



# Dose Difference To Target Volume and Organs At Risk With Three -Dimensional Conformal Radiation Therapy (3DCRT) Versus Intensity Modulated Radiation Therapy (IMRT) In Carcinoma Left Breast Post Mastectomy Patient: A study from a rural cancer centre in INDIA”

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**ABSTRACT: Objective:** To study the dose difference to target volume and organs at risk with three -dimensional conformal radiation therapy (3DCRT) versus intensity modulated radiation therapy (IMRT) in carcinoma left breast post mastectomy patients.

**Material & Methods:** Forty consecutive histopathologically proven non metastatic post left mastectomy female breast cancer patients, attending radiation oncology OPD between September 2018 and September 2020 fulfilling the inclusion criteria were included. All patients received 50 Gy in 25 fractions to the PTV over 5 weeks. Dosimetric assessment of both IMRT and 3DCRT plans were done for all patients. Planning target volume (PTV) parameters- $D_{near-max}$  ( $D_2$ ),  $D_{near-min}$  ( $D_{98}$ ),  $D_{mean}$ ,  $V_{95}$ , and  $V_{110}$ -homogeneity index (HI), and conformity index (CI) were compared. The mean doses of lung and heart, percentage volume of ipsilateral lung and heart receiving 5 Gy ( $V_5$ ), 10 Gy ( $V_{10}$ ), 20 Gy ( $V_{20}$ ) and 30 Gy ( $V_{30}$ ) were extracted from dose-volume histograms and compared.

**Results:** The PTV parameters were comparable in both the groups. HI and CI were significantly improved with IMRT (0.13 vs 0.17,  $p < 0.001$ , CI-0.96 vs 0.95,  $p < 0.001$ ) compared to 3DCRT. IMRT in comparison to 3DCRT showed significant reduction in the high-dose volumes of lung ( $V_{20}$ , 26.67% vs. 31.43%;  $V_{30}$ , 15.67% vs. 15.87%;  $p < 0.001$ ) and heart ( $V_{30}$ , 6.96% vs. 14.65%;  $p < 0.001$ ); mean dose of lung and heart (14.12 vs. 15.87 Gy and 9.62 vs. 10.08 Gy, respectively;  $p < 0.001$ ) Whereas, the low-dose volume ( $V_5$  lung, 70.61% vs. 43.22%;  $V_{10}$  44.98 vs 36.01,  $V_5$  heart, 65.85% vs. 24.45%;  $V_{10}$  38.57% vs 20.87  $p < 0.001$ ) showed significant reduction in 3DCRT compared to IMRT.

**Conclusion:** For post -mastectomy radiotherapy to the left chest wall, IMRT significantly improves the

conformity, homogeneity of the plan and reduce the high -dose volumes of ipsilateral lung and heart compared to 3DCRT, but 3DCRT is superior in terms of low dose volume. IMRT compared with conventional or conformal radiation therapy technique for the breast cancer has benefits in terms of dose, toxicity and quality of life but there are issues in clinical implementation of Intensity modulated radiotherapy, especially in post mastectomy treatment such as high cost, Complex and time consuming procedures, dedicated quality assurance programs, management of inter-fraction changes-(set up errors) and management of intra-fraction changes- (movement with respiratory motion).

**KEYWORDS-** Left Breast Cancer, Modified Radical Mastectomy, Three -Dimensional Conformal Radiation Therapy (3DCRT), Intensity Modulated Radiation Therapy (IMRT)

## I. INTRODUCTION:

Breast cancer is the most common site-specific cancer in women and is the leading cause of death from cancer for women age 40 to 44 years. It accounts for 33% of all female cancers and is responsible for 20% of the cancer related deaths in women.<sup>[1]</sup>

Breast cancer was the leading cause of death until 1985, when it was surpassed by lung cancer. There is a tenfold variation in breast cancer incidence among different countries worldwide. England and Wales have highest age adjusted mortality for breast cancer while South Korea has the lowest. Women living in less industrialized countries have a lower incidence of breast cancer than women living in industrialized countries.<sup>[2]</sup>

GLOBOCAN 2018 has estimated over 1.1 million new cancer cases and 0.78 million cancer deaths in India in 2018. Both sexes combined, breast cancer is the most commonly observed cancer (14% of the



total cases) and it is the leading cause of cancer death (11.1% of the total cases) in India. In 2018, 1, 62,468 new cases and 87,090 deaths were reported for breast cancer in India.<sup>[3]</sup>

The management of invasive breast cancer is based on the clinical extent and pathological characteristic of tumor, in addition to the age of patient (menopausal status), biological prognostic factors and preference of the patient. Although surgery is the mainstay of treatment in non-metastatic breast cancers, the other modalities including chemotherapy, endocrine therapy, targeted therapy and radiation therapy have added benefits if administered according to the indications. Introduction of multimodality treatment (surgery, chemotherapy and radiation therapy) reduced breast cancer mortality by 18% and improved overall survival.<sup>[4]</sup>

Radiation therapy has a central role in the management of breast cancer after either breast-conserving surgery or mastectomy, with attendant improvements in local control and survival.<sup>[5]</sup>

In contrast to western world, modified radical mastectomy (MRM) is performed more often than breast conservation surgery (BCS) in India. Post operatively patients are given adjuvant chemotherapy as per disease stage and receptor status. Most of the patients required post mastectomy radiotherapy (PMRT) to decrease loco-regional recurrence, improved disease free and overall survival.<sup>[6-9]</sup> PMRT is recommended in patients with four or more positive axillary lymph nodes. In Patients with negative nodes, PMRT is indicated for tumors more than five centimeters or positive pathological margins.<sup>[10]</sup>

Intensity Modulated Radiotherapy Therapy (IMRT) has proved to be superior to three-dimensional conformal radiation therapy (3DCRT) in various sites like head & neck, central nervous system, lung, prostate etc.<sup>[11]</sup>

IMRT by virtue of multi leaf collimators modulates fluence and divide a beam into small beamlets to prescribe maximum dose to the target with minimum dose to critical organs. In case of chest wall irradiation, lung and heart remain two most important vital organs, irradiation of which always causes concern to radiation oncologist. In this study, we evaluated the dosimetry in post MRM patients of carcinoma of left breast undergoing PMRT using IMRT versus conventional 3DCRT techniques carried out at our department.

## II. MATERIAL & METHODS

Forty consecutive histopathologically proven non metastatic post leftmastectomy female

breast cancer patients (18-75 years), attending radiation oncology OPD between September 2018 and September 2020 fulfilling the inclusion criteria were included. All patients were planned for adjuvant radiotherapy to the chest wall with inclusion of mastectomy scar and supraclavicular region. All patients were immobilized while free breathing using a thermoplastic mould in supine position over a breast board on the couch with left arm extended above their head onto arm rests, abducted and externally rotated. Marker CT scan with contiguous 2mm slice thickness were taken once optimal patient position was confirmed on Siemens CT Scan Machine.

The chest wall, axilla, supraclavicular region and organs at risk was contoured according to the RTOG guidelines for breast Cancers and treatment planning was done according to Practical Radiotherapy Planning by Jane Dobbs. All of 40 patients were treated with Linear Accelerator (6MV photons) VARIAN DBX. The total dose received by every patient was 50Gy in 25 fractions to the PTV with 2 Gy per fraction, 1 fraction per day for 5 days per week. In 3 DCRT two tangential semi-opposed beams (to avoid divergence), physical wedges (usually 15° or 30°), and a multileaf collimator were used. The beam angles, wedge angles, and beam weighting (usually minimal) were chosen to optimize coverage of the PTV, while minimizing exposure to the ipsilateral lung, heart and contralateral breast. Gantry angles ranged from, 300° to 320° for the medial tangential fields and from 120° to 140° for the lateral tangential fields. The supraclavicular field was marked with separate anterior field. Attention was given to geometric match of SCF field and chest wall field to avoid junctional overdose or underdose. In IMRT, chest wall was irradiated using 7-9 fields creating a butterfly shaped planning using dynamic MLC. IMRT planning was inverse planned. Gantry angled ranged from 300 to 180 degrees. The monitor units ranged from 85 to 100 for each beam.

## III. DOSIMETRIC ANALYSIS

Dosimetric assessment of both IMRT and 3DCRT plans were done for all 40 patients. Planning target volume (PTV) parameters- $D_{near-max}$  ( $D_2$ ),  $D_{near-min}$  ( $D_{98}$ ),  $D_{mean}$ ,  $V_{95}$ , and  $V_{110}$  - homogeneity index (HI), and conformity index (CI) were compared. The mean doses of lung and heart, percentage volume of ipsilateral lung and heart receiving 5 Gy ( $V_5$ ), 10 Gy ( $V_{10}$ ), 20 Gy ( $V_{20}$ ) and 30Gy ( $V_{30}$ ) were extracted from dose-volume histograms and compared.



#### IV. RESULTS & OBSERVATIONS:

This study included 40 female left breast cancer patients who underwent mastectomy and were planned for adjuvant radiotherapy with either

3DCRT or IMRT. The following baseline characteristics and dosimetric analysis of the study subjects were noted.

**TABLE 1-Patient's characteristics**

CHARACTERISTICS	3DCRT	IMRT
<b>AGE GROUP</b> (median)	53.50years	52.50 years
<b>MENOPAUSAL STATUS</b>		
PRE	7(35%)	6(30%)
POST	13(65%)	14(70%)
<b>GRADE</b>		
1	1(5%)	0
2	14(70%)	14(70%)
3	5(25%)	6(30%)
<b>STAGE</b>		
1	1(5%)	1(5%)
2	10(50%)	10(50%)
3	9(45%)	9(45%)
<b>CHEMOTHERAPY</b>		
NEOADJUVANT	0%	4(20%)
ADJUVANT	20(100%)	20(100%)

**Table 2: Dose Distribution to the PTV of the study subjects based on the following parameter**

S.NO			Mean	Std. Deviation	P Value
1	D <sub>MAX</sub> (Gy)	3DCRT	53.86	± 0.810	0.115
		IMRT	53.421	± 0.914	
2	D <sub>MIN</sub> (Gy)	3DCRT	44.775	± 1.230	0.336
		IMRT	46.430	± 2.220	
3	D <sub>MEAN</sub> (Gy)	3DCRT	50.61	± 0.839	0.116
		IMRT	50.889	± 0.734	
4	V <sub>95%</sub> (Gy)	3DCRT	96.360	± 0.886	0.091
		IMRT	96.956	± 0.879	
5	V <sub>110%</sub> (Gy)	3DCRT	0.150	± 0.398	0.170
		IMRT	0.060	± 0.134	
6	HI	3DCRT	0.170	± 0.054	0.001
		IMRT	0.130	± 0.026	
7	CI	3DCRT	0.957	± 0.008	0.001
		IMRT	0.968	± 0.010	

**Table 3: Dose Distribution of the study subjects based on the Left lung parameters**

		Mean	Std. Deviation	P Value
Left Lung-V5%(Gy)	3DCRT	43.22	±4.70	0.001
	IMRT	70.61	± 5.47	
Left Lung-V10%(Gy)	3DCRT	36.01	± 4.15	0.001
	IMRT	44.98	± 2.280	
Left Lung-V20%(Gy)	3DCRT	31.43	± 4.10	0.001
	IMRT	26.67	± 4.10	
Left Lung-V30%(Gy)	3DCRT	28.99	±3.70	0.001
	IMRT	15.67	± 3.50	
Left Lung-DMEAN	3DCRT	15.87	± 1.71	0.001
	IMRT	14.12	± 1.07	



**Table 4:** Dose Distribution of the study subjects based on the heart parameters

		Mean	Std. Deviation	P Value
Heart-V5%(Gy)	3DCRT	24.45	± 5.64	0.001
	IMRT	65.85	± 5.45	
Heart-V10%(Gy)	3DCRT	20.87	± 5.61	0.001
	IMRT	38.57	± 11.73	
Heart-V20%(Gy)	3DCRT	17.39	± 4.33	0.22
	IMRT	17.83	± 6.22	
Heart-V30%(Gy)	3DCRT	14.65	± 4.12	0.05
	IMRT	6.96	± 2.61	
Heart-DMEAN	3DCRT	10.08	± 1.41	0.001
	IMRT	9.62	± 1.33	

## V. DISCUSSION:

Breast cancer is the most common cancer in females worldwide. Radiotherapy after radical mastectomy is an important treatment modality for the patients with advanced breast cancer, which can significantly reduce the recurrence rate and improve the survival rate. At present, the main modalities of postoperative radiotherapy for patients with advanced breast cancer include three-dimensional conformal radiotherapy (3DCRT), intensity modulated radiotherapy (IMRT), volumetric modulated arc therapy (VMAT), and the combination of 3DCRT and IMRT. With this background, we conducted a study to understand the dosimetric properties of IMRT and 3DCRT in the present study.

A number of studies have demonstrated dosimetric benefit of IMRT compared to 3DCRT for the whole breast in early breast cancer patients but for post mastectomy chest wall irradiation, such data is scarce. Many studies have reported lower doses to the ipsilateral lung, contralateral lung, contralateral breast, heart, and left anterior descending artery using IMRT technique for whole breast radiotherapy [12]. Fiorentino et al. [13] compared 3DCRT and 4-fields IMRT treatment plans, and concluded 4-fields IMRT technique significantly reduced the dose to OARs and normal tissue, with a better target coverage compared to 3DCRT. Since the anatomy of chest wall is entirely different from that of the whole breast, differences exist between the target volumes of these two. This might have an impact on the resulting dose distribution, both to the PTV and OARs.

This study included 40 subjects with left breast carcinoma, post mastectomy, who were evaluated for dose difference to the target volume and organs at when they were subjected to radiotherapy using either IMRT or 3DCRT

In a study conducted by Li et al, [14] the planning target volume of treatment, showed no statistically significant difference in Dmax, Dmin,

Dmean, V95%, V110% parameters between the IMRT and 3D-CRT groups, [Dmax (Gy) 3DCRT- 54.58 ± 0.92 IMRT- 54.67 ± 0.86, Dmin (Gy) 3DCRT-47.52 ± 0.61 IMRT-47.48 ± 0.56, Dmean (Gy) 3DCRT- 51.63 ± 0.58 IMRT- 51.59 ± 0.42 V95%-3DCRT- 98% ± 2% IMRT- 98% ± 1%, V110% 3DCRT- 2% ± 2% IMRT-2% ± 1%]. This study supported the results established by Li et al. In literature, [15] various planning studies have shown the PTV95% coverage values ranging from 90% to 97%. and our results fell exactly within that range. Hong et al. have showed that the use of equally spaced gantry angles not only improves HI and CI but also reduces the volume of critical normal tissues. [16] Beckham et al. [17] reported that IMRT significantly improved not only CI (0.91 vs. 0.48, p < 0.05) but also HI (0.95 vs. 0.74, p < 0.05). Similarly, Xie X et al, [18] compared 3D-CRT plan, with both IMRT and hybrid plans. Compared with 3D-CRT plans, both CI and HI showed significant improvements through IMRT-involved plans. In this study also, statistically significant improvement was noted in CI and HI with IMRT compared to 3DCRT (CI-0.968 vs. 0.957, p < 0.001, HI -0.130 vs. 0.170, p < 0.001). Whereas, Moorthy et al [19] (CI, 0.14 vs. 0.18, p = 0.01; HI, 1.01 vs. 1.03, p = 0.45) and Rudat et al. [20] (CI, 0.32 vs. 0.25, p = 0.03; HI, 0.73 vs. 0.77, p > 0.05) concluded that IMRT only improves CI but difference in HI was non -significant. Phansopkar DA et al., [21] concluded that the CI with 3D-CRT was 0.953 vs. 0.951 with IMRT (P=0.327).

In a study conducted by Rudat et al [20], for over 20 unselected patients, tangential beam IMRT significantly reduced the ipsilateral mean lung dose by an average of 21% (11.29 Gy vs. 14.37 Gy, p < 0.01) and D30 by 43% (9.60 Gy vs. 16.95 Gy, p < 0.01). Similarly, in a study by , Li et al. [14] concluded that V<sub>20</sub> and V<sub>30</sub> of ipsilateral lung were significantly higher (p < 0.001) in the 3DCRT group (32% ± 6% and 22% ± 5%) than in the IMRT group (29% ± 2% and 21% ± 2%).





Similarly, in Phansopkar DA et al.,<sup>[21]</sup> the ipsilateral lung V20% received significantly higher dose with 3D-CRT than with IMRT (151.2 cGy vs. 115.4 cGy)  $P=0.019$ . All the above mentioned studies, were in accordance to this study results of the left lung dosimetric parameters, in which the average values of left lung V5% and V10% were significantly higher among IMRT group when compared to 3DCRT group but the average values of V20%, V30% and Dmean was significantly higher among 3DCRT when compared to IMRT.

Moorthy et al.,<sup>[19]</sup> concluded that IMRT in comparison to 3DCRT had significantly lower V40 heart (2.13% vs. 7.5%). Rudat et al.<sup>[20]</sup> concluded that tangential beam IMRT statistically significantly reduced the V55 by an average of 43% (5.7% vs. 10.6%) and the mean heart dose by an average of 20% (7.04 Gy vs. 8.77 Gy,  $p = 0.03$ ). Similarly, Smith et al.<sup>[22]</sup> also concluded that IMRT lowered heart V30. On the similar lines, El-Mesidy S et al.,<sup>[23]</sup> concluded that the parameters used to evaluate the radiation doses to the heart (V30Gy, V40Gy, Dmax and NTCP) were better in IMRT than in 3D-CRT technique with a statistically significant differences ( $P.value < 0.05$ ). This study results were similar to the above mentioned studies, where, the mean dose distribution for the heart at V5% and V10% for 3DCRT were 24.45 and 20.87 as against 65.85 and 38.57 respectively for IMRT and these differences were statistically significant proving that heart volume receiving low dose distribution was lower for 3DCRT when compared to IMRT. V20% was the only parameter which showed non-significant values comparable to each other (17.39 vs 17.83) whereas V30% showed statistically significant values in favor of IMRT (14.65 vs 6.96). The D mean (9.62 Gy vs. 10.08 Gy) had a significant difference ( $P < 0.05$ ),

Beckham et al.<sup>[17]</sup> have shown that IMRT increased the volume of normal tissues receiving low-dose RT: V5 right lung (13.7% vs. 2.0%), V5 right breast (29.2% vs. 7.9%), and V5 normal high tissue volume (31.7% vs. 23.6%) (all  $p < 0.001$ ). Li et al.<sup>[31]</sup> concluded that V5 of ipsilateral lung was significantly lower ( $p < 0.001$ ) in the 3DCRT group ( $52\% \pm 7\%$ ) than in the IMRT group ( $65\% \pm 9\%$ ); V10 was similar for both groups ( $41\% \pm 7\%$  vs.  $44\% \pm 4\%$ ). This may translate into secondary malignancies in long term. Hall and Wu<sup>[24]</sup> predicted an increase in incidence of secondary cancer from 1% in conventional planning to 1.75% in IMRT planning for patient's surviving 10 years. Similar finding was seen in this study also where V5 which was significantly higher for IMRT compared with 3DCRT for the heart (65.85% vs.

24.45%,  $p < 0.001$ ) and the lungs (70.61% vs. 43.22%,  $p < 0.001$ ). A study conducted by Rastogi K et al.,<sup>[10]</sup> concluded that for lung, IMRT in comparison to 3DCRT significantly reduced the high-dose volumes (V20, 22.09% vs. 30.16%; V55, 5.16% vs. 10.27%;  $p < 0.001$ ) and the mean dose (11.39 Gy vs. 14.22 Gy,  $p < 0.001$ ). Similarly, for heart also, IMRT in comparison to 3DCRT significantly reduced the high-dose volumes (V25, 4.59% vs. 9.19%; V45, 1.85% vs. 7.09%;  $p < 0.001$ ) and the mean dose (4.57 Gy vs. 8.96 Gy,  $p < 0.001$ ). However, 3DCRT proved to be superior to IMRT in terms of low-dose volume for both the lung (V5, 51.05% vs. 61.48%;  $p < 0.001$ ) and the heart (V5, 23.27% vs. 31.02%;  $p < 0.001$ ). They concluded that both the methods achieved adequate target coverage, IMRT reduces maximum doses and improves Conformity and Homogeneity indices of target volumes, also reduces dose to OAR. The conclusions drawn from the above-mentioned studies are corresponding to this study findings.

## VI. CONCLUSION:

For post -mastectomy radiotherapy to the left chest wall, IMRT significantly improves the conformity, homogeneity of the plan and reduce the high -dose volumes of ipsilateral lung and heart compared to 3DCRT, but 3DCRT is superior in terms of low dose volume. IMRT compared with conventional or conformal radiation therapy technique for the breast cancer has benefits in terms of dose, toxicity and quality of life but there are issues in clinical implementation of Intensity modulated radiotherapy, especially in post mastectomy treatment such as high cost, Complex and time consuming procedures, dedicated quality assurance programs, management of inter-fraction changes-(set up errors) and management of intra-fraction changes- (movement with respiratory motion).

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