

Response Assessment of Post Operated Carcinoma Breast Patients Treated by Volumetric Modulated ARC Therapy (VMAT): A Prospective Clinical Study

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Abstract

Background: Breast cancer is the most common cancer and the leading cause of cancer-related deaths among women worldwide. The annual global incidence of breast cancer is estimated to be >1.3 million cases and approximately 465,000 women die of this disease every year. Postoperative radiotherapy plays an important role in the management of breast cancer and reduces the local and regional recurrence, thereby improving outcomes.

Objective: Response assessment of post operated carcinoma breast patients treated by volumetric modulated arc therapy (VMAT).

Method: This prospective clinical study involves 40 histopathologically proven cases of carcinoma breast patients conducted during October 2020 to October 2021 in Department of Radiation Oncology at Regional Cancer Centre of Pt JNM Medical College Raipur, Chhattisgarh. Response was assessed and analyzed on every month post radiation.

Result: In this study the mean age of patients was 47.8 years with standard deviation of 7.63 years. Our most of the cases (57.5%) belongs to age group 41 – 50 years. 7 (17%) patients were premenopausal, 12 (30%) patients were perimenopausal and 21(52%) were postmenopausal. distribution of the site of tumor among patients were reported as 16 (40.0%) patients had UOQ, 5 (12.5%) patients had UIQ, 12 (30.0%) patients had central quadrant, Further 4 (10%) and 3 (7.5%) patients had LOQ and LIQ respectively, among patients were reported as IA were 0 (0.0%), IB were 7 (17.5%), IIA were 5 (12.5%), IIB were 7 (17.5%), IIIA were 6 (15.0%), IIIB were 11(27.5%) and IIIC were 4 (10.0%), ipsilateral lung dose data analysis was reported as the average total volume of I/L lung is 922.18 ± 218.21 cc, D min 448.83 ± 489.83 c Gy, D max 4192.1 ± 116.94 c Gy, D mean 1871.70 ± 523.92 c Gy, V5 $90.28 \pm 7.96\%$, V10 $62.5 \pm 12.49 \%$, V20 $25.28 \pm 3.28 \%$.

Conclusion: In our study we recorded 95% of complete response at the end of 3 months clinically and radiologically while in 5% of cases progressive disease were observed. An ipsilateral lung dose volume constraint of $V_{20} \leq 30\%$ reduced rate of radiation pneumonitis was observed.

Keywords: Response, VMAT, Radiation Therapy, Lung, Breast Cancer.

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Introduction

Breast cancer is the most common cancer among women and is the leading cause of cancer deaths in women globally. In developing countries, locally advanced breast cancers (LABCs) account for the majority of the cases. Treatment of LABC involves a multimodality approach including surgery usually mastectomy, chemotherapy, radiotherapy, and targeted therapy. Global cancer burden according to GLOBOCAN 2020 estimates of cancer incidence and mortality produced by International Agency for Research on cancer, Worldwide an estimated 19.3 million new cancer cases and 10.0 million cancer deaths occurred in 2020.

Among women, breast cancer accounts for 1 in 4 cancer cases and for 1 in 6 cancer deaths.[1] In India, breast cancer is the most common cancer among women accounting for 26.3% followed by cervical cancer as the 2nd most common cancer accounting for 18.3% of all cancer. [2] As per cancer statistics of India in 2020, number of registered female breast cancer is 205,424 with cumulative risk of 1 in 29 females in their lifetime. [3]

Many factors are associated with incidence rates of breast cancer; these are genetic mutation, more on nullipara women, hormonal, environmental, lifestyle and dietary habits etc. Management of breast cancer has changed drastically from surgical intervention alone to multimodality treatment including chemotherapy, radiation, hormonal and targeted therapy owing to better understanding of the biology and molecular characteristics. [4] Postoperative radiotherapy plays an important role in the management of breast cancer and reduces the locoregional recurrence, thereby improving outcomes. [5]

Objective

Response assessment of post operated carcinoma breast patients treated by volumetric modulated arc therapy (VMAT).

Material and Methods

The present prospective clinical study involving 40 patients of carcinoma breast undergoing radiotherapy was conducted during October 2020 to October 2021 in Department of Radiation Oncology at Regional Cancer Centre of Pt JNM Medical College Raipur, Chhattisgarh.

Patient Inclusion criteria

- Cytologically and histopathologically proven cases of carcinoma breast.
- Post operated patient of breast cancer having normal PFT test and undergoing Volumetric Modulated Arc Therapy.
- Age less than 65 years.
- ECOG performance score of 0 to 2.
- Patient with normal liver function test, renal function test and haematological parameters.
- Patient with normal 2D Echo
- Normal HRCT Test

Image Acquisition and Treatment Planning

- The planning CT images of the patients were acquired and transferred to the Eclipse treatment planning system (TPS) (Varian Medical Systems, USA. The target (chest-wall and supraclavicular region), OARs (ipsilateral lung, contralateral lung, heart and contralateral breast).
- The single isocenter VMAT tangential arc conformal treatment plans were generated in the Eclipse TPS images. 6

MV and 15 MV photon beams were used for the chest wall and supraclavicular regions respectively.

- The hypo fractionation regimen of 4006 cGy in 15 fractions over a period of 3 weeks was used for all the patients in this study.
- To evaluate treatment toxicities during course of radiation follow up was done at every 5 fractions of radiation therapy.
- Post Radiation therapy Follow up and evaluation of patient was done monthly for 6 months to assess treatment response and toxicities.

Results

Age: In our study the mean age was 47.8 years with standard deviation of 7.63 years. Our most of the cases (57.5%) belongs to age group 41 – 50 years.

Table 1: Age wise Distribution of Patients

Age Groups (years)	All Patients No.	(%)
21-30	1	2.5
31-40	5	12.5
41-50	23	57.5
51-60	12	30.0

Menopausal status: In our study 7 (17%) patients were premenopausal, 12 (30%) patients were perimenopausal and 21(52%) were postmenopausal.

Table 2: Menopausal Status of the patients

Menopausal Status	All Patients No.	(%)
Premenopausal	7	17%
Perimenopausal	12	30%
Postmenopausal	21	52%

Site wise distribution: In our study, distribution of the site of tumor among patients were reported as 16 (40.0%) patients had UOQ, 5 (12.5%) patients had UIQ, 12 (30.0%) patients had central quadrant, Further 4 (10%) and 3 (7.5%) patients had LOQ and LIQ respectively.

Table 3: Site wise distribution

Location	Frequency (n)	Percentage (%)
Upper outer quadrant	16	40.0%
Upper inner quadrant	5	12.5%
Lower outer quadrant	4	10.0%
Lower inner quadrant	3	7.5%
Central quadrant	12	30.0%

Composite stage wise distribution: In our study, stage wise distribution among patients were reported as IA were 0 (0.0%), IB were 7 (17.5%), IIA were 5 (12.5%), IIB were 7 (17.5%), IIIA were 6 (15.0%), IIIB were 11(27.5%) and IIIC were 4 (10.0%).

Table 4: Composite Stage Wise Distribution

Composite Stage	Frequency (n)	Percentage (%)
IA	0	0.0%
IB	7	17.5%
IIA	5	12.5%
IIB	7	17.5%
IIIA	6	15.0%
IIIB	11	27.5%
IIIC	4	10.0%

Dose distribution in left breast and ipsilateral lung: In our study of 25 patients, in left breast ipsilateral LUNG dose data analysis was reported as the volume 1004.6 ± 235.14 , Dmin 55.21 ± 787.82 , Dmax 4187.33 ± 149.1 c Gy, Dmean 1869.07 ± 621.64 c Gy, V5 90.38 ± 8.46 %, V10 64.10 ± 12.75 %, V20 25.05 ± 3.69 %.

Table 5: Dose distribution in left breast and ipsilateral lung

	Volume (cc)	Minimum Dose (cGy)	Maximum Dose (cGy)	Mean Dose (cGy)
Mean Dose	1004.60	550.21	4187.33	1869.07
Standard Deviation	235.14	787.82	149.1	621.64
Minimum Dose	623	112	3940	1504
Maximum Dose	1459	3327	4448	4045

The volume of Lung Received Radiation

Table 6: Volume of Lung Received Radiation

%	V5 (Gy)	V10 (Gy)	V20 (Gy)
Mean Dose	90.38	64.10	25.05
Standard Deviation	8.46	12.75	3.69
Minimum Dose	77	49	20
Maximum Dose	100	90	30

Dose distribution in right breast and ipsilateral lung: In our study of 15 patients, in case of carcinoma right breast with their ipsilateral lung doses and the average total volume is 872.72 ± 195.78 cc, Dmin 388 ± 132.4 c Gy, Dmax 4194.96 ± 96.09 c Gy, Dmean 1873.28 ± 469 .

Table 7: Dose distribution in right breast and ipsilateral lung

%	volume (cc)	Minimum Dose (cGy)	Maximum Dose (cGy)	Mean Dose (cGy)
Mean Dose	872.72	388	4194.96	1873.28
Standard Deviation	195.78	132.49	96.09	469.70
Minimum Dose	458	99.4	4035	1506
Maximum Dose	1237	605	4386	4035

The volume of Lung Received Radiation

Table 8: Volume of Lung Received Radiation

%	V5 (Gy)	V10 (Gy)	V20 (Gy)
Mean Dose	87.82	56.82	25.27
Standard Deviation	8.59	14.46	3.35
Minimum Dose	76	23	20
Maximum Dose	99	79	29

Dose distribution in left breast and Total lung: In our study of 40 patients, In case of carcinoma left breast the total LUNG dose data analysis was reported as the average total volume is 1912 .07 \pm 397.5cc, Dmin 142.37 \pm 49.15c Gy, Dmax 4203 .53 \pm 139.74c Gy, Dmean 1112 .8 \pm 101. 10c Gy, V5 51.0 \pm 11.6%, V10 29.7 \pm 6.5%, V20 9.93 \pm 3.7%.

Table 9: Dose distribution in left breast and Total lung

%	volume (cc)	Minimum Dose (cGy)	Maximum Dose (cGy)	Mean Dose (cGy)
Mean Dose	1912 .07	142.37	4203.53	1112.87
Standard Deviation	397.5	49.15	139.74	101.10
Minimum Dose	1103	38.6	4006	948
Maximum Dose	2690	220	4448	1274

The volume of Lung Received Radiation

Table 10: Volume of Lung Received Radiation

%	V5 (Gy)	V10 (Gy)	V20 (Gy)
Mean Dose	51	29.71	9.93
Standard Deviation	11.62	6.52	3.71
Minimum Dose	24	21	4.20
Maximum Dose	68	40	19

Dose distribution in right breast and Total lung: In our study of 40 patients, In case of carcinoma right breast the total LUNG dose data analysis was reported as the average total volume is 1910 .80 \pm 402.87cc, Dmin 141. 7 \pm 54.3cGy, Dmax 4186.7 \pm 89.5 c Gy, Dmean 1034. 5 \pm 185.70c Gy, V5 50.82 \pm 8.4%, V10 29.4 \pm 4.5%, V20 10.3 \pm 4.5%.

Table 11: Dose distribution in right breast and Total lung

%	volume (cc)	Minimum Dose (cGy)	Maximum Dose (cGy)	Mean Dose (cGy)
Mean Dose	1910.80	141.71	4186.76	1034.52
Standard Deviation	402.87	54.37	89.54	185.71
Minimum Dose	1168	17	4040	426
Maximum Dose	2682	267	4386	1316

The volume of Lung Received Radiation

Table 12: Volume of Lung Received Radiation

%	V5 (Gy)	V10 (Gy)	V20 (Gy)
Mean Dose	50.82	29.45	10.36
Standard Deviation	8.42	4.52	4.51
Minimum Dose	29	20	5.40
Maximum Dose	60	67	19

Response Assessment: In our study, post radiation therapy response in term of locoregional control in 1st month follow up, all patients (100%) presented with complete response (CR), in 3rd month follow up 39(97.5%) patient presented with complete response (CR) and patient developed recurrence over post of scar in form of multiple satellite nodules, in 6th month follow up 1patient developed lung metastasis and 1 patient presented with local recurrence hence 2 (5.0%) shows progressive disease (PD) and 38 (95.0%) patients presented with complete response.

Table 13: Response analysis

Locoregional Response	CR	PR	PD	SD	CR %
1 st Month	40	0	0	0	100
2 nd Month	39	1	0	0	97.5
3 rd Month	38	0	2	0	95.0

Discussion

In our study all patients participated were female. The minimum age was 30 years and the maximum age was 60 years. The most of the patients were belonged to 41 to 50 years which is 57.5% (n=23), and the median age was 47.8 years with standard deviation 7.63 years incidence was observe. Similar incidence was observed in the study by Chopra, Brinder *et al* (2014), they reported that the majority of the Indian patients were in between 40 years to 50 years, which is 42% (n=42) and the median age was 50 years. [6] Similarly DS Sandhu *et al* (2010) found in their study that majority of the patients (65.8%) were of the age group of 31years to 50 years with the mean age was 47.39 years with standard deviation of 10.90 years. [7]

In our study, the premenopausal patients were 7(17.5%) and Postmenopausal patients were 21 (52.5%). K Mc Pherson *et al* (2000) and Freddie Bray *et al* (2004) reports that the incidence of breast cancer increases until menopause and slows down dramatically after that probably due to diminishing levels of circulating estrogens.[8,9] which is not seen in our study. Composite Staging among the patients was reported as IA 0(0%), IB 7(17.5%), IIA 5(12.5%), IIB 7(17.5%), IIIA 6(15%), IIIB 11(27.5%), and IIIC 4(10%) respectively.

Similar incidence was observed in the study by Gaurav Agrawal and Pooja Ramakant (2008) they reported that almost 50% of patients present with locally advanced disease. Majority of patients present with Stage IIIB (35%) followed by Stage IIIA (27%) and Stage IIb (16%), some 8-10% have Stage IV and very few (approximately 5%) have Stage I disease. [10] In our study,

PTV dose data analysis was reported as the average total volume of PTV 1076± 303cc, PTV Dmax 4445±102cGy, PTV Dmin 3542±402 cGy, PTV Dmean 4027±68cGy, D2% 4241±54.17cGy, D5% 4205±45.5cGy, D95% 3808.9±155cGy, D98% 3736±177 cGy, V95% 94±3 (or V38Gy% ≥94±3), HI 10.75±2 and CI 9.46±2.9. K R Murlidhar *et al* 2015 reported PTV median dose coverage 100% with range 0 %, PTV median min dose 63.36 % with range 68.7 %, PTV median max dose 111% with range 12.5% and PTV median mean dose 100% with range 0 % in VMAT respectively. [11]

In our study, ipsilateral LUNG dose data analysis was reported as the average total volume of I/L LUNG is 922.18±218.2cc, Dmin 448.83±489.83cGy, Dmax 4192.1±116.94cGy, Dmean 1871.70±523.92cGy, V5 90.28±7.96%, V10 62.5±12.49%, V20 25.28±3.28%. Kim Y J *et al* (2016) in their study reported that I/L lung V5 97.3%, V10 74.9% and V20 33.4%. [12]

In our study, contralateral LUNG dose data analysis was reported as the average total volume of C/L LUNG is 934.68±219.48cc, Dmin 149.87±44.42cGy, Dmax 1856±738.58 cGy, Dmean 416.49±96.6cGy, V5 20.78±4.98%, V10 2.00±1.17%, V20 is negligible. LUNG TOTAL dose data analysis were reported as the average total volume of LUNG TOTAL is 1911.28±395cc, Dmin 141.96± 51.83cGy, Dmax 4193.05±109.6cGy, Dmean 1063±162.38cGy, V5 51.36±10.44%, V10 30.14±5.88%, V20 10.06±3.83%. Kim Y J *et al* (2016) in their study reported that C/L breast mean dose 5.4Gy and V5% 42.4. [12]

Their study reported that C/L breast Dmin $1.7\pm 1\text{Gy}$ [153] Ranger *et al* 2018 in. Jian Hu *et al* 2020 reported Mean Contralateral Breast Dose (Gy) 3.11 ± 0.28 in VMAT. [13,14] Narudom Supkalin *et al* 2018 reported Mean Contralateral Breast Dose (Gy) 4.98 ± 0.57 in VMAT. [15] After observation, we found that the dose to ipsilateral lung in case of carcinoma left breast is more compare than carcinoma right breast. RP was rare with the applied ipsilateral lung dose-volume constraint V2030%.

Mild RP was detected in four patients, and one patient developed moderate RP. When we applied the ipsilateral lung volume constraint of V2030% in our planning of LRRT in Breast cancer, symptomatic RP was rare and less frequent. [16]

Conclusion

In our study we recorded 95% of complete response at the end of 3months clinically and radiologically while in 5% of cases progressive disease were observed.

An ipsilateral lung dose volume constraint of $V20\leq 30\%$ reduced rate of radiation pneumonitis was observed. Further follow up and a large number of patients are needed to evaluate the late response and toxicity.

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