

## Original Research Article

# A STUDY TO COMPARE THE DOSIMETRIC ADVANTAGES AND DISADVANTAGES BETWEEN VOLUMETRIC MODULATED ARC THERAPY, INTENSITY MODULATED RADIOTHERAPY AND THREE DIMENSIONAL CONFORMAL RADIOTHERAPY IN POST MASTECTOMY LEFT SIDED CHEST WALL AND SUPRA-CLAVICULAR IRRADIATION

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## ABSTRACT

**Background:** The aim is to dosimetrically analyze Volumetric Modulated Arc Therapy (VMAT), Intensity Modulated Radiotherapy (IMRT) and Three Dimensional Conformal Radiotherapy (3D-CRT) to find the optimal technique in the treatment of post mastectomy left sided chest wall and supra-clavicular irradiation.

**Materials and Methods:** Twenty consecutively treated left sided breast cancer patients were selected. Radiation therapy plans were generated on Radiation Planning CT Scan with each Radiotherapy Modalities (IMRT, VMAT, 3D-CRT). Three plans were generated for each patient and compared.

**Results:** VMAT technique provided a statistically significant homogenous ( $p < 0.0001$ ) and conformal dose distribution ( $p < 0.00001$ ) with a mean HI of ( $0.16 \pm 0.03$ ) and mean CI of ( $0.94 \pm 0.01$ ), compared to mean HI of ( $0.22 \pm 0.06$ ) and mean CI of ( $0.91 \pm 0.04$ ) with IMRT technique and mean HI of ( $0.27 \pm 0.06$ ) and mean CI of ( $0.83 \pm 0.04$ ) with 3D-CRT. For ipsilateral lung and heart, VMAT technique significantly reduced the high-dose volumes where the mean V20 to lung was ( $32.93 \pm 3.16$ ) vs ( $39.17 \pm 2.43$ ) vs ( $46.65 \pm 4.16$ ) for VMAT, IMRT and 3D-CRT respectively ( $p < 0.0001$ ) and mean V30 to heart was ( $6.81 \pm 2.28$ ) vs ( $11.29 \pm 3.44$ ) vs ( $19.85 \pm 7.98$ ) in VMAT, IMRT and 3D-CRT techniques respectively ( $p < 0.0001$ ). But 3D-CRT was found to be superior in case of reducing low dose volumes to the ipsilateral lung, heart, contralateral lung and breast.

**Conclusion:** VMAT plans in left sided chest wall irradiation should be used in selected cases keeping the dose distribution and normal tissue dose constrains in mind.

**Keywords:** CI: Conformity Index, CTV: Clinical Target Volume, DVH: Dose Volume Histogram, 3DCRT: 3 Dimensional Radiation Therapy, GTV: Gross Tumor Volume, HI: Homogeneity Index, MLC: Multi Leaf Collimator, MU: Monitor Units, OAR: Organ at Risks, RT: Radiation Therapy, PTV: Planning Target Volume, SCF: Supra-clavicular Fossa

## INTRODUCTION

Among the most commonly diagnosed cancers, breast cancer alone accounts for 24.2% of all new cancers among women in 2018.<sup>[1]</sup> A combination of three treatment modalities, namely surgery, radiation therapy and chemotherapy forms the standard protocol in patients with early breast cancer. However for advanced stages, a combination of surgery and chemotherapy remains the primary treatment, followed by selective use of post-mastectomy radiation therapy in high risk population. Post mastectomy radiotherapy (PMRT) has been found to be beneficial in patients with lymph node-positive breast cancer. It efficiently reduces the loco-regional recurrence rate and improves the overall survival rate.<sup>[2]</sup>

Different modalities have been tried for the left-breast irradiation and have been the subject of various studies. This includes the use of conventional radiotherapy (3D-CRT), Intensity Modulated Radiation Therapy (IMRT), and Volumetric Modulated Arc Therapy (VMAT).<sup>[3]</sup>

Irradiation of two most important vital organs, lung and heart, are of utmost concern in case of chest wall irradiation. The result of various planning techniques varies with the planning target volume (PTV). In other words, a PTV only with chest wall is comparatively simpler than the PTV with chest wall, internal mammary (IM) and supra-clavicular (S/C) field. A simple 3D plan to include the above nodal regions would result in irradiation of a larger volume of heart and ipsilateral lung and also create match line issues as it would require a separate IMN and S/C fields in addition to the two tangential fields.

IMRT is superior in terms of dose homogeneity and sparing normal tissue. On the other hand, the time for radiation delivery is more for IMRT compared to 3D techniques due to more fields and monitor units (MU).<sup>[4-6]</sup> IMRT also increases integral dose to normal healthy tissue, increasing concern about second malignancy in long-term survivors.<sup>[4]</sup>

Volumetric modulated arc therapy (VMAT) is a novel extension of IMRT, in which an optimized three-dimensional (3D) dose distribution may be delivered in a single gantry rotation.<sup>[6]</sup> VMAT technique has shown an improved target coverage and better dose homogeneity.

This study was conducted in an effort to identify the dosimetric differences between 3D-CRT, IMRT and VMAT delivery techniques for the patients receiving radiation therapy to the left chest wall and supraclavicular region. The dose volume histograms (DVH) of 3D-CRT plans were analyzed and compared with IMRT and VMAT in 20 breast cancer patients.

## MATERIALS AND METHODS

**Patients:** From March 2018, the first twenty left-sided breast cancer patients treated in our

department were enrolled in the study. All patients had undergone modified radical mastectomy and received the combined chemotherapy with or without trastuzumab. Patients with distant metastases were excluded from the study.

**Methods:** Patients were set up on a breast board with the sternum parallel to the table, arms raised above their heads and head turned towards the right side. CT images for treatment planning were acquired from the level of mandible to the lung base with a slice thickness of 3 mm. All the images were exported to the Oncentra External Beam version 4.5 for contouring and treatment planning.

### Target volume and organ at risks (OARs)

**delineation:** The clinical target volume (CTV) was delineated as the ipsilateral chest wall and supraclavicular field according to the recommendations of the Radiation Therapy Oncology Group (RTOG) breast cancer consensus definitions. A 5 mm margin was given to the CTV to generate the planning target volume (PTV) to account for the patient movements and set up errors. The PTV was then cropped 3 mm from the skin to exclude the buildup region.

Organs at risk (OAR) contoured included heart, left and right lung, spinal cord and contralateral breast. The heart was contoured from the first CT slice below the pulmonary artery to the apex inferiorly; the entire ipsilateral and contralateral lung contoured; and the contralateral breast outlined based on the visible breast parenchyma.<sup>[2]</sup>

### Treatments:

#### Radiation techniques

The treatments were planned for delivery on an Elekta Synergy linear accelerator with 3 mm width multileaf collimator (MLC). A 1cm tissue-equivalent bolus was placed on the patient's skin with the coverage of PTV and surgical scar to increase the skin dose. In the present dosimetric study, one 3D-CRT, one step and shoot IMRT and one VMAT treatment plan were created for each patient. The prescription dose was 50 Gy in 25 fractions.

#### 3D-CRT

A paired, field-in-field technique for parallel opposed beams was applied.

#### IMRT

A tangential beam IMRT plan with six beams (145, 120, 95, 0, 335 and 310 degree) was created for each patient for homogeneous dose delivery to the PTV using a step and shoot MLC. An angle of 25° separated the two beams, which were oriented 3 in each tangential direction.

#### VMAT

Two arcs were used for the VMAT plan. The first arc started from 160° to 308°. The second arc had exactly opposite starting and ending angles relative to the first arc.

#### Plan evaluation

The DVH was used to dosimetrically analyze the various data. For the targets, D98% (the minimum dose received by 98% of the target volume), D2%

(the maximum dose received by 2% of target volume), D50%, homogeneity index (HI), conformity index (CI), V95% (percentage of the PTV receiving at least 95% of the prescription dose), V107% and V110% (volume of PTV receiving 107% and 110% of the prescription dose) were evaluated.

**The homogeneity index was calculated as follows:**

$$HI = D2\% - D98\%$$

$$D50\%$$

Where, D2%, D50% and D98% are the dose received by 2% (Dnear-max), 50% and 98% (Dnear-min) of PTV volume.

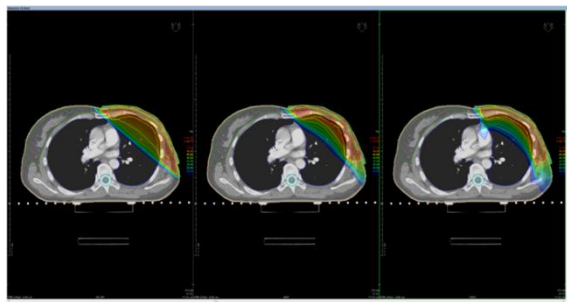
$$CI = \frac{\text{Volume receiving at least 95\% of the prescribed dose}}{\text{Volume of PTV}}$$

For the critical structures, the mean dose, V5, V10 and V30 of the heart; V5, V10, V20 and mean dose of ipsilateral lung; mean and V5 of contralateral lung and contralateral breast were calculated.

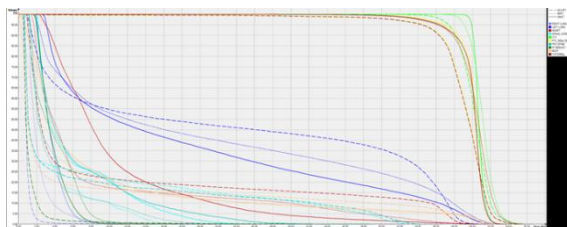
**Statistical analysis:** One-way analysis of variance test was performed to compare dosimetric differences between the 3 techniques. The statistical tests were performed using Microsoft excel version 13. The results were represented as mean  $\pm$  standard deviation (SD) and the differences were considered statistically significant at a p-value of  $<0.05$ .

## RESULTS

**Target coverage:** A comparative dose distribution of PTV between 3D-CRT, IMRT and VMAT is shown in [Figure 1] and the corresponding DVHs in Figure 2 for a single patient.



**Figure 1: 3DCRT /IMRT/VMAT**



**Figure 2: DVH (---- 3dcrt, ....IMRT, — VMAT)**

There was a statistically significant ( $p < 0.0001$ ) difference in maximum dose (D2%) and minimum dose to the PTV (D98%). VMAT technique had a mean HI of  $(0.16 \pm 0.03)$  and mean CI of  $(0.94 \pm 0.01)$ , thereby providing a statistically significant homogenous ( $p < 0.0001$ ) and conformal dose distribution ( $p < 0.00001$ ), compared to mean HI of  $(0.22 \pm 0.06)$  and mean CI of  $(0.91 \pm 0.04)$  with IMRT technique and mean HI of  $(0.27 \pm 0.06)$  and mean CI of  $(0.83 \pm 0.04)$  with 3D-CRT. The p values of V110% and V107% were 0.01 and 0.00001 respectively, favoring VMAT technique in lowering hot spots. The mean MU delivered by 3D-CRT technique was  $(444.00 \pm 21.04)$  compared to  $(1061.60 \pm 91.99)$  by VMAT and  $(1446.60 \pm 162.74)$  by IMRT. Hence indicating a statistically significant difference in the treatment time ( $p < 0.00001$ ).

**Normal tissue sparing:** For ipsilateral lung, compared to 3D-CRT and IMRT, VMAT technique significantly reduced the high-dose volumes, where the mean V20 was  $(32.93 \pm 3.16)$  vs  $(39.17 \pm 2.43)$  vs  $(46.65 \pm 4.16)$  for VMAT, IMRT and 3D-CRT respectively ( $p < 0.0001$ ). In the same manner VMAT also significantly reduced the high-dose volumes to the heart with the mean V30 of  $(6.81 \pm 2.28)$  vs  $(11.29 \pm 3.44)$  vs  $(19.85 \pm 7.98)$  in VMAT, IMRT and 3D-CRT techniques respectively ( $p < 0.0001$ ). But in case of the low dose volumes to the ipsilateral lung and the heart, 3D-CRT was found to be superior to VMAT and IMRT with the mean V5 of the ipsilateral lung being  $(62.39 \pm 3.31)$  vs  $(66.20 \pm 3.87)$  vs  $(72.14 \pm 6.83)$  for 3D-CRT, IMRT and VMAT respectively ( $p < 0.0001$ ) and the mean V5 for heart was  $(32.86 \pm 8.57)$  vs  $(44.42 \pm 21.23)$  vs  $(60.72 \pm 31.86)$  for 3D-CRT, IMRT and VMAT respectively ( $p < 0.0012$ ). It was also found that the VMAT plans achieved lower mean dose to the left lung than the 3D-CRT and IMRT, i.e.  $(22.10 \pm 1.76)$  vs  $(19.74 \pm 0.89)$  vs  $(17.13 \pm 1.29)$  ( $p < 0.0001$ ). There was no significant difference in the mean dose of the heart between the 3 plans. 3D-CRT plans were found to be significantly better in reducing dose to the opposite lung compared to IMRT and VMAT with the mean dose to right lung being  $(1.02 \pm 0.05)$  vs  $(2.52 \pm 0.63)$  vs  $(3.79 \pm 0.78)$  ( $p < 0.0001$ ). The mean dose to the contralateral breast was highest in VMAT compared to IMRT and 3D-CRT  $(3.94 \pm 0.71)$  vs  $(3.62 \pm 0.28)$  vs  $(1.59 \pm 0.49)$  ( $p < 0.0001$ ).

**Table 1: Dosimetric comparison of various parameters for PTV between 3DCRT, IMRT and VMAT**

PTV	3DCRT	IMRT	VMAT	p-VALUE
D2% (Gy)	53.48 ± 0.81	53.64 ± 0.28	52.22 ± 0.34	<0.0001
D98% (Gy)	40.20 ± 3.34	42.30 ± 2.95	44.02 ± 1.20	<0.0001
HI	0.27 ± 0.06	0.22 ± 0.06	0.16 ± 0.03	<0.0001
CI	0.83 ± 0.04	0.91 ± 0.04	0.96 ± 0.01	<0.00001
V110% (cm3)	0.40 ± 0.69	0.22 ± 0.17	0.00 ± 0.00	0.01
V107%	3.68 ± 3.42	2.51 ± 0.89	0.05 ± 0.06	<0.00001
MU	444.00 ± 21.04	1446.60 ± 162.74	1061.60 ± 91.99	<0.00001

**Table 2: Dosimetric comparison of parameters for lung, heart and opposite breast**

ORGAN AT RISK	PARAMETER	3DCRT	IMRT	VMAT	p-VALUE
Heart	Mean (Gy)	12.26 ± 3.85	10.64 ± 1.64	11.42 ± 1.55	0.15
	V30 (%)	19.85 ± 7.98	11.29 ± 3.44	6.81 ± 2.28	<0.0001
	V10 (%)	26.77 ± 8.16	28.41 ± 8.03	37.96 ± 10.17	<0.0003
	V5 (%)	32.86 ± 8.57	44.42 ± 21.23	60.72 ± 31.86	<0.0012
Left Lung	Mean (Gy)	22.10 ± 1.76	19.74 ± 0.89	17.13 ± 1.29	<0.0001
	V20 (%)	46.65 ± 4.16	39.17 ± 2.43	32.93 ± 3.16	<0.0001
	V10 (%)	53.27 ± 3.93	55.28 ± 4.53	47.71 ± 4.12	<0.0001
	V5 (%)	62.39 ± 3.31	66.20 ± 3.87	72.14 ± 6.83	<0.0001
Right Lung	Mean (Gy)	1.02 ± 0.05	2.52 ± 0.63	3.79 ± 0.78	<0.0001
	V5 (%)	0.26 ± 0.19	10.63 ± 6.51	15.94 ± 4.63	<0.0001
Opposite breast	Mean (Gy)	1.59 ± 0.49	3.94 ± 0.71	3.62 ± 0.28	<0.0001

## DISCUSSION

The chest wall anatomy being entirely different from that of the whole breast, might have an impact on the resulting dose distribution, both to the PTV and OAR because of the differences that exist between the target volumes of the two. Potential long-term sequelae of post mastectomy radiotherapy include cardiac toxicity, radiation pneumonitis, lymphedema, rib fractures, brachial plexopathy, and radiation-induced second malignancy.<sup>[10]</sup>

In the present study we compared radiotherapy planning with VMAT, IMRT and 3D-CRT techniques for the left chest wall and supraclavicular lymph nodes. VMAT plans were found to be superior in terms of target volume coverage and had more homogenous and conformal dose distribution. Similar results were obtained in a comparison done by Zang et al,<sup>[2]</sup> between VMAT and IMRT in postmastectomy patients, it was concluded that VMAT achieved similar or superior target coverage and better normal tissue sparing, as compared with 5-beam step and shoot IMRT. Popescu CC et al,<sup>[5]</sup> compared VMAT and IMRT in left sided chest wall irradiation and observed that VMAT was able to achieve equivalent PTV coverage and to significantly spare OARs and healthy tissue than IMRT. Similarly, a study by Muralidhar et al,<sup>[7]</sup> showed that IMRT plans with four to five tangential beams provide comparable coverage of the PTV relative to VMAT plans in breast cancer but with lesser dose to adjacent normal tissue and integral dose. In our study we also found that VMAT technique used fewer monitor units and short end delivery time like the above mentioned studies.

One of the most common adverse effect following PMRT is radiation pneumonitis. For patients treated with 3D-CRT, the volume of lung receiving 20 Gy i.e. V20 has been found to predict the risk of symptomatic radiation pneumonitis in

literature.<sup>[11,12]</sup> In the same manner the clinical effects of radiation induced heart disease have been observed with therapeutic doses of  $\geq 35$  Gy to partial volumes of the heart. There is potentially no threshold dose below which risk of cardio-toxicity does not exist.<sup>[4]</sup> However, development of cardiotoxicity could be multifactorial and depends upon a number of risk factors such as elderly age, physical inactivity, obesity, tobacco, diabetes, hypertension, pre-existing cardiovascular diseases and the chemotherapeutic agents used in breast carcinoma which possess cardiotoxic potential like anthracyclines, taxanes and trastuzumab. Hence the volume of irradiated heart is kept to as minimum as possible without compromising the target coverage. In our study VMAT technique was found to be superior in terms of reducing high dose volumes to the left lung (V20) and heart (V30) compared to IMRT and 3D-CRT. Also, VMAT plans were found to achieve lower mean dose to left lung than 3D-CRT and IMRT. However, the low dose volume, V5 was significantly higher for IMRT and VMAT compared with 3D-CRT for both the lung and the heart. 3D-CRT plans also significantly reduce mean dose and V5 to the contralateral lung and breast, while VMAT was found to be inferior. These results were comparable to the study by Muralidhar et al. where it was observed that VMAT technique produced relatively larger volumes of lung, heart, and spinal cord exposed to the radiation. Beckham et al,<sup>[16]</sup> concluded that IMRT increased the volume of normal tissues receiving low-dose RT; V5 right lung and V5 right breast (all  $p < 0.001$ ). This may translate into secondary malignancies in long term. Hall and Wu,<sup>[18]</sup> has suggested an increase in incidence of secondary cancer from 1% in conventional planning to 1.75% in IMRT planning for patient's surviving 10 years. We have to wait long to reach a firm conclusion on this.



In the present study we have not included the internal mammary nodal region (IMN) in the treatment volume, which may be very often required in majority of the cases. Inclusion of the IMN will further increase the lung and heart dose. Therefore improved RT techniques are required to treat the left-breast to reduce the heart dose and hence minimize the associated risk of radiation pneumonitis and cardiac mortality. Retrospective nature, small sample size, exclusion of IMN and short follow-up are the major limitations of the present study.

## CONCLUSION

In conclusion, VMAT was found to have an upper hand over IMRT and 3D-CRT in having a better target volume coverage, dose homogeneity and conformality. VMAT also reduced the mean dose to the heart and high dose volumes of the ipsilateral lung and heart. The use of fewer MUs and shorter treatment time also adds to the advantage of VMAT in reducing the intra-fraction errors. In terms of low dose volume to the heart, ipsilateral lung and contralateral breast and lung, VMAT and IMRT were found to be inferior, compared to 3D-CRT. Now, the advantages of reducing high-dose volumes and the disadvantages of higher low dose volumes with VMAT needs to be weighed and decided on an individual case basis, where 3D-CRT may not be able to give the desired dose coverage such as in complex chest wall anatomies and where IMN has to be included.

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