

# Assessment of Treatment Plan Quality between Flattening Filter and Flattening Filter Free Photon Beam for Carcinoma of the Esophagus with IMRT Technique

Dinesh Kumar Saroj (PhD Candidate)<sup>1,2\*</sup>, Suresh Yadav (PhD)<sup>3</sup>, Neetu Paliwal (PhD)<sup>2</sup>, Subhas Haldar (MSc)<sup>4</sup>, Amol Jagtap (PhD Candidate)<sup>1</sup>, Arvind Kumar (MSc)<sup>5</sup>

## ABSTRACT

**Background:** As compared to the flattened photon beam, removing the flattening filter (FF) from the head of a gantry decreases the average energy of the photon beam and increases the dose rate, leading to an impact on the quality of treatment plans.

**Objective:** This study aimed to compare the quality of intensity-modulated radiation therapy (IMRT) treatment plans for esophageal cancer with and without a flattened filter photon beam.

**Material and Methods:** In this analytical study, 12 patients, who had already been treated with a 6X FF photon beam, were treated based on new IMRT methods using a 6X the flattening filter-free (FFF) photon beam. Both 6X FF IMRT and 6X FFF IMRT plans used identical beam parameters and planning objectives. All plans were evaluated with planning indices and doses for organs at risk (OARs).

**Results:** Insignificant dose variation was for HI, CI,  $D_{98\%}$ , and  $V_{95\%}$  between FF and FFF photon beam IMRT plans. FF-based IMRT plan delivered a 15.51% and 11.27% higher mean dose to both lungs and heart than the FFF plan, respectively. The integral dose (ID) for the heart and lungs was 11.21% and 15.51%, respectively, less in the IMRT plan with an FFF photon beam.

**Conclusion:** In contrast to the FF photon beam, a filtered photon beam-oriented IMRT plan provides significant OAR sparing without losing the quality of the treatment plan. High monitor units (MUs), low ID, and Beam on Time (BOT) are major highlights of the IMRT plan with FFF beam.

**Citation:** Saroj DK, Yadav S, Paliwal N, Haldar S, Jagtap A, Kumar A. Assessment of Treatment Plan Quality between Flattening Filter and Flattening Filter Free Photon Beam for Carcinoma of the Esophagus with IMRT Technique. *J Biomed Phys Eng.* 2023;13(3):227-238. doi: 10.31661/jbpe.v0i0.2108-1381.

## Keywords

Intensity Modulated; Linear Accelerator; Radiotherapy; Photons; Radiotherapy Planning; Radiotherapy, Conformal

## Introduction

Esophagus cancer (Ca-esophagus) is considered under the category of lethal diseases with therapeutic challenges to multidisciplinary oncology. Patients with advanced stages are not suitable for surgical resection. For such cases, chemo-radiation is the prime mode of treatment in the management of the Ca-esophagus. Earlier 2-dimensional conformal radiotherapy (2D-CRT) with anterior-posterior (AP-PA) field arrangement was used to treat the ca-esophagus. Due to the presence of normal organs, such as the spinal cord, the heart, and the lung, 2D-CRT, and 3D-CRT delivery techniques limit the dose esca-

<sup>1</sup>Department of Radiotherapy, Alexis Multispecialty Hospital Nagpur-440030 (Maharashtra), India

<sup>2</sup>Department of Science, Rabindranath Tagore University, Bhopal, Madhya Pradesh, India

<sup>3</sup>Department of Radiotherapy, Gandhi Medical College, Bhopal-462001 (M.P.), India

<sup>4</sup>Department of Radiotherapy, Saroj Gupta Cancer Center and Research Institute, Kolkata-700063 (West Bengal), India

<sup>5</sup>Department of Radiation Oncology, All India Institute of Medical Sciences (AIIMS), Rishikesh-249203 (U.K.), India

\*Corresponding author: Dinesh Kumar Saroj Medical Physics, Department of Radiotherapy, Alexis Multispecialty Hospital Nagpur-440030 (Maharashtra), India E-mail: dinesh.saroj@gmail.com

Received: 12 August 2021  
Accepted: 17 March 2022

tion of the target dose. Radiotherapy for Esophageal cancer has shifted from 3D-CRT to intensity-modulated radiation therapy (IMRT) to take advantage of the clinical potential of lung and spinal cord sparing.

IMRT has a better ability to paint a target dose and provides better dose conformity around the target and superior sparing of surrounding normal healthy tissue compared to the 3D-CRT [1]. Furthermore, the probability of increased low dose to adjoining healthy cells is higher with IMRT than the 3D-CRT, and the number of Monitor Units (MU) is 3 to 5 times higher as well. Greater dose conformity and steeper dose gradient beyond the target structure are important aspects of the IMRT. Higher MU leads to a rise in the gantry head leakage scattered dose and greater dose to the normal tissues as well as the whole body. As a result, minimizing excess scatter from the gantry head and shortening the treatment plan delivery time for IMRT delivery is preferable. With progress in linear accelerator (Linac) design and radiotherapy treatment delivery, it is now possible to strip the flattening filter (FF) from the head of the gantry. Elimination of the flattening filter (FF) from the route of the photon beam was considered a logical decision to limit the scatter contribution from FF; the flattening filter was initially designed to provide flattened dosage profiles at a specific depth. In modern linac systems, the development of IMRT can result in removing the need for a FF. The usage of unfiltered photon beams has been widely studied in recent years [2-6]. The main characteristic of the flattening filter-free (FFF) beam is its forward peaked dose profile [7-11]. The dose rate of the FFF photon beam is relatively high than that of the flattened photon beam [12], a lower dose to the organ at risk (OAR) [13], and less neutron contamination with high energy beams (>15 MV). Accordingly, therapeutic use of the FFF beam will result in a shorter treatment time and a lower risk of secondary cancer caused by radiation [14]. From a physics point of view, the more im-

portant major changes are the decrease in the mean energy and the increase in the dose rate in the FFF beam. The quality of the treatment plan has a strong correlation with the reduction of beam energy. The purpose of this study was to compare the efficacy of treatment plans with FF and FFF photon beams for esophageal carcinoma using the IMRT technique. In the analysis, dosimetric indices were utilized for the radiotherapy planning target volume (PTV), normal structure, MUs, beam on time, and integral dose to check the efficacy of the FFF photon beam to generate the clinical acceptable and desirable plan concerning the FF photon beam.

## Material and Methods

In this analytical study, Varian Linac with millennium multi-leaf collimator (M120, MLC) was used for patient treatment, which was capable of producing both photon and electron beams. Linac was also equipped with 6 MV (6X\_FF), 10 MV (10X\_FF), 15 MV (15X\_FF) FF and 6 MV (6X\_FFF), 10 MV (10X\_FFF) FFF photon beam. A total of 120 leaves were applied with 40 leaf pairs in the middle and 10 leaf pairs on each side. The middle leaf thickness is estimated at the isocenter to be 5 mm, while the outer leaves were wider at 10 mm. The maximum speed of leaves was 2.5 cm/sec with Eclipse Treatment Planning System (Version 13.7.29, Varian Medical System) for the treatment plans. Photon optimizer (PO) (Version 13.7.29, Varian Medical System) was selected for inverse optimization. The resulting dose was calculated using the Anisotropic Analytical Algorithm (AAA) (Version 13.7.29, Varian Medical System). M120 MLC was used for both types of photon beam treatment plans. Varian's leaf motion calculator (version 13.7.29) was used to generate the IMRT leaf series.

## CT simulation and Patient selection

In this research, 12 patients with a diagno-

sis of ca-esophageal cancer participated from Alexis Multispecialty Hospital, Nagpur, India (Department of Radiotherapy); they had already been treated in the hospital with IMRT (6X\_FF photon beam) treatment technique. For all patients, computed tomography (CT) images were acquired in a supine position with the arm extended above the shoulder. CT simulation was performed on Siemen's CT using routine protocols and a slice spacing of 2.5 mm. Acquired CT images were then imported to the treatment planning workstation for target and OARs contouring.

An additional IMRT treatment plan was created using the 6X\_FFF photon beam in retrospect. Finally, using the 6X\_FF and 6X\_FFF photon beams, we were able to generate two separate treatment plans for each patient. Gross tumor volume (GTV), clinical target volume (CTV), PTV, and nodes were delineated by a radiation oncologist according to the RTOG 0436 protocols [15]. The GTV contained the gross tumor as well as any involved lymph nodes as determined by diagnostic CT and Positron Emitted Tomography (PET) scan. The CTV was described by superior-inferior margins of 3–5 cm and lateral and anterior-posterior margins of 1 cm about the GTV. The PTV was delineated with a margin of 0.5 cm from the CTV. On each CT slice, the spinal cord, lung, and heart were contoured as OARs by the radiation oncologist.

### Treatment Plan Strategy

Two separate IMRT plans were produced for each patient with FF and FFF 6 MV photon beam. The prescription doses for original and re-planned IMRT plans were 50.4 Gy in 28 fractions. A total of 9 equally spaced beams were used to produce the IMRT treatment plans, as follows: 0°, 40°, 80°, 120°, 160°, 200°, 240°, 280, and 320°. The collimator setting was kept at 0° without any couch rotation. A maximum dose rate was utilized to have a shorter treatment delivery time that was 600 MU/min in the case of 6X\_FF photon beam

### Integral Dose for FF and FFF Photon Beam.

and 1400 MU/min in 6X\_FFF photon beam. Since the patient was already treated with a 6X\_FF flattened photon beam, retrospectively each patient was again re-planned with a 6X\_FFF photon beam with the same dose, dose constraints, and inverse optimization parameter.

### Treatment plan evaluation

The target coverage and dosage of OARs were assessed to analyze the treatment strategies, normalized for all individuals; accordingly, 95% of the specified dose covered 95% of the PTV. The dose constraints used during inverse optimization are listed in Table 1. After optimization, the dose was computed using the optimized MU value and the AAA calculation algorithm with a dose grid size of 2.5 mm. The dose pattern was then evaluated, and the Dose Volume Histograms (DVHs) were analyzed to ensure that the necessary dose constraints are met here. During planning, the major goal was to obtain uniform PTV coverage for all patients, and the secondary objective was to lower OAR doses as much as possible individually. For PTV coverage, the conformity index (CI) and the homogeneity index (HI) were used. The radiation doses for PTV and OARs were reported using DVHs, and the integral doses of the OARs were calculated

**Table 1:** Inverse Dose Planning Constraints.

PTV	<b>V<sub>95%</sub> ≥95% &amp; Maximum point dose inside the PTV should be less than 107% of the prescribed dose</b>	
Spinal Cord	Maximum dose	45 Gy
	V <sub>30Gy</sub>	≤20%
Heart	V <sub>20Gy</sub>	≤30%
	Mean	≤30 Gy
Lungs	V <sub>20Gy</sub>	≤30%
	Mean	≤20 Gy

PTV: Planning treatment volume, Gy=Gray, V<sub>95%</sub>=95% of volume receiving 95% of prescribed dose

with the help of DVHs.

### Plan evaluation indices

#### Conformity Index (CI)

According to ICRU Report 83 (International Commission on Units and Measurements) [16]. The conformity index is defined as the prescription isodose volume ( $V_{Rx}$ ) divided by the PTV volume. The recommended value of CI is unity, but it is usually greater than one.

$$CI = V_{Rx} / V_{PTV} \quad (1)$$

Where,  $V_{Rx}$  is a prescription isodose volume, and  $V_{PTV}$  is total PTV volume.

#### Homogeneity index (HI)

The homogeneity Index is defined as follows [16]:

$$HI = (D_{2\%} - D_{98\%}) / (D_{50\%}) \quad (2)$$

where  $D_{2\%}$ ,  $D_{50\%}$ , and  $D_{98\%}$  are the dose values by 2%, 50%, and 98 percent volumes of PTV, respectively.

The HI scales from 0 to 1 that 0 shows the ideal value. A higher HI represents a lack of homogeneity.

#### Integral Dose (ID)

The integral dose refers to the whole amount

of energy absorbed within the organ [17]. The mean organ dose, mean organ density, and mean organ volume are used to determine the ID, defined by:

$$\text{Integral Dose ID} = D_{\text{mean}} \times V_{\text{mean}} \times \rho_{\text{mean}} \text{ (Gy-L)} \quad (3)$$

where  $D_{\text{mean}}$  is mean organ dose,  $V_{\text{mean}}$  is organ volume, and  $\rho_{\text{mean}}$  is mean organ density.

In this study, all the organs have an equal density ( $\rho=1$ ); therefore, ID is calculated by the following equation:

$$\text{Integral Dose ID} = D_{\text{mean}} \times V_{\text{mean}} \text{ (Gy-L)} \quad (4)$$

### Statistical Tools

The statistical differences in target coverage for patients were examined based on a paired sample t-test (statistical significance,  $P \leq 0.05$ ) using SPSS (release 20, SPSS Inc., Chicago, IL, USA). A paired sample t-test (statistical significance,  $P \leq 0.05$ ) was used to investigate the statistical differences in planning indices and dose to normal organs for patients.

### Results

Table 2 shows the patient's characteristics and tumor location, staging, and dimensions.

**Table 2:** Patient demographic, tumor extent, and clinical target volume (PTV) characteristics.

Patients	Sex (M/F)	Age (Yrs.)	Tumor location	Tumor staging	PTV Long axis (cm)	CTV Volume (cm <sup>3</sup> )	PTV Volume (cm <sup>3</sup> )
1.	M	65	Middle Third	III	14.5	477.5	789.3
2.	M	72	Middle Third	III	20.7	362.5	656.2
3.	F	76	Middle Third	IVB	13	165.6	310.3
4.	F	64	Middle Third	IV	15.2	293.2	478.1
5.	F	60	Middle Third	IV	13.2	122.1	264.3
6.	F	52	Middle Third	IIIB	10	219.1	299.4
7.	M	67	Upper Third	IIIC	18	68.9	120.9
8.	M	62	Middle Third	IVB	13.85	214.3	381.9
9.	M	79	Lower Third	IIIC	13.6	120.8	232.7
10.	M	56	Middle Third	IIB	16.15	192.5	363.9
11.	F	75	Middle Third	III	21.6	402.8	659.8
12.	M	68	Middle Third	IIIA	13.1	155.8	309.4
(Mean±SD)					15.24±3.22	236.6±125	405.52±192.07

M: Male, F: Female, Yrs.: Years, PTV: Planning treatment volume, CTV: Clinical Target Volume, SD: Standard deviation

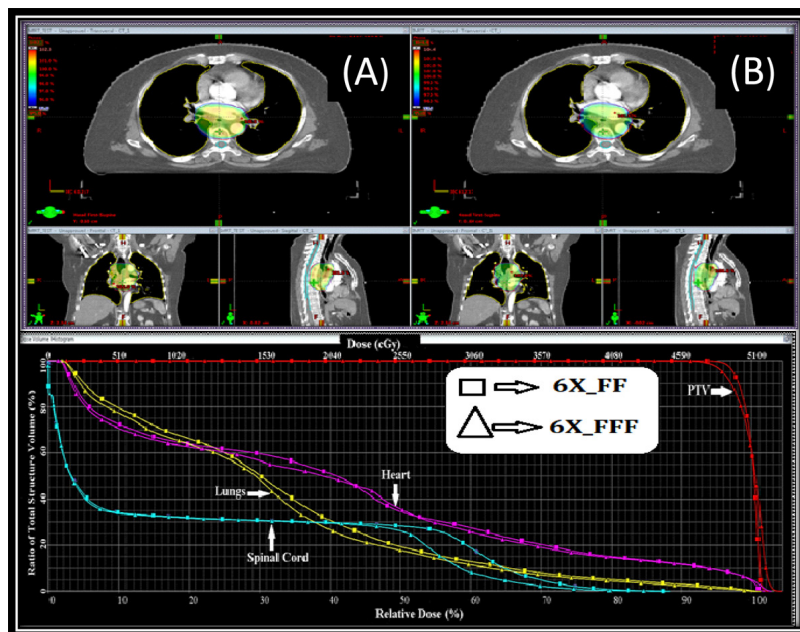


Out of 12 patients, 10 had tumors located at the middle one third, one was at the upper one third, and the remaining one was at the lower one third. The average value of PTV length was  $15.24 \pm 3.37$  cm, and the average PTV and CTV volume were  $236.6 \pm 131.04$  cc and  $405.51 \pm 200.62$  cc, respectively. PTV volume ranged from 232.7 cc to 789.3 cc. The maximum dose ( $D_{\max}$ ) inside the PTV was  $52.18 \pm 0.48$  Gy and  $51.97 \pm 0.56$  Gy in 6X\_FF and 6X\_FFF IMRT plans, respectively ( $P > 0.05$ ). In the instances of 6X\_FF and 6X\_FFF IMRT, the lowest dose recorded within the PTV was  $43.63 \pm 3.40$  Gy and  $43.49 \pm 3.30$  Gy ( $P > 0.05$ ). In 6X\_FF and 6X\_FFF IMRT, the mean dose ( $D_{\text{mean}}$ ) to a PTV was  $50.36 \pm 0.0$  Gy and  $50.53 \pm 0.32$  Gy ( $P > 0.05$ ), respectively.

Figure 1 illustrates the color dose wash of 95% of the prescribed dose and the DVHs of PTV and various OARs for one of the patients.  $D_{98\%}$  was higher  $49.16 \pm 0.56$  Gy in case of 6X\_FF than  $48.60 \pm 0.85$  Gy in 6X\_FFF plan ( $P > 0.05$ ). Table 3 shows the DVH for PTV in both types of planning strategies. The 6X\_FF plan was reported with a higher  $V_{95\%}$  in com-

parison with the 6X\_FFF IMRT plan ( $P > 0.05$ ). CI values for 6X\_FF and 6X\_FFF IMRT plans were  $0.990 \pm 0.012$  and  $0.989 \pm 0.013$ , respectively. HI value for 6X\_FF and 6X\_FFF plan was  $0.042 \pm 0.018$  and  $0.055 \pm 0.018$  ( $P > 0.05$ ).

Table 4 shows the doses to the OARs between 6X\_FF and 6X\_FFF IMRT plans. The spinal cord receives an average maximum dose of  $37.97 \pm 4.89$  Gy and  $34.24 \pm 4.60$  Gy in 6X\_FF and 6X\_FFF IMRT plans ( $P < 0.05$ ).  $V_{5\text{Gy}}$  of the lung was  $77.97 \pm 17.03\%$  and  $75.97 \pm 16.82\%$  in 6X\_FF and 6X\_FFF IMRT plan ( $P > 0.05$ ).  $V_{10\text{Gy}}$  for lungs gains  $60.95 \pm 13.42\%$  in 6X\_FF IMRT plans in comparison to  $56.44 \pm 13.15\%$  in 6X\_FFF IMRT plans ( $P > 0.05$ ).  $V_{20\text{Gy}}$  for lungs was  $24.96 \pm 9.65\%$  in 6X\_FF plans, and for 6X\_FFF plans, it was  $22.08 \pm 8.65\%$  ( $P > 0.05$ ). Lungs were recorded with an average dose of  $15.00 \pm 2.94$  Gy and  $12.62 \pm 2.53$  Gy in 6X\_FF and 6X\_FFF IMRT plans, respectively ( $P < 0.05$ ).  $V_{20\%}$  of heart was  $46.46 \pm 22.86\%$  and  $40.51 \pm 20.20\%$  in 6X\_FF and 6X\_FFF IMRT plans ( $P > 0.05$ ).  $V_{30\%}$  of heart received  $23.17 \pm 11.80\%$  in 6X\_FF and  $19.54 \pm 10.45\%$  in 6X\_FFF IMRT plan ( $P > 0.05$ ). The mean



**Figure 1:** Provides a comparison of isodose and Dose Volume Histogram for intensity-modulated radiation therapy between (A) a flattened 6 MV filter and (B) a flattening filter free 6 MV flattening filter.

**Table 3:** The Dosimetric Parameter for the clinical target volume (PTV) in 6X\_FF (Flattened Filter) & 6X\_FFF (Flattened Filter Free) intensity-modulated radiation therapy (IMRT) plan.

Variables	Treatment Plans		P-Value
	6X_FF (Mean±SD)	6X_FFF (Mean±SD)	
D <sub>max</sub> (Gy)	51.97±0.56	52.18±0.48	0.33
D <sub>min</sub> (Gy)	43.63±3.40	43.49±3.30	0.9
D <sub>mean</sub> (Gy)	50.36±0.0	50.53 ±0.13	0.22
D <sub>98%</sub> (Gy)	49.16 ±56.01	48.60±85.36	0.08
V <sub>95%</sub> (cc)	401.49±199.63	400.90±198.89	0.99
CI	0.990±0.012	0.989±0.013	0.83
HI	0.042±0.018	0.055±0.018	0.13

FF: Flattened Filter, FFF: Flattened Filter Free, D<sub>max</sub>: Maximum Dose, D<sub>min</sub>: Minimum Dose, D<sub>mean</sub>: Average dose, SD: Standard Deviation, D<sub>98%</sub>: Dose received by 98% volume, V<sub>95%</sub>= Volume receiving 95% dose in cc, CI: Conformity Index, HI: Homogeneity Index

**Table 4:** The dosimetric indices for the organs at risk (OARs).

Variables	Treatment Plans		P-Value
	6X_FF (Mean±SD)	6X_FFF (Mean±SD)	
Spinal Cord (D <sub>max</sub> ) (Gy)	37.97±4.89	34.24±4.60	0.06
Lungs V <sub>5Gy</sub> (%)	77.97±17.03	75.97±16.82	0.77
Lungs V <sub>10Gy</sub> (%)	60.95±13.42	56.44±13.15	0.41
Lungs V <sub>20Gy</sub> (%)	24.96±9.65	22.08±8.65	0.44
Lungs Mean (Gy)	15.00±2.94	12.62±2.53	0.04
Heart V <sub>20%</sub> (%)	46.46±22.86	40.51±20.20	0.5
Heart V <sub>30%</sub> (%)	23.17±11.80	19.54±10.45	0.43
Heart V <sub>40%</sub> (%)	11.45±5.57	9.16±4.26	0.27
Heart Mean (Gy)	20.87±7.95	18.52±7.02	0.45

FF: Flattened Filter, FFF: Flattened Filter Free, SD: Standard Deviation, D<sub>max</sub>: Maximum Dose, V<sub>xx</sub>: XX Gy dose received by % of the volume

dose to the heart was 20.8 7±7.95 Gy and 18.52±7.02 Gy in 6X\_FF and 6X\_FFF IMRT plans (P>0.05).

Table 5 shows the distribution of ID, MU, and Beam on Time (BOT). ID for heart was 1163.8±504.62 (Gy-L) and 1033.34±451.13 (Gy-L) in 6X\_FF and 6X\_FFF, respectively (P>0.05). The monitor unit in the case of 6X\_FF was 507.04±106.49 and for 6X\_FFF IMRT plans, it was 580.01±105.71 (P>0.05). BOT for the 6X\_FF plan was 0.845±0.18 min

and the same for 6X\_FFF was.414±0.08 min (P<0.05).

### Discussion

Based on the studies, FFF photon irradiation is superior to FF photon beam irradiation [18-19]. The current research shows that a 6X FFF photon beam can treat ca-esophagus malignancies in comparison to a 6X FF photon beam. Clinically appropriate treatment plans were produced with an Eclipse treatment

planning system (TPS) and 6X FFF photon beam. The dosimetric indices showed an insignificant difference in PTV dose distribution between 6X\_FFF, and 6X\_FF photon beams. When IMRT plans generated with FFF photon beam were compared to FF photon beam, the maximal dose within the PTV was insignificantly greater. In both cases, it is well below 107% of the prescription dose. No relative significant dose difference was for the average dose to the PTV between 6X\_FF and 6X\_FFF IMRT plans. Daniel et al, [20] discovered similar findings in prostate cancers using IMRT with a flattening filter-free beam.

$D_{98\%}$  and  $V_{95\%}$  were insignificantly higher in 6X\_FF plans compared to 6X\_FFF. Figure 2 shows the distribution of CI and HI across the treatment plan for both types of a

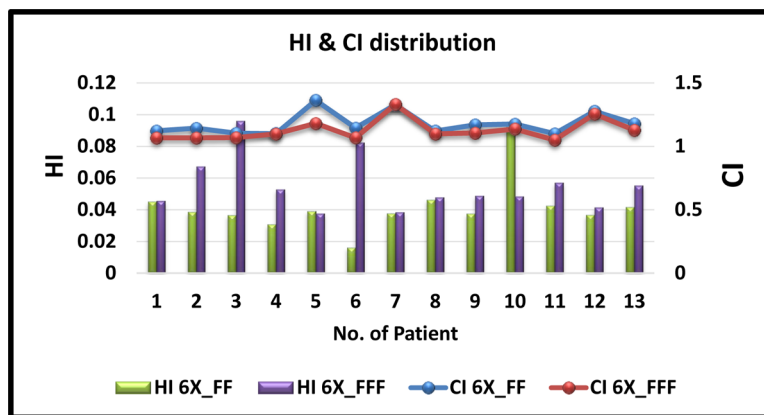
planning strategy, in which CI was relatively 4.4% higher in the 6X\_FF IMRT plan compared to the 6X\_FFF IMRT plan. The HI value for 6X\_FF was insignificantly better in comparison to 6X\_FFF IMRT plans. When interacting with smaller treatment areas, flattened and unflattened beams produced equivalent dose coverage, effectively eliminating the need for a uniform beam [21].

IMRT plans with FFF photon beams have better OARs sparing capability in comparison to FF photon beam plans. Kumar Saroj et al. [22] concluded the better sparing of OARs with FFF photon beams with the same findings in the case of Glioma. Dose restriction to the spinal cord is of prime interest in Ca-esophagus treatment planning. The spinal cord is the serial structure and its maximum

**Table 5:** The Summary of integral dose, monitor unit (MU), and beam-on time (BOT) for 6X\_FF (Flattened Filter) & 6X\_FFF (Flattened Filter Free) treatment plans.

Variables	Treatment Plans		P-Value	
	6X_FF (Mean±SD)	6X_FFF (Mean±SD)		
ID (Gy-L)	Heart	1163.8±504.62	1033.34±451.13	0.66
	Lungs	3863.29±1141.22	3263.99±1011.79	0.68
	Liver	0.998±0.619	0.949±0.588	0.2
Number of MUs	507.04±106.49	580.01±105.71	0.1	
BOT (min.)	0.845±0.18	0.414±0.08	0.00	

FF: Flattened Filter, FFF: Flattened Filter Free, SD: Standard Deviation, ID: Integral Dose, Gy-L: Gray-Liter, MUs: Monitor Unit, BOT: Beam on Time



**Figure 2:** The variation of the Homogeneity Index (HI) and the Conformity Index (CI) for intensity-modulated radiation therapy with filtered and filter-free photon beams.

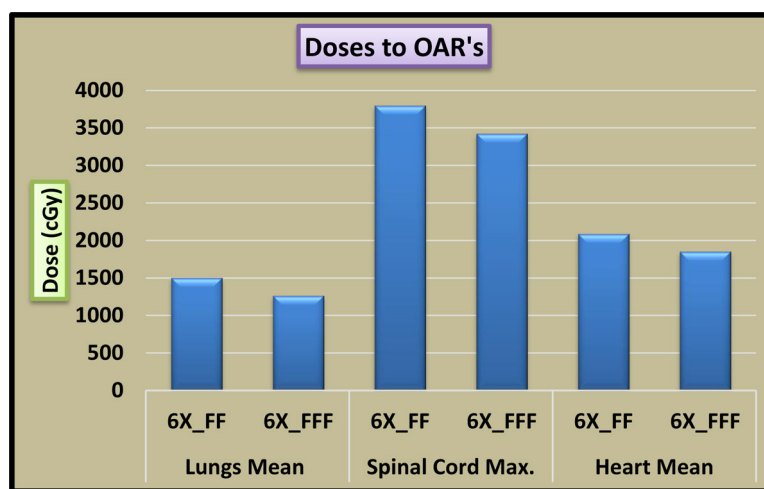
dose must be evaluated carefully. The mean maximum dose for the spinal cord and the mean doses for the lungs and heart are shown in Figure 3. Compared to 6X\_FF IMRT plans, the spinal cord dose was 9.8% lower in 6X\_FFF IMRT plans. Heart toxicity is a major potential side effect of esophageal cancer treatment that its doses must be accounted. In addition, the bilateral lung doses are important during evaluating the plan. Several studies with contradicting parameters for assessing lung toxicity had already been described [22, 23]. In this study,  $V_{5Gy}$ ,  $V_{10Gy}$ , and  $V_{20Gy}$  were compared to evaluate lung toxicity. According to Graham MVMary V.G, the lung receiving  $V_{20Gy} < 25\%$  implies a minimal risk of pneumonitis [24].

For the two different planning groups, the average value of  $V_{5Gy}$ ,  $V_{10Gy}$ , and  $V_{20Gy}$  were lower in 6X\_FFF IMRT plans by 2.56%, 7.4%, and 11.53% in comparison to 6X\_FF IMRT plans, respectively. When compared to the contrast group, the mean radiation dose to the entire lung in 6X\_FFF plans was considerably lower. There was a 15.90% lesser mean dose received by total lung in 6X\_FFF plans.

Dose to the heart is the second most important issue considered in the ca-esophagus. Numerous studies have indicated that radiation causes severe heart damage whenever the

heart absorbs more than  $V_{40Gy}$ ; accordingly, lowering  $V_{40Gy}$  is critical in minimizing cardiac toxicities [24-25].  $V_{40Gy}$  was 9.16% in FFF beam plans while comparatively reported 11.45% higher value in FF beam plan;  $V_{20Gy}$  and  $V_{30Gy}$  were lower in FFF beam plans. Pericardial edema occurred in just 13% of patients when  $V_{30Gy}$  to the heart was kept below 46%, according to Wei et al, [26]. In this research mean,  $V_{30Gy}$  was bellowed in both the planning schemes; however, the  $V_{30Gy}$  was 15.67% lower in FFF beam plans.  $V_{20Gy}$  was 11.87 % lower in the FFF beam plan compared to FF beam Plan. A total of 20% lower average mean dose was received by the heart in the FFF beam plan in comparison to the FF beam plan.

The integral dose is the absorbed dose inside the organ of interest. Figure 4 shows an integral dose comparison between 6X\_FF and 6X\_FFF IMRT plan for the heart and lungs. The inclusion of a greater number of tiny aperture and monitor units in IMRT is usually reported to increase the integral dose. Although the FFF beam plan had higher MUs, the OARs had a lower ID due to less scattered dose. ID for the heart was 11.21% less in patients planned with FFF beam as compared to FF photon beam, and ID for lungs and liver were reported as 15.51% and 4.94% in the Treatment plan with

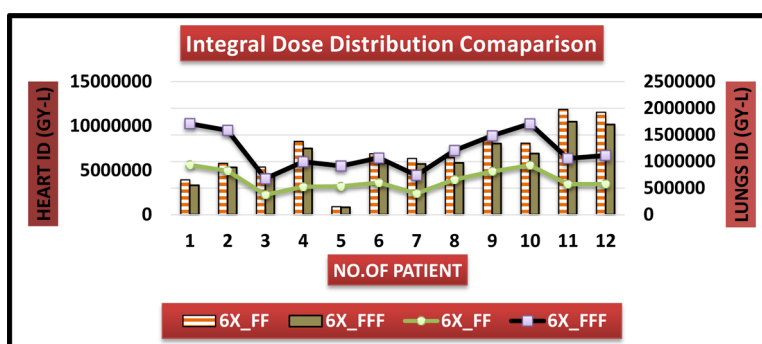


**Figure 3:** A comparison of mean doses to the lungs, the heart, and maximum dose to the spinal cord with filtered and filter-free photon beams for intensity-modulated radiation therapy.

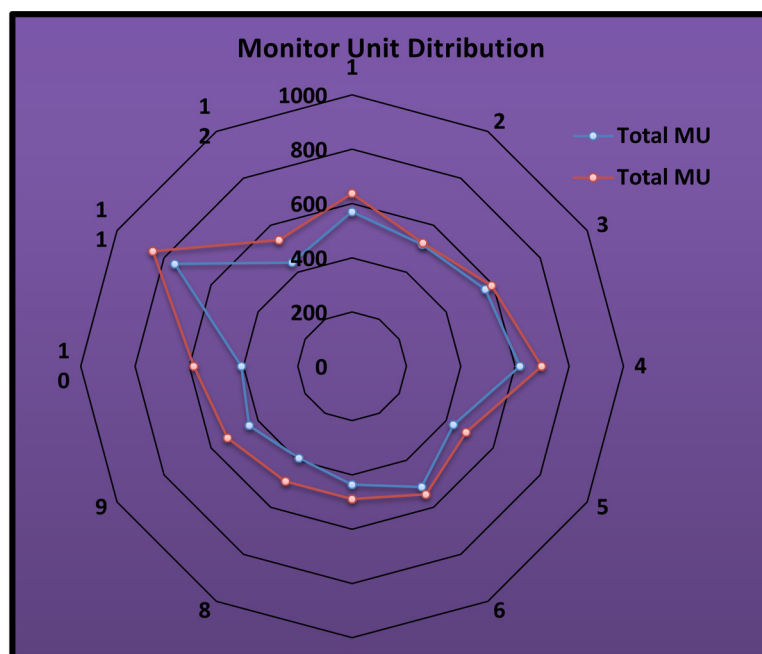


FFF beams compared to the FF beam plan. Cashmore et al. [27] claimed a 70% reduction in undesired and superfluous scatter dose for IMRT utilizing FFF beams. Furthermore, Kargl et al. [28] demonstrated a 52% and a 65% reduction in 6 and 10 MVs in the therapy of head leakage in prostate IMRT utilizing the FFF beam. Figure 5 shows the MU variation among the 6X\_FF and 6X\_FFF IMRT treatment plans. As reported in most of the earlier studies, the increase in MU and the decrease in BOT were also seen in the current study

[29-30]. As opposed to the FF beam plan, the FFF beam plan had 14.39 % greater MU. The increased amount of MUs was mainly to achieve a uniform dose pattern and a higher number of small fragments, and MUs are required to compensate for the FFF beam profile. BOT had a 50.97% reduction for the 6X\_FFF IMRT plan as compared to the FF beam plan as the FFF beam can deliver a larger dose in a shorter amount of time. A shorter treatment delivery time will be advantageous in the case of a tumor that is more prone to motion.



**Figure 4:** The intensity-modulated radiation therapy, integral dose comparison between 6X\_FF (Flattened Filter) and 6X\_FFF (Flattened Filter Free) for the heart & lungs.



**Figure 5:** The variation of the Homogeneity Index (HI) and the Conformity Index (CI) for intensity-modulated radiation therapy with filtered and filter-free photon beams. Orange line is for 6X\_FFF Total MU, Blue Line is for 6X\_FF Total MU.

## Conclusion

The FFF photon beams in comparison to the FF photon beam provide a clinically desirable and physically acceptable treatment plan without any distinguishable dose difference for target coverage between FF and FFF IMRT plan for Ca-esophagus. Furthermore, better OARS sparing is seen for patients planned with FFF photon beam, improving the quality of life of patients with a short life expectancy and ensuring that the treatment process runs smoothly. In addition, higher MU for the FFF IMRT plan can be compensated by a high dose rate. Reduction in overall treatment time has added a benefit in decreasing in-room time for patients and helps in motion management of the target. Lesser scattered dose for a treatment plan with FFF photon beam benefiting in lowering the integral dose to the Oars. Therefore, the FFF photon beam can be used dosimetrically for Ca-esophagus treatment planning.

## Authors' Contribution

DK. Saroj conceived the idea. The introduction of the paper was written by DK. Saroj, S. Haldar, and S. Yadav. DK. Saroj, A. Jagtap, S. Yadav and A. Kumar gathered the images and the related literature and also helped with the writing of the related works. The method implementation was conducted by DK. Saroj, S. Haldar, N. Paliwal and A. Kumar. Results and analysis were performed by DK. Saroj, S. Haldar, S. Yadav and N. Paliwal. The research work was proofread and supervised by S. Yadav, N. Paliwal and A. Jagtap. All the authors read, modified, and approved the final version of the manuscript.

## Ethical Approval

This study conducted with valid consent at Alexis Multispecialty Hospital, Nagpur, Maharashtra, India.

## Informed consent

All patients signed the informed consent.

## Conflict of Interest

None

## References

1. Cahlon O, Hunt M, Zelefsky MJ. Intensity-modulated radiation therapy: supportive data for prostate cancer. *Semin Radiat Oncol.* 2008;**18**(1):48-57. doi: 10.1016/j.semradonc.2007.09.007. PubMed PMID: 18082588.
2. Ong CL, Dahele M, Slotman BJ, Verbakel WF. Dosimetric impact of the interplay effect during stereotactic lung radiation therapy delivery using flattening filter-free beams and volumetric modulated arc therapy. *Int J Radiat Oncol Biol Phys.* 2013;**86**(4):743-8. doi: 10.1016/j.ijrobp.2013.03.038. PubMed PMID: 23773394.
3. Georg D, Knöös T, McClean B. Current status and future perspective of flattening filter free photon beams. *Med Phys.* 2011;**38**(3):1280-93. doi: 10.1118/1.3554643. PubMed PMID: 21520840.
4. Huang Y, Siochi RA, Bayouth JE. Dosimetric properties of a beam quality-matched 6 MV unflattened photon beam. *J Appl Clin Med Phys.* 2012;**13**(4):3701. doi: 10.1120/jacmp.v13i4.3701. PubMed PMID: 22766941. PubMed PMCID: PMC5716519.
5. Vassiliev ON, Titt U, Kry SF, Pönisch F, Gillin MT, Mohan R. Monte Carlo study of photon fields from a flattening filter-free clinical accelerator. *Med Phys.* 2006;**33**(4):820-7. doi: 10.1118/1.2174720. PubMed PMID: 16696457.
6. Reggiori G, Mancosu P, Castiglioni S, Alongi F, et al. Can volumetric modulated arc therapy with flattening filter free beams play a role in stereotactic body radiotherapy for liver lesions? A volume-based analysis. *Med Phys.* 2012;**39**(2):1112-8. doi: 10.1118/1.3679858. PubMed PMID: 22320821.
7. Hawkins MA, Bedford JL, Warrington AP, Tait DM. Volumetric modulated arc therapy planning for distal oesophageal malignancies. *Br J Radiol.* 2012;**85**(1009):44-52. doi: 10.1259/bjr/25428720. PubMed PMID: 21427179. PubMed PMCID: PMC3473937.
8. Kwa SL, Lebesque JV, Theuws JC, Marks LB, et al. Radiation pneumonitis as a function of mean lung dose: an analysis of pooled data of 540 patients. *Int J Radiat Oncol Biol Phys.* 1998;**42**(1):1-9. doi: 10.1016/s0360-3016(98)00196-5. PubMed PMID: 9747813.
9. Wang SL, Liao Z, Vaporciyan AA, Tucker SL, Liu H, et al. Investigation of clinical and dosimetric factors associated with postoperative pulmonary compli-

- cations in esophageal cancer patients treated with concurrent chemoradiotherapy followed by surgery. *Int J Radiat Oncol Biol Phys.* 2006;**64**(3):692-9. doi: 10.1016/j.ijrobp.2005.08.002. PubMed PMID: 16242257.
10. Lee HK, Vaporciyan AA, Cox JD, Tucker SL, et al. Postoperative pulmonary complications after preoperative chemoradiation for esophageal carcinoma: correlation with pulmonary dose-volume histogram parameters. *Int J Radiat Oncol Biol Phys.* 2003;**57**(5):1317-22. doi: 10.1016/s0360-3016(03)01373-7. PubMed PMID: 14630268.
  11. Chapet O, Fraass BA, Ten Haken RK. Multiple fields may offer better esophagus sparing without increased probability of lung toxicity in optimized IMRT of lung tumors. *Int J Radiat Oncol Biol Phys.* 2006;**65**(1):255-65. doi: 10.1016/j.ijrobp.2005.12.028. PubMed PMID: 16618580.
  12. Titt U, Vassiliev ON, Pönisch F, Dong L, Liu H, Mohan R. A flattening filter free photon treatment concept evaluation with Monte Carlo. *Med Phys.* 2006;**33**(6):1595-602. doi: 10.1118/1.2198327. PubMed PMID: 16872067.
  13. Kry SF, Vassiliev ON, Mohan R. Out-of-field photon dose following removal of the flattening filter from a medical accelerator. *Phys Med Biol.* 2010;**55**(8):2155-66. doi: 10.1088/0031-9155/55/8/003. PubMed PMID: 20305334.
  14. David HI, Jennifer M, Mohan S, Adam D, Lisa AK, Andre A, et al. RTOG 0436: A phase III trial evaluating the addition of cetuximab to paclitaxel, cisplatin, and radiation for patients with esophageal cancer treated without surgery. *Journal of Clinical Oncology.* 2014;**32**(15\_suppl):4007. doi: 10.1200/jco.2014.32.15\_suppl.4007.
  15. Cashmore J. Surface dose variations in 6 and 10 MV flattened and flattening filter-free (FFF) photon beams. *J Appl Clin Med Phys.* 2016;**17**(5):293-307. doi: 10.1120/jacmp.v17i5.6284. PubMed PMID: 27685127. PubMed PMCID: PMC5874110.
  16. ICRU. Report 83: Prescribing, Recording, and Reporting Photon-Beam Intensity-Modulated Radiation Therapy (IMRT). *Journal of ICRU.* 2010;**10**(1):1-3.
  17. Yadav S, Singh OP, Choudhary S, Saroj DK, Yogi V, Goswami B. Estimation and comparison of integral dose to target and organs at risk in three-dimensional computed tomography image-based treatment planning of carcinoma uterine cervix with two high-dose-rate brachytherapy sources: 60Co and 192Ir. *J Cancer Res Ther.* 2021;**17**(1):191-7. doi: 10.4103/jcrt.JCRT\_199\_19. PubMed PMID: 33723154.
  18. Treutwein M, Hipp M, Koelbl O, Dobler B. Volumetric-modulated arc therapy and intensity-modulated radiation therapy treatment planning for prostate cancer with flattened beam and flattening filter free linear accelerators. *J Appl Clin Med Phys.* 2017;**18**(5):307-14. doi: 10.1002/acm2.12168. PubMed PMID: 28857432. PubMed PMCID: PMC5875831.
  19. Vassiliev ON, Kry SF, Kuban DA, Salehpour M, Mohan R, Titt U. Treatment-planning study of prostate cancer intensity-modulated radiotherapy with a Varian Clinac operated without a flattening filter. *Int J Radiat Oncol Biol Phys.* 2007;**68**(5):1567-71. doi: 10.1016/j.ijrobp.2007.04.025. PubMed PMID: 17544596.
  20. Fu W, Dai J, Hu Y, Han D, Song Y. Delivery time comparison for intensity-modulated radiation therapy with/without flattening filter: a planning study. *Phys Med Biol.* 2004;**49**(8):1535-47. doi: 10.1088/0031-9155/49/8/011. PubMed PMID: 15152690.
  21. Saroj D, Yadav S, Ghosh G, Shukla S, Gupta G, Choudhary S. Dosimetric Comparison between 6MV Flattened Filter and Flattening Filter Free Photon Beams in the Treatment of Glioblastoma with IMRT Technique: A Treatment Planning Study. *Iranian Journal of Medical Physics.* 2020;**17**(3):188-96. doi: 10.22038/ijmp.2019.39054.1515.
  22. Kim TH, Cho KH, Pyo HR, Lee JS, Zo JI, et al. Dose-volumetric parameters for predicting severe radiation pneumonitis after three-dimensional conformal radiation therapy for lung cancer. *Radiology.* 2005;**235**(1):208-15. doi: 10.1148/radiol.2351040248. PubMed PMID: 15703313.
  23. Kong FM, Hayman JA, Griffith KA, Kalemkerian GP, et al. Final toxicity results of a radiation-dose escalation study in patients with non-small-cell lung cancer (NSCLC): predictors for radiation pneumonitis and fibrosis. *Int J Radiat Oncol Biol Phys.* 2006;**65**(4):1075-86. doi: 10.1016/j.ijrobp.2006.01.051. PubMed PMID: 16647222.
  24. Graham MV, Purdy JA, Emami B, Harms W, et al. Clinical dose-volume histogram analysis for pneumonitis after 3D treatment for non-small cell lung cancer (NSCLC). *Int J Radiat Oncol Biol Phys.* 1999;**45**(2):323-9. doi: 10.1016/s0360-3016(99)00183-2. PubMed PMID: 10487552.
  25. Ishikura S, Nihei K, Ohtsu A, Boku N, Hironaka S, et al. Long-term toxicity after definitive chemoradiotherapy for squamous cell carcinoma of the thoracic esophagus. *J Clin Oncol.* 2003;**21**(14):2697-702. doi: 10.1200/JCO.2003.03.055. PubMed PMID: 12860946.

26. Wei X, Liu HH, Tucker SL, Wang S, Mohan R, Cox JD, Komaki R, Liao Z. Risk factors for pericardial effusion in inoperable esophageal cancer patients treated with definitive chemoradiation therapy. *Int J Radiat Oncol Biol Phys.* 2008;**70**(3):707-14. doi: 10.1016/j.ijrobp.2007.10.056. PubMed PMID: 18191334.
27. Cashmore J, Ramtohum M, Ford D. Lowering whole-body radiation doses in pediatric intensity-modulated radiotherapy through the use of unflattened photon beams. *Int J Radiat Oncol Biol Phys.* 2011;**80**(4):1220-7. doi: 10.1016/j.ijrobp.2010.10.002. PubMed PMID: 21167659.
28. Kragl G, Baier F, Lutz S, Albrich D, Dalaryd M, et al. Flattening filter free beams in SBRT and IMRT: dosimetric assessment of peripheral doses. *Z Med Phys.* 2011;**21**(2):91-101. doi: 10.1016/j.zemedi.2010.07.003. PubMed PMID: 20888199.
29. Lohse I, Lang S, Hrbacek J, Scheidegger S, et al. Effect of high dose per pulse flattening filter-free beams on cancer cell survival. *Radiother Oncol.* 2011;**101**(1):226-32. doi: 10.1016/j.radonc.2011.05.072. PubMed PMID: 21733592.
30. Zhuang M, Zhang T, Chen Z, Lin Z, Li D, Peng X, Qiu Q, Wu R. Volumetric modulation arc radiotherapy with flattening filter-free beams compared with conventional beams for nasopharyngeal carcinoma: a feasibility study. *Chin J Cancer.* 2013;**32**(7):397-402. doi: 10.5732/cjc.012.10182 PubMed PMID: 23237224. PubMed PMCID: PMC3845599.