Dosimetric Analysis of Organs at Risk and its Correlation with Radiation Techniques in Left-Sided Breast Radiotherapy

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Abstract: *Background:* Breast cancer (BC) burden has increased drastically and has been ranked 2nd worldwide and most common in India, with an incidence of 13.5% of all newly diagnosed cancers. Surgery is the main modality of treatment. The aim of adjuvant radiation therapy is to reduce local recurrence and improve survival. In breast radiotherapy, the proximity of the target to sensitive structures together with the uncertainty introduced by respiratory movement, make this treatment one of the most studied to increase its effectiveness. Various techniques like 3DCRT (Three-Dimensional Conformal Radiation Therapy), IMRT (Intensity Modulated Radiation Therapy) and VMAT (Volumetric Modulated Arc Therapy) are used in RT (Radiation Therapy). Although 3DCRT lowers radiation exposure to normal tissues, it can result in suboptimal dosing of the tumor volume. Conversely, IMRT and VMAT achieve better tumor dose coverage but pose greater challenges in protecting organs at risk (OARs).

Objectives: This retrospective study aims to highlight the Dosimetric study of OARS, and compare Dosimetric values of different RT Techniques in patients receiving left-sided breast irradiation.

Methods: A total of 142 left breast carcinoma patients receiving either whole-breast irradiation or chest wall irradiation were enrolled in this study. The Dosimetric parameters of the heart, left lung and right breast were evaluated and compared, and possible correlations were studied.

Results: Of the 142 patients assessed, 62 patients were stage III, 93 patients underwent post-mastectomy radiotherapy and 49 patients with Whole Breast Radiotherapy (WBRT). Majority of patients were treated by 3DCRT technique. Patients were planned for the 50 Gy in 25 fractions (n-72) and 40 Gy in 15 fractions (n-70) radiation dose regimens. Heart mean dose in 3DCRT, IMRT and VMAT is 6, 7.8 and 7.1Gy respectively (p-0.002).On comparing V_{20} (Volume of lung receiving 20Gy) of ipsilateral (I/L) Lung with 3DCRT, IMRT and VMAT (p-0.998) is 24.8%, 27.5 % and 22.5% respectively. Contralateral (C/L) breast mean dose in 3DCRT was 0.8Gy whereas 5.3Gy and 4Gy respectively in IMRT and VMAT which was statistically significant (p-0.05)

Conclusion: Significant correlations for dosimetric parameters were registered between the OARs and RT Techniques. Our results suggest that heart mean dose and C/L breast dose is minimal in 3DCRT compared to IMRT and VMAT techniques.

Keywords: Breast, radiotherapy, mean dose, dosimetry, irradiation, RT, lung, heart.

INTRODUCTION

Breast cancer (BC) burden has increased drastically and has been ranked 2nd worldwide as per the GLOBOCON data 2022.The incidence (42.9%) and mortality rates (47.3%)of BC is highest among Asian countries [1]. Amongst the Indian women, BC is the most common of all cancers with an incidence of 13.5% in all newly diagnosed cancers [2]. There are many risk factors that have been studied in the causation of BC such as early menarche, late menopause, use of hormone Replacement Therapies and nulliparity. The relative risk increases by 2-4 fold in first degree relatives and more than 4 fold in patients with BRCA gene mutations and previous history of irradiation to chest wall [3-5]. The role of screening significantly helps in detecting lumps in an earlier stage which helps in better survival. Women with high risk as per the Gail models can be screened at an earlier stage as per the ACS guidelines [6,7]. Treatment approach is based on the stage of the disease and hormonal status. Neoadjuvant chemotherapy is given to patients with tumour size more than 2cm and node positive. Chemotherapy regimens are based on hormonal status of the patient. Type of surgery is then planned with Sentinel Lymph Node Biopsy or Axillary Lymph node Dissection based on nodal status of the patient. Adjuvant radiotherapy is planned based on the type of surgery and post-operative HPE (Histo-pathological Examination) features. Hormonal therapy or targeted therapy is then given as maintenance. In cases of less than 2 cm tumor size, approach is upfront surgery followed by Chemotherapy with/ without radiation [8].

The aim of post mastectomy RT (PMRT) is to decrease the incidence of local recurrence which in turn improves survival. PMRT is recommended in patients with Tumor size >5 cm and node positive status [8,15]. Breast conservative surgery (BCS) itself remains the indication for Whole Breast RT followed by

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Lumpectomy boost [9,10]. In the era of2D technique, in which a box was drawn to cover the breast volume, but the target volume was reduced to meet constraints of heart leading to under treatment of disease or organ toxicities like cardiotoxicity, pneumonitis and secondary malignancies [12]. This insufficiency lead to evolution of better techniques like 3DCRT followed by IMRT and VMAT. These advanced techniques delivered lesser dose to OARs while not compromising dose to target volumes. Darby *et al*., studied 2D technique versus 3D technique in 2168 patients which showed 7% increase in relative risk per Gray of mean heart dose, whereas 2DRT had 35% of relative risk [11].

This study aims to analyse V_{20} of I/L lung and D mean (average dose received by the organ) of heart and C/L breast in various RT techniques and correlate the doses in each technique. This study reinforces the importance of selecting appropriate irradiation techniques to minimize exposure to critical organs during breast radiotherapy.

MATERIALS AND METHODS

Study Design

This is a retrospective study which was conducted at a tertiary care cancer centre in South India from January 2020 to March 2024. A total of 142 left breast carcinoma patients receiving either whole-breast irradiation or chest wall irradiation were enrolled in this study.

The main objective of the study was to Analyse Dosimetric parameters of OARs in left breast cancer patients treated with radiation therapy and to correlate Dosimetric values of OARs in different RT techniques (3DCRT, IMRT and VMAT). All the left breast cancerwith Post mastectomy or post BCS requiring radiotherapy were included in the study. Patients with metastatic carcinoma breast, patients requiring Palliative radiotherapy and Recurrent/ secondary breast cancer patients previously treated with RT were excluded. Organs at risk- heart, ipsilateral lung and contralateral breast were contoured according to Radiation Therapy Oncology Group (RTOG) breast cancer atlas guidelines [18]. The dosimetric parameters such as D mean to heart, right breast and V_{20} of left lung were evaluated and possible correlations were studied across 3DCRT, VMAT and IMRT techniques. In patients undergoing Hypofractionation Equivalent Dose (EQD2) was calculated for OARs before correlation across RT Techniques.

STATISTICAL ANALYSIS

The data were analysed using IBM SPSS version 25. Continuous and categorical variables were

Table 1: Patient and Tumour Characteristics

Patient and Tumour Characteristics			
Variable		**N(Number)**	**Percentage**
Age	Mean	54	
Stage	I	27	19
	IIa	28	20
	IIb	36	25
	III	30	21
	IV	21	15
RT	3DCRT	83	58
	IMRT	46	32
	VMAT	13	10
RT Dose	50Gy/25 #	74	52
	40Gy/15#	68	48
Total		142	100

Table 2: Comparison of D-Mean of Heart Across the Three Techniques Using ANOVA

Technique	N	Mean (Gy)	Standard deviation	P value
3DCRT	83	6.03	2.78	.002
IMRT	46	7.83	2.74	
VMAT	13	7.11	2.22	

presented as mean ± standard deviation and percentages respectively. Comparison of the dosages against different techniques and total radiation doses was done using ANOVA followed by Tukey's post-hoc analysis. A p value of ≤.05 was considered significant for all analyses.

RESULTS

142 patients diagnosed with left BC who have received adjuvant RT were included in our study and were analysed retrospectively. The age at diagnosis was found to be 26-79 years with a mean age of 54years. The most common stage at diagnosis was Stage IIB (25.4%) followed by Stage III. 65.5% (n=93) of patients underwent MRM, 29.6% (n=42) underwent BCS and 4.9% (n=7) underwent Wide Local Excision (WLE).

All patients were planned for Adjuvant RT based on Tumor characteristics and post operative histologic features. 52.1% (n=74) patients received 50Gy in 25 fractions and 47.9% (n= 68) received 40Gy in 15 fractions. Of these patients, 83 (45.8%) were treated by 3DCRT technique, 46 (32.4%) by IMRT technique and 13 (9.2%) by VMAT technique.

The dose to the heart (D-mean) was noted and compared across the three techniques using ANOVA analysis, the p-value was found to be p - 0.002. A further Tukey's post-hoc analysis revealed that the dose was higher for IMRT and VMAT compared to 3DCRT which was statistically significant.

The V_{20} (Volume receiving 20Gy) to the left lung was calculated and analysedover the three techniques. The p-value was 0.998 and it was found that the dose to lungs (V_{20}) did not vary significantly with RT different techniques.

Comparison of mean dose of C/L breast across the three techniques using ANOVA varied significantly with the technique. Tukey's post-hoc analysis revealed that the dose was significantly lesser for 3DCRT than IMRT and VMAT (P value-0.005).

DISCUSSION

In this study, over 45% and 21% of cases are in stages II and III respectively, revealing that breast cancer frequently presents at later stages in Indian population. This makes radiotherapy an indispensable tool for preventing local recurrence in carcinoma breast [13]. The proximity of breast to critical organs at risk makes it challenging to optimize tumor control while achieving minimal normal tissue exposure with better planning techniques. The main objective of the study was to Analyse Dosimetric parameters of OARs in left breast cancer patients treated with radiation therapy and to correlate Dosimetric values of OARs in different RT techniques (3DCRT, IMRT and VMAT).

A study done by Darby SC *et al*. reported that exposure of the heart to ionizing radiation during radiotherapy for breast cancer increases the subsequent rate of ischemic heart disease, with increase in 7.4% per Gray (mean) to the heart, with increased absolute risk in previously existing cardiac risk factors [11]. Kryszak *et al.* conducted a study on heart mean dose in different techniques, which showed no better OAR protection in IMRT and VMAT compared to 3DCRT [16]. Ma *et al*. [14] found that IMRT had a better tumor coverage, but their results showed no significant difference in heart mean dose between IMRT and 3DCRT. Our study showed the mean heart

Table 3: Comparison of V_{20} of l/Llung Across the Three Techniques Using ANOVA

Technique	N	V_{20}	Standard deviation	P value
3DCRT	83	24.82	10.87	.998
IMRT	46	24.71	6.80	
VMAT	13	24.83	4.85	

Table 4: Comparison of C/L Breast Mean Dose Across the Three Techniques Using ANOVA

Technique	N	Mean(Gy)	Standard deviation	P value
3DCRT	83	.896	2.41	.005
IMRT	46	3.56	1.062	
VMAT	13	3.83	1.24	

dose was higher with IMRT and VMAT techniques when compared to 3DCRT (p-0.002) attributing to beam angles and MLC placement.

Radiation pneumonitis is one of the most common side effects following PMRT. For patients treated with 3DCRT, the volume of lung receiving 20Gy i.e., V_{20} has been found to predict the risk of symptomatic radiation pneumonitis in literature [19,20]. However, there is no absolute safe dose below which there is no pneumonitis [18]. Moorthy *et al*., [21] study showed that V_{20} of I/L lung was 37.9% for 3DCRT and 22.4% ($p< 0.01$) for IMRT, concluding IMRT had better lung dose when compared to 3DCRT. A similar study, Li *et al*., [22] concluded that V_{20} and V_{30} of I/L lung were significantly higher 32% and 29% respectively ($p < 0.001$) in 3DCRT and IMRT group respectively. Ma *et al.* [14] concluded an increase in mean lung dose by VMAT compared to 3DCRT and IMRT. Our results also shows that V_{20} to I/L lung is 24.82% in 3DCRT technique whereas 24.71% in IMRT and 24.83% in VMAT technique. This result was not statistically significant, although lung dose was minimally lesser in IMRT technique.

Various literatures have shown approximately 2-3% risk for C/L BC after 5 years of radiation. However, other factors also play a role in secondary malignancies including age and BRCA gene mutation. Taylor *et al*., is a meta-analysis which showed relative risk of C/L BC of 1.20 in post - RT BC, with an increase in absolute risk to 1% in 15 years follow up[(17).] ICRP models and the BEIR VII report Lifetime Attributable Risk (LAR) of 5% per Gy of mean dose to the contralateral breast in young women [23].

Ahmad *et al*., compared C/L breast dose in 3DCRT, IMRT and VMAT which were 1.3Gy, 2.1Gy and 3.47Gy respectively concluding better OAR dose tolerance in 3DCRT technique followed by IMRT and VMAT [24]. Bhatnagar *et al*., study observed reduced C/L breast dose in IMRT when compared to conventional technique [25]. In our study, the radiation dose to the C/L breast in patients receiving IMRT, VMAT, and 3DCRT were 3.56Gy, 3.83Gy and 0.896Gy respectively. Increased dose to C/L breast in VMAT and IMRT can be due to beam angles. A similar study, Khosla *et al*., reported C/L breast dose of 1.02Gy and 2.6Gy in 3DCRT and VMAT techniques respectively [26]. Based on the above mentioned studies and this study, it is found that modern techniques like IMRT and VMAT increased the dose to the C/L breast. The study highlighted the need for careful planning in techniques like IMRT and VMAT to minimize unnecessary radiation exposure to healthy tissues, including the C/L breast [27,28].

The main limitations of our study were single institute and retrospective study with a smaller number of sample size. Large prospective studies are required to analyse the dosimetric parameters of these critical structures and a long term follow up would reveal a late toxicity associated with the different radiation techniques.

CONCLUSION

In conclusion, techniques with tangential fields' arrangement resulted in overall better OARs dosimetry compared to those with multi-fields and arcs arrangements. 3DCRT offered better C/L breast dose and similar doses to I/L lung and heart when compared to IMRT and VMAT. This study collectively reinforces that while modern radiation techniques like IMRT and VMAT offer improved targeting of the tumor, they also require careful consideration of their effects on surrounding healthy tissues.

CONFLICT OF INTEREST

The authors have no conflict of interest to declare.

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