Original Article

Is Synchronous Bilateral Breast Irradiation Using Flattening Filter-Free Beam-Based Volumetric-Modulated Arc Therapy Beneficial? A Dosimetric Study

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Abstract

Objective: The aim of this study is to validate the clinical use of flattening filter-free (FFF) beam-based volumetric-modulated arc therapy (VMAT) in synchronous bilateral breast carcinoma (SBBC) patient treatments and to compare with flattening filtered (FF) beam-based VMAT. **Materials and Methods:** Computed tomography images of 15 SBBC patients were taken for this study. A dose of 50 Gy in 25 fractions was prescribed to planning target volume (PTV). VMAT plans were generated using both FFF and FF 6 MV X-ray beams in Eclipse treatment planning system. PTV and organs at risk (OARs) doses were analyzed quantitatively using dose–volume histograms (DVHs) to meet plan objectives. Pretreatment point and planar dosimetry were performed. **Results:** The findings were reported as mean ± 1 standard deviation. PTV volume receiving 95% of the prescribed dose was 95.71% ± 0.65% for FF-VMAT and 95.45% ± 1.33% for FFF-VMAT ($P = 0.743$). Conformity index was 1.12 ± 0.31 (FF-VMAT) and 1.12 ± 0.02 (FFF-VMAT). Right lung mean dose was 10.95 ± 1.33 Gy (FF-VMAT) and 10.60 ± 98.5 (FFF-VMAT). Left lung mean dose was 9.73 ± 1.56 (FF-VMAT) and 9.61 ± 1.53 Gy (FFF-VMAT). Tumor control probability (TCP) was 99.68% ± 0.02% (FF-VMAT) and 99.67% ± 0.01% (FFF-VMAT) ($P = 0.390$). Uncomplicated TCP was 98.72% ± 0.02% (FF-VMAT) and 98.72% ± 0.01% (FFF-VMAT) ($P = 0.508$). **Conclusion:** The planning objective parameters achieved using FFF-based VMAT showed that FFF can also be used clinically to treat bilateral breast carcinomas and the low-dose lung volumes were still lesser with FFF-VMAT plans than FF-VMAT.

Keywords: Bilateral breast, breast radiotherapy, flattening filter free, SBBC, synchronous bilateral breast, volumetric-modulated arc therapy

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Introduction

The incidence of breast cancer is one of the highest among women.[1,2] In breast cancer itself, the incidence of cancer in both the breasts (bilateral) is very rare. Bilateral breast cancers are divided into metachronous and synchronous depending on the time gap between detection of cancer in both the breasts. If detected less than a year gap, it is called synchronous bilateral breast carcinoma (SBBC); otherwise, it is called metachronous. The incidence rate of SBBC is lesser than metachronous. Many studies are indicating the range of synchronous bilateral breast carcinoma to be from 0.4% to 2.8% of total breast cancers.[3-6] Compared to other breast cancers, the incidence of distant metastasis is higher and also disease-free survival is significantly less in synchronous bilateral breast carcinoma patients.[4,5]

Surgery followed by adjuvant radiation therapy is the well-known treatment process of early-stage breast cancers. The radiation therapy techniques used for synchronous bilateral breast irradiation are the same as unilateral breast cancers, except the beam orientation, and the junction of both breasts makes the planning more complex. Furthermore,

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achieving the dose constraints of total lung and heart is very critical in the treatment of SBBC.[7-9] Many studies compared three-dimensional conformal radiotherapy (3DCRT) techniques with intensity-modulated radiotherapy (IMRT) for SBBC and shown that IMRT was more optimal with respect to organs at risk (OAR) dose and planning target volume (PTV) dose conformity in the selected cases.[5] The disadvantage of conventional IMRT is that the time required to deliver dose was much higher than 3DCRT and hence reduces the patient throughput in any busy radiotherapy department.

The introduction of volumetric-modulated arc therapy (VMAT) makes the special form of IMRT to deliver the dose in time comparable to 3DCRT and hence providing optimal radiation therapy treatments to breast cancer patients.[10-12] The advantage of VMAT has been more pronounced in the current radiotherapy practices. Helical tomotherapy is also another rotational method of treatment, but lags in the treatment time compared to VMAT.[13]

The radiation beams used mostly are flattening filtered (FF) beam from the accelerator head. The use of flattening filter-free (FFF) beam has increased more rapidly in recent years. Technical evolution of high-performance computers and accurate dose calculation algorithms enhance the treatment planning systems (TPSs) to counter the complex intensity modulation involving FFF. With FFF beam, the treatment time is considerably reduced for stereotactic treatments where higher dose per fraction is employed.

Vendors are coming up with linear accelerators enabled with FFF alone in recent times [e.g., Varian Edge™ manufactured by Varian Medical Systems (Palo Alto, USA), providing the option of buying high-intensity FFF beams alone]. The extent of usefulness of FFF is well established in hypofractionated treatments in the form of SRS and SBRT where the tumor size is smaller and the treated volumes are much lower than conventional RT with larger size tumors (with or without positive lymphatic nodes).[14-17] SBBC is one such site, which requires large-field arrangements.

The advantage of using flattened beam-based VMAT for SBBC had been reported by Nicolini *et al*.[5] There are very scarce papers in literature, which suggest the role of FFF beam-based VMAT in the treatment of SBBC. Hence, we decided to validate the usefulness of FFF beam-based VMAT (FFF-VMAT) to treat SBBCs in comparison with FF beam-based VMAT (FF-VMAT) for conventional dose of 2 Gy per fraction.

Materials and Methods

Patient characteristics

In this study, 15 synchronous bilateral breast carcinoma patients registered in our institute from 2010 to 2018 were selected. Among these 15 patients, 5 were right side total mastectomy, 6 were left side total mastectomy, and 4 were both breast conservative surgery performed patients. Of these 15 patients, 13 were treated using FF-VMAT and 2 were treated using forward IMRT.

Simulation

All patients were immobilized by following the institutional protocol using thermoplastic masks and VacLok with positions supine, head straight, and hands above head. All the patients were simulated in free breathing condition. Both plain and contrast-enhanced three-dimensional computed tomography (CT) images were acquired using 16-slice Siemens Somatom Scope (Siemens AG, Germany) with a slice thickness of 3 mm for contouring and treatment planning. Among these 15 patients, six patients underwent PET-CT and these images were rigid registered with the planning CT images to assist target delineation.

Planning

In 2013, we had upgraded our existing C-Series linear accelerator with FFF beam mode of delivery along with Eclipse TPS version 11 (Varian medical systems, Palo Alto, USA). For all 15 patients, new contours and plans (FF-VMAT and FFF-VMAT) were created regardless of old plan and technique in Eclipse TPS version 11. The Radiation Therapy Oncology Group (RTOG) breast contouring guidelines[18] were followed for contouring. The structures such as CTV (clinical target volume), PTV, PTV_{Eval} (PTV cropped by 5 mm from body for evaluation), right lung, left lung, heart, spinal cord, and healthy tissue were contoured. VMAT treatment plans were created using upgraded Clinac iX (Varian medical systems, Palo Alto, USA) linear accelerator, which is capable of delivering 6 MV FF and FFF beams. It is equipped with millennium 120 multileaf collimator and On-Board imager where kV and MV planar images and cone-beam computed tomography volume images can be acquired to verify the patient position before treatments.

The dose prescription to PTV was 50 Gy in 25 fractions. Planning goals were set as follows: for PTV, minimum 90% of the PTV volume should receive 95% of the prescribed dose and no volume should receive dose more than 115% of the prescribed dose as well as the global dose maximum should be inside the PTV. For OAR, lung dose constraints were 20 Gy volume should be <30% and mean lung dose should be <15 Gy; heart dose to be minimized as low as possible (mean <5 Gy was suggested in RTOG 1005) and spinal cord maximum dose should be <45 Gy.[19]

For all the patients, 6 MV FF VMAT plans were created in the TPS using two isocenters with four partial coplanar arcs, with two partial arcs placed at each isocenter as shown in Figure 1. The first isocenter was placed on the right side breast PTV and the second isocenter was placed in the same transverse plane on the left side breast PTV by moving lateral coordinate without changing vertical and longitudinal plane. For the right side target, the arc angle ranged from 230° to 60° clockwise (CW) and from 60° to 230° counterclockwise (CCW) with collimator rotation of 15° or 345°. For the left side target, it was 300° to 130° CW as well as CCW with collimator rotation of 15° or 345°.

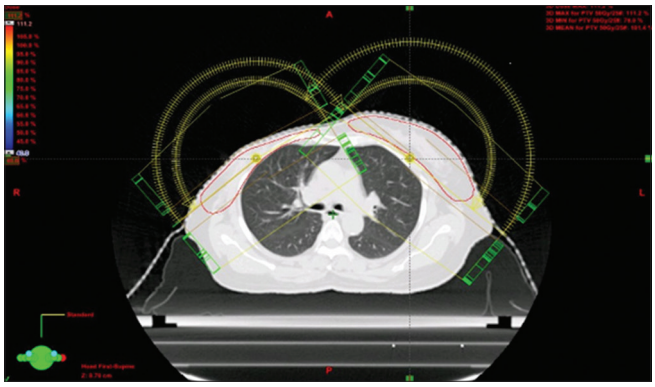

Figure 1: Isocenter placement and volumetric-modulated arc therapy: arc beam geometry in axial plane

The direct aperture optimizer progressive resolution optimizer version 3 in Eclipse allows VMAT optimization of multiple isocenters as well as multiple arcs simultaneously in the same plan. The VMAT optimization was performed to get optimal dose distribution by giving lower and upper dose constraints along with priority. Both lower and upper constraints were used for PTV, while only upper constraints were used for critical structures. Priority ranks of 1, 2, 3, and 4 were given to PTV, lungs, heart, and spine, respectively. Normal tissue objective function available in Eclipse was used to reduce the dose to normal tissues. The dose was calculated on planning CT using analytical anisotropic algorithm in Eclipse TPS with calculation grid size of 2.5 mm. The final plan was taken as the reference. In the same way, FFF-based VMAT plans were created by keeping the same planning objectives as of the reference FF-VMAT plans only by changing the energy from 6 MV FF to 6 MV FFF, and the highest dose rate available for the respective energy was used. These two plans were compared using dosimetric and biological parameters.

Dosimetric evaluation

Cumulative dose–volume histograms (DVHs) were used to compare the dose coverage and plan quality parameters. For PTV, $V_{95\%}$ (% of volume receiving 95% of the prescribed dose that is 47.5 Gy), $V_{90\%}$ (volume receiving 90% of the prescribed dose), and D_{1cc} (dose received by 1cc of the PTV volume) were used to compare dose coverage to PTV.[5] Conformity index (CI) and heterogeneity index (HI) were used to compare the quality of plans. The following formulas were used to compute the CI and HI.

$$CI_{95\%} = V_{95\%}/V_{PTV} \quad (1)$$

where $V_{95\%}$ = volume covered by 95% of the dose (cc), V_{PTV} = volume of the PTV (cc)

$$HI = D_{5\%}/D_{95\%} \quad (2)$$

where $D_{5\%}$ = dose received by 5% volume of PTV (Gy), $D_{95\%}$ = dose received by 95% volume of PTV (Gy). To compare dose to lungs, the parameters $V_{5\ Gy}$ (% of volume receiving dose of 5 Gy), $V_{10\ Gy}$ (% of volume receiving dose of 10 Gy), $V_{20\ Gy}$ (% of volume receiving dose of 20 Gy), and D_{mean} (mean dose) were used. For heart, parameters such as D_{mean}, $D_{2\%}$ (dose received by 2% of volume), $V_{10\ Gy}$ (% of volume receiving dose of 10 Gy), and $V_{45\ Gy}$ (% of volume receiving dose of 45 Gy) were used.

Healthy tissue (body subtracted from PTV) dose was compared using D_{mean}, $V_{3\ Gy}$ (% of volume receiving dose of 3 Gy), $V_{10\ Gy}$ (% of volume receiving dose of 10 Gy), external volume index (EI), and integral dose (ID).[5] EI was calculated as $V_D/V_{PTV,}$ where V_D is the volume of healthy tissue receiving dose more than the prescribed dose and V_{PTV} is the volume of PTV.

Biological evaluation

Biological parameters, tumor control probability (TCP) and normal tissue complication probability (NTCP), were also calculated to check the quality of plans using cumulative DVHs. The cumulative DVHs were exported with dose bin size of 1cGy in text format and converted to tabular format in Microsoft Excel for calculating equivalent uniform dose (EUD), TCP, and NTCP. The dose in DVH was converted to equivalent dose of 2 Gy ($EQD_{2\ Gy}$) using L-Q model[20] to find the EUD. The formula used to calculate $EQD_{2\ Gy}$ is as follows:

$$EQD_{2\ Gy} = D(\alpha/\beta + D/n)/(\alpha/\beta + 2) \quad (3)$$

where D = nd (d is the dose per fraction and n is the number of fractions); α/β = ratio that gives the dose at which linear (α) and quadratic (β) components of cell killing are equal. EUD was calculated to convert the heterogeneous dose distribution to homogeneous dose that produces the same biological effect based on the Niemierko's model.[21]

$$EUD = (\Sigma_i v_i D_i^a)^{1/a} \quad (4)$$

where D_i is the equivalent dose of 2 Gy corresponding to i^{th} bin and v_i is the partial volume receiving the dose D_i, a is the model parameter.

The calculated EUD was used to calculate the TCP of PTV and NTCP of normal structures based on Niemierko's models.[22-26] The formulas used were as follows:

$$TCP = 1 / [1 + (TCD_{50} / EUD)^{\wedge}4\gamma_{50}] \quad (5)$$

$$NTCP = 1 / [1 + (TD_{50/5} / EUD)^{\wedge} 4\gamma_{50}] \quad (6)$$

Where γ_{50} = slope of the dose response curve at a dose of 50% complication or control probability; TCD_{50} = tumor dose for 50% TCP; and $TD_{50/5}$ = normal tissue dose for 50% complication probability in 5 years. The values used in the calculation of EQD, EUD, TCP, and NTCP are given in Table 1. The therapeutic gain can be obtained using uncomplicated TCP (UTCP). UTCP was calculated as follows:

$$UTCP = (TCP \times \pi_i (1 - NTCP_i)) \quad (7)$$

where NTCPi is the NTCP of organ i (e.g., if i = lung, NTCPi = NTCP of organ lung).

Pretreatment verification

Pretreatment plan verification was done by point dose and planar dose measurements. Verification plans were created

for both plans without resetting the collimator angles and with preset MU values as of original plans in TPS for point dose and planar dose measurements. Both FF-VMAT and FFF-VMAT plans were executed on verification phantoms as like actual plan setup just by moving the couch lateral values as shown in Figure 2.

Point dose

Point doses were measured at isocenter for all fields using CC13 (IBA Dosimetry, Gmbh, Germany) (cavity volume 0.13cc) cylindrical chamber and slab phantom made up of PMMA plastic material (30 cm × 30 cm × 10 cm). The point of measurement was kept in the low-gradient high-dose regions. Two points from the left side and right side high dose as well as low gradient were identified in the lateral direction and measured the dose in those points by keeping the couch separation same as of the original plan. The cumulative variations of measured dose from the TPS-predicted dose for both techniques were tabulated.

Planar dose

Multicube phantom with I-matrix array detectors (31.5 cm × 34 cm × 22 cm) and OmniPro IMRT software (IBA Dosimetry, Gmbh, Germany) were used for planar dosimetry. The detector plane in coronal view was taken for comparison and dose plane was exported in DICOM format to Omnipro IMRT software to compare with the corresponding measured dose maps. In this process, a setup field was introduced in the verification plan at coordinates as of user origin in the middle of the detector as shown in Figure 2 and used to align all the fields when exporting the plan in DICOM format. The 2D gamma evaluation was done to evaluate both the plans on the usable detector area of central 24 cm × 24 cm. Distance to agreement (DTA) and dose difference (DD) criteria of 3 mm and 3%, 2 mm and 3%, and 2 mm and 2% were used to compute the gamma value for comparison of both the plans. The percentage of points passing the 2D gamma value of ≤1 was calculated and tabulated.

Table 1: Biological parameters for planning target volume and organs at risks

Parameter	Breast PTV	Heart	Lung	Spinal cord
γ_{50}	2	3	2	4
α/β	3.4	3	3.1	3
$TD_{50/5}$ (Gy)	-	48	24.5	66.5
TCD_{50} (Gy)	25	-	-	-
a	−7.2	3	1	13
End point	Tumor control	Pericarditis	Pneumonitis	Myelopathy
Reference	[24-26]	[24]	[24]	[24]

PTV: Planning target volume, TCD: Tumor dose for 50% TCP, TD: Normal tissue dose for 50%, TCP: Tumor control probability

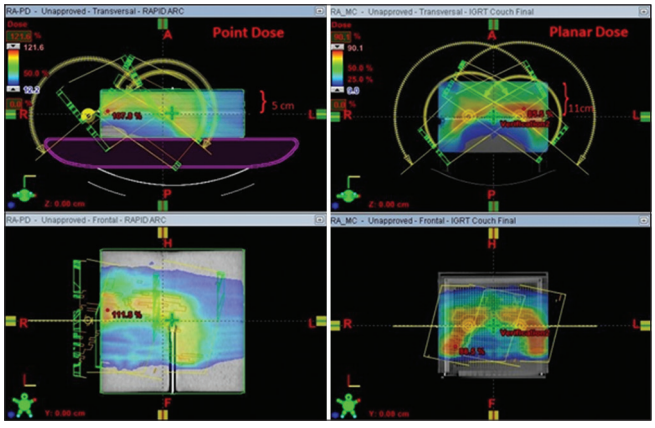

Figure 2: Phantom and detector setup for point and planar dosimetry

Efficiency of plan

Efficiency of both the plans was compared using the total number of monitor units (MU) and beam ON time for each plan by considering the rest of the setup and simulation procedures were the same for both the techniques.

Statistical analysis

Statistical analyses were made using Microsoft Excel spreadsheet. To find the significance of difference, Student's paired *t*-test with two tails was used. The null hypothesis set was that both FF-VMAT and FFF-VMAT were having the same mean with 95% confidence limit. Thus, if the probability value (*P*) is ≤0.05, the differences in the two techniques are statistically significant.

Results

The plans which satisfied the clinical goals with acceptable limitations for both FF-VMAT and FFF-VMAT plans were taken for comparison. The dose distribution achieved by both the plans for a sample patient is shown in Figure 3 with dose levels of 47.5, 45 , and 20 Gy.

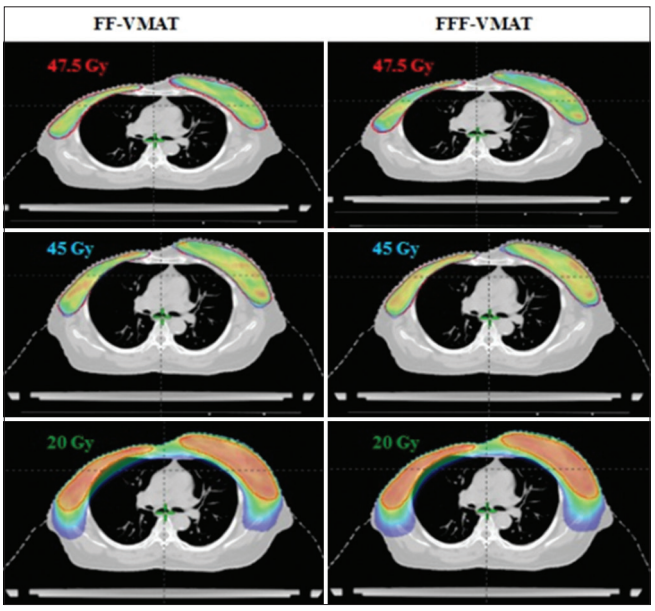

Figure 3: Dose distribution using flattening filtered volumetric-modulated arc therapy (left) and flattening filter-free volumetric-modulated arc therapy (right) for the sample patient

The mean results of all patients were reported with one standard deviation for all evaluating parameters. The results of physical and biological parameters for PTV are given in Table 2 with their *P* values. Dosimetric and biological parameters for OARs and normal healthy tissue are given in Table 3. The corresponding *P* values were also given for each parameter under evaluation for both the techniques. The UTCP was 98.72% ± 0.02% (FF-VMAT) and 98.72% ± 0.01% (FFF-VMAT) ($P = 0.508$).

The gamma analysis window of both the techniques of a sample patient is shown in Figure 4 for different gamma index analysis (GIA) criteria. The analysis was made first by taking the entire measured area (GIA total) and then by keeping the region of interest in junction where the overlap occurs usually (GIA at junction) as indicated with red rectangle in Figure 4. Patient's plan verification measurement results were tabulated along with the number of MUs and treatment beam ON time in Table 4.

Table 2: Planning target volume: dosimetric and biological comparison results

Parameter	FF-VMAT		FFF-VMAT		*P*
	Mean	SD	Mean	SD	
$V_{90\%}$ (%)	99.47	0.37	99.55	0.32	0.762
$V_{95\%}$ (%)	95.71	0.65	95.45	1.33	0.743
$D_{2\%}$ (%)	107.37	1.89	107.39	1.34	0.942
D_{1CC} (Gy)	54.37	1.07	54.53	0.61	0.803
$CI_{95\%}$	1.12	0.31	1.12	0.02	0.662
HI	1.63	1.03	1.12	0.02	0.396
EUD	51.22	0.42	51.07	0.29	0.370
TCP (%)	99.68	0.02	99.67	0.01	0.390

PTV: Dosimetric and biological comparison results

Table 3: Organs at risk: dosimetric and biological comparison results

Structure	Parameter	FF-VMAT		FFF-VMAT		*P*
		Mean	SD	Mean	SD	
Lung Left	D_{mean} (Gy)	9.73	1.57	9.62	1.53	0.916
	V_{20Gy} (%)	11.69	4.53	11.70	4.28	0.998
	V_{10Gy} (%)	26.78	3.53	26.50	4.04	0.922
	V_{5Gy} (%)	62.82	3.79	59.62	4.47	0.318
	EUD (Gy)	7.40	1.56	7.32	1.50	0.581
	NTCP (%)	0.02	0.03	0.02	0.02	0.329
Lung Right	D_{mean} (Gy)	10.95	1.34	10.61	9.85	0.696
	V_{20Gy} (%)	14.60	5.16	14.42	4.85	0.960
	V_{10Gy} (%)	33.62	4.02	32.10	4.14	0.616
	V_{5Gy} (%)	68.05	2.73	63.34	2.30	0.039
	EUD (Gy)	8.36	1.25	8.31	1.29	0.700
	NTCP (%)	0.03	0.03	0.03	0.03	0.861
Lung Total	D_{mean} (Gy)	10.41	0.29	10.22	0.40	0.472
	V_{20Gy} (%)	13.32	0.86	13.25	0.73	0.905
	V_{10Gy} (%)	30.47	1.60	29.49	2.26	0.503
	V_{5Gy} (%)	65.70	2.62	61.54	3.30	0.096
Heart	D_{mean} (Gy)	11.80	3.45	12.24	3.86	0.869
	V_{10Gy} (%)	42.27	14.64	44.25	11.52	0.483
	V_{45Gy} (%)	1.17	1.53	1.22	1.60	0.495
	EUD (%)	16.50	3.97	16.34	4.89	0.783
	NTCP (%)	0.00	0.00	0.00	0.00	0.331
Spinal Cord	Dmax (Gy)	31.52	4.19	31.70	3.62	0.954
	EUD (%)	23.93	2.83	24.90	3.75	0.340
	NTCP (%)	0.00	0.00	0.00	0.00	0.389
Healthy Tissue	D_{mean} (Gy)	7.45	1.32	7.32	1.10	0.487
	V_{3Gy} (%)	48.13	7.11	45.87	6.96	0.001
	V_{10Gy} (%)	24.19	4.34	23.05	4.07	0.022
	EI (%)	0.28	0.08	0.27	0.06	0.459
	ID ($Gy.cm^3 \times 10^5$)	170.94	22.79	168.42	2.70	0.513

OARs: Dosimetric and biological comparison results

Discussion

In contrast to unilateral breast irradiation, the treatment planning to SBBC is complex due to the involved critical organ's doses. It was already proved that VMAT showed better distribution than IMRT with FF for SBBC.[5] In this dosimetric study, the feasibility of using FFF beam-based VMAT to treat SBBC was investigated and compared with FF beam-based VMAT. The results of this study showed that the FFF-VMAT plans were as good as FF-VMAT plans.

Planning target volume and dose-volume comparison

Dose distributions achieved with respect to PTV in both FF-VMAT and FFF-VMAT plans were equivalent and the differences were very minimal [Figure 2]. The maximum doses to all patients were less than 110% of the prescribed dose, and in these patients, the variations of maximum doses for PTV between both the plans were from 1% to 2%. The DVH data also showed that the PTV coverage for both the plans were similar and the differences were statistically insignificant for parameters such as PTV $V_{95\%}$, $V_{90\%}$, D_{1cc}, $CI_{95\%}$, and HI [Table 2]. It was established that the PTV results were equivalent to FF-VMAT results of single-side breast cancer.[27,28] The average DVH of all 15 patients for each structure under evaluation (PTV, healthy tissue, lungs, heart, and spinal cord) are given in Figure 5 for comparison.

Lung dose–volume histogram comparison

With respect to lungs, the left side lung showed no statistically significant differences in the mean lung dose, 20 Gy lung volume and 5 Gy lung volume between both FF-VMAT and FFF-VMAT. The *P* values were much higher than 0.05 as shown in Table 3. The mean dose and V_{20Gy} for right lung from both the plans showed that the differences were insignificant as shown in Table 3. Whereas, FFF-VMAT showed statistically significant reduction in V_{5Gy} volume for right lung compared to FF-VMAT with *P* value of 0.039.

Although both the lungs are having the mean dose lesser than 15 Gy, the mean doses are higher for right side than the left side for all patients. The lung volume near to the PTV is always less in the left side due to the presence of heart and hence reducing the mean dose to left side lung.

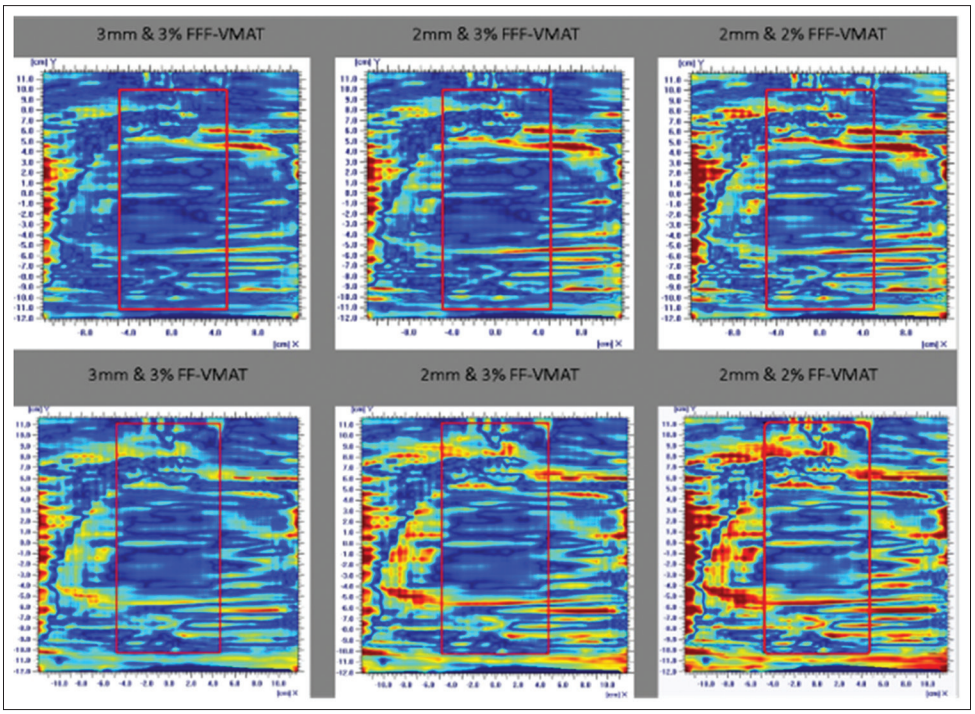

Figure 4: Gamma analysis window of different sets of analysis criteria of the sample patient's planar dosimetry for both the techniques

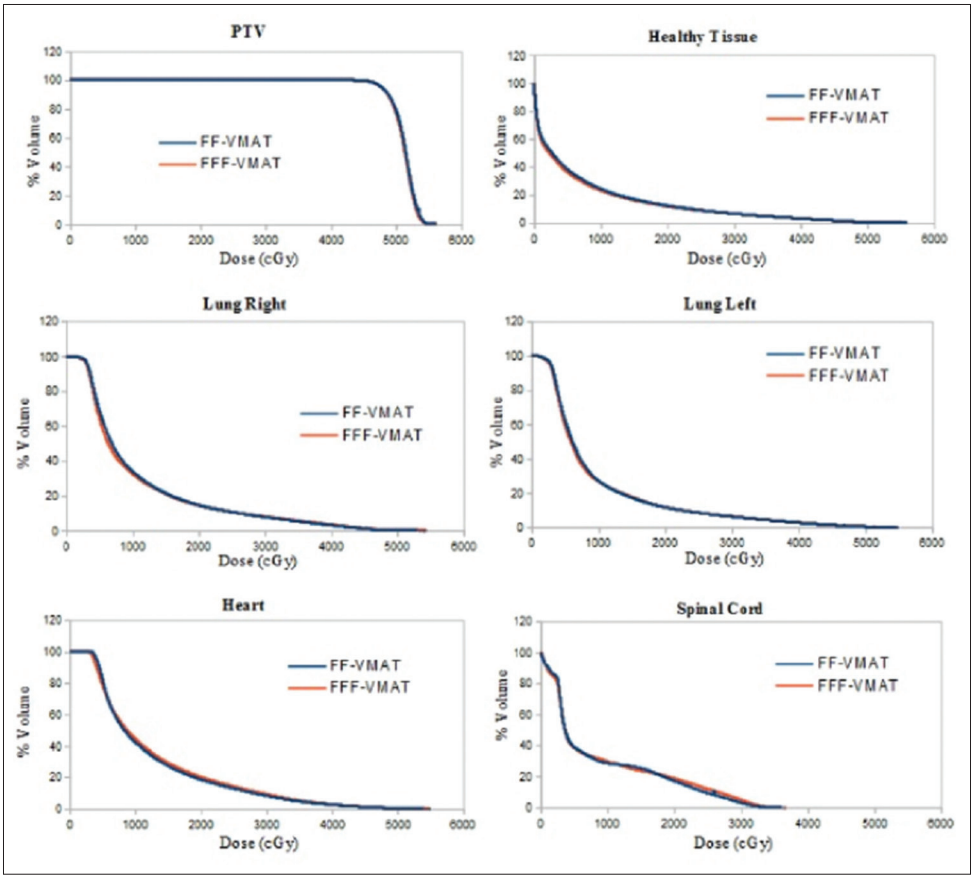

Figure 5: Average dose–volume histograms of all 15 patients under study

Table 4: Delivery parameters result

Parameter	FF-VMAT		FFF-VMAT		*P*
	Mean	SD	Mean	SD	
MU	963.25	23.75	1120.25	55.34	0.006
Beam ON time (min)	2.79	0.03	2.72	0.06	0.088
Point Dose Variation (%)	0.96	0.11	0.94	0.23	0.828
GIA (3mm & 3%)					
Total (%)	96.45	0.92	96.22	1.01	0.172
At Junction (%)	97.75	1.06	98.06	1.60	0.564
GIA (2mm & 3%)					
Total (%)	93.32	0.62	93.83	0.08	0.494
At Junction (%)	95.85	0.07	96.54	0.75	0.445
GIA (2mm & 2%)					
Total (%)	89.76	0.37	89.84	0.27	0.458
At Junction (%)	92.20	0.42	93.56	0.94	0.324

FFF: Flattening filter free, VMAT: Volumetric-modulated arc therapy, SD: Standard deviation, FF: Flattening filtered, MU: Monitor units, GIA: Gamma index analysis

Heart, spine, and healthy tissue

Heart mean doses showed random variations for both the plans [Figure 5] and statistically insignificant with *P* value of 0.869 [Table 3]. However, the mean heart dose (<5 Gy) was not achieved in all cases since we attempted to keep as low as possible without compromising the PTV coverage. The maximal heart distance and maximal heart length were found to be more in free breathing condition for these patients, which contributed significantly to high mean dose to heart.[28] It can be reduced further using the combinations of breath-hold techniques and gated delivery systems.[29]

Spinal cord maximum dose was always <45 Gy in all patients for both the plans. The *P* value of 0.954 for spine maximum dose showed that there was no significant difference between the two plans.

Healthy tissue 3 Gy volume and 10 Gy volume showed a statistically significant difference and FFF-VMAT was superior to FF-VMAT. The difference may be because of the reduced average energy of FFF. On the other hand, there are no significant difference between two techniques in EI and ID.

Biological comparisons

Biological parameter EUD for all structures showed no statistically significant difference with *P* value much higher than 0.05. For PTV, the TCP values for all the patients were above 99% for both the plans, and the differences were insignificant statistically. NTCP and UTCP values also suggested that there were no statistically significant differences between FFF-VMAT and FF-VMAT. Hence, these two plans can be considered equivalent to each other based on biological and physical parameters irrespective of shape of the beams before intensity modulation.

Efficiency comparisons

Lesser MU and lesser beam ON time are the desired characteristics of a better plan of similar distributions. The plan which has lesser overall treatment time is considered to be the best plan with respect to patient throughput. From Table 4, FF-VMAT was better with respect to lesser MU than FFF-VMAT with a *P* value of 0.006. At the same time, beam ON time showed no statistically significant difference between both plans, which means that both the plans can be delivered in the same time with more number of MUs for FFF-VMAT. The availability of high dose rates in FFF mode compensates the time of beam ON for FFF-VMAT. We had expected relatively less treatment time with FFF-VMAT, but because of the conventional dose of 2 Gy per fraction, the maximum dose rate was not boosting more than the conventional level of 600 MU/min.[30] Hence, the overall treatment time remained the same for both the plans.

Deliverability comparison

The plan deliverability check with point dose and planar dose measurements also showed no significant difference between these two VMAT plans. Point dose variations were well within the institutional protocol limit of 3% for all patients in both techniques. Furthermore, the gamma passing rates were more than 95% for both the plans with clinically accepted GIA criteria of 3 mm and 3%. This indicates that both plans deliverability are equivalent in accordance with TPS.

Future study

Although the standard conventional dose of 50 Gy in 25 fractions has been followed in our center for SBBCs, the FAST-Forward trial (26 Gy in 5 fractions)[31] is being adopted in many centers across the world for breast cancers. The introduction of FFF may reduce the treatment time for the dose of 5.2 Gy per fraction and we want to study its significance in our future work and we would like to elaborate this study with deep inspiration breath-hold gated therapy.

Conclusion

There is always a conflict in using FFF beams for large-field treatments and our results showed that there were no dosimetric differences between FFF-VMAT and FF-VMAT plans and also proved that FFF beams could also be used to treat large-field breast cancers. It is inferred that even though the MU for FFF beams were higher than FF beams, the beam ON time remained the same for conventional dose of 2 Gy per fraction. Moreover, the low-dose lung volumes are quite less with FFF beams. Thus, FFF-based VMAT delivery can also be preferred equally for SBBCs as of FF-VMAT.

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Conflicts of interest

There are no conflicts of interest.

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