RESEARCH ARTICLE

Treatment Planning With Unflattened as Compared to Flattened Beams for Bilateral Carcinoma of the Breast

Suresh Tamilarasu[1], Madeswaran Saminathan[2]*, S K Sharma[1], Anjali P[1], Abhinav Dewan[1]

Abstract

Aim: To evaluate the plan quality of 6MV unflattened (UFB) and flattened beam (FB) photon energy using AAA dose calculation algorithms for volumetric arc therapy. **Materials and Methods:** Plans were generated for bilateral carcinoma of breast and the dose prescribed was 50.4Gy in 28 fractions. Two different plans were made for each patient using 6MV FB and 6MV UFB. Dose calculations were performed on an AAA dose calculation algorithm. Plans were generated on Eclipse TPS and were capable of being delivered with a true beam STx linear accelerator. The homogeneity index (HI), conformity index (CI), normal tissue integral dose (NTID), and effect of low dose volume on normal tissue and monitor units (MU) were noted. **Results:** All the plans were clinically acceptable. The HI and CI of 6MV UF rapid arc (RA) plans were higher than with the 6MV FB plan (1.16±0.05 and 0.12±0.00 respectively). There was no appreciable difference observed in Organ at risk (OAR) doses. The mean NTID and low dose volume were significantly low with 6MV RA UFB as compared to FB. 6MV RA UFB required a 35% higher MU than with the 6MV RA plan ($p<0.05$). **Conclusion:** RA plans generated with UFB on Eclipse TPS achieved target volume coverage and preserved OAR's essentially similar to 6MV RA FB plans. However RA plans generated in Varian Eclipse of UFB were superior with respect to mean NTID and low dose volumes in normal tissue.

Keywords: Flattened beam- unflattened beam- rapid arc and volumetric arc therapy

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Introduction

Bilateral breast carcinoma (Bib) is a rare clinical entity. However, with increasing awareness and better diagnostic tools, the incidence of synchronous BiB cancer is on a rise. It is well known that conventional tangential technique with or without wedges fails to give a homogenous dose distribution throughout the target volume. The drawback of these techniques included hot spots and high maximum dose (>107%), especially in large-breasted patients, which leads to worse/poor cosmetic outcomes after irradiation and under dosage may result in increased chance of local recurrence. In the past decade (Moorthy et al., 2013), 3-Dimensional Conformal Radiotherapy (3DCRT) became a standard treatment technique, which reduced the doses to lung, heart, and other critical structures in the breast cancer treatment. However, using 3DCRT, it is not always possible to achieve adequate normal tissue constraints, especially when treating left sided tumor. This is mainly due to the overlying concave shape of the target, which can result in more doses to adjacent structures such as heart and lung. By modulating photon beam (Hong L et al., 1999), it is possible to obtain concave and convex shape dose distributions with IMRT and has the ability to conform radiation dose to irregular target volumes, thereby sparing the underlying critical structures with better tumor control probability (TCP).

In most of the radiotherapy plans, the photon beam energy is selected depending up on tumor depth and location. The choosen optimal energy in a busy department depends upon the beam energy to target volume (TV) achieve the coverage and OAR sparing. Recently, so many modification / innovation like VMAT, UFB have been proposed and implemented clinically. At high energy greater than 10MV, the neutron contamination and exit dose is prominent. The advantage of treatment with high energies is more skin sparing as compared to lower energies (less than 6MV). The exit dose is low at lower energies which will help in OAR sparing. The advances in technique will improve target coverage, homogeneity, conformity and reduce toxicity that will help reduce chronic breast edema. Many authors compared 3DCRT, IMRT and VMAT techniques for different anatomical sites. Already, VMAT plays an important role in reducing delivery time compared to IMRT (Rana S et al., 2013). However limited as numbers of publication are available for bilateral breast cancer cases. In this present study we will discuss the advantage of UFB or Flattening filter free

*[1]Department of Radiotherapy, Rajiv Gandhi Cancer Institute and Research Centre, Rohini, New Delhi, [2]Department of Physics, VIT University, Vellore, Tamil Nadu, India. *For Correspondence: madeswaran.s@vit.ac.in*

beam in VMAT technique for bilateral breast carcinoma cases.

Materials and Methods

In VMAT or Rapid arc planning, a single isocentre was placed at the middle of sternum for easy setup and to further reduce the treatment duration. There were two partial arcs placed around each breast, the arc angle being 200°. The collimator jaws were fixed for the both breast and angulated to take are the tongue and groove. Similarly, treatment planning of photon beam for 6MV FB and 6MV UFB Rapid Arc was performed on Eclipse Treatment Planning system using Anisotropic analytical algorithm (AAA) with 0.25 cm grid size was used. Plans were capable of delivering treatment on Varian True Beam Linear Accelerator equipped with HD 120 MLC (MLC of 60 pair, inner 32 leaf pair of 0.25 cm, and outer 28 leaf pair of 0.50 cm projection width at isocenter and a maximum leaf speed of 2.5 cm/s). The VMAT and Rapid Arc delivery mode were same, however the vendor's trades name their products diffently. The Varian arc technique is called Rapid Arc and Elekta was VMAT.

All the photon beams were calibrated at 1 cGy/MU at dmax on the central axis for a 10 cm x 10 cm field with SSD of 100 cm, for both flattened and UF beams as per Technical Reports Series No. 398 (TRS-398, 2000) of International Atomic Energy Agency. Plans were optimized selecting a maximum dose rate of 600MU/min in 6MV FB and 1400 MU/min for 6MV UFB in Varian.

Patients Characteristics

Five patients who had undergone bilateral mastectomy with axillary lymph node clearance were identified. These five patients' detailed post-operative histopathology report warranted radiotherapy to the chest wall on both sides.

Imaging and contouring

Patients were taken up in the CT simulator room and made to lie in the supine position on AIO (All In One) base plate with head rest below the head and both arms abducted above the head. Room lasers were used to align the patient. A topograph was obtained for ensuring correct alignment of the patient. Radio-opaque markers and wires were placed to mark the area of interest. Then a 4 clip thermoplastic orfit cast (Orfit industries, Belgium) was made to immobilize the thorax and upper abdomen of the patient for simulation and daily treatment. Three reference fiducials (one in midline and two lateral) were placed on the cast on a bony landmark preferably in the area of interest with the help of room lasers which guide the isocentre shift during first day of treatment delivery.

A CT scan was obtained on the CT Simulator (Sensation Open Duo Wide Bore version Syngo CT 2007 by Siemens Medical Solutions, Germany) for treatment planning with 5 mm slices from the angle of the mandible to 5 cm below the inferior border of the breasts. DICOM (Digital Imaging and Communication System) images from the CT simulator were transferred to the contouring station. The TV and OAR's were contoured. Target volumes were defined by radiation oncologists: PTV included the entire breast (combination left and right breast). PTV was restricted to the skin by cropping at least 5 mm from the skin surface and to exclude the ribs.

PTV is defined medially at the lateral edge of the sternum, inferiorly at the infra-mammary fold, superiorly at the inferior edge of the medial head of the clavicle, and laterally to include all apparent breast tissue. OAR's such as heart, and common lung were also delineated. PTV, Common lung, and heart volumes were 878.6 ± 389.5cc, 2791.5 ± 811.2cc, and 410.5 ± 76.5cc respectively.

Dose Prescription and Optimization objective used for Inverse Treatment planning

Dose prescribed to PTV was 50.4Gy (1.8Gy/fraction) in 28 fraction. Planning objective was to deliver 100% prescription dose (PD) to 95% of PTV as recommended in International Commission on Radiation Units and Measurements (ICRU-50, 1999) Report 50 & 83 (ICRU Report 83, 2010). The normal dose constraint used were heart V25Gy ≤ 10%, Common lung V20Gy ≤ 30%, as per institutional protocol.

Plan Evaluation and statistical Methods

Homogeneity index (HI): A ratio evaluating the dose homogeneity (D2%-D98%)/D50%, in TV, where D2%, D98%, and D50% are the minimum dose delivered to 2%, 98%, and 50% volume of the TV, respectively. HI of zero indicates the dose distribution to be homogeneous.

Conformity index (CI): A ratio evaluating the coverage of the prescription dose in treatment Plans. CI = Volume within 98% isodose line / TV. CI of one indicates good dose conformity.

Parameters selected for comparison of heart V25Gy and common lung V20Gy were chosen because there was evidence that dose beyond these values could cause acute or late clinical symptoms. To assist in further analysis, V10Gy, and V35Gy for heart, as well as V45Gy and V5Gy for common lung, were noted. Healthy tissues, common lung dosimetric parameters (mean doses and V5Gy) were compared as they may represent doses that might be associated with a carcinogenic risk.

Normal tissue integral dose (NTID) (D'Souza WD et al., 2003) was defined as the integral of the absorbed dose extending to overall voxels excluding those within the TV. It was calculated to assess the plan quality based on the following formula. Normal tissue integral dose (NTID) = Mean dose × Volume of normal tissue outside TV.

In addition, the treatment parameters including the monitor units (MU) and beam on time (BOT) for each treatment plan were recorded for evaluation. BOT was defined as the radiation delivery time and did not include the patient positioning and imaging procedures.

In order to quantify the differences between plans a test of significance was required. All statistical tests were done using paired sample t-test for comparisons of data, performed using the IBM Statistical Package for Social Sciences (SPSS) software (release 20.0, SPSS Inc., Chicago, IL, USA). Statistical significance was defined as $p < 0.05$.

Results

Target volume Coverage

The target volume coverage of 6MV RA UFB was clinically acceptable. However there was significant p value $p<0.05$ were observed in homogeneity and conformity index in both plans. The V110% was greater than 3% in 6MV RA UFB plan in comparison to 6MV RA FB plan. The CI, HI, and target coverage (D98%, D95%, D50%, and D2%,) values were mentioned in table 1 and isodose color wash of one patient in all three views is shown in Figure1.

Organ at risk

Dose to common lung and heart are mentioned in table 1. The common lung V20Gy, V45Gy and mean dose found to be less in 6MV RA FB plan and similarly for heart V45Gy, V25Gy, and V10Gy.

Normal Tissue Integral Dose

The NTID and body minus PTV volume receiving low dose of 1Gy, 2Gy, 3Gy, 4Gy and 5Gy were comparatively less in 6MV UFB RA plans. The p value of less than 0.05 is observed and mentioned in the Table 1.

Monitor units and beam on time

In this study, 6MV UFB RA plans generate higher MU's compared to 6MV RA FB plan. The significant p value (< 0.05) observed in both the plans. However the BOT was less in 6MV RA UFB and a significant p value was observed.

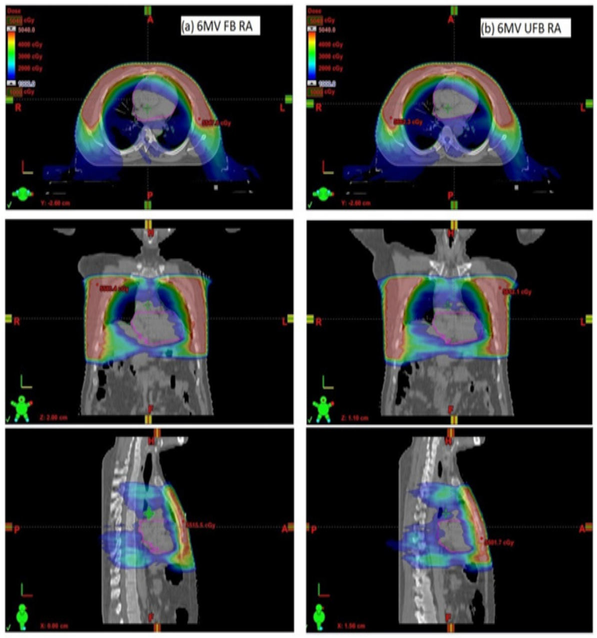

Figure 1. The Isodose Distribution of both the Plans in Axial, Saggital and Coronal View of One Patient (a) 6MV FB RA and (b) 6MV UFB RA. The isodose color wash for 50.4Gy, 30Gy and 10Gy were shown

Table 1. PTV Coverage and OAR's Doses for 6MV FB and UFB. SD, Standard Deviation

Target and OARS	Parameters	6MV_FB RA Mean ± SD	6MV_UFB_RA Mean ± SD	6MV RA FB Vs UFB (p value)
	$D_{98\%}$ (Gy)	49.45 ± 0.2	49.31 ± 0.13	NS
	$D_{95\%}$ (Gy)	50.34 ± 0.1	50.26 ±0. 74	NS
	$D_{50\%}$ (Gy)	53.00 ± 0.3	53.20 ± 0.3	p<0.05
	$D_{2\%}$ (Gy)	55.31 ± 0.3	55.74 ± 1.5	p<0.05
PTV	HI	0.11 ± 0.01	0.12 ± 0.00	p<0.05
	CI	1.12 ± 0.04	1.16 ± 0.05	p<0.05
	$V_{110\%}$	1.8 ± 1.4	3.4 ± 1.04	NS
	V_{20Gy}(%)	26.6 ± 4.5	26.9 ± 3.9	p<0.05
	V_{45Gy}(%)	3.1 ± 1.5	3.7 ± 1.5	p<0.05
Common Lung	V_{5Gy}(%)	84.0 ± 14.7	84.2 ± 14.9	p<0.05
	Mean dose (Gy)	15.47 ± 1.3	15.82 ± 1.4	p<0.05
	V_{10Gy}(%)	34.3 ± 6.7	37.8 ± 9.6	p<0.05
	V_{25Gy}(%)	9.5 ± 4.2	10.6 ± 4.4	p<0.05
Heart	V_{35Gy}(%)	3.0± 2.1	3.6 ± 2.3	p<0.05
	Mean dose (Gy)	10.17 ± 2.6	10.84± 3.1	p<0.05
NTID (105Gy cm3)		142.44 ± 45	141.44 ± 45	p<0.05
	V_{1Gy} (%)	62.33 ± 11.05	61.50 ± 10.8	p<0.05
	V_{2Gy} (%)	51.16 ± 9.20	50.41 ± 9.03	p<0.05
	V_{3Gy} (%)	47.19 ± 8.33	46.76 ± 8.21	p<0.05
Low Dose Volume	V_{4Gy} (%)	44.81 ± 7.89	43.45 ± 7.74	p<0.05
	V_{5Gy} (%)	42.37 ± 7.56	41.89 ± 8.13	p<0.05
	V_{10Gy} (%)	28.55 ± 6.19	27.12 ± 5.89	p<0.05
MU	Monitor Unit	1214 ± 66	1638.4 ± 78	p<0.05
BOT	minutes	3.01 ± 0.13	2.50 ± 0.12	p<0.05

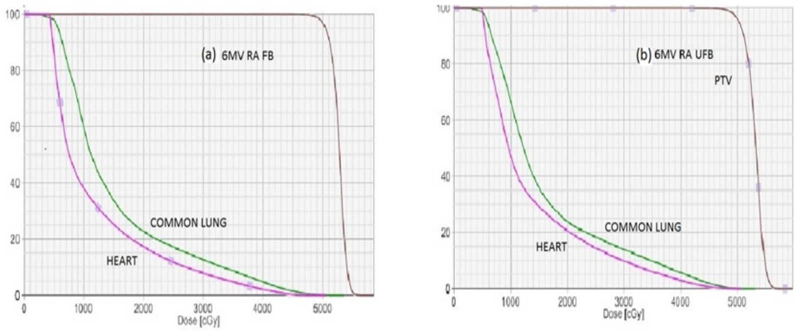

Figure 2. Dose Volume Histograms of PTV, Common Lung and Heart of One patient (a) 6MV FB RA and (b) 6MV UFB RA

Discussion

Treatment planning of bilateral breast is a challenge case due to involvement of the bilateral lungs, heart and a large treatment volume in comparison to other sites. Many authors (Jobsen J et al., 2002; Yamauchi C et al., 2005; Graham M Purdy et al., 1999) suggested that radiation therapy is the best choice in bilateral breast cancer. The present study was the first study, to compare the arc planning of 6MV RA plans using flatten and unflattened beam in bilateral breast case. Johannes Maier et al., (2016) noted that rapid arc (RA) conformity is better than VMAT. Elekta VMAT plans generate lesser NTID and low dose volume (V2Gy, V5Gy, and V10Gy) due to jaw tracking. However in low and high dose regions no significant difference in dose calculation accuracy was noted in FB and UFB or FFFB (Flattening filter free beam) in both IMRT and VMAT modality. More MU's were generated in FFFB generated IMRT and VMAT plans due to the shape of the FFF beam profile, particularly at off axis region to achieve the dose constraint. FFF beam quality was superior in tVMAT and VMAT technology. The dose to contralateral OARS was found to be less in FFFB. For right side breast cases, the FFFB VMAT MU were 1.2 time was higher, due to higher dose rate, the treatment times reduced by 7%. The present study also noted that UFB needs 35% more MU's in RA plan as compared to FB. (1214±66 for FB and 1638±78 for UFB). The MU ratio of FB/UFB factor was 1.35, hence the UFB drop the BOT by 17%.

Wiant et al., (2014) observed the intra-fractionional movement in breast cases, the result were significant as treatment time increased. Koivumaki et al., (2015) found that tangential VMAT plan showed time advantage in FFF beam as compared to tangential IMRT in breast cases. Spruijt et al., (2013) noted that treatment times reduced in IMRT with use of FFF beam plans.

Giorgia Nicolini et al., (2009) found that there was no significant difference ($p<0.14$) in the beam on time (BOT) observed, by comparing IMRT versus VMAT in bilateral breast planning. The Beam on time was 2.3min for IMRT and 2.23 min for VMAT. However p value was significant ($p<0.01$) for total treatment delivery. The rapid arc delivery time (3min) was 74% lesser in comparison to IMRT(11.45min), which will reduce the intrafractional movement of the patient. By comparing the mean and integral dose to non-tumor tissue volume the was more in RA plan due to higher low dose volume contribution, however the high dose volume contribution was less, therefore reducing the cosmetic effects. In our study, there is significant p value significant were observed in BOT between 6MV RA FB versus UFB plans. (2.5±0.12 min for UFB and 3.01±0.13 min for FB). But the mean NTID and low dose volume of V1Gy, V2Gy, V3Gy, V4Gy, V5Gy, and V10Gy, in non-tumor tissue for 6MV RA UFB plans was lesser in comparison to 6MV FB plan, due to UFB physical properties. (Like lesser head scatter, leakage etc.,)

ICRU Report 50 recommends a dose variation to the PTV to be within−5% to 7% of the prescription dose. Mundt et al., (2002) reported that the high dose volume V110 (%) and V115 (%) in the PTV was 9.8% and 0.2% respectively. In our study, V110 (%) was less than 3.0% (except 6MV UFB RA plan) and V110 (%) is zero. Many authors (Pirzkall A et al., 2000; Verhey LJ et al., 1999) noted longer delivery time in IMRT due to more MU's and multiple beam angles. Faster treatment delivery time is needed to take care of patient comfort during delivery. The UF beam VMAT and IMRT plans dose distribution was clinically acceptable and added benefit of reduction in treatment time helped in imaging and gating.

In Conclusion, this study compared the UFB with FB in VMAT plans for bilateral breast cancer patients. All the plan achieved the better target coverage and OAR sparing. We conclude in this study that UFB also produces better plans. Ours is a dosimetric study where only one of the generated plans was implemented on the patient. Hence, no comparison could be made between the long term clinical outcomes on the heart, the ipsilateral lung, opposite breast or the loco-regional control. A randomization of patients with similar clinical characteristics between the various planning algorithms would provide more robust information about the clinical implication of these dosimetric techniques. Though the rarity of the scenario of bilateral breast carcinoma may make it difficult due to small sample size in each sub group. Further investigations were required to study the performance of TPS for different energies and different anatomical sites.

References

D'Souza WD, Rosen II (2003). Non-tumor integral dose variation in conventional radiotherapy treatment planning.

Med Phys, **30**, 2065-71.
Graham M Purdy J, Emami B, Harms W, et al (1999). Clinical dose-volume histogram analysis for pneumonitis after 3D treatment for non small cell lung cancer (NSLC). *Int J Radiat Oncol Biol Phys*, **45**, 323-9.
Hong L, Hunt M, Chui C, et al (1999) Intensity modulated tangential beam irradiation of the intact breast. *Int J Radiat Oncol Biol Phys*, **44**, 1155-64.
IAEA (2000). An international code of practice for dosimetry based on absorbed dose to water, IAEA technical series No. 398, absorbed dose determination in external beam radiotherapy. Vienna: IAEA.
ICRU Report 83 (2010) Prescribing, recording, and reporting photon-beam intensity-modulated radiation therapy (IMRT). International commission on radiation units and measurements, Bethesda.
International commission on radiation units and measurements: Prescribing, recording and reporting photon beam therapy. (1993). ICRU report 50. Bethesda.
Jobsen J, Palen J van der, Ong F, Meerwaldt J (2002). Synchronous bilateral breast cancer: prognostic value and incidence. *Breast*, **12**, 83-8.
Johannes M, Bernadette K, Manuel M (2016). Simultaneous integrated boost (SIB) radiation therapy of right sided breast cancer with and without flattening filter A treatment planning study. *Radiation Oncol*, **11**, 111.
Koivumaki T, Heikkila J, Vaananen A, et al (2015). Flattening filter free technique in breath-hold treatments of left-sided breast cancer: The effect on beam-on time and dose distributions. *Radiother Oncol*, **18**, 194–8.
Moorthy S, Sakr H, Hasan S, et al (2013). Dosimetric study of SIB-IMRT versus SIB-3DCRT for breast cancer with breath hold gated technique. *Int J Cancer Ther Oncol*, **3**, 10110.
Mundt AJ, Lujan AE, Rotmensch J, et al (2002). Intensity-modulated whole pelvic radiotherapy in women with gynecologic malignancies. *Int J Radiat Oncol Biol Phys*, **52**, 1330–7.
Nicolini G, Clivio A, Fogliata A, et al (2009). Simultaneous integrated boost radiotherapy for bilateral breast: a treatment planning and dosimetric comparison for volumetric modulated arc and fixed field intensity modulated therapy. *Radiation Oncol*, **4**, 27
Pirzkall A, Carol M, Lohr F, et al (2000). Comparison of intensity-modulated radiotherapy with conventional conformal radiotherapy for complex-shaped tumors. *Int J Radiat Oncol Biol Phys*, **48**, 1371-80.
Rana S (2013). Intensity modulated radiation therapy versus volumetric intensity modulated arc therapy. *J Medical Radiation Sci*, **60**, 81-3
Skowronek J, Piotrowski T (2003). Bilateral breast cancer. *Neoplasma*, **49**, 49-54.
Spruijt KH, Dahele M, Cuijpers JP, et al (2013). Flattening filter free vs flattened beams for breast irradiation. *Int J Radiat Oncol Biol Phys*, **85**, 506–13.
Verhey LJ (1999). Comparison of three-dimensional conformal radiation therapy and intensity-modulated radiation therapy systems. *Semin Radiat Oncol*, **9**, 78–98.
Wiant DB, Wentworth S, Maurer JM, et al (2014). Surface imaging-based analysis of intrafraction motion for breast radiotherapy patients. *J Appl Clin Med Phys*, **15**, 4957.
Yamauchi C, Mitsumori M, Nagata Y, et al (2005). Bilateral breast-conserving therapy for bilateral breast cancer: results and consideration of radiation technique. *Breast Cancer*, **12**, 135-9.