JHWCR JOURNAL OF HEALTH, WELLNESS AND COMMUNITY RESEARCH 3007-0570

https://doi.org/10.61919/t7espy64

Original Article

Study of Acute and Late Side Effects in Breast Cancer Patients Treated with Ultra-Hypo-Fractionated Radiation Therapy

Muhammad Ikrama Tanveer[1], Daniyal Ahmed Sami[1], Anusha Haider[1], Maria Qureshi[1]

[1] Department of Radiation Oncology, Shaukat Khanum Hospital, Lahore, Pakistan

*** Corresponding author: Muhammad Ikrama Tanveer, Ikramatanveer@gmail.com**

ABSTRACT

Background: Breast cancer imposes a substantial clinical burden in Pakistan, and shorter radiotherapy schedules may improve patient convenience and optimize limited oncology resources. Ultra-hypofractionated breast radiotherapy has gained increasing acceptance internationally, but local real-world toxicity data remain limited. Objective: To evaluate the acute and late side effects of ultra-hypofractionated adjuvant breast radiotherapy in patients with breast cancer treated at a tertiary cancer center in Pakistan. Methods: This retrospective observational study included 86 adult female patients with node-negative breast cancer treated between January 2021 and December 2022 with 26 Gy in 5 fractions, with or without a boost of 10 Gy in 5 fractions. Toxicities were assessed using Common Terminology Criteria for Adverse Events version 5 at the end of treatment, 4, 8, and 12 weeks, and at 6 and 12 months. Results: The mean age was 43.8 years. Most patients received field-in-field radiotherapy (82.6%). Radiation dermatitis was the most frequent acute toxicity, with 59.3% Grade 0, 38.4% Grade 1, and 2.3% Grade 2 events; no Grade 3-4 dermatitis occurred. Radiation pneumonitis was observed in 4.7%, acute lymphedema in 2.3%, and skin hyperpigmentation in 2.3%, all of low grade. Among 57 patients with long-term follow-up, breast fibrosis occurred in 14.0% and late lymphedema in 3.5%. Conclusion: Ultra-hypofractionated breast radiotherapy showed an overall favorable and clinically manageable toxicity profile in this cohort, supporting its practical use in routine care, although larger prospective comparative studies are needed. Keywords: Breast radiotherapy, ultra-hypofractionation, radiation dermatitis, radiation pneumonitis, breast fibrosis, toxicity

"Cite this Article" | Received: 20 September 2025; Accepted: 18 March 2026; Published: 30 March 2026.

Author Contributions: Concept: MIT; Design: MIT, DAS; Data Collection: MIT, AH, MQ; Analysis: DAS, AH; Drafting: MIT, DAS, AH, MQ. **Ethical Approval**: Ethical Approval was obtained by respective Institute**.** Informed Consent: Written informed consent was obtained from all participants; Conflict of Interest: The authors declare no conflict of interest; Funding: No external funding; Data Availability: Available from the corresponding author on reasonable request; Acknowledgments: N/A.

INTRODUCTION

Breast cancer remains the most frequently diagnosed malignancy among women worldwide and continues to impose a major clinical and public health burden, particularly in low- and middle-income countries where delayed diagnosis, restricted access to comprehensive oncology services, and limited radiotherapy capacity can adversely affect outcomes (1). In Pakistan, the burden of breast cancer is especially substantial, with a high annual case load that places sustained pressure on diagnostic, surgical, systemic, and radiation treatment services (1). Within this context, adjuvant radiotherapy is a fundamental component of breast cancer management after breast-conserving surgery and in selected post-mastectomy settings because of its established role in reducing local recurrence and improving long-term disease control (2). The increasing demand for radiotherapy, however, has amplified the need for treatment schedules that maintain safety and therapeutic effectiveness while also improving patient convenience and optimizing institutional resources.

Conventionally fractionated and moderately hypofractionated whole-breast irradiation schedules have long been accepted in routine clinical practice, but growing evidence has supported the use of ultra-hypofractionated regimens that deliver treatment over a substantially shorter time period (3,4). This shift has been driven by both clinical and logistical considerations, including patient travel burden, treatment adherence, machine availability, and overall health system efficiency. Shorter regimens are

particularly attractive in resource-constrained settings because they may reduce waiting times and improve treatment access without increasing the burden on patients who must repeatedly travel for therapy. In addition, technical advances in treatment planning and delivery, including three-dimensional conformal radiotherapy and field-in-field intensity-modulated approaches, have improved dose homogeneity and reduced unnecessary exposure to surrounding normal tissues, thereby supporting the feasibility of shorter fractionation schedules in appropriately selected patients (5,6).

Despite the increasing international acceptance of ultra-hypofractionated breast radiotherapy, local real-world toxicity data remain limited, especially in South Asian populations and routine clinical environments outside of controlled trial settings. Acute skin reactions, radiation pneumonitis, lymphedema, pigmentation changes, and late fibrosis remain clinically relevant endpoints because tolerability strongly influences treatment completion, patient satisfaction, and the practical adoption of abbreviated protocols. Previous work has shown that short-course breast irradiation can produce acceptable acute skin toxicity profiles, but the pattern and severity of treatment-related adverse effects may still vary according to patient characteristics, treatment technique, institutional workflow, and follow-up practices (7,8). Accordingly, locally generated outcome data are important for determining whether these regimens remain well tolerated in routine practice and whether their implementation is justified in settings with finite radiotherapy infrastructure.

The present study was undertaken to address this evidence gap by evaluating the acute and late treatment-related toxicities observed in breast cancer patients treated with ultra-hypofractionated adjuvant radiotherapy at a tertiary cancer center in Pakistan. The specific objective was to describe the frequency, timing, and severity of acute dermatitis, pneumonitis, lymphedema, skin hyperpigmentation, and selected late toxicities after delivery of 26 Gy in 5 fractions with or without boost, and to assess whether the observed toxicity profile supports the practical use of this shortened schedule in routine breast cancer care (1-8).

MATERIALS AND METHODS

This retrospective observational study was conducted in the Department of Clinical and Radiation Oncology at Shaukat Khanum Memorial Cancer Hospital and Research Centre, Peshawar, Pakistan, and included patients treated between January 2021 and December 2022. The study was designed to evaluate the acute and late toxicity profile of ultra-hypofractionated adjuvant breast radiotherapy delivered in routine clinical practice. A retrospective design was appropriate because the objective was to assess real-world tolerability using existing treatment and follow-up records from patients who had already completed radiotherapy according to institutional protocols. Ethical approval was obtained from the Institutional Review Board of Shaukat Khanum Memorial Trust under reference number EX-03-01-23-01-A1. Patient confidentiality was maintained throughout data extraction, handling, and analysis by using institutional records solely for research purposes and restricting access to de-identified study data.

The study population comprised adult female patients aged more than 18 years with histologically confirmed breast cancer who underwent adjuvant external beam radiotherapy to the breast or chest wall using an ultra-hypofractionated schedule of 26 Gy in 5 fractions, with or without an additional boost of 10 Gy in 5 fractions. Eligible patients had node-negative disease within the clinical stage range cT1 to cT3 and had undergone breast-conserving surgery before radiotherapy. Patients were included if their records contained sufficient treatment and follow-up documentation for assessment of acute toxicity outcomes. Patients were excluded if they had a prior history of ipsilateral chest irradiation, bilateral breast involvement, pre-existing connective tissue disorders likely to alter radiation-related skin sensitivity, or incomplete clinical records preventing reliable toxicity grading during scheduled follow-up. To reduce selection ambiguity and improve reproducibility, the analysis was restricted to all eligible cases meeting these criteria during the study period, thereby reflecting a consecutive real-world institutional cohort rather than a selectively sampled subgroup.

Clinical, pathological, treatment, and toxicity data were extracted from the institutional electronic hospital information system using a structured review of the medical records. Variables collected included patient age, menopausal status where available, tumor laterality, histopathological subtype, nodal status, radiotherapy planning technique, dose schedule, and treatment-related toxicities recorded during follow-up. The principal study outcomes were acute and late radiation-related toxicities. Acute toxicities were operationally defined as adverse events recorded from the end of treatment up to the 12-week post-treatment period, whereas late toxicities were defined as adverse events documented at 6 and 12 months after treatment completion.

Toxicity severity was assessed according to the Common Terminology Criteria for Adverse Events version 5, which provided standardized grading for radiation dermatitis, radiation pneumonitis, lymphedema, skin hyperpigmentation, and fibrosis. This use of a recognized toxicity framework strengthened consistency in outcome classification across patient records.

All patients received treatment on linear accelerators in the supine position using a breast board for immobilization. Treatment planning was performed using either three-dimensional conformal radiotherapy or field-in-field intensity-modulated radiotherapy according to institutional practice and dosimetric suitability. The target volume for adjuvant therapy included the whole breast, with boost treatment delivered where indicated to the tumor bed.

The planning objective was to ensure adequate target coverage while minimizing dose exposure to adjacent healthy tissues. Image guidance procedures included cone-beam computed tomography during the first three treatment days when required for setup verification, with additional cone-beam imaging in patients receiving a boost to improve precision of dose delivery. Quality assurance procedures included an independent double-check of treatment planning and delivery parameters to enhance treatment accuracy and patient safety.

Follow-up assessments were organized according to routine departmental practice at the end of treatment and again at 4, 8, and 12 weeks after treatment, followed by late evaluations at 6 and 12 months. This schedule was used to capture both the immediate onset and short-term resolution pattern of acute toxicity, as well as selected persistent or delayed adverse effects.

The primary analytical focus was the frequency and grade distribution of acute toxicities, particularly radiation dermatitis and pneumonitis, while secondary outcomes included lymphedema, skin hyperpigmentation, and late fibrosis. Recording toxicity at prespecified follow-up intervals improved temporal consistency in outcome ascertainment and allowed the pattern of adverse effects to be interpreted in relation to treatment completion.

Several measures were applied to strengthen internal validity and reduce bias within the constraints of retrospective design. Eligibility criteria were defined before data extraction to reduce case selection inconsistency. Standardized CTCAE grading was used to limit outcome misclassification.

Because treatment technique was not randomly assigned and may have been influenced by routine clinical judgment, technique-related comparisons were interpreted descriptively and with caution as potentially confounded by baseline or planning-related factors. Missing late follow-up data were not imputed; instead, acute toxicity analyses were based on the full eligible cohort with available early follow-up records, whereas late toxicity analyses were restricted to patients with documented 6- and 12-month assessments. This complete-case approach was appropriate for a retrospective dataset but was recognized as a potential source of attrition bias in interpretation of long-term findings.

The sample size was determined by the total number of eligible patients treated during the predefined study period, yielding 86 patients for the acute toxicity analysis. Rather than estimating effect size through prospective power calculation, the study was designed as a census of all available eligible cases in the institutional database over 23 months, which improved representativeness of local practice and

allowed a pragmatic evaluation of tolerability in this treatment setting. For late toxicity outcomes, only patients with available long-term follow-up data were included in the corresponding analysis set.

Data were entered, cleaned, and analyzed using Microsoft Excel and SPSS version 26. Continuous variables were summarized using means and distributions, while categorical variables were presented as frequencies and percentages.

Toxicity grades were tabulated across follow-up intervals and by treatment technique where relevant. For exploratory comparison of categorical toxicity outcomes between planning techniques, appropriate significance testing was undertaken and p-values were reported, with statistical significance interpreted at a two-sided threshold of less than 0.05. Because the study was primarily descriptive and retrospective, findings were interpreted with emphasis on magnitude, frequency, and clinical pattern rather than causal inference. Data integrity was supported through record cross-checking during extraction and consistency review before final analysis.

RESULTS

A total of 86 women were included in the study and received ultra-hypofractionated adjuvant radiotherapy at a dose of 26 Gy in 5 fractions, with or without sequential boost. The cohort was relatively young, with a mean age of 43.8 years, and the age distribution peaked between 35 and 50 years. Right-sided disease was slightly more frequent than left-sided disease, accounting for 54.7% (47/86) versus 45.3% (39/86), respectively. Invasive ductal carcinoma was the predominant histological subtype, and no patient had lymph node involvement. Most patients were treated using the field-in-field technique, which was used in 82.6% (71/86) of cases, whereas 17.4% (15/86) received three-dimensional conformal radiotherapy. This distribution reflects a clear institutional preference for forward-planned field-in-field treatment in routine breast irradiation practice.

Table 1. Baseline Clinical and Treatment Characteristics of the Study Population (n = 86)

Variable	Category	n	%
Age	**Mean age, years**	**43.8**	**—**
Tumor laterality	**Left breast**	**39**	**45.3**
	Right breast	**47**	**54.7**
Histology	**Invasive ductal carcinoma**	**Predominant**	**—**
Nodal status	**Node-negative**	**86**	**100.0**
Radiotherapy technique	**3D conformal radiotherapy**	**15**	**17.4**
	Field-in-field IMRT	**71**	**82.6**
Fractionation schedule	**26 Gy in 5 fractions ± boost**	**86**	**100.0**

Radiation dermatitis was the most frequent acute toxicity. Overall, 59.3% (51/86) of patients had no dermatitis, 38.4% (33/86) developed Grade 1 dermatitis, and 2.3% (2/86) developed Grade 2 dermatitis, while no Grade 3 or Grade 4 events were reported.

The highest burden of acute skin toxicity occurred at the end of treatment, indicating that most reactions were early, mild, and self-limiting. When dermatitis grades were compared by planning technique, higher-grade reactions remained uncommon in both groups, and the association between technique and dermatitis severity was not statistically significant ($p = 0.43$). These findings support the tolerability of the regimen across both treatment approaches, although the larger field-in-field subgroup contributed most observed Grade 1 events by absolute count.

Table 2. Acute Radiation Dermatitis Overall and by Planning Technique (n = 86)

Outcome	Category	3D-CRT n (%)	FiF n (%)	Total n (%)	p-value
Radiation dermatitis	Grade 0	Not fully disaggregated	Not fully disaggregated	51 (59.3)	0.43
	Grade 1	Not fully disaggregated	Not fully disaggregated	33 (38.4)	
	Grade 2	0 reported in text	2 reported in text	2 (2.3)	
	Grade 3–4	0	0	0 (0.0)	

Skin hyperpigmentation was distinctly uncommon. Grade 0 hyperpigmentation was observed in 97.7% (84/86) of patients, while only 2.3% (2/86) developed Grade 1 hyperpigmentation; both cases occurred in the field-in-field group. Given the overwhelming predominance of Grade 0 findings, this endpoint further supports the skin-sparing profile of the abbreviated schedule. Acute pulmonary toxicity was also infrequent. Radiation-induced pneumonitis was absent in 95.3% (82/86) of patients, and only 4.7% (4/86) experienced Grade 1 pneumonitis, with no higher-grade events documented. Acute lymphedema was similarly rare, occurring in only 2.3% (2/86) of patients, both at Grade 1 intensity. Collectively, these findings indicate that non-dermatologic acute toxicities remained uncommon and clinically manageable in this cohort.

Table 3. Acute Non-Dermatologic Toxicities After Ultra-Hypofractionated Radiotherapy (n = 86)

Toxicity	Grade 0 n (%)	Grade 1 n (%)	Grade 2+ n (%)	Total with Any Toxicity n (%)
Skin hyperpigmentation	84 (97.7)	2 (2.3)	0 (0.0)	2 (2.3)
Radiation pneumonitis	82 (95.3)	4 (4.7)	0 (0.0)	4 (4.7)
Acute lymphedema	84 (97.7)	2 (2.3)	0 (0.0)	2 (2.3)

Long-term assessment was available for 57 patients, as 27 of the original 86 patients were excluded from chronic toxicity analysis because 6- and 12-month follow-up data were not available by the time of study closure. Among evaluable patients, late toxicities remained limited. Symptomatically tolerable lymphedema was present in 3.5% (2/57) and breast fibrosis in 14.0% (8/57). Fibrosis therefore emerged as the most frequent late adverse effect, but even this remained confined to a minority of patients. The pattern suggests that while acute toxicity was dominated by mild skin reactions, the principal late concern was fibrosis rather than persistent edema or pulmonary morbidity.

Table 4. Late Toxicities Among Patients With Available Long-Term Follow-Up (n = 57)

Toxicity	No Toxicity n (%)	Toxicity Present n (%)
Late lymphedema	55 (96.5)	2 (3.5)
Breast fibrosis	49 (86.0)	8 (14.0)

A clinically relevant pattern emerges when acute and late toxicities are considered together. Any-grade dermatitis affected 40.7% (35/86), making it the dominant adverse event overall, whereas any pneumonitis occurred in only 4.7% (4/86) and acute lymphedema in 2.3% (2/86). Among late events, fibrosis affected 14.0% (8/57), exceeding late lymphedema at 3.5% (2/57). This indicates that the toxicity

profile was characterized primarily by mild early skin reactions and relatively infrequent late structural sequelae, with pulmonary and lymphatic complications remaining rare.

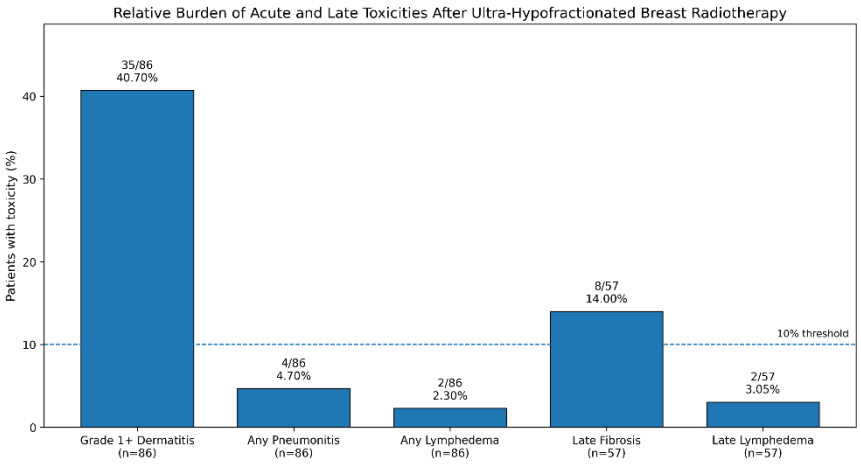

Figure 1

The figure demonstrates a strongly asymmetric toxicity profile in which any-grade radiation dermatitis was the dominant adverse event, affecting 40.7% (35/86) of patients, whereas any pneumonitis and acute lymphedema remained low at 4.7% (4/86) and 2.3% (2/86), respectively. Among late outcomes, fibrosis was the most frequent delayed toxicity at 14.0% (8/57), exceeding late lymphedema at 3.05% (2/57), but still remaining well below the burden of acute skin toxicity. Clinically, this pattern indicates that the regimen was associated mainly with early mild cutaneous reactions rather than substantial pulmonary or lymphatic morbidity, while late fibrosis represented the principal persistent toxicity signal within the available follow-up subset.

DISCUSSION

This study evaluated the acute and late toxicity profile of ultra-hypofractionated adjuvant breast radiotherapy delivered as 26 Gy in 5 fractions, with or without boost, in a real-world Pakistani cohort treated at a tertiary cancer center. The findings indicate that the regimen was generally well tolerated, with most adverse events being mild and transient. Acute radiation dermatitis was the most frequent toxicity, affecting 40.7% of patients overall, but nearly all events were limited to Grades 1–2, with no Grade 3 or 4 dermatitis reported. Non-cutaneous acute toxicities were uncommon, as radiation pneumonitis occurred in 4.7% of patients and acute lymphedema in 2.3%, while skin hyperpigmentation was observed in only 2.3%. Among the subset with available long-term follow-up, late fibrosis was identified in 14.0% and late lymphedema in 3.5%, indicating that persistent toxicity was present in a minority of evaluable patients. Taken together, these results support the practical tolerability of ultra-hypofractionated breast irradiation in routine clinical practice within a resource-constrained setting (3,4,7,8).

The predominance of low-grade acute skin toxicity observed in this study is consistent with the broader evolution of breast radiotherapy toward shorter fractionation schedules supported by improved planning and delivery techniques. Prior clinical evidence has shown that abbreviated breast irradiation regimens can maintain acceptable normal tissue toxicity while reducing treatment burden, and the present data align with that trajectory by demonstrating that more than half of the cohort remained free of dermatitis and only 2.3% experienced Grade 2 skin toxicity (3,7,8). The absence of severe dermatitis is clinically important because skin toxicity is one of the most visible and treatment-limiting adverse effects in breast radiotherapy. The temporal pattern in this cohort, with the highest frequency of dermatitis at the end of treatment and subsequent decline across follow-up, further suggests that most acute reactions were self-limited and compatible with routine outpatient management. These findings are relevant for patient

counseling, as they support the expectation that abbreviated treatment can reduce overall time on therapy without substantially increasing acute toxicity burden (7,8).

The low incidence of radiation pneumonitis in this study also supports the feasibility of this regimen. Only 4.7% of patients developed pneumonitis, all of which were Grade 1, with no more severe pulmonary events documented. This is reassuring because pulmonary toxicity remains a key concern in breast irradiation, particularly in left-sided cases and when normal tissue dose constraints are not rigorously maintained (9).The low pneumonitis rate in this cohort likely reflects careful treatment planning, patient positioning, and image-guided verification practices, all of which were incorporated into routine delivery. Likewise, the rarity of acute lymphedema and skin hyperpigmentation suggests that the radiation schedule and associated planning techniques did not impose a substantial short-term burden on lymphatic or superficial cutaneous structures in most patients. These findings collectively indicate that ultra-hypofractionated treatment was associated mainly with manageable skin reactions rather than clinically substantial pulmonary or lymphatic morbidity (5,6).

An additional point of clinical interest is the distribution of treatment techniques used in this cohort. Most patients were treated with field-in-field radiotherapy rather than conventional 3D conformal planning, reflecting institutional preference for a technique that offers improved dose homogeneity and reduced hot spots within the breast tissue (6). Although a statistical comparison of dermatitis grade by technique did not show significance, and the reported p-value was 0.43, this finding should be interpreted cautiously because the groups were imbalanced in size and the study was not designed or powered for comparative effectiveness analysis. Nevertheless, the predominance of field-in-field planning in a setting where severe skin toxicity remained absent is operationally relevant. It suggests that the safe implementation of short-course regimens may depend not only on fractionation schedule but also on the quality of treatment planning and delivery infrastructure available at the treating institution (5,6).

The observed late toxicity profile also merits careful interpretation. Among patients with available long-term follow-up, fibrosis was the most frequent delayed adverse event, identified in 14.0%, whereas late lymphedema remained uncommon at 3.5%. This pattern suggests that although acute toxicity was predominantly mild and reversible, a subset of patients may develop persistent tissue changes after treatment completion. However, the late toxicity estimates should not be overinterpreted because only 57 of the original 86 patients were evaluable for chronic outcomes. The exclusion of 27 patients due to unavailable 6- and 12-month follow-up data introduces the possibility of attrition bias, and the true incidence of late effects may therefore be somewhat different from the observed estimates. This limitation is particularly important because late fibrosis can influence cosmesis, comfort, and long-term patient satisfaction even when oncologic treatment has been successfully completed. Accordingly, future studies should prioritize more complete longitudinal follow-up and standardized late-effect reporting to better characterize durability of tolerability in this population (7,8).

This study has several strengths. It provides real-world evidence from Pakistan, where local toxicity data on ultra-hypofractionated breast radiotherapy remain limited despite the practical relevance of shorter schedules in busy oncology centers. It also reflects routine institutional practice rather than tightly controlled trial conditions, thereby offering insight into how abbreviated treatment performs under standard service delivery conditions. At the same time, important limitations should be acknowledged. The retrospective single-center design limits causal inference and external generalizability. The study did not include a concurrent comparison arm treated with conventional or moderately hypofractionated radiotherapy, and therefore the findings should not be framed as evidence of non-inferiority. The sample size was based on all eligible cases over the study period rather than formal prospective power estimation, and toxicity analyses were primarily descriptive. Some results in the source text were also not fully granular by subgroup, which restricted deeper comparative tabulation. In addition, the inconsistency in one reported dermatitis percentage at the third follow-up highlights the need for stricter numeric verification during manuscript preparation. These limitations do not negate the findings, but

they indicate that the results should be interpreted as supportive observational evidence rather than definitive comparative proof (3,4,7,8).

From a health-system perspective, the findings remain meaningful. In a country where radiotherapy access, machine time, travel costs, and patient throughput can all influence treatment completion, a 5-fraction regimen that demonstrates low rates of serious toxicity has practical value. Shorter schedules may reduce demand on institutional resources, improve patient convenience, and support more efficient use of radiotherapy infrastructure without materially worsening short-term tolerability. For breast cancer services in resource-limited environments, this is a highly relevant operational advantage. Future work should expand on these findings through prospective multicenter studies with longer follow-up, predefined primary toxicity endpoints, more robust inferential analysis, and comparison against standard fractionation pathways so that safety, patient-reported outcomes, cosmetic results, and service-delivery benefits can be evaluated in a more comprehensive and methodologically rigorous manner (1,3,4,7).

CONCLUSION

Ultra-hypofractionated adjuvant breast radiotherapy delivered as 26 Gy in 5 fractions, with or without boost, demonstrated an overall favorable toxicity profile in this single-center retrospective cohort, with most acute adverse effects limited to mild dermatitis, very low rates of pneumonitis, lymphedema, and hyperpigmentation, and relatively infrequent late toxicity among patients with available follow-up. These findings support the practical tolerability of this shortened regimen in routine breast cancer care and suggest that it may be a clinically useful option in resource-constrained settings; however, the results should be interpreted within the limitations of retrospective design, incomplete long-term follow-up, and absence of a comparator group.

REFERENCES

1. Roonjha Q, Murtaza A, Kumar R, Sarwar A, Hussain T. Evaluation of knowledge and practice regarding breast self-examination by lady health workers working with Health Department Lasbela, Baluchistan, Pakistan. SSRN. 2020:3544845. doi:10.2139/ssrn.3544845.

2. Kikuchi K, Koyama H, Masuda H, Nomura Y, Sakai D, Sugimachi K, et al. Effects of radiotherapy and of differences in the extent of surgery for early breast cancer on local recurrence and 15-year survival. Lancet. 2005;366:2087-106. doi:10.1016/S0140-6736(05)67887-7.

3. Ratosa I, Chirilă ME, Steinacher M, Kozma E, Vojtíšek R, Franco P, et al. Hypofractionated radiation therapy for breast cancer: Preferences amongst radiation oncologists in Europe-results from an international survey. Radiother Oncol. 2021;155:17-26. doi:10.1016/j.radonc.2020.10.008.

4. Machiels M, Weytjens R, Bauwens W, Vingerhoed W, Billiet C, Huget P, et al. Accelerated adaptation of ultrahypofractionated radiation therapy for breast cancer at the time of the COVID-19 pandemic. Clin Oncol (R Coll Radiol). 2021;33:e166-71.

5. Nielsen MH, Berg M, Pedersen AN, Andersen K, Glavicic V, Jakobsen EH, et al. Delineation of target volumes and organs at risk in adjuvant radiotherapy of early breast cancer: National guidelines and contouring atlas by the Danish Breast Cancer Cooperative Group. Acta Oncol. 2013;52:703-10. doi:10.3109/0284186X.2013.765064.

6. Sameeullah F, Harrison DS, Greer DM, Coffey BJ. Fifth Toe Abduction in Brain Death/Death by Neurologic Criteria: Description of a New Spinal Reflex. Neurocritical Care. 2025 Dec 16:1-3.

7. Sasaoka M, Futami T. Dosimetric evaluation of whole breast radiotherapy using the field-in-field technique in early-stage breast cancer. Int J Clin Oncol. 2011;16:250-6. doi:10.1007/s10147-010-0175-1.

8. Brunt AM, Wheatley D, Yarnold J, Somaiah N, Kelly S, Harnett A, et al. Acute skin toxicity associated with a 1-week schedule of whole breast radiotherapy compared with a standard 3-week regimen delivered in the UK FAST-Forward Trial. Radiother Oncol. 2016;120:114-8. doi:10.1016/j.radonc.2016.02.027.

9. Lewis P, Brunt AM, Coles C, Griffin S, Locke I, Roques T. Moving forward fast with FAST-Forward. Clin Oncol (R Coll Radiol). 2021;33:427-9.