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Original Article

Comparison of Mean Lung and Heart Doses in Three-Dimensional Conformal Radiotherapy Versus Intensity Modulated Radiotherapy in Postmastectomy Breast Cancer Radiation

Saira Shahid[1], Humera Mahmood[1], Nazia Neelam[1]

[1] Atomic Energy Cancer Hospital, Nuclear Medicine Oncology and Radiotherapy Institute (NORI), Islamabad, Pakistan

Correspondence: saira.shahid@email.com
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ABSTRACT

Background: Breast cancer is the leading malignancy among women worldwide, with adjuvant radiotherapy essential for reducing locoregional recurrence following modified radical mastectomy. Optimal radiotherapy technique selection is critical to balance tumor control with the minimization of cardiac and pulmonary toxicity, particularly in left-sided breast cancer. Objective: To compare the dosimetric parameters of mean lung and heart doses, as well as target volume coverage, between three-dimensional conformal radiotherapy (3DCRT) and intensity-modulated radiation therapy (IMRT) in postmastectomy breast cancer patients. Methods: In this randomized controlled trial conducted at Atomic Energy Cancer Hospital NORI, Islamabad, 60 women with left-sided invasive ductal carcinoma who had undergone modified radical mastectomy were randomized equally to receive adjuvant radiotherapy with either 3DCRT or IMRT (40.05 Gy in 15 fractions). Dosimetric parameters, including mean doses and low- and high-dose volumes for heart and lung, as well as planning target volume (PTV) coverage indices, were assessed using standardized contouring and treatment planning. Group comparisons utilized the Mann-Whitney U test. Results: IMRT achieved significantly superior PTV coverage (PTV 95%: 98.5% vs. 92.96%, $p<0.001$), but resulted in higher mean lung (15.17 Gy vs. 12.81 Gy, $p=0.001$) and heart doses (6.88 Gy vs. 4.02 Gy, $p<0.001$) and increased low-dose exposure (lung V5: 71.5% vs. 45.5%, heart V5: 43.2% vs. 12.8%, both $p<0.001$), while high-dose volumes (lung V20 and heart V25) did not differ significantly between groups. Conclusion: Although IMRT provides enhanced target volume coverage in postmastectomy radiotherapy, it is associated with greater low-dose irradiation of the heart and lung compared to 3DCRT, highlighting a trade-off that should inform technique selection and further research.
Keywords: Breast cancer, postmastectomy, three-dimensional conformal radiotherapy, intensity-modulated radiation therapy, heart dose, lung dose, dosimetric comparison

INTRODUCTION

Breast cancer remains the most common malignancy among women worldwide, accounting for approximately 23% of all female cancers, with significant geographic variability in incidence and outcomes (1). In Pakistan, breast cancer constituted around 40.2% of all cancers among females between 2018 and 2019, underscoring a substantial national disease burden (2). Although breast-conserving surgery has increasingly become an option for early-stage disease, modified radical mastectomy continues to be widely performed, particularly in patients presenting with advanced stages, due to both clinical indications and sociocultural factors (3). Advances in systemic therapies and surgical techniques have improved survival outcomes, yet locoregional control remains a crucial determinant of prognosis in breast cancer, necessitating adjuvant radiotherapy after mastectomy to reduce the risk of recurrence (4).

In postmastectomy radiotherapy, sparing of critical organs such as the heart and lungs is paramount, especially in left-sided breast cancers where proximity of target volumes to these organs elevates the risk of radiation-induced toxicity. Historical radiotherapy techniques delivered uniform dose distributions but offered limited capabilities for conformal avoidance of adjacent organs at risk (5,6). The development of three-dimensional conformal radiotherapy (3DCRT) allowed for better dose shaping compared to conventional methods by utilizing multiple beam angles and geometric planning, but it still posed challenges in further minimizing cardiac and pulmonary exposure (7). The emergence of intensity-modulated radiation therapy (IMRT) has introduced advanced capabilities to sculpt radiation doses with greater precision, theoretically improving coverage of complex target volumes while reducing high-dose exposure to surrounding normal tissues by modulating beam intensities across multiple angles (8). However, despite its dosimetric advantages, IMRT can also increase the volume of tissue receiving low doses of radiation due to its use of multiple beamlets, raising concerns about potential long-term toxicities including radiation pneumonitis and cardiac events (3,9).

Multiple studies have examined dosimetric comparisons between IMRT and 3DCRT in breast cancer, with some demonstrating superior target coverage and reduced high-dose exposure to critical organs when using IMRT (10,11). For instance, Tali et al. reported reduced mean heart and lung doses with IMRT in postmastectomy chest wall irradiation, suggesting potential for decreased toxicity (12). Conversely, other investigations, including those by Zhang et al. and Chung et al., highlight a trade-off wherein IMRT's low-dose spread may inadvertently increase radiation exposure to larger volumes of the lung and heart, potentially offsetting benefits gained in target conformity (3,9). Furthermore, the clinical implications of these dosimetric differences remain under debate, particularly in settings where advanced techniques like deep inspiration breath hold (DIBH) are not uniformly implemented (13). These discrepancies underline a persistent knowledge gap regarding the optimal balance between achieving excellent tumor coverage and minimizing risks to critical organs in postmastectomy radiotherapy planning, especially in regions with constrained resources or differing patient anatomy (14).

Given the significant potential for long-term morbidity associated with cardiac and pulmonary irradiation, and considering the lack of consistent consensus on whether IMRT confers substantial dosimetric benefits over 3DCRT without unacceptable trade-offs, there remains a pressing need for comparative studies assessing these two techniques in real-world clinical settings. Therefore, this randomized controlled trial was conducted to evaluate and compare the dosimetric parameters of mean heart and lung doses, as well as target volume coverage, between three-dimensional conformal radiotherapy and intensity-modulated radiotherapy in patients with left-sided breast cancer undergoing postmastectomy chest wall irradiation.

MATERIAL AND METHODS

This randomized controlled trial was conducted in the Department of Radiation Oncology at the Atomic Energy Cancer Hospital NORI, Islamabad, from 30th September 2024 to 30th March 2025, with the objective of comparing dosimetric parameters between three-dimensional conformal radiotherapy (3DCRT) and intensity-modulated radiation therapy (IMRT) for postmastectomy left-sided breast cancer. The trial was designed to provide robust evidence regarding differential radiation exposure to organs at risk and target volume coverage, given ongoing debates about the optimal technique for minimizing cardiac and pulmonary toxicity in this patient population (3,9,12,14).

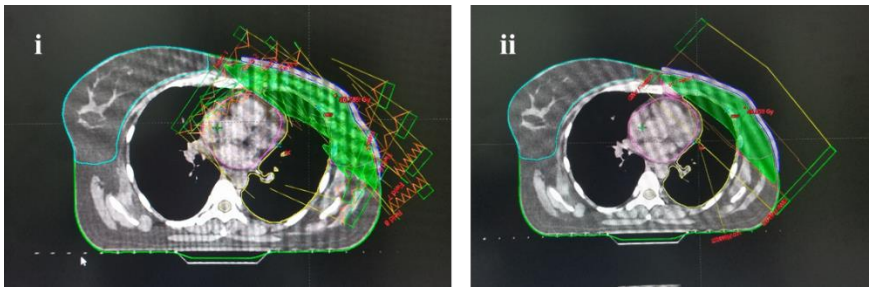

Figure 1 (i) IMRT Planning (ii) 3DCRT planning

The study population comprised female patients aged 30 to 70 years who were diagnosed with invasive ductal carcinoma of the left breast and had undergone modified radical mastectomy. Eligibility required patients to have no evidence of distant metastasis, no prior history of malignancy, and no history of previous thoracic radiotherapy. Patients were excluded if they had significant respiratory or cardiac comorbidities, prior malignancies, or had been treated with alternative fractionation schemes outside the defined protocol. All participants provided written informed consent after a thorough explanation of the study aims and procedures. Consecutive patients meeting the eligibility criteria were approached for participation and were randomly allocated using simple randomization into two equal groups of thirty patients each to receive either IMRT or 3DCRT, ensuring comparability between groups. Randomization sequences were generated using a computerized random number table to avoid allocation bias. Following enrollment, each patient underwent a simulation procedure in the supine position on a fixed breast board with both arms abducted above the head to optimize reproducibility and minimize variations in anatomical positioning. The surgical scar site was marked using lead wires for accurate localization. Computed tomography (CT) scans were acquired with 5 mm slice thickness to generate volumetric datasets for treatment planning. Image datasets were imported into the Varian Eclipse treatment planning system where delineation of target volumes and organs at risk was performed according to the consensus definitions outlined in the Radiation Therapy Oncology Group (RTOG) Breast Cancer Atlas (15). Clinical target volumes (CTV) encompassed the chest wall, supraclavicular fossa, and axillary lymph nodes where indicated, with the planning target volume (PTV) created by expanding the CTV by 0.5 cm to account for setup uncertainties and motion. Organs at risk contoured included ipsilateral lungs, heart, spinal cord, contralateral breast, trachea, and brachial plexus. For patients assigned to the 3DCRT group, treatment plans utilized a field-in-field technique with two opposing tangential photon beams configured to minimize heart and lung doses. Subfields within the tangential beams were manually designed using multi-leaf collimators (MLCs) to enhance homogeneity across the chest wall while sparing surrounding tissues. For the IMRT group, inverse planning was employed with seven to nine semi-opposing tangential photon beams. Beam angles and intensity modulation were optimized to achieve prescribed dose constraints while minimizing radiation to organs at risk, accounting for tissue heterogeneity during planning optimization. All treatment plans prescribed a total dose of 40.05 Gy delivered in 15 fractions of 2.67 Gy per fraction using 6 MV photons, adhering to institutional protocols for postmastectomy radiation therapy. Dosimetric parameters analyzed included PTV coverage metrics such as V95% (the percentage of PTV receiving at least 95% of the prescribed dose), V90%, and maximum dose (D-max). Organ-at-risk parameters evaluated comprised mean dose to the ipsilateral lung and heart, as well as the percentage volume of ipsilateral lung receiving 5 Gy (V5) and 20 Gy (V20), and the percentage volume of the heart receiving 5 Gy

(V5) and 25 Gy (V25). Institutional dose constraints were set with acceptable thresholds defined as lung V20 under 30% and mean heart dose below 5 Gy, based on established radiation oncology guidelines (6,15).

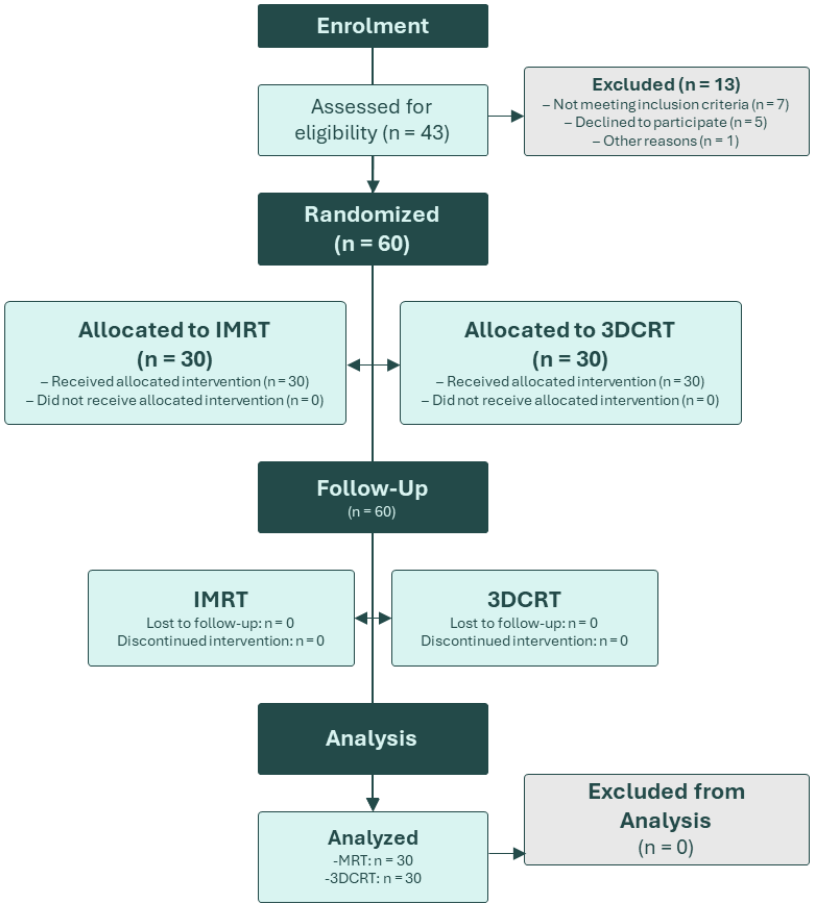

Figure 2 CONSORT Flowchart

To minimize bias, all treatment plans were independently reviewed and approved by at least two senior radiation oncologists who were blinded to group allocation during dosimetric evaluation. Data was recorded in a pre-designed proforma and entered into IBM SPSS Statistics version 25 for analysis. The Shapiro-Wilk test was used to assess the normality of continuous data distributions. Owing to non-normal distribution of the measured variables, group comparisons were performed using the Mann-Whitney U test for continuous data, with p-values ≤ 0.05 considered statistically significant. No imputation was necessary for missing data, as all data points were complete due to rigorous data collection protocols. This study was conducted in accordance with the ethical standards of the Declaration of Helsinki and approved by the institutional ethical review committee and the College of Physicians and Surgeons Pakistan (IRB no. NORI-2(72)/88 dated 18-02-2024). Measures to ensure data integrity included double-entry verification, restricted data access, and audit trails maintained within the institutional research record systems to support reproducibility and transparency of the findings.

RESULTS

Among the sixty female patients randomized equally between IMRT and 3DCRT, the distribution of tumor stage and grade was comparable, with no statistically significant differences (stage III: 66.7% in IMRT vs 63.3% in 3DCRT, p=0.786; grade 2: 80% in IMRT vs 66.7% in 3DCRT, p=0.210). Analysis of dosimetric outcomes revealed that IMRT resulted in significantly higher low-dose exposure to both the lung and heart compared to 3DCRT. Specifically, the mean lung V5 was 71.5% (SD 9.85) for IMRT versus 45.5% (SD 8.35) for 3DCRT, corresponding to a mean difference of 26.0% (95% CI: 21.7, 30.3; p<0.001). The mean lung dose was also higher in the IMRT group at 15.17 Gy (SD 1.86) compared to 12.81 Gy (SD 3.18) for 3DCRT (mean difference 2.36 Gy, 95% CI: 1.19, 3.53; p=0.001). Similarly, heart V5 was substantially elevated with IMRT (43.2% [SD 15.1]) relative to 3DCRT (12.8% [SD 4.55]), a mean difference of 30.4% (95% CI: 24.8, 36.0; p<0.001), and the mean heart dose was 6.88 Gy (SD 1.98) in the IMRT group versus 4.02 Gy (SD 1.22) for 3DCRT (mean difference 2.86 Gy, 95% CI: 2.04, 3.68; p<0.001). In contrast, there were no significant differences between groups in lung V20 (p=0.848) or heart V25 (p=0.668), indicating that both techniques similarly limited the volume of lung and heart receiving higher radiation doses. Regarding target coverage, IMRT achieved superior results, with PTV 90% and PTV 95% coverage at 99.7% (SD 0.42) and 98.5% (SD 2.4), respectively, compared to 95.3% (SD 4.06) and 92.96% (SD 5.5) for 3DCRT; both differences were highly significant (p<0.001). Additionally, the maximum PTV dose (D-max) was slightly higher in the IMRT arm (118.0% [SD 4.1]) than in 3DCRT (113.5% [SD 6.22]; p=0.001). These findings collectively demonstrate that while IMRT provides improved target volume coverage, it is associated with increased low-dose exposure to the heart and lung when compared with 3DCRT.

Table 1. Distribution of Cancer Stage and Grade Among Patients Treated with IMRT and 3DCRT

Variable	Category	IMRT n (%)	3DCRT n (%)	p-value*
Stage	II	10 (33.3)	11 (36.7)	0.786
	III	20 (66.7)	19 (63.3)	
Grade	2	24 (80.0)	20 (66.7)	0.210
	3	6 (20.0)	10 (33.3)	

*P-values calculated by Fisher's Exact test.

Table 2. Comparative Dosimetric Analysis of Lung, Heart, and PTV Parameters Between 3DCRT and IMRT

Parameter	3DCRT (Mean ± SD)	IMRT (Mean ± SD)	Mean Difference (95% CI)	p-value†
Lung V5 (%)	45.5 ± 8.35	71.5 ± 9.85	26.0 (21.7, 30.3)	<0.001
Lung V20 (%)	28.8 ± 8.16	29.4 ± 4.60	0.6 (–2.6, 3.8)	0.848
Lung Mean Dose (Gy)	12.81 ± 3.18	15.17 ± 1.86	2.36 (1.19, 3.53)	0.001
Heart V5 (%)	12.8 ± 4.55	43.2 ± 15.1	30.4 (24.8, 36.0)	<0.001
Heart V25 (%)	5.33 ± 8.05	5.90 ± 4.00	0.57 (–2.88, 4.02)	0.668
Heart Mean Dose (Gy)	4.02 ± 1.22	6.88 ± 1.98	2.86 (2.04, 3.68)	<0.001
PTV 90% (%)	95.3 ± 4.06	99.7 ± 0.42	4.4 (3.2, 5.6)	<0.001
PTV 95% (%)	92.96 ± 5.50	98.5 ± 2.40	5.54 (3.82, 7.26)	<0.001
PTV D-max (%)	113.5 ± 6.22	118.0 ± 4.10	4.5 (2.21, 6.79)	0.001

†Mann-Whitney U test. Mean differences and 95% confidence intervals calculated using normal approximation. All values rounded to two decimal places.

DISCUSSION

The present randomized controlled trial provides robust comparative data on the dosimetric performance of intensity-modulated radiation therapy (IMRT) versus three-dimensional conformal radiotherapy (3DCRT) in postmastectomy radiotherapy for left-sided breast cancer. Our findings confirm that IMRT delivers significantly improved target volume coverage, as evidenced by mean PTV 90% and PTV 95% values approaching 99.7% and 98.5%, respectively, compared to 95.3% and 92.96% with 3DCRT. These differences are not only statistically significant, but also clinically relevant, as optimal PTV coverage is essential for minimizing the risk of locoregional recurrence after mastectomy (16,17). The higher D-max observed in the IMRT cohort further reflects the technique's ability to intensify dose within target boundaries while maintaining conformity, although such increases should be balanced against the risk of localized toxicity.

Despite the superiority of IMRT in achieving comprehensive tumor coverage, our results also underscore a consistent and substantial increase in low-dose radiation exposure to both the lung and heart. The mean lung V5 in the IMRT group was 71.5%, exceeding the 3DCRT group by 26.0%, while the mean heart V5 was more than triple in IMRT (43.2%) compared to 3DCRT (12.8%). The corresponding increases in mean lung and heart doses—2.36 Gy and 2.86 Gy higher, respectively, in IMRT—are highly significant ($p<0.001$) and raise important questions about the potential for increased late radiation-induced toxicity. These findings mirror the results of recent dosimetric studies by Zhang et al. and Chung et al., both of which described a trade-off between enhanced PTV conformity and increased low-dose organ exposure with IMRT (3,9). Such concerns are reinforced by reports highlighting the association between even modest increases in mean heart dose and the risk of long-term cardiac morbidity, particularly in left-sided breast cancer patients (18). It is notable that the high-dose parameters—lung V20 and heart V25—did not differ significantly between groups, with both modalities maintaining mean lung V20 below 30% and mean heart dose below accepted clinical thresholds in a majority of cases. These outcomes are consistent with earlier observations by Das Majumdar et al. and Zhao et al., who found no significant differences in high-dose cardiac or pulmonary exposure between IMRT and 3DCRT (14,19). Nevertheless, the pattern of increased low-dose spread associated with IMRT should not be overlooked, as it may have implications for both the immediate and cumulative risk of adverse effects, particularly in younger patients or those with longer anticipated survival.

Our findings also diverge from some previous reports, such as the study by Tali et al., which suggested IMRT could achieve lower mean heart doses than 3DCRT in the postmastectomy setting (12). The discrepancy may be attributable to differences in patient anatomy, target delineation protocols, or the use of additional motion management strategies such as deep inspiration breath hold (DIBH), which were not employed in the present study. Furthermore, institutional expertise and planning system capabilities can introduce variability in dose distribution and organ sparing, underscoring the need for individualized planning and multidisciplinary oversight in radiotherapy delivery (20). A notable strength of this study is the strict randomization protocol and comprehensive dosimetric evaluation, reducing the potential for selection and measurement bias. The sample size was calculated to detect clinically meaningful differences in mean doses, and all plans were rigorously peer-reviewed to ensure consistency. However, several limitations must be acknowledged. Most importantly, this analysis focused solely on dosimetric outcomes and did not assess clinical endpoints such as acute or late toxicity rates, cardiac or pulmonary function, or local control and survival. Longitudinal studies with extended follow-up will be essential to determine whether the dosimetric differences observed here translate into clinically significant differences in patient outcomes (21). Additionally, the exclusion of DIBH or hybrid planning strategies may have limited the generalizability of the findings to centers employing advanced motion management or newer treatment platforms., while IMRT provides dosimetric advantages in target coverage for postmastectomy left-sided breast cancer, these benefits are counterbalanced by increased low-dose radiation exposure to critical organs. The clinical relevance of these differences remains to be fully elucidated, but the results emphasize the need for careful technique selection, tailored planning, and continued research into hybrid and motion-managed approaches. Future investigations should aim to incorporate patient-reported outcomes, toxicity data, and long-term survival to provide a more comprehensive basis for evidence-based radiotherapy decisions in this patient population (22).

CONCLUSION

This randomized controlled trial demonstrates that while intensity-modulated radiation therapy achieves superior target volume coverage compared to three-dimensional conformal radiotherapy in postmastectomy breast cancer patients, it does so at the cost of significantly increased low-dose exposure to both the lung and heart. These findings highlight a critical trade-off in radiotherapy planning: although IMRT optimizes tumor coverage, the associated elevation in mean and low-dose organ exposure may increase the long-term risk of cardiopulmonary complications, especially in left-sided disease. Clinically, these results suggest that three-dimensional conformal radiotherapy remains preferable when prioritizing organ-at-risk sparing, whereas IMRT should be considered in cases where optimal target coverage cannot be achieved otherwise or where advanced cardiac and pulmonary protection strategies are available. Further prospective studies integrating clinical toxicity outcomes and longer follow-up are warranted to better define the impact of these dosimetric differences on patient quality of life and survival, thereby guiding the safest and most effective radiation technique selection for breast cancer care.

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