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Comparison Of Acute Skin Toxicity In Simultaneous Integrated Boost Vs Sequential Boost In Early Breast Cancer

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Article Details

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ABSTRACT

Objectives: To compare the acute skin toxicity in hypo fractionated radiotherapy with sequential boost vs simultaneous integrated boost. Materials and Methods: This Prospective comparative observational study was conducted in the Department of Radiation Oncology, CMH Rawalpindi from June 2024 to June 2025. After ethical approval, 50 eligible patients were enrolled with consent and divided into SIB and SEQ groups. SIB received 50.4 Gy with a simultaneous boost to 60.2 Gy, while SEQ received 50 Gy followed by 10–16 Gy sequential boost. Acute skin toxicity was assessed weekly using RTOG criteria by a blinded oncologist. Data were collected via a questionnaire and analyzed using SPSS version 25. Results: The mean patient age was 46.38 ± 12.22 years. Age distribution differed significantly between groups ($p = 0.02$). Higher-grade skin toxicity (Grade 3) was less frequent in the SIB group (12%) than SEQ (32%), but the overall difference in skin toxicity was not statistically significant ($p = 0.16$). Conclusion: It was concluded that the present study highlights the comparative safety of SIB versus SEQ in breast-conserving therapy, with a lower incidence of higher-grade skin toxicity seen in the SIB group despite no significant difference. Larger studies with longer follow-up are needed to confirm these findings and evaluate long-term outcomes..

INTRODUCTION

Breast cancer is most common cancer in females worldwide.(1, 2) It is the second leading cause of deaths amongst women.(3) Pakistan has the highest incidence of Breast Cancer in Asia.(4) It is estimated that 1 in 9 women may develop Breast Cancer in their lifetime.(5) Post-operative radiotherapy is the mainstay of the treatment of early breast cancer after breast conserving surgery for prevention of local recurrence and improvement of overall survival.(6) The 2011 meta-analysis conducted by the Early Breast Cancer Trialists' Collaborative Group demonstrated a 15.7% reduction in overall breast cancer recurrence at 10 years post-treatment, which translated into a 3.8% improvement in breast cancer-specific survival at 15 years. The addition of a boost to the tumor bed has been shown to further enhance local control. Notably, the 20-year results of the EORTC boost trial reported an absolute reduction in local recurrence of 4.4%, with a hazard ratio of 0.65.

Breast-conserving therapy, consisting of breast-conserving surgery followed by adjuvant radiotherapy, is now an established standard in the treatment of early breast cancer.(7) To reduce the risk of local recurrence, a boost an additional dose of radiation is often delivered to the tumor bed.(8)

Traditionally, this so-called "sequential boost" (SEQ) is administered after completion of whole-breast radiation therapy.(9) A modern alternative is "simultaneous integrated boost" (SIB), in which the boost dose is delivered simultaneously with whole-breast radiation therapy, shortening overall treatment time and potentially offering dosimetric advantages.(10)

An important consideration in the evaluation of both techniques is acute skin toxicity, as it can impact patients' quality of life and complicate the treatment process. The aim of this study is to compare acute skin toxicity between the SIB and SEQ procedures in patients with early breast cancer in order to better assess the tolerability and potential benefits of each method.

Objective: To compare the acute skin toxicity in hypo fractionated radiotherapy with sequential boost vs simultaneous integrated boost.

MATERIALS AND METHODS

STUDY DESIGN: Prospective comparative observational study.

STUDY SETTING: Department of Radiation Oncology, CMH Rawalpindi.

DURATION OF THE STUDY: Duration of the study was one year (from June 2024 to June 2025).

SAMPLING TECHNIQUE: • Simple Random Sampling technique was used for the recruitment of patients.

INCLUSION CRITERIA

- Only female patients.
- Patients of age 18-70 years.
- Patients who had undergone breast-conserving surgery (BCS).
- Patients who were diagnosed with carcinoma of the breast, classified as clinical stage T1 to T3 with any nodal status (cT1–cT3N).

EXCLUSION CRITERIA

- Pregnant women.
- Those with pre-existing skin diseases such as systemic lupus erythematosus (SLE) or erythroderma.
- Patients who had previously received radiotherapy to the chest or breast region.
- Patients with recurrent or metastatic breast cancer.

METHODS: Following approval from the Ethical Committee of CMH Rawalpindi, patients who fulfilled the inclusion criteria were identified and enrolled after obtaining written informed consent, either from the patients themselves or their guardians. Each participant underwent a detailed medical history review along with a comprehensive physical examination. A total of 50 patients divided into two groups (Group A= Simultaneous Integrated Boost (SIB) and Group B= sequential boost) were included in the study. Simultaneous Integrated Boost (SIB) group received whole-breast radiotherapy with a concurrent boost to the tumor bed in a single treatment plan using intensity-modulated radiation therapy (IMRT) or volumetric-modulated arc therapy (VMAT). The total dose was typically 50.4 Gy in 28 fractions to the whole breast with a simultaneous boost of 60.2 Gy to the tumor bed. While Sequential Boost (SEQ) group received 50 Gy in 25 fractions to the whole breast followed by a sequential tumor bed boost of 10–16 Gy in 5–8 fractions.

Acute skin toxicity was evaluated weekly throughout the course of radiotherapy and again two weeks after treatment completion, using the Radiation Therapy Oncology Group (RTOG) grading criteria. These criteria classify skin reactions as follows: Grade 0 indicates no change; Grade 1 denotes faint erythema or dry desquamation; Grade 2 reflects moderate to brisk erythema with patchy moist desquamation; Grade 3 represents confluent moist desquamation or bleeding; and Grade 4 indicates ulceration or necrosis. All assessments were conducted by an experienced radiation oncologist who was blinded to the treatment group allocation. A predesign questionere was used to collect data. The collected data were entered and analyzed using the Statistical Package for Social Sciences (SPSS) Version 25 software.

RESULTS: The mean age of the patients was 46.38 ± 12.22 years. In terms of age distribution, 16% of patients were between 18–30 years, 10% were between 31–40 years, 42% were in the 41–50 year age group, 14% were between 51–60 years, and 18% were older than 60 years (Table 1). Among the 25 patients in each group, the age distribution showed that in the SIB group, 20% were aged 18–30 years, none were in the 31–40 years range, 36% were 41–50 years, 12% were 51–60 years, and 32% were above 60 years. In comparison, the SEQ group had 12% aged 18–30 years, 20% aged 31–40 years, 48% aged 41–50 years, 16% aged 51–60 years, and 4% above 60 years, with a statistically significant difference between the groups (p = 0.02). Regarding acute skin toxicity based on RTOG grading, Grade 0 was observed in 12% of the SIB group and 4% of the SEQ group; Grade 1 in 40% and 20%, respectively; Grade 2 in 36% and 44%; and Grade 3 in 12% and 32%, with no statistically significant difference between the two groups (p = 0.16) (Table 2).

TABLE 1: DISTRIBUTION OF PATIENTS BY AGE *(N=50)*

Variables	
Age (Years)	46.38±12.22
Age Groups	
18-30 years	16(16.0%)
31-40 years	5(10.0%)
41-50 years	21(42.0%)
51-60 years	7(14.0%)
>60 years	9(18.0%)

TABLE 2: COMPARISON OF AGE GROUPS AND RTOG SKIN TOXICITY GRADES BETWEEN SIB AND SEQ GROUPS (N = 50)

Variables	**Groups**		**p-value**
	SIB Group	**SEQ Group**	

	(n = 25)	(n = 25)	
Age Groups			
18-30 years	5(20.0%)	3(12.0%)	
31-40 years	0(0.0%)	5(20.0%)	
41-50 years	9(36.0%)	12(48.0%)	0.02
51-60 years	3(12.0%)	4(16.0%)	
>60 years	8(32.0%)	1(4.0%)	
RTOG Skin Toxicity Grade			
Grade 0	3(12.0%)	1(4.0%)	
Grade 1	10(40.0%)	5(20.0%)	
Grade 2	9(36.0%)	11(44.0%)	0.16
Grade 3	3(12.0%)	8(32.0%)	

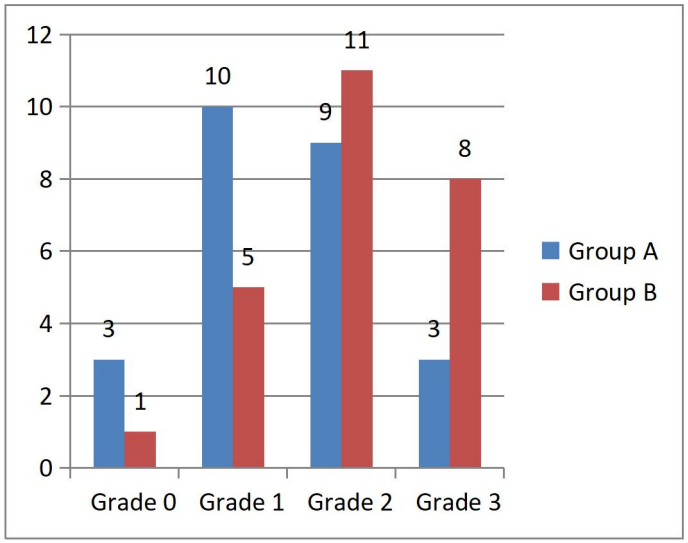

FIG 1: FREQUENCY OF PATIENTS ON THE BASIS OF RTOG SKIN TOXICITY GRADE

DISCUSSION: The main aim of the present study was to compare the incidence and severity of acute skin toxicity between SIB and SEQ radiotherapy techniques in patients with early-stage breast cancer. Our findings revealed that while the SIB group demonstrated a lower incidence of higher-grade acute skin toxicity compared to the SEQ group, the difference was not statistically significant. Specifically, the proportion of patients developing Grade 3 toxicity was notably lower in the SIB group (12%) compared to the SEQ group (32%). This suggests a potential clinical benefit of the SIB approach in minimizing severe skin reactions, although the limited sample size may have affected the ability to detect a statistically significant difference. Our study was supported by the study conducted by Paelinck et al. that observed a significantly higher incidence of acute grade 2/3 skin toxicity with a sequential boost as compared to SIB.(11) Van Parijs et al.(12) reported that there was no difference in acute skin tolerance between patients treated with a normofractionated schedule followed by a sequential boost and those receiving moderate hypofractionation combined with a simultaneous boost in their randomized trial. Findings from the IMPORT-High trial indicated that the use of a simultaneous integrated boost (SIB) is a safe technique that also reduces the number of hospital visits required for treatment.(13) Our study finding are consistent with a number of studies,

which have reported that the SIB technique, by delivering the boost dose concurrently with whole breast irradiation, reduces overall treatment time and may offer better dose conformity and skin sparing.

The observed trend favoring SIB may be attributed to the advanced radiation delivery techniques such as IMRT and VMAT, which allow for precise dose modulation, reducing unnecessary radiation exposure to the surrounding healthy skin and tissues. Moreover, reducing the overall treatment duration with SIB could improve patient convenience and compliance, which is particularly valuable in clinical practice.

However, this study has certain limitations. The sample size was relatively small, which may limit the generalizability of the findings. Additionally, the follow-up period was focused on acute toxicity, and longer-term follow-up would be necessary to assess late skin effects, cosmetic outcomes, and local tumor control. Moreover, the baseline skin characteristics and other confounding factors such as BMI, smoking status, and comorbidities, which may influence skin toxicity, were not controlled in this study. Despite these limitations, the study provides valuable insights into the safety profile of SIB compared to sequential boost techniques in breast-conserving therapy. Future studies with larger cohorts and longer follow-up periods are warranted to confirm these findings and evaluate long-term outcomes, including cosmesis, fibrosis, and tumor control.

CONCLUSION: It was concluded that the present study offers meaningful insights into the comparative safety of the SIB versus SEQ techniques in breast-conserving therapy. Although no statistically significant difference in acute skin toxicity was observed, the lower incidence of higher-grade toxicity in the SIB group suggests a potential clinical advantage. Future research involving larger patient populations and extended follow-up is essential to validate these findings and to assess long-term outcomes such as cosmetic results, fibrosis, and local tumor control.

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