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"ANALYTICAL STUDY OF RADIATION INDUCED PNEUMONITIS IN CASES OF POST OPERATED CARCINOMA BREAST USING VOLUMETRIC MODULATED ARC THERAPY (VMAT)"

Oncology/Radiotherapy

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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. The treatment, however, deliver some unwanted irradiation to the lung and heart. Radiation induced lung injury including radiation pneumonitis and radiation fibrosis, is common among patients who have received radiation therapy, and it is the most common treatment limiting toxicity. **Objective** To study and analyze the incidence of radiation induced pneumonitis in post operated cases of carcinoma breast undergoing radiotherapy with 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. Radiation induced pnuemonitis was assessed and analyzed. **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 ±218.21cc, D min 448.83 ± 489.83c Gy, D max 4192.1 ±116.94c Gy, D mean 1871.70 ±523.92c Gy, V5 90.28 ± 7.96%, V10 62.5 ±12.49 %, V20 25.28 ±3.28 %. In our study, 4 patients developed radiation pneumonitis which shown by changes in radiation port in CECT Thorax (CO – RADS, Grade – 1). None of the patients developed symptoms related to radiation pneumonitis for eg. Low grade fever, cough, chest pain or breathing difficulties within three months of post radiation therapy. **Conclusion:** In this study we found that incidence of radiation pneumonitis in patients of carcinoma breast post operative who are treated with hypofractionation radiotherapy with VMAT technique, shows less incidence (2.5%) of radiation pneumonitis in irradiated ipsilateral lung volume with better coverage of PTV (D95% is ≥95% of prescribed dose) patient remained asypmtomatic and with less radiation exposer to organs at risk. An ipsilateral lung dose volume constraint of V20≤30% reduced rate of radiation pneumonitis was observed.

KEYWORDS

Pneumonitis, VMAT, Radiation Therapy, Lung

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. [4] Postoperative radiotherapy plays an important role in the management of breast cancer and reduces the locoregional recurrence, thereby improving outcomes. [5] During treatment however, some unwanted irradiation to the lung and heart are delivered. Radiation induced lung injury including radiation pneumonitis and radiation fibrosis, is common among patients who have received radiation therapy, and it is the most common treatment limiting toxicity. [5]

OBJECTIVE:-

To study and analyze the incidence of radiation induced pneumonitis in post operated cases of carcinoma breast undergoing radiotherapy with VMAT.

MATERIALAND 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%

Pneumonitis (Acute Pulmonary Toxicities)

In our study, 4 patients developed radiation pneumonitis which shown by changes in radiation port in CECT Thorax (CO – RADS, Grade – 1). None of the patients developed symptoms related to radiation pneumonitis for eg. Low grade fever, cough, chest pain or breathing difficulties within three months of post radiation therapy. After 6 months of radiations only 1 patient shown persistent changes in CECT Thorax (CO – RADS, Grade – 1).

Table 5 Pneumonitis (Acute pulmonary toxicities)

PNEUMONITIS	GRADE 0	GRADE 1	GRADE 2	GRADE 3	GRADE 4
1st WEEK	40	0	0	0	0
2nd WEEK	40	0	0	0	0
3rd WEEK	40	0	0	0	0
1st MONTH	40	0	0	0	0
3rd MONTH	36	4	0	0	0
6th MONTH	39	1	0	0	0

Dose distribution of ipsilateral lung

In our study of 40 patients, ipsilateral lung dose data analysis was reported as the average total volume of I/L lung is 922.18 ±218.21cc, D min 448.83 ± 489.83c Gy, D max 4192.1 ±116.94c Gy, D mean 1871.70 ±523.92c Gy, V5 90.28 ± 7.96%, V10 62.5 ±12.49 %, V20 25.28 ±3.28 %.

Table 6 Dose distribution of ipsilateral lung

	volume (cc)	Minimum Dose (cGy)	Maximum Dose (cGy)	Mean Dose (cGy)
Mean Dose	922.18	448.83	4192.1	1871.70
Standard Deviation	218.21	489.83	116.94	523.92
Minimum Dose	458	99.4	3940	1504
Maximum Dose	1459	3327	4448	4045

Dose distribution of Contralateral lung

In our study of 40 patients, contralateral lung dose data analysis was reported as the average total volume of C/L LUNG is 934. 68 ±219.48cc, Dmin 149.87 ±44.42c Gy, Dmax 1856 .83 ±738.58c Gy, Dmean 416.49 ±96.60c Gy, V5 20.78 ±4.98 %, V10 2.00 ± 1.17 %, V20 negligible.

Table 7 Dose distribution of Contralateral lung

	volume (cc)	Minimum Dose (cGy)	Maximum Dose (cGy)	Mean Dose (cGy)
Mean Dose	934.68	149.87	1856.83	416.49
Standard Deviation	219.48	44.42	738.58	96.60
Minimum Dose	479	66.7	814	219
Maximum Dose	1444	266	3637	677

Dose distribution of total lung

In our study of 40 patients, Total lung dose data analysis was reported as the average total volume is 1911 .28 ±395.73cc, Dmin 141.96 ±51.83c Gy, Dmax 4193 .05 ±109.6 cGy, Dmean 1063.90 ±162.38c Gy, V5 51.36 ± 10.44%, V10 30.14 ±5.88 %, and V20 10.06 ±3.83%.

Table 8 Dose distribution of total lung

	volume (cc)	Minimum Dose (cGy)	Maximum Dose (cGy)	Mean Dose (cGy)
Mean Dose	1911.28	141.96	4193.05	1063.90
Standard Deviation	395.73	51.83	109.6	162.38
Minimum Dose	1103	17	4006	426
Maximum Dose	2690	267	4448	1316

Dose Data Analysis

Structure	Parameter	Mean	Standard Deviation	Minimum	Maximum
PTV	Vol. (cc)	944.23	371.02	219.00	1704.00
	Dmin (cGy)	2541.00	772.04	579.40	3549.00
	Dmax (cGy)	4431.59	119.75	4200.00	4989.00
	Dmean (cGy)	3957.83	587.53	399.00	4673.00
	D2% (cGy)	4241.50	54.78	4100.00	4376.00
	D5% (cGy)	4205.63	45.59	4127.00	4339.00
	D95% (cGy)	3808.98	155.68	3228.00	4007.00
	D98% (cGy)	3736.35	172.00	3116.00	4056.00
Ipsilateral lung	Vol. (cc)	922.18	218.21	458.00	1459.00
	Dmin (cGy)	448.83	489.83	99.40	3327.00
	Dmax (cGy)	4192.10	116.94	3940.00	4448.00
	Dmean (cGy)	1871.70	523.92	1504.00	4045.00
	V5 (Gy)	90.28%	7.96%	76.00%	100.00%
	V10 (Gy)	62.05%	12.49%	23.00%	90.00%
	V20 (Gy)	25.28%	3.28%	20.00%	30.00%
Contralateral lung	Vol. (cc)	934.68	219.48	479.00	1444.00
	Dmin (cGy)	149.87	44.42	66.70	266.00
	Dmean (cGy)	1856.83	738.58	814.00	3637.00
	Dmean (cGy)	416.49	96.60	219.00	677.00
	V5 (Gy)	20.78%	4.98%	8.005	28.00%
	V10 (Gy)	2.00%	1.17%	0.00%	4.70%
	V20 (Gy)	0.00%	0.00%	0.00%	0.00%

DISCUSSION

This prospective Analytical study was carried out in 40 patients in the

department of Radiation Oncology, Regional Cancer Center, Pt JNM Medical College, Raipur (C.G.), After assessment of all the patients with respect to inclusion and exclusion criteria, it included 40 patients, which were biopsy-proven, post operated breast cancer who received chemotherapy were assessed with complete hemogram, ECG, 2D echo, PFT, and radiological examination and then underwent volumetric modulated arc therapy. Treatment toxicities were evaluated every week during radiation therapy. Post radiation therapy follow-up and evaluation of patients was done after 1 month, 3months and 6 months with clinical examination, complete hemogram, ECG, 2D echo, PFT, and radiological examination CECT Thorax to assess treatment response and lung (radiation induced pneumonitis) toxicities . Doses to PTV and the dose to ipsilatral, contralatral lung and lung total and OAR were calculated (as Mean, max and SD). In our study all patients 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] 4(10%) patients showed Grade I Pneumonitis after 3 months of completion of radiation in which all patients were asymptotic and diagnosed by CECT Thorax which is done in routine follow up.

The sign of CECT Thorax gradually resolved and 1 (2.5%) patients show Grade 1 pneumonitis after six months of RT. In our study Radiation pneumonitis Grade 1 was seen in 1(2.5%) patient without any symptoms which is similar to study done by **Byung Min Lee et al**. [11] **Platanioties GA et al.** Evaluated radiation pneumonitis in hypofractionation setting (42.5Gy/16#) by HRCT in early breast cancer patients and reported minimal and minor effects on the underlying lung parenchyma. [12] **Kim Y J et al (2016)** [13] in their study reported that clinical result of VMAT technique for radiation therapy treating IMN in patients with locally advanced breast cancer with median 2 year follow up the radiation induced pneumonitis grade 1 was 32.2% and grade 2 was 3.2%.

In our study, acute toxicities were observed and we found that no skin toxicity was reported in patients during 1st week, in the 2nd week 28 (70%) developed Grade I toxicity and 21(52.5%) developed Grade II and 10(25%) developed Grade III skin reaction during the 3rd week. **Kim Y J et al (2016**) in their study reported that clinical result of VMAT technique for radiation therapy treating IMN in patients with locally advanced breast cancer, grade 2 skin toxicity was 19% in 2 year follow-up[140]. [13] **Susan GR, MC Duff, and others (2018)** in their study report that the time course for lymphedema development depends on the breast cancer treatment received. Axillary lymph node dissection (ALND) is associated with early-onset lymphedema, and regional lymph node irradiation (RLNI) is associated with late- onset lymphedema. [14]

CONCLUSION

In this study we found that incidence of radiation pneumonitis in patients of carcinoma breast post operative who are treated with hypofractionation radiotherapy with VMAT technique, shows less incidence (2.5%) of radiation pneumonities in irradiated ipsilateral lung volume with better coverage of PTV (D95% is ≥95% of prescribed dose) and with less radiation exposer to organs at risk. An ipsilateral lung dose volume constraint of V20≤30% reduced rate of radiation pneumonities was observed. Further follow up and a large number of patients are needed to evalute the late response and toxicity.

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