# **Annals of Radiation Therapy and Oncology**

പ

# **Dose-Volume Comparison for Optimal Beam Findings for Stereotactic Body Radiation Therapy in Lung Carcinoma**

Priyanka Agarwal<sup>1\*</sup>, Rajesh Kinhikar<sup>2</sup>, Rakhi Berman<sup>2</sup>, Naveen Mummudi<sup>2</sup>, Shrikant Kale<sup>2</sup> and Jaiprakash Agarwal<sup>2</sup>

<sup>1</sup>Homi Bhabha Cancer Hospital (Tata Memorial Center), Varanasi, India <sup>2</sup>Tata Memorial Hospital, Mumbai, India

## Abstract

Aim: To study the dosimetric differences of using different energy in the case of Lung SBRT VMAT treatment planning.

Materials and Methods: A total of 12 patients with stage I non-small cell lung cancer (36 plans) with PTV of 63.3 cc to 115.4 cc were selected for this study retrospectively. Three different treatment plans were generated using 6XFF, 6XFFF, and 10XFFF energies with same optimization constraints to deliver 60 Gy in 8 fractions with two partial arcs on Eclipse TPS. A progressive resolution optimizer and Acuros algorithm were employed for optimization and dose calculation, respectively. Planning evaluation was carried out qualitatively and quantitatively for PTV and OARs doses, as per RTOG guidelines (0813/0915). Delivery quality assurance for each plan was performed using the PTW Octavius-4D phantom. In addition, the point dose was verified using a thimble ion chamber.

Results: The Coverage Index (CI) (p<0.05) was the same 96% ± 0.008 for 6XFF and 6XFFF, while 94% ± 0.012 for 10XFFF. The mean Conformity Index (COIN) (p>0.05) for 6XFF, 6XFFF and 10XFFF was 0.956  $\pm$  0.036, 0.957  $\pm$  0.037, and 0.936  $\pm$  0.043, respectively. Mean treatment time (p<0.05) for 6XFF, 6XFFF and 10XFFF was  $3.7 \pm 0.41$ ,  $1.55 \pm 0.21$  and  $1.13 \pm 0.13$  minutes, respectively. Mean gamma (3%, 3 mm) was  $96.5 \pm 1.12$ ,  $96.3 \pm 1.03$  and  $97.4 \pm 1.3$  for 6XFF, 6XFFF and 10XFFF, respectively. Mean point dose difference in % between TPS and measurement was 2.2  $\pm$  0.4, 2.4  $\pm$  0.9 and 2.68  $\pm$  0.9 for 6XFF, 6XFFF and 10XFFF respectively.

Conclusion: We found 6XFFF to be the optimal choice based on OAR sparing with no compromise for coverage and conformity index.

**OPEN ACCESS** 

#### \*Correspondence:

Priyanka Agarwal, Department of Radiation Oncology, Homi Bhabha Cancer Hospital, Tata Memorial Centre, India, Tel: 9454536365 Received Date: 04 Aug 2023 Accepted Date: 22 Aug 2023 Published Date: 26 Aug 2023

### Citation:

Agarwal P, Kinhikar R, Berman R, Mummudi N, Kale S, Agarwal J. Dose-Volume Comparison for Optimal Beam Findings for Stereotactic Body Radiation Therapy in Lung Carcinoma. Ann Radiat Ther Oncol. 2023; 4(1): 1023.

Copyright © 2023 Priyanka A. This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Keywords: Lung SBRT; Flattening Filter Free (FFF) beam; Non-small Cell Lung Cancer (NSCLC); Lung dosimetry

## Introduction

Stereotactic Body Radiotherapy (SBRT), Stereotactic Ablative Radiotherapy (SABR) and Stereotactic Radiosurgery (SRS) are advanced treatment techniques and effective modalities for cancer treatment at sites such as the lung, liver, kidney, brain, spine, and pancreas. In SBRT, a high dose of radiation is delivered over a short period; therefore, the accuracy of treatment delivery is of paramount importance to ensure adequate target coverage and sparing of the normal tissues.

SBRT is considered a viable treatment option for early stage-I Non-Small Cell Lung Cancer

(NSCLC), in both operable and inoperable settings [1]. There are several complexities and challenges in generation of lung SBRT plans for heterogeneous targets. Moreover, planning algorithms are based on electron densities, which add uncertainties to dose calculations [2,3]. Other challenges include the proximity of Organs at Risk (OARs), such as the spinal cord, normal lung, esophagus, heart, Proximal Bronchus Tree (PBT), and chest wall, and if the target location is peripherally located, skin sparing seems to be a concern.

In the entire course of treatment, respiratory motion of the target is unpredictable. While delineating the target as well as normal structures, it is necessary to keep in mind inter and intrafraction motion strategies. Hence, several methods have been developed to account for respiratory motion during simulation and treatment to reduce the uncertainty in target delineation and treatment delivery, such as respiratory gating and breath-hold techniques [4]. All these techniques reduce variability throughout the treatment. However, such methods increase the treatment time on the couch, resulting in patient discomfort and treatment delivery uncertainty.

At present, linear accelerators can deliver treatment using both Flattening Filter (FF) beams and

Flattening Filter-Free (FFF) beams [5]. There are numerous technical benefits of FFF beam over the FF beam for Volumetric Modulated Arc Therapy (VMAT) planning. First, the major benefit of the FFF beam is its high dose rate, which results in a shorter treatment time. The primary beam has a non-uniform profile and offers less energy variation in the lateral direction when the flattening filter is removed [6,7]. This characteristic of a linear accelerator supports limiting head scattering, less peripheral dose, high conformity, limiting the body integral dose, Multileaf Collimator (MLC) transmission, and leakage [8]. Because of the numerous variabilities in FFF and FF beams, the dosimetric outcomes have been variable.

Therefore, we compared the dosimetric differences among 6XFF, 6XFFF, and 10XFFF beam for previously treated cases of lung SBRT. Plan Delivery Quality Assurance (DQA) for absolute dose and gamma analysis was performed for each plan.

# **Materials and Methods**

## Study design, target delineation and treatment unit

For this study, a total of 12 previously treated lung patients (5 left and 7 right) with stage-I non-small lung cell carcinoma was enrolled from the institutional database. This was a retrospective study to evaluate the dosimetry impact of changing beam energy for plan evaluation. The patients were simulated using a Four-Dimensional Computed Tomography (4DCT) GE CT scanner (Light Speed 16, Version, Waukesha, WI, USA) and were immobilized with Vaclok. The image slice width of 1 mm was acquired for the target and OAR delineation. These images were transferred for contouring and planning purposes to the Eclipse treatment planning system (Varian Medical System, Palo Alto, USA), version 13.5. Target delineation was carried out according to the guidelines for lung SBRT [9].

First, Gross Tumor Volume (GTV) and Clinical Target Volume (CTV) were segmented. Furthermore, the phase-based Internal Target Volume (ITV) was segmented in each phase so that the target was drawn throughout the respiratory cycle. Therefore, the Planning Target Volume (PTV) was delineated by considering all phases of the ITVs, with an appropriate additional margin of 5 mm for setup accuracy. Subsequently, the organs at risk (spinal cord, esophagus, normal lung, heart, and skin) were drawn.

The plans were generated for True Beam linear accelerator (Varian Associates, Palo Alto, CA, USA), version 2.5. It has five photon energies with Photon energy 6XFF, 10XFF, 15XFF having a maximum dose rate of 600 MU/min. The maximum dose rates for the photon energies 6XFFF and 10XFFF is 1400 MU/min and 2400 MU/min respectively. The linear accelerator was tuned for 1cGY per MU at a 100 cm Target to Surface Distance (TSD) at a depth of 10 cm from the surface for 10 cm × 10 cm field size. True Beam linear accelerator comprises of a total of 60 pairs of tertiary Millennium MLC [9] with a maximum field size of 40 cm × 40 cm at 100 cm TSD. Further, the central 40 MLC pairs width at isocenter (20 cm treatment length) is 5 mm, and the remaining peripheral MLC width is of 10 mm at isocenter. Hence all the plans were generated only using 5 mm width central MLC.

## **Treatment planning**

First, the VMAT plans were generated using a 6XFF beam with the highest available dose rate. All VMAT plans were generated using Eclipse TPS, and optimization was performed using the Progressive Resolution Optimizer (PRO) algorithm. The final dose calculation was carried out with the Acuros XB algorithm, which takes into accounts all the inhomogeneity corrections during dose calculation (calculation dose to medium), depending on Linear Boltzmann Transport Equation (LBTE) [10]. The grid size for planning was kept at 1.25 mm. All the dynamic VMAT plans were generated with two co-planar partial arcs (contralateral lung saved while choosing a partial arc) and the collimation angle for each patient plan was set at 45°. For sharp dose gradient fall-off, the Normal Tissue Objective (NTO) value was kept at 30% fall-off at 0.5 cm a distance of PTV. The plans were generated using jaw tracking, and the total dose was prescribed 60 Gy in 8 fractions means 7.5 Gy per fraction. The best possible plan using a 6XFF beam was generated with one optimization without changing any dose constraints during the optimization for each patient and was assumed as a base plan.

Further, for each patient, two new plans were generated with FFF beams, 6XFFF and 10XFFF, with their maximum available dose rates for the same treatment unit. For the true planning comparison, the arc angles, collimator angles, and optimization parameters were kept the same for each patient plan. Data collection was performed after the completion of the plans in the same manner, without allowing further improvements to any constraints. A total of 36 plans were generated for 12 patients included in the study.

#### **Plan evaluation**

Plan acceptance was set using the Radiation Therapy Oncology Group (RTOG) guidelines 0813 and 0915 [11,12]. All 6XFFF and 10XFFF plans were compared with respect to their 6XFF plans using a cumulative Dose-Volume Histogram (DVH). For dosimetry comparison of OARs of each plan w.r.t. 6XFF plan, the ratios of the 6XFFF and 10XFFF plans were analyzed as 6XFF/6XFFF and 6XFF/10XFFF.

The following PTV parameters were used to evaluate the plan quality Coverage Index (CI) [13] (institutional acceptance criteria: 95% of the prescription dose to 95% of PTV volume), Conformity Index (COIN) [14], Homogeneity Index (HI) [15], Dose to Healthy Tissue (DHT=body-PTV), D2 cm (maximum dose point in cGy at any 2 cm diameter farther away from PTV in any direction) [11,12], R50% (ratio of volume of 50% prescription isodose volume to the volume of PTV) [11,12], body integral dose (body mean dose), Monitor Units (MU), treatment time, and average dose rate. The remaining organs at risk doses to the spinal cord, esophagus, brachial plexus, and heart were recorded.

## Plan delivery quality assurance

Delivery Quality Assurance (DQA) is required prior to accepting the plan because of the significant level of uncertainty in such a heterogeneous lung target. Each of the 36 plans in this study had its validity confirmed twice. Data from the TPS and measurements were compared in terms of absolute dosage. For fluency verification, a gamma evaluation [16,17] was carried out.

Here, fluence verification was performed on the Truebeam through an Octavius phantom (Seven29, PTW, Freiburg, Germany). Gamma Evaluation Scores (GES) were determined for a Dose Difference (DD), a distance to agreement (DTA) of 3%, 3 mm, and 2%, 2 mm, with a 10% threshold. Absolute dose measurements were also performed using a solid water phantom (PTW, RW3 phantom) and a thimble chamber (volume 0.13 cc). In addition, the acceptance criteria for the absolute dose variation between the actual and delivered plans was approved within 3%.

#### Statistical analysis

In order to determine the statistical significance of all parameters that were studied, a one-way repeated ANOVA test was applied using SPSS software (version 26.0, IBM Corp., South Asia Pvt. Ltd., India). For Statistical significance was set at p<0.05. It was decided to assess the coverage index using a box-and-whisker graphic.

# **Results**

#### **Patient's characteristics**

The GTV and PTV volume range from minimum to maximum was from 7.4 cc to 62.1 cc and 63.3 cc to 115.4 cc, respectively. The mean ( $\pm$  SD) and median GTV were 31.6 ( $\pm$  38.9) cc and 29.7 cc. Similarly, the mean ( $\pm$  SD) and median PTV were 86.3 ( $\pm$ 17.6) cc and 85.7 cc respectively.

#### Planning target volume assessment

The mean coverage indices of the PTV for the 6XFF and 6XFFF plans were 96%  $\pm$  0.008 and 94%  $\pm$  0.012 for 10XFFF plan respectively. The cumulative DVH of the three-beam plans 6XFF, 6XFFF, and 10XFFF are showed. The mean coverage index for PTV (p<0.01) of 6XFFF was 1.002 times more than that of 6XFF, while opposite for 10XFFF, it was 0.989 times less than that of 6XFF. The mean Conformity Index (COIN) of the PTV was 0.956 ± 0.036,  $0.957 \pm 0.037$ , and  $0.936 \pm 0.043$  for the 6XFF, 6XFFF and 10XFFF plans respectively. The results showed that 6XFFF plans were more conformal than 6XFF and 10XFFF plans. The mean homogeneity index (p<0.007) for 6XFF, 6XFFF, and 10XFFF was 1.109  $\pm$  0.01,  $1.108 \pm 0.01$ , and  $1.128 \pm 0.02$ , respectively. R50% was obtained 3.59  $\pm$  0.58, 3.55  $\pm$  0.56 and, 3.55  $\pm$  0.59 for 6XFF, 6XFFF and 10XFFF plans, respectively. Similarly, D2 cm was 47.97 Gy ± 4.2 Gy, 48.38 Gy  $\pm$  4.27 Gy and, 48.3 Gy  $\pm$  4.07 Gy for 6XFF, 6XFFF, and 10XFFF plans, respectively.

The Monitor Units (MU) obtained from the plans was subjected to depth, plan complexity, and dose constraint modulation. The average monitor units for 6XFF, 6XFFF, and 10XFFF plans were 2029.5  $\pm$  253.3, 2161.5  $\pm$  305.1, and 2103.9  $\pm$  323.7 respectively, which were 1.07 and 1.04 times more for 6XFFF and 10XFFF as compared to 6XFF. A statistically significant difference was found in treatment time (p<0.001). The estimated average treatment time for the 6XFF base plan was 3.37  $\pm$  0.41 min, while it was reduced 0.46 times for plan 6XFFF and 0.33 times for 10XFFF than the 6XFF plan. The average dose rate was 2350 MU/min for the 10XFFF plan. The 6XFF Annals of Radiation Therapy and Oncology

and 6XFFF plans were delivered with constant maximum dose rates. The average integral dose of the body for 6XFF, 6XFFF, and 10XFFF was 352.6 cGy  $\pm$  96.3 cGy, 348.1 cGy  $\pm$  96.9 cGy, and 351.3 cGy  $\pm$  97.1 cGy, respectively. The 6XFFF beam produced the lowest integral dosage.

In summary, 6XFFF plan was the optimum plan in terms of coverage index and conformity index compared to the base plan. 10XFFF was the best option in terms of therapy delivery time.

### Evaluation of organ at risks

Table 1 provides a summary of the OARs results for the 6XFF base plan. OAR doses with 6XFFF and 10XFFF plans were normalized in relation to 6XFF summarized in Table 2. The predominant OAR was the normal lung during planning. With decreases of 0.979, 0.971, and 0.978 times for V5, V20, and mean lung dosage, respectively, the result demonstrates a statistically significant difference (p<0.01) in the normal lung dose for the 6XFFF plans compared to the 6XFF plan, making it extremely useful for plan evaluation. Now, V5 for the heart was reduced by 0.953 times for the 6XFFF plan, while it was 1.037 times more for 10XFFF as compared to 6XFF plan. The spinal cord dose was higher in the 6XFFF plan as compared to base plan, but the difference was not statistically significant.

The skin dose (10 cc dose), proximal bronchial tree maximum dose, and chest wall dose volume (V30 and V60) were higher for 6XFFF than for 6XFF, but the difference was not statistically significant. However, the Skin dose for 10 cc and chest wall dose-volume V30 was less compared to 6XFF.

#### Delivery quality assurance

Table 3 lists the DQA outcomes for gamma evaluation and absolute dose variation. The results show, for 10XFFF plans, the average gamma passing rate was 97.4% for 3%, 3 mm (p=0.07). This was 1.01% more than the base plan, while the opposite was reduced 0.99 times for the 6XFFF plans compare to the base plan. One set of plans had gamma passing rates of 94.7%, 94%, and 94.1% for the 6XFFF, 6XFFF, and 10XFFF plans respectively, which were not acceptable. In short, the gamma fluence for the 6XFFF plan was less than that for the 6XFF and 10XFFF plans, but acceptable except for one plan.

The absolute dose variation (p=0.41) was better in the 6XFF plan than that in both beam plans. In one patient plan, the absolute dose discrepancy was found to be 3.08% in the case of the 6XFF base plan.

Table	1: '	The mean	doses o	of the C	Drgans	at Risk	(OARs)	for 6XFF	plans	along	with ra	nges (	(min-m	ıax).

OAR Name	Evaluated Parameters	Observed Dose	Range (min-max)	
	V5	32.17% ± 11.8	12.4% - 47.1%	
Normal Lung	V20	9.55% ± 5.2	4.7% - 12.2%	
	Mean Lung Dose (Gy) 5.98 Gy ± 2.0		2.44 Gy - 8.52 Gy	
Ipsilateral Lung	V25 (cc)	471.9 cc ± 200	84.6 cc - 805.6cc	
	V5	25.87% ± 24.7	8.0% - 82.5%	
Heart	Mean Heart Dose (Gy)	1.96 Gy ± 0.8	1.04 Gy - 3.72 Gy	
Esophagus	D (5cc) (Gy)	12.1 Gy ± 7.3	0.5 Gy - 17.03 Gy	
Spinal Cord	D (0.5 cc) (Gy)	10.05 Gy ± 2.3	4.3 Gy - 12.9 Gy	
Skin	V10 (cc)	16.97 Gy ± 4.12	9.8 Gy - 20.4 Gy	
Proximal Bronchial Tree (PBT)	Max Dose (cGy)	52.2 cGy ± 14.6	25.3 cGy - 64.9 cGy	
	V 30 (cc)	93.7 cc ± 50.6	19.6 cc - 113.1 cc	
Chest waii	V 60 (cc)	5.5 cc ± 6.8 cc	0.7 cc - 19.7 cc	

OAR NAME	Evaluated Parameters	6XFF/6XFF	6XFFF/6XFF	10XFFF/6XFF	p-value
	V5	1	0.979	1.062	<0.01
Normal Lung	V20	1	0.971	1.011	0.01
	Mean Lung Dose (GY)	1	0.978	1.021	<0.01
11	V5	1	0.953	1.037	0.015
nean	Mean Heart Dose (Gy)	1	0.984	0.984	0.18
Spinal Cord	V0.5 (cc)	1	1.013	1.06	0.12
Esophagus	V5 (cc)	1	0.986	1.001	0.95
Body Integral Dose	Mean Dose	1	0.984	0.995	0.09
Ipsilateral Lung	V25	1	0.98	1.005	0.98
Skin	V10 (cc)	1	1.06	0.89	0.25
Proximal Bronchial Tree (PBT)	Max Dose (cGy)	1	1.01	1.007	0.99
Chaotwall	V 30 (cc)	1	1.002	0.97	0.98
Criest wall	V 60 (cc)	1	1.08	1.06	0.98

Table 2: The organs at risk doses for 6XFF, 6XFFF and 10XFFF plans, normalized w.r.to 6XFF plans along with p-value, for dosimetry comparison.

Table 3: Summarizing the DQA for 3%, 3 mm fluence, 2%, 2 mm fluence and absolute dose variation between TPS and measurements with range.

Energy	Gamma Value	Range in % (min-max)	Gamma Value	Range in % (min-max)	Difference between TPS & Measurements	Range in % (min-max)
	3%, 3 mm	3%, 3 mm	2%, 2 mm	2%, 2 mm	%	%
6XFF	96.5 ± 1.12	(94.7-98.7)	86.1 ± 3.28	(80.8-90.3)	2.22 ± 0.38	1.16-3.08
6XFFF	96.± 1.04	(94-97.5)	84.7 ± 3.08	(78.5-89.1)	2.40 ± 0.97	1.06-4.15
10XFFF	97.4 ± 1.31	(94.1-99.1)	88.4 ± 3.41	(81.4-93.6)	2.68 ± 0.96	0.75-4.23

In the case of the 6XFFF plan, two plans did not satisfy the acceptance criteria (4.08% and 4.15%), and for 10XFFF, four plans were out of acceptance criteria (3.06%, 3.38%, 3.99%, and 4.23%).

## **Discussion**

The focus of this study was to estimate the optimal beam consistency for non-homogeneous cases in terms of PTV evaluation, OARs comparison, and treatment delivery time among all beam plans. The low dosage rate and lengthy treatment delivery time of the 6XFF beam are two of its key potential drawbacks. 6XFF is one of the most commonly used beams for conventional fractionation, but is not appropriate for hypo-fractions. In the case of hypo-dose fractions, many of the publications concluded that a shorter treatment delivery time is the only advantage of the FFF beam over the FF beam.

FFF beam is not a new concept. Brien et al. [18] reported, in 1991, the benefits of radiosurgery with unflattened 6MV photon beam over flattened 6MV photon beam for small fields (but not clinical). Furthermore, Tomotherapy [19] is the only treatment unit that results in an unflattened 6XFFF single beam. To the best of our knowledge, Vassiliev et al. [20] reported the first dosimetry advantages of the FFF beam over the FF beam (6XFFF *vs.* 6XFF) for lung SBRT on Clinac 21-EX, however, the calculation algorithm was a Pencil-Beam Calculation (PBC) algorithm with Batho power law inhomogeneity correction.

In this paper, the authors report both dosimetric comparison and reduction in the treatment time. Evaluating the target coverage is the first step in figuring out whether planning is clinically acceptable. Vassiliev et al. [21] reported electronic disequilibrium for the comparison of flattened and unflattened beams. In this study, the authors considered various conditions of the target, such as different sizes, electron densities, and modalities. The authors came to the conclusion that under-dosing is unquestionably shown for small targets and lower lung density based on these criteria. In some cases, the target coverage may be reduced by up to 10% of the prescribed dose. However, the authors finalized the report with a conclusion; the modest coverage can be increased by replacing the FF beam by the FFF beam.

Figure shows the box and whisker plots for the coverage index for the overall percentage error. The middle line shows the median (which is less than the mean, except for 10XFFF), while the lower and upper boundaries of the boxes represent the 25<sup>th</sup> and 75<sup>th</sup> percentiles. The plot shows the largest range in 10XFFF. The minimum and maximum ranges for 6XFF and 6XFFF ranged from 95.4% to 97.7% and 95.6% to 97.8% (which is acceptable), respectively, while for 10XFFF it ranged from 93.9% to 97.1% (not acceptable for a few plans). Following a very thorough dosimetry study of 6XFF, 6XFFF, and 10XFFF beams, Hrbacek et al. [22] came to the conclusion that 6XFFF increases the conformity of dose distribution. However, 10XFFF cuts down on the lengthy beam-on time. However, this study used the AAA algorithm for the final dose calculation. The dose calculation in the present study was carried out by Acuros XB algorithm, considering heterogeneity.

Han et al. [23] reported that in the case of lung targets, the dose differences between the Acuros XB and AAA algorithms were 0.9% and 11.6%, respectively, showing a 10% overestimation of the dose by the AAA algorithm [24]. Kragl et al. [25] evaluated the peripheral dose for various sites of SBRT (H&N, prostate, and lung) in the case of FFF beams and compared them with FF beams. Kragl et al. [25] reported that the peripheral dose was reduced by 23% and 31% for 6XFFF and 10XFFF beams, respectively. Our study clearly shows a reduction in the body integral dose and greater conformity in the case of the 6XFFF beam. For 6XFFF and 10XFFF, the mean body integral dose was recorded 98% and 99% times as compared to 6XFF beam. Due to beam hardening, the transmission through the MLC and jaw will be greater; hence the body integral dose in the 6XFF beam

may need to be raised [5-7]. For OARs doses, the 6XFFF beam is statistically superior to spare healthy OARs, except for the skin dose. Using a 10XFFF beam, skin-sparing is more effective, but at the cost of other predominant OARs.

Lu et al. [26] compared 6XFFF and 10XFFF beams with different fractionation schemes of 4X12 Gy, 3X18 Gy, and 1X34 Gy respectively, and concluded the report on the basis of the OARs spring, Normal Tissue Complication Probability (NTCP) estimation, and treatment efficacy. The authors recommended the 6XFFF beam to be more efficient for OARs sparing and lower NTCP for SBRT stage I lung cancer, whereas 10XFFF was better for treatment efficacy. Hence, the authors concluded in favor of 6XFFF for more than one fraction. Our results are in agreement with this conclusion.

Karan et al. [27] investigated the instantaneous dose rate impact on cell survival and irradiated the lung cell line sample by FF beam and FFF beam with the same dose, but different dose rates, and found no difference in any protraction scheme. The authors did not find any variation in DNA double-strand breaks *via*  $\gamma$ H2AX by either type of beam or no detrimental effect on in vitro cell irradiation.

Apart from *in vitro* studies, it is important to know the outcome of patients treated with FFF beams. Stieb et al. [28] reported the outcomes of 75 lung SBRT patients in a median follow-up and found no unexpected toxicity. The patient outcome treated with the FFF beam, for toxicity and treatment efficacy was found to be within the same range as with the FF beam. Therefore, the authors recommended patient treatment with the FFF beam, because of the short treatment time and OARs dose benefits. In a review of numerous clinical outcomes articles, Agarwal et al. [29] found that the predominant radiation toxicities-rather than skin-appear as pneumonitis, myocardial infarction, and ribs. In summary, 6XFFF beam is the best among the three. The increase in the skin dose is only a potential limitation when using the 6XFFF beam compared to the 10XFFF beam, additional more treatment time.

The plan fluence verification was tested using a phantom 2D array IBA matriXX by Durmus et al. [30] and reported that the gamma passing result was better in 10XFFF compared to 6XFFF for 3%, 3 mm and 2%, 2 mm. Our results revealed agreement when comparing the range of the gamma passing rate for all energies. Specifically, 6XFFF is the optimal beam choice for target coverage, conformity, and organs at risk perspective.

# **Study Limitations**

The sample size was smaller for dosimetry comparison. However, this seems quite appropriate, as many authors have reported a dosimetry comparison with this sample size.

# Conclusion

Our study demonstrates that 6XFFF and 10XFFF both beams are beneficial for reducing the treatment delivery time compared to the 6XFF beam plan. Optimal lung SBRT plan can be obtained using the 6XFFF beam with an average delivery dose rate of 1400 MU/ min without compromising the coverage index, conformity index, integral dose of the body, and OAR doses. 6XFFF delivers slightly less OARs doses but the reductions in few OARs were not statistical significance. The 10XFFF beam plan provides a lower skin dose and treatment time but at the cost of less coverage and conformity. Longterm clinical outcomes are required in future studies.

# **References**

- Donovan EK, Swaminath A. Stereotactic Body Radiation Therapy (SBRT) in the management of non-small-cell lung cancer: Clinical impact and patient perspectives. Lung Cancer (Auckl). 2018;9:13-23.
- 2. Fogliata A, Nicolini G, Clivio A, Vanetti E, Cozzi L. Critical appraisal of Acuros XB and anisotropic analytic algorithm dose calculation in advanced non-small-cell lung cancer treatments. Int J Radiat Oncol Biol Phys. 2012;83(5):1587-95.
- 3. Brandner ED, Chetty IJ, Giaddui TG, Xiao Y, Huq MS. Motion management strategies and technical issues associated with stereotactic body radiotherapy of thoracic and upper abdominal tumors: A review from NRG oncology. Med Phys. 2017;44(6):2595-612.
- Sharma SD. Unflattened photon beams from the standard flattening filter free accelerators for radiotherapy: Advantages, limitations and challenges. J Med Phys. 2011;36(3):123-5.
- Verbakel W, Ong C, Senan S, Cuijpers JP, Slotman BJ, Dahele M. Flattening filter-free beams for SBRT: Advantages and risks. Int J Radiat Oncol Biol Phys. 2012;84(3):S826-7.
- Xiao Y, Kry SF, Popple R, Yorke E, Papanikolaou N, Stathakis S, et al. Flattening filter-free accelerators: A report from the AAPM therapy emerging technology assessment work group. J Appl Clin Med Phys. 2015;16(3):5219.
- Vassiliev ON, Titt U, Pönisch F, Kry SF, Mohan R, Gillin MT. Dosimetric properties of photon beams from a flattening filter free clinical accelerator. Phys Med Biol. 2006;51(7):1907-17.
- 8. Varian Medical Systems. Millennium MLC Systems and Maintenance Guide. Palo Alto, CA: Varian Medical Systems; 2010.
- 9. Videtic G, Donington J, Giuliani M, Heinzerling J, Karas TZ, Kelsey CR, et al. Stereotactic body radiation therapy for early-stage non-small cell lung cancer: Executive summary of an ASTRO evidence-based guideline. Pract Radiat Oncol. 2017;7(5):295-301.
- Fogliata, A, Nicolini, G, Clivio A, Vanetti E, Cozzi L. Dosimetric evaluation of Acuros XB advanced dose calculation algorithm in heterogeneous media. Radiat Oncol. 2011;6:82.
- 11. Bezjak A. Seamless phase I/II study of Stereotactic Lung Radiotherapy (SBRT) for early stage, centrally located, Non-Small Cell Lung Cancer (NSCLC) in medically inoperable patients. RTOG. 2012;0813:1-75.
- 12. Videtic GMM, Hu C, Singh AK, Chang JY, Parker W, Olivier KR, et al. A Randomized phase 2 study comparing 2 stereotactic body radiation therapy schedules for medically inoperable patients with stage I peripheral non-small cell lung cancer: NRG oncology RTOG 0915 (NCCTG N0927). Int J Radiat Oncol Biol Phys. 2015;93(4):757-64.
- International commission on radiation units and measurements. ICRU 62. Prescribing, recording and reporting photon beam therapy (supplement to ICRU report 50) Report No: 62. Washington DC. 1999.
- 14. Lomax NJ, Scheib SG. Quantifying the degree of conformity in radiosurgery treatment planning. Int J Radiat Oncol Biol Phys. 2003;55(5):1409-19.
- Report 83: Report 83: Prescribing, recording, and reporting photon-beam intensity-modulated radiation therapy. (IMRT). J ICRU. 2010;10(1):1-2.
- Low DA, Harms WB, Mutic S, Purdy JA. A technique for the quantitative evaluation of dose distributions. Med phys. 1998;25(5):656-61.
- 17. Daniel LA, Dempsey JF. Evaluation of the gamma dose distribution comparison method. Med phys. 2003;30(9):2455-64.
- Brien PFO', Gillies BA, Schwartz M, Young C, Davey P. Radiosurgery with unflattened 6MV photon beams. Med Phy. 1991;18(3):519-21.
- 19. Mackie TR, Holmes T, Swerdloff S, Reckwerdt P, Deasy JO, Yang J, et al. Tomotherapy: A new concept for the delivery of dynamic conformal radiotherapy. Med Phys. 1993;20(6):1709-19.

- 20. Vassiliev O, Kry SF, Chang JY, Balter PA, Titt U, Mohan R. Stereotactic radiotherapy for lung cancer using a flattening filter free Clinac. J App Clin Med Phys. 2009;10(1):14-21.
- 21. Vassiliev ON, Kry SF, Wang HC, Peterson CB, Chang JY, Mohan R. Radiotherapy of lung cancers: FFF beams improve dose coverage at tumor periphery compromised by electronic disequilibrium. Phys Med Biol. 2018;63(19):195007.
- 22. Hrbacek, J, Lang S, Graydon, SN, Klöck S, Riesterer O. Dosimetric comparison of flattening and unflattening beams for stereotactic ablative radiotherapy of stage I non-small cell lung cancer. Med Phy. 2014;41(3):031709.
- 23. Han T, Mikell JK, Salehpour M, Mourtada F. Dosimetric comparison of Acuros XB deterministic radiation transport method with Monte Carlo and model-based convolution methods in heterogeneous media. Med Phys. 2011;38(5):2651-64.
- 24. Fogliata A, Nicolini G, Clivio A, Vanetti E, Cozzi L. Critical appraisal of Acuros XB and anisotropic analytic algorithm dose calculation in advanced non-small-cell lung cancer treatments. Int J Radiat Oncol Biol Phys. 2012;83(5):1587-95.

- 25. Kragl G, Baier F, Lutz S, Albrich D, Dalaryd M, Kroupa B, et al. Flattening filter free beams in SBRT and IMRT: Dosimetric assessment of peripheral doses. Z Med Phys. 2011;21(2):91101.
- 26. Lu JY, Lin Z, Lin PX, Huang BT. Optimizing the flattening filter free beam selection in Rapid Arc-based stereotactic body radiotherapy for Stage I lung cancer. Br J Radiol. 2015;88(1053):20140827.
- 27. Karan T, Moiseenko V, Gill B, Horwood R, Kyle A, Minchinton AI. Radiobiological effects of altering dose rate in filter-free photon beams. Phys Med Biol. 2013;58(4):1075-82.
- Stieb S, Lang S, Linsenmeier C, Graydon S, Riesterer O. Safety of highdose-rate stereotactic body radiotherapy. Radiat Oncol. 2015;10:27.
- 29. Agarwal P, Kinhikar R. In regard to the article 'Effectiveness of robust optimization in volumetric modulation arc therapy using 6 and 10 MV flattening filter-free beam therapy planning for lung stereotactic body radiation therapy with a breath-hold technique. J Radiat Res. 2021;62(4):740-2.
- 30. Durmus IF, Atalay ED. Dosimetric comparison of flattening filter-free energies for lung SBRT. IJES. 2018;7(11):17-21.