum available dose rates of 600 and 1400 monitor unit (MU)/min for 6-MV FF and 6-MV FFF beams, respectively. A dose rate of 1400 MU/min can be delivered, which is about 2.3 times faster than the commonly used dose rate. The dose prescription was 48 Gy in four fractions to deliver a biological equivalent dose (BED) exceeding 100 Gy. A plan normalization point in the center of the PTV was created and assigned a dose of 48 Gy. In order to compare the plan using the FF beam, we re-optimized the SABR plan using a 6-MV FF beam under the condition of the same dose constraints and beam settings used in the plan employing 6-MV FFF beams to have the equivalent plan quality. The dose distributions were calculated using by the Acuros (AXB) dose algorithm with the inhomogeneity correction. The calculation grid was 2.5 mm.

According to the RTOG protocol (RTOG 0618 and 0915), the optimization goals were to ensure that the PTV cover 95% of the volume that received 95% of the prescribed dose, with no PTV hot spot receiving 110% or more of the prescribed dose. Doses exceeding 110%

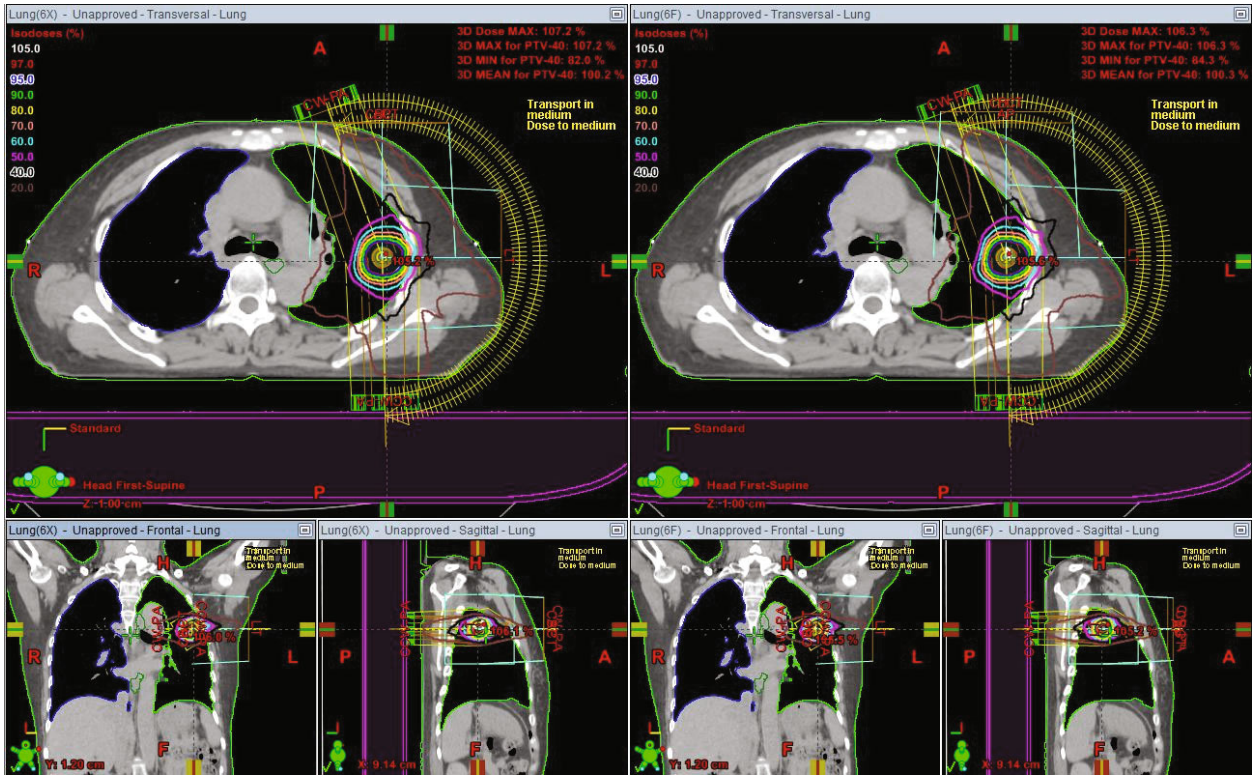

Fig. 1. (Color online) Example dose distributions for the lung SABR plan achieved with 6-MV FF (left) and FFF (right) beams.

Table 1. Dose volume constraints of organs at risk adopted for the planning study.

Volume	Constraints
Contralateral lung	$V_{20} < 10\%$
Ipsilateral lung	$V_{20} < 30\%$
	$V_{12.5} < 15\%$
Heart	$D_{max} < 30$ Gy
Spinal cord	$D_{max} < 20$ Gy

V_{20}, $V_{12,5}$: the volumes receiving 20 Gy, 12.5 Gy, respectively.

were permitted only inside the target. The dose volume constraints of the OARs are defined in Table 1.

3. Evaluation of Dosimetric and Technical Parameters

The cumulative dose-volume histograms (DVHs) and technical parameters were compared for all cases. The mean doses, maximum doses, minimum doses, R_{100} and R_{50} (Rx: ratio of x% isodose volume to PTV) for the PTV were measured. To represent the target coverage, we evaluated $V_{95\%}$ of the PTV (PTV receiving more than 95% of the prescribed dose) and the $V_{100\%}$ of the CTV. To quantify the dose uniformity in the PTV, we analyzed the homogeneity index (HI) for each plan. The HI of the PTV (as defined by the International Commission on Radiation Units and Measurements report 83 [12]) is defined as

$$HI = \frac{(D_{2\%} - D_{98\%})}{D_{50\%}}, \quad (1)$$

where $D_{2\%}$ means the maximum dose received by 2% of the PTV, $D_{98\%}$ means the minimum dose received by 98% of the PTV, and $D_{50\%}$ means the dose received by 50% of the PTV. A lower HI represents a more homogeneous plan because $D_{2\%}$ and $D_{98\%}$ are surrogate markers of the maximum dose and the minimum dose in the PTV, respectively [13]. The conformity index (CI) is defined as

$$CI = \frac{TV_{RI}^2}{TV \times TV_{RI}}, \quad (2)$$

where TV and TV_{RI} represent the PTV volume and the volume covered by 95% of the prescribed dose. A CI equal to 1 corresponds to an ideal conformation, and a CI greater than 1 represents healthy tissues that are irradiated [14]. To consider the irradiation of healthy tissue, we evaluated the conformation number (CN). The CN is the product of two fractions, TV_{RI}/TV and TV_{RI}/V_{RI}. V_{RI} is defined a volume covered by 95% of the prescribed

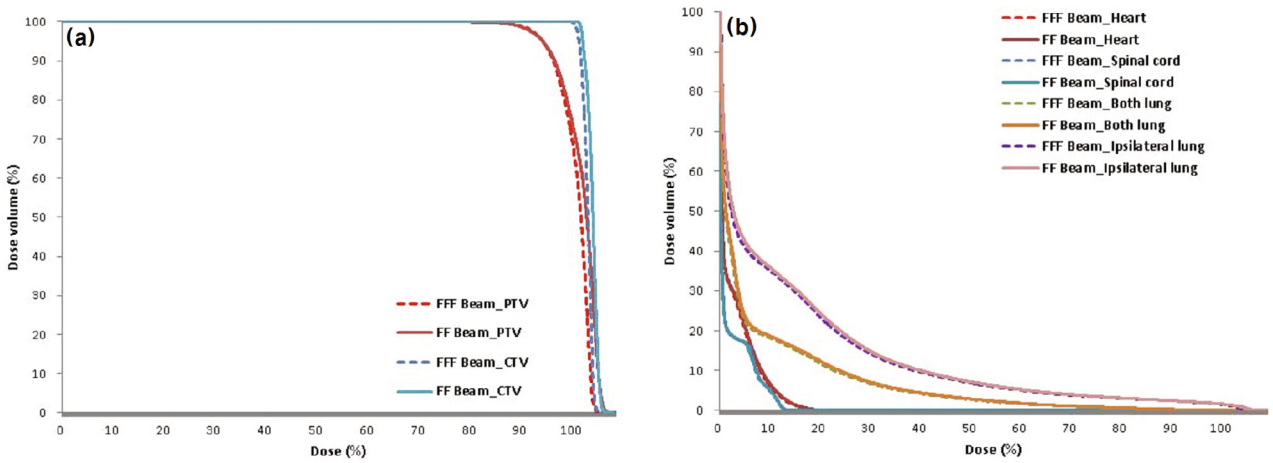

Fig. 2. (Color online) Average dose volume histogram (DVH) for (a) target volumes (PTVs and CTVs) and (b) all OARs in the lung SABR plan achieved with 6-MV FF and FFF beams.

dose. The first fraction represents the quality of target coverage, and the second factor represents the volume of healthy tissue irradiated with the reference isodose or more [15]. In the current study, we used the 95% isodose as the reference isodose.

For the lungs, the mean dose, maximum dose, and percentage volumes receiving 5 and 10 Gy (V_{5Gy} and V_{10Gy}, respectively), as well as V_{20Gy}, were compared. The maximum dose was evaluated for the heart and spinal cord. Additionally, the technical parameters of delivery, such as the total monitor units (MUs) and beam delivery time, were recorded for each plan. The beam delivery time was only a beam-on time and excluded patient setup imaging and immobilization time for the overall treatment process. The beam delivery time was defined as the aggregate time during which the machine delivered photons for two arcs in a given plan.

III. RESULTS AND DISCUSSION

In VMAT-SABR planning for lung cancer, we investigated the impact on the dose distribution and technical parameters of using 6-MV FF and 6-MV FFF beams. Figure 1 illustrates example dose distributions achieved with 6-MV FF and FFF beams for the same patient. Figure 2 shows the average DVH of the target volumes (PTV and CTV) and all OARs for the two beams. Table 2 shows the detailed dosimetric results for the target volumes as obtained from DVH analysis for each patient. There was not much difference in the CTV and the PTV doses between the FF and the FFF beams, but the maximum doses to the CTV and the PTV exhibited relatively high differences; specifically, the PTV dose for the FFF beam plan was lower than that for the FF beam plan (52.63 Gy vs. 53.99 Gy). FFF beam plans delivered higher minimum doses for the PTV and the CTV than the FF beam, but the difference was small. Concerning the target coverage, all the plans achieved the planning objectives for the PTV (*i.e.*, $V_{95\%} > 95\%$) and the maximum dose (*i.e.*, $D_{max} < 110\%$) revealing adequate target coverage for the 6-MV FF and FFF beams. The 6-MV FFF beam, however, generated conformal dose distributions slightly higher than the ones achieved with the 6-MV FF beam. The HI values were lower (0.122 vs. 0.142) with the 6-MV FFF beam than with the 6-MV FF beam. A lower HI indicates a more homogeneous plan because $D_{2\%}$ and $D_{98\%}$ are surrogate markers for the maximum and the minimum doses to the PTV, respectively. The CI value, which indicates the $V_{95\%}$ in the lung SABR plans show that the CI value for the FF beam was slightly higher (1.053 vs. 1.048), than that for the FFF beam, which means that 6-MV FFF plan exhibited better conformity. The R_{50} and the R_{100} values were always lower in plans with the FFF beam than in those with the FF beam by average differences of 2.48% and 1.75%, respectively. The results indicate that plans using the FFF beam generated more conformal dose distributions and produced lower intermediate-dose spillage than these using the FF beam.

Table 3 presents the dosimetric results for all OARs. OAR constraints were met in all plans using both the FF and the FFF beams. For the plan generated with the FFF beam, the mean V_5, V_{10}, and V_{20} for the ipsilateral lung were 35.30%, 22.86%, and 15.90%, respectively, when a dose of 48 Gy was delivered to the isocenter. After a recalculation using the FF beam, these values were 35.42%, 22.90%, and 15.93%, respectively. The V_{20Gy} values for the ipsilateral lung were always higher on all plans with the FF beam compared to these with the FFF beam. The V_{5Gy} and V_{10Gy} were also slightly reduced in the plans using the FFF beam when compared to the ones with the FF beams. The reason for this phenomenon is a reduction of the out-of-field dose with reduced head scatter and leakage dose from the FFF beam.

Table 2. Summary of dosimetric results from dose volume histogram analyses of the PTV, and the CTV, on lung SABR plans using the 6-MV FFF and FF beams.

	FFF (Mean ± SD)	FF (Mean ± SD)	Relative difference (%) (FFF-FF)/FF × 100
CTV			
Maximum dose (Gy)	52.63 ± 2.11	53.99 ± 1.79	−2.52
Mean dose (Gy)	48.48 ± 1.53	48.55 ± 1.55	−0.14
Minimum dose (Gy)	46.59 ± 3.04	46.32 ± 2.71	0.58
$V_{95\%}$ (%)	100.52 ± 0.83	100.63 ± 0.36	−0.10
$V_{100\%}$ (%)	99.38 ± 1.23	99.92 ± 0.63	0.15
PTV			
Maximum dose (Gy)	52.83 ± 2.98	54.27 ± 2.13	−2.65
Mean dose (Gy)	48.68 ± 1.51	48.16 ± 1.49	1.08
Minimum dose (Gy)	42.12 ± 3.79	41.88 ± 3.25	0.57
$V_{95\%}$ (%)	95.35 ± 5.53	95.31 ± 3.35	0.04
$V_{100\%}$ (%)	86.75 ± 5.81	86.50 ± 4.33	0.29
$V_{105\%}$ (%)	3.08 ± 2.58	2.87 ± 1.05	4.32
Homogeneity index	0.122 ± 0.012	0.142 ± 0.025	−14.08
Conformity index	1.048 ± 0.071	1.053 ± 0.093	−0.47
Conformation number	0.916 ± 0.49	0.912 ± 0.10	0.44
R_{50}	3.93 ± 0.64	4.03 ± 0.65	−2.48
R_{100}	1.12 ± 0.14	1.14 ± 0.14	−1.75

FFF: flattening-filter-free, FF: flattening filter, SD: standard deviation, V95%, V100%, V105%: the volumes receiving 95%, 100%, and 105% of the prescribed dose, respectively, RX: ratio of X% isodose volume to PTV volume.

Table 3. Surmmary of dosimetric results for all organs at risk on lung SABR plans using the 6-MV FFF and FF beams.

	FFF (Mean ± SD)	FF (Mean ± SD)	Relative difference (%) (FFF-FF)/FF × 100
Both lung			
V_{5Gy} (%)	22.11 ± 6.13	22.60 ± 5.61	−2.21
V_{10Gy} (%)	13.37 ± 4.31	13.69 ± 4.69	−2.34
V_{20Gy} (%)	4.86 ± 1.33	5.33 ± 1.36	−8.82
MLD (Gy)	4.26 ± 1.14	4.44 ± 1.25	−4.05
Ipsilateral lung			
V_{5Gy} (%)	35.30 ± 3.83	35.42 ± 3.50	−0.34
V_{10Gy} (%)	22.86 ± 2.44	22.90 ± 2.43	−0.17
V_{20Gy} (%)	15.90 ± 2.02	15.93 ± 2.01	−0.19
MLD (Gy)	8.40 ± 0.66	8.42 ± 0.65	−0.24
Spinal cord			
Maximum dose (Gy)	8.40 ± 2.19	8.45 ± 1.73	−0.59
Heart			
Maximum dose (Gy)	12.36 ± 9.58	12.46 ± 9.47	−0.80

FFF: flattening-filter-free, FF: flattening filter, MLD: mean lung dose, V_{5Gy}, V_{10Gy}, V_{20Gy}: the percentage volumes receiving 5, 10, and 20 Gy dose, respectively.

However, the differences in the corresponding values for both lungs were comparable (within approximately 1%) between plans with the FFF and the FF beams as shown in Table 2. Concerning the spinal cord and heart, a negligible difference was observed in the plans between the two different beam types.

Table 4. Comparison of technical data on lung SABR plans using the 6-MV FFF and FF beams.

Beams	FFF (Mean ± SD)	FF (Mean ± SD)	Relative difference (%) (FFF-FF)/FF × 100
Delivery time (min)	2.22 ± 0.59	4.72 ± 0.72	−52.97
MU	2813.2 ± 478.2	2688.2 ± 446.5	4.65

FFF: flattening-filter-free, FF: flattening filter, MU: monitor unit.

Table 4 exhibits the mean treatment delivery times and total MUs. The mean delivery times for the 6-MV FFF and the 6-MV FF beams were 2.22 ± 0.59 min and 4.72 ± 0.72 min, respectively. Overall mean dose rates, considering all plans, were 1267 ± 125 MU/min and 578 ± 15 MU/min, for the 6-MV FFF and the 6-MV FF beams. The average delivery time of the 6-MV FFF beam was reduced by 52.97% when compared with that of the FF beam. This was the higher dose rate being 2.3 higher with the FFF beam. The reduction in the delivery time was the most obvious benefit of the FFF beam. The use of the FFF beam for lung SABR could allow faster and safer radiation treatment delivery to the patients compared to radiation delivery techniques with the FF beam due to the reduced tumor position uncertainty related to intrafraction motion and patient movement error between setup and treatment completion [9,16,17]. In the study reported by Stieb *et al.*, the use of the FFF beam at the available maximum dose rate, if carefully applied, appear to be safe for SABR [18].

All plans using the 6-MV FFF beam required more MUs than ones using the 6-MV FF beam. The relative difference in MUs between the FF and the FFF beams was 4.65%. The increase in the MUs for the FFF beam was associated with the increasing target volume for patients and the conical profile of the beam. Because of the larger target volumes, the dose uniformity within an irradiated larger PTV will need to be modulated by MLC movement to cut down the higher beam intensity near the central positions of FFF beams. Therefore, the MUs in the plans using the FFF beam had to be increased to obtain suitable PTV coverage as in the plans using the FF beam. This was in line with several previous studies in which increasing numbers of MU were reported [11, 19,20]. The spectrum of a 6-MV FFF beam is typically softer than that of a 6-MV FF beam because beam hardening is generated by the flattening filter. The spectrum difference of the FFF beam may impact the number of MUs and the depth-dose distribution. Vassiliev *et al.* reported that the depth-dose distribution of a 6-MV FFF beam was similar to that of 4 and 5-MV beams [7].

Several previous studies have evaluated the plan quality for VMAT with FFF beams compared to VMAT with FF beam, especially in the lung, prostate, and other sites [9, 11, 16, 19–21]. Most of the studies showed that the FFF beam produced a dose distribution and an OAR dose similar to FF beam as we found here. In contrary, Zhuang *et al.* found in their study that the FF beam was superior to the FFF beam due to the lower dose to most OARs and to the better conformity and homogeneity of the PTV for the treatment of nasopharyngeal carcinoma [21]. However, all studies observed a marked reduction in the delivery time for the VMAT-SABR with FFF beams.

One limitation of this study is that no definitive clinical data have been reported for the short- and the long-term outcome results for lung SABR. Our current study focused mainly on the feasibility and the efficiency of using the FFF beam in SABR treatment for lung cancer. Therefore, for safe use of the FFF beam, future studies are required to evaluate the clinical outcomes and the toxicity for lung SABR treatment.

IV. CONCLUSION

Dose distributions of the lung SABR plan using 6-MV FFF beams was closely similar to the ones generated in the plan using 6-MV FF beams. However, this study confirmed that the use of the FFF beam at maximum dose rate for lung SABR offer obviously shorter delivery time compared to the FF beams. The strategy is associated with high dose conformity to the lung, excellent patient stability, and decreased intra-fraction movements resulting from the large fraction dose because of the shorter treatment delivery time. Therefore, the results of this study suggest that the lung SABR using a 6-MV FFF beam is a feasible technique for treating cancer. For the safe clinical use of the FFF beam, future follow-up studies are necessary to assess the clinical outcome and toxicity for lung SABR.

ACKNOWLEDGMENTS

This research was supported by Choonhae College of Health Sciences.

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