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Feasibility and tolerability of hypofractionated post-mastectomy radiotherapy in breast cancer patients: A prospective study

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Abstract
Background: Hypofractionated post-mastectomy radiotherapy (PMRT) offers a shorter treatment regimen for breast cancer patients, potentially improving patient compliance and resource efficiency. While studies support its safety in breast-conserving settings, its application in post-mastectomy scenarios requires further assessment.
Materials and Methods: This prospective study involved 25 breast cancer patients who underwent modified radical mastectomy and received hypofractionated PMRT. Patients were evaluated for acute toxicities weekly over six weeks. Treatment dosimetry followed established guidelines, with attention to clinical target volume (CTV) and organs-at-risk (OAR) dose limits.
Results: Most patients tolerated the treatment well, with no Grade IV toxicities. Acute side effects included dermatitis (56% Grade I, 16% Grade II) and mild fatigue. Only one patient developed Grade III dermatitis. Analysis revealed that higher BMI correlated with increased toxicity, though within tolerable limits. No significant dose violations occurred, and treatment completion rates were high.
Conclusion: Hypofractionated PMRT is a feasible, well-tolerated approach for post-mastectomy breast cancer patients, achieving acceptable toxicity levels and supporting future research into its standardization. BMI-specific dose adaptations may enhance treatment tolerance.

Keywords: Hypofractionated radiotherapy, breast cancer, post-mastectomy radiotherapy, acute toxicity, BMI, feasibility study

Introduction
Breast cancer remains one of the most prevalent malignancies worldwide, significantly impacting women's health with an estimated 2.3 million new cases in 2020 alone [1]. It accounts for the highest cancer incidence among women globally, with an increasing prevalence due to lifestyle factors, genetics, and age-related risk [2]. Although mortality rates have declined in recent years, largely due to early detection and advanced treatments, breast cancer still leads as a cause of cancer-related deaths among women [3].
Treatment options vary based on cancer stage and subtype, including surgery, chemotherapy, radiation therapy, hormonal therapy, and targeted biological agents [4]. Hypofractionated radiotherapy has emerged as an alternative treatment approach in post-mastectomy breast cancer care, aiming to reduce the duration and cost of radiotherapy while maintaining treatment efficacy and tolerability.
Standard post-mastectomy radiotherapy (PMRT) traditionally involves fractionated doses administered over five to six weeks, a regimen that can pose logistical challenges, financial burdens, and increased healthcare costs for patients and providers alike [5]. Hypofractionated PMRT, where higher doses are delivered over a shorter period, has demonstrated promising outcomes in terms of tumor control, survival, and patient quality of life, especially in breast-conserving settings. However, there remains a need to substantiate its feasibility and tolerability in post-mastectomy settings, particularly in patients with advanced-stage breast cancer, who are at high risk of local recurrence and systemic disease spread [6].
Recent studies have shown that hypofractionated radiotherapy can potentially reduce side effects, enhance patient compliance, and maintain local control rates comparable to conventional fractionation schedules [7, 8]. The Royal College of Radiologists and the National Comprehensive Cancer Network (NCCN) guidelines increasingly endorse

hypofractionated approaches in early-stage breast cancer treatment, yet data on its effectiveness and safety in post-mastectomy settings are limited [9]. Several trials, such as the START A and START B, have provided foundational evidence on hypofractionated radiotherapy's tolerability and efficacy, yet the applicability of these findings to the post-mastectomy population is not fully understood [10].

The present study aims to evaluate the feasibility and tolerability of hypofractionated PMRT in patients who have undergone mastectomy for carcinoma breast. The study will assess treatment tolerance, focusing on acute and late toxicities, as well as overall patient quality of life throughout the treatment course.

Materials and Methods

This single-arm prospective trial assessed the feasibility and tolerability of hypofractionated post-mastectomy radiotherapy in breast cancer patients. Conducted from April 2020 to November 2020 in the Department of Radiation Oncology at Kamineni Academy of Medical Sciences and Research Centre the study received approval from the Institutional Review Board and Ethics Committee. Eligible patients were selected based on criteria including age (18-70 years) and the need for post-mastectomy radiotherapy within 42 days of surgery or last chemotherapy cycle. Exclusions included prior breast conservation surgery, pregnancy, metastatic disease, and severe comorbidities.

A total of 25 female patients requiring adjuvant radiotherapy after mastectomy were enrolled after informed consent. Patients received treatment once their surgical wounds healed or after a minimum of three weeks following chemotherapy. Each patient underwent routine blood tests, positioning on a breast board for immobilization, and computed tomography (CT) scans to establish clinical boundaries and target volume for radiotherapy. The scans, performed from the fourth cervical vertebra to the adrenal glands, followed RTOG contouring guidelines for defining the clinical target volumes (CTV) and organs at risk (OAR).

Treatment planning used the Eclipse External Beam Planning System, with the chest wall and supraclavicular regions identified as target areas. The radiation dose was set at 40.05 Gy, delivered in 15 fractions over three weeks. Quality assurance followed criteria for dose limits, with the heart and ipsilateral lung closely monitored to minimize risk. Patient setup was verified with digitally reconstructed radiographs before each treatment.

Patients were assessed weekly for acute toxicities, with dermatitis graded according to RTOG Acute Radiation Morbidity Criteria. Treatment was paused if Grade 3 dermatitis occurred, resuming only when reactions reduced to Grade I. Post-treatment follow-ups included a six-week assessment for dermatitis and a pulmonary function test three months post-radiotherapy. Data were analyzed using SPSS, with frequencies for discrete variables and statistical tests to determine association.

Results

The study recruited 25 patients with breast carcinoma who had undergone a modified radical mastectomy. Patient demographics varied, with the majority originating from Telangana (n=13), followed by Kerala (n=4), Andhra Pradesh (n=3), and other states, including one patient from Bhutan. The age distribution was primarily in the 46-55 age groups (56%), with a mean age of 50 years. Body mass index (BMI) varied, with 40% classified as overweight and 16% with Grade I or II obesity. Common comorbidities included diabetes and hypertension, present in 48% of participants. Most cases involved left-sided breast cancer (60%), and staging revealed that 40% of patients were at Stage IIIA, followed by 32% at Stage IIA. Hormone receptor statuses were as follows: 68% were estrogen receptor-positive, and 48% were progesterone receptor-positive, while 16% were HER2/neu positive and 16% had triple-negative breast cancer. Clinical details are summarized in Table 1.

Table 1: Patient Demographics and Clinical Characteristics

Characteristic		N (%)
Origin	Telangana	13 (52%)
	Kerala	4 (16%)
	Andhra Pradesh	3 (12%)
	Other	5 (20%)
Age (years)	<35	2 (8%)
	36-45	4 (16%)
	46-55	14 (56%)
	>55	5 (20%)
BMI	Healthy	10 (40%)
	Overweight	10 (40%)
	Obese (Grade I)	3 (12%)
	Obese (Grade II)	2 (8%)
Comorbidities	Diabetes	6 (24%)
	Hypertension	6 (24%)
Laterality	Left	15 (60%)
	Right	10 (40%)
Stage	IIA	8 (32%)
	IIIA	10 (40%)
	IIIB	4 (16%)
	IV	3 (12%)
Receptor Status	Estrogen Receptor Positive	17 (68%)
	Progesterone Receptor Positive	12 (48%)
	HER2/neu Positive	4 (16%)
	Triple Negative	4 (16%)

All patients completed treatment without significant complications. Radiotherapy dosimetry was analyzed, focusing on clinical target volume (CTV) and organ-at-risk (OAR) parameters. The lower dose limit achieved over 90% coverage for CTV, while upper dose limits (V105% and V107%) remained within tolerance across all patients. Treatment regions included the chest wall in 60% of patients and both chest wall and supraclavicular area in 40%. Analysis showed no statistically significant differences in CTV coverage between single-region and combined-region groups ($p>0.05$).

Table 2: Dose-Volume Histogram Parameters

Parameter	Chest Wall Only (Median)	Chest Wall & Supraclavicular (Median)	p-value
V90%	98.34%	97.38%	0.530
V95%	92.52%	91.60%	0.755
V100%	47.99%	60.6%	0.343

Table 3: Incidence of Acute Toxicities

Toxicity	Week 1	Week 2	Week 3	Week 4	Week 5	Week 6	Total Cases (%)
Fatigue	2	5	3	1	0	0	11 (44%)
Dermatitis (Grade I)	3	7	10	4	2	1	14 (56%)
Dermatitis (Grade II)	0	1	2	1	0	0	4 (16%)
Dermatitis (Grade III)	0	0	0	1	0	0	1 (4%)
Cough	0	3	2	0	0	0	5 (20%)
Throat Irritation	0	2	1	0	0	0	3 (12%)

The study reported minimal acute toxicities, with mild fatigue in 20% and Grade I or II dermatitis in 40% of patients. No cases of Grade IV toxicity or acute radiation pneumonitis were observed. Patients were followed up for six weeks, with only one case showing distant metastasis. Heart and lung dose constraints were achieved in 75% of cases, with slightly higher volumes in left-sided irradiation.
The data confirmed that hypo-fractionated post-mastectomy radiotherapy was feasible and tolerable, supporting further investigation into its potential as a standard treatment approach.

Discussion

Breast cancer is one of the most commonly diagnosed cancers globally, with significant morbidity and mortality, particularly in women [11]. While advancements in early detection and treatment have improved survival rates, effective local control remains essential to reduce recurrence. Surgery, chemotherapy, and radiotherapy are integral components of breast cancer management, tailored to each patient's cancer stage, molecular subtype, and overall health status [12]. Post-mastectomy radiotherapy (PMRT) is widely used to lower the risk of local recurrence, especially in patients with high-risk features, such as large tumors or lymph node involvement [13]. Conventionally, PMRT is administered over five to six weeks; however, hypofractionated PMRT—delivering higher doses over a shorter period—has gained attention as a time-efficient and potentially less costly alternative [14]. While research in breast-conserving settings supports hypofractionation's efficacy, studies on its safety and tolerability in the post-mastectomy context are ongoing.
Our study of 25 breast cancer patients treated with hypofractionated PMRT found this regimen to be feasible and well-tolerated, with low incidences of severe toxicity. Acute toxicities were manageable: 56% of patients experienced Grade I dermatitis, 16% Grade II, and only one patient (4%) had Grade III. Mild fatigue was common but did not interrupt treatment. This is consistent with findings by Hasan *et al*., who reported that 54% of patients in their study had Grade I dermatitis, with only 2% experiencing Grade III [15]. Similarly, a study by Fowble *et al*. on 35 post-mastectomy patients reported tolerability levels in line with ours, with a majority experiencing only mild-to-moderate skin reactions, indicating a low risk for high-grade toxicity in hypofractionated PMRT [16].
Another relevant study by De Boer *et al*. examined hypofractionated PMRT outcomes in a cohort of 70 patients and found that only 4% experienced severe (Grade III or higher) skin toxicity, with most patients developing Grade I or II dermatitis [17]. The De Boer study reinforces our findings, demonstrating hypofractionation's tolerability. Moreover, Khanna *et al*. found a positive correlation between higher BMI and toxicity incidence in their study of 60 patients, similar to our results where patients with higher BMI were more likely to develop skin reactions [18].

Conclusion

This study demonstrates that hypofractionated post-mastectomy radiotherapy is a feasible and well-tolerated treatment option for breast cancer patients, with minimal severe toxicity and manageable side effects. The findings support hypofractionation as a safe and efficient alternative to conventional PMRT, particularly beneficial in reducing treatment time and patient burden. Notably, BMI influenced toxicity, suggesting the need for further investigation into personalized dose modifications for overweight patients. Additional studies with larger cohorts and extended follow-up are recommended to confirm these results and optimize PMRT protocols.

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Conflicts of Interest

The authors declare no conflicts of interest related to this study.

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