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ORIGINAL ARTICLE

FAST- Forward Radiotherapy in Breast Cancer Patients from a Turkish Cohort: A Study on Acute Skin Toxicity

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OBJECTIVE

This study aimed to evaluate early skin reactions in patients with breast cancer treated with the FAST -Forward radiotherapy regimen after surgery.

METHODS

Between December 2019 and August 2022, 60 patients with breast cancer received the FAST-Forward radiotherapy protocol: 26 Gy delivered in five fractions of 5.2 Gy each, using tangential field-in-field techniques.Treatments were administered on consecutive weekdays, and skin reactions were graded using the Radiation Therapy Oncology Group (RTOG) system in the second and sixth weeks after radiotherapy. The radiotherapy area and contralateral breast were photographed, and the patients were asked to report any breast swelling as a subjective symptom.

RESULTS

The median patient age was 71 years (range: 51-86). All had T1-2 and N0-1 disease and received adjuvant radiotherapy following surgery. In the second week after radiotherapy, 7 patients (11.6%) had grade 1 skin reactions and 1 patient (1.6%) had a grade 2 reaction. By the sixth week, five of the seven grade 1 reactions had resolved, with one remaining in grade 1 and one increasing to grade 2. The initial grade 2 reaction improved to a grade 1 reaction. None of the patients reported breast swelling in the second and sixth weeks after radiotherapy.

CONCLUSION

Considering the impact of skin reactions on the patients' quality of life, the FAST-Forward protocol appears to be a safe and comfortable option for patients who meet the appropriate criteria.

Keywords: Breast cancer; FAST-Forward protocol; hypofractionated radiotherapy; skin toxicity.

INTRODUCTION

The incidence of breast cancer continues to increase globally, presenting ongoing challenges in oncological care and treatment modalities. As one of the most prevalent cancers, effective treatment modalities such as radiotherapy are crucial. The ideal radiotherapy fractionation for breast cancer is still debated, with recent studies supporting five-fraction courses for efficacy and reduced treatment burden. Conventional fractionated radiotherapy (CFRT) has been reported to result in severe skin reactions such as moist desquamation in up to 8% of patients, underscoring a significant challenge in managing side

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effects.[1] Implementation of the hypofractionated schemes into our routine practice scared us at first, but when we started using it in our appropriate patients and saw that the toxicity was low, we were encouraged to use them in more patients.

The FAST-Forward radiotherapy protocol represents a pivotal advancement in this regard. It was initially developed and tested in the United Kingdom, and this study marks its first application in Turkey, providing unique insight into its effectiveness and adaptation to a new demographic setting. This research aims to evaluate the early skin reactions associated with this protocol, offering critical data on its viability as a global standard in breast cancer treatment.[2]

Hypofractionated schedules have demonstrated a lower incidence of such severe reactions, suggesting a more favorable profile for acute skin toxicity.[2,3] Notably, the FAST-Forward study highlighted an even lower incidence of severe skin reactions, approximately 5%, suggesting that this ultrahypofractionated approach could offer substantial benefits in reducing treatment-related skin toxicity.[4]

The objective of this study was to explore the frequency and intensity of skin toxicity that occurs early in breast cancer patients who undergo radiotherapy with a one-week FAST-Forward regimen.

MATERIALS AND METHODS

This retrospective study included 60 patients diagnosed with breast cancer between December 2019 and August 2022. The eligibility criteria included patients undergoing the FAST-Forward radiotherapy protocol with available post-treatment skin follow-up images. This study was approved by the Koc University Ethics Committee, with the approval number (2024.212.IRB2.098).

Before initiating treatment, each patient underwent a thorough 3D-computerized tomography (CT) scan to facilitate precise treatment planning. Special care was taken to protect the heart, particularly in patients receiving left-sided breast radiation, by using the deep inspiration breath-hold technique. The delineation process was improved by utilizing optimized medial and lateral tangential beams of megavoltage X-rays that conform to the intricate geometries of the target regions. The patients received a total dose of 26 Gy in five daily fractions of 5.2 Gy using tangential field-in-field techniques. A typical margin of 10 mm was added around the breast or chest wall clinical target volume, accounting for setup errors, breast swelling, and breathing, to create a planning target volume (PTV). For all patients, a full 3D CT set of outlines covering the entire breast and organs at risk was collected with a slice separation of up to 5 mm. Organs at risk were prospectively outlined. A tangential opposing pair beam arrangement encompassed the entire breast or chest wall PTV, minimizing ipsilateral lung and heart exposure. The treatment plan was optimized with 3D dose compensation to achieve the following PTV dose distribution: more than 95% of the PTV received 95% of the prescribed dose, less than 5% of the PTV received 105% or more, less than 2% of the PTV received 107% or more, and a global maximum of less than 110%. Dose constraints for the five-fraction schedules were as follows: volume of ipsilateral lung receiving 8 Gy less than 15%, and volume of heart receiving 1.5 Gy less than 30%, and that receiving 7 Gy less than 5%.[2]

Panthenol is routinely used as prophylaxis for skin toxicity in all patients. Acute skin reactions were assessed using the RTOG system during the second and sixth week after RT.[5] Photographic documentation of the treated and untreated areas facilitated comparison, and patient-reported symptoms, such as breast swelling, were recorded to evaluate the impact of treatment. Photographs of the radiotherapy area and contralateral breast were taken by a nurse for comparison at specific time points, including simulation and the second and sixth weeks of radiation treatment. These images were captured at a distance of 1 m using a standard gray card scale to ensure consistent lighting and color in the photos. This standardized approach allows for accurate assessment and comparison of post-treatment skin reactions. Example images of a patient were shown in Figure 1a-c.

RESULTS

We analyzed the data of 60 breast cancer patients who underwent the FAST-Forward radiotherapy protocol, which included 60 breast cancer patients with a median age of 71 years (range, 51–86 years). All patients had T1-2 and N0-1mi disease and received adjuvant radiotherapy after breast-conserving surgery. Two patients had stage T2N1mi (micrometastasis) breast cancer. They were 79 and 76 years old. Because of their age and axilla staging, they received radiotherapy with the FAST-Forward protocol without axilla irradiation. The average Body Mass Index (BMI) was calculated at

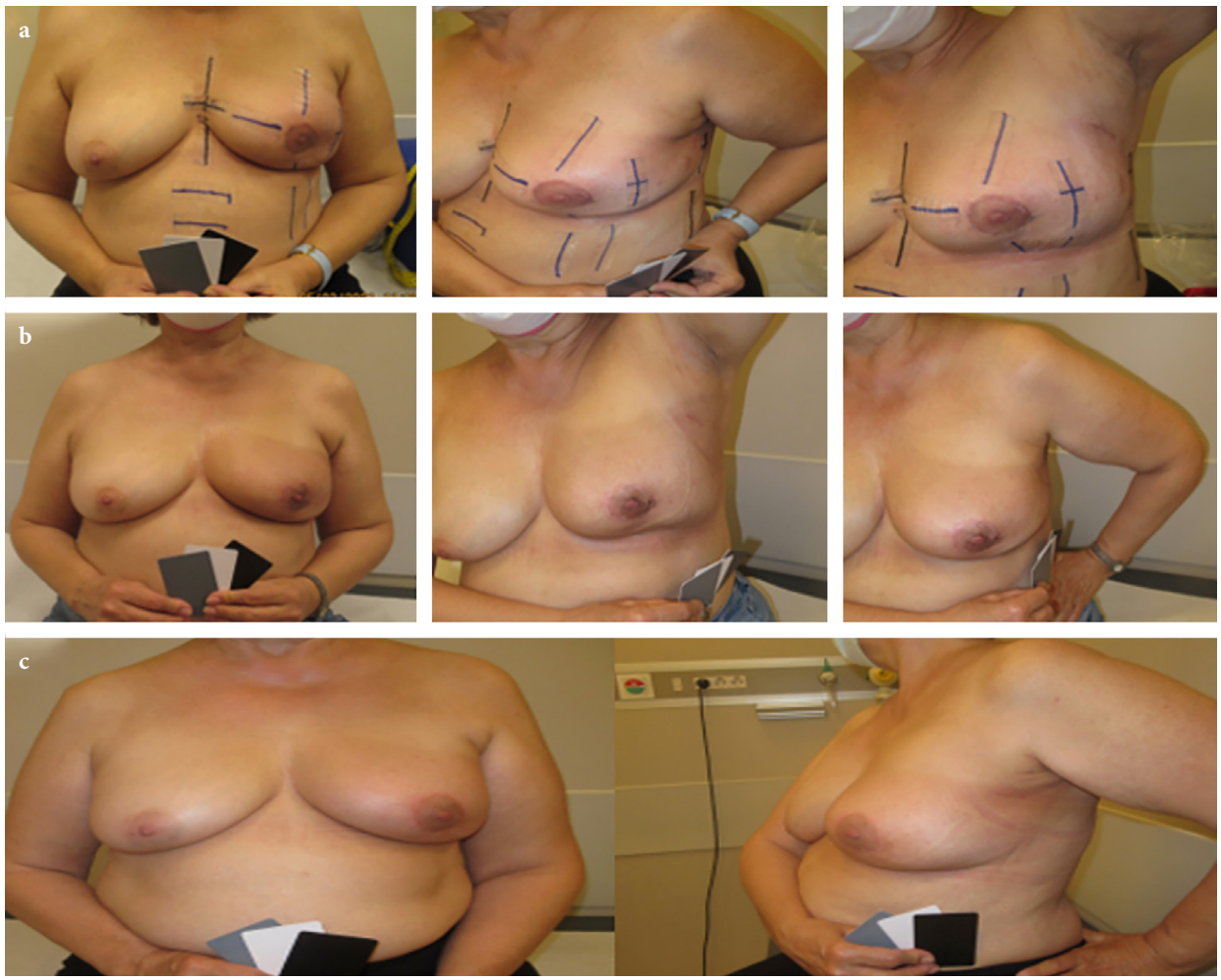

Fig. 1. 71 years old female patient, T2N0, invasive ductal carcinoma, estrogen receptor (+), progesterone receptor (+), cerbB2 (-), Ki67 25%, illustration of the photographic setup used to capture consistent images of the treatment areas, employing a grey card for color and lighting standardization. This setup ensured that all the photographs were taken under identical conditions, facilitating an accurate comparison across different time points. (a) Day of simulation. (b) Second week after the completion of the radiation treatment. (c) Sixth week after the completion of the radiation treatment.

26.76±7.23 kg/m^2. The smoking rate was 33.3% (n=20). Detailed patient demographics and clinical characteristics are summarized in Table 1, which provides a comprehensive overview of the study cohort.

All patients were treated with a total radiation dose of 26 Gy in five fractions. The treatment was delivered using tangential field-in-field techniques, with special attention paid to cardiac protection using the deep inspiration breath-hold technique in patients with left-sided breast cancer.

During toxicity evaluation in the second week post-radiotherapy, seven patients (11.6%) had grade 1 skin reactions, and one patient (1.6%) experienced a grade 2 skin reaction. By the sixth week of follow-up, five of the seven patients with initial grade 1 reactions showed complete normalization of the skin. The remaining two patients had varied outcomes: one continued to have grade 1 reactions, whereas the other experienced an escalation to grade 2. The initial grade 2 reaction improved to a grade 1 reaction. Among the patients with grade 1 and 2 reactions in the sixth week, all three were aged ≥79 years. Apart from this, there were no clinical differences in distinguishing the skin reactions in these patients. None of the patients reported breast swelling in the second and sixth weeks after radiotherapy completion (Table 2).

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Table 1 Patient charactherictics and treatment parameters

Patient characteristics and treatment parameters	Value
Total number of patients	60
Age	Median: 71 years (Range: 51–86 years)
Tumor stage	All had T1-2 and N0-N1mi (2/60) disease
Radiation dose	26 Gy in 5 fractions
BMI (body mass index)	Mean: 26.76±7.23 kg/m^2
Smoking status	Smokers: 20 (33.33%)
Skin reactions at week 2	Grade 1: 7, Grade 2: 1
Skin reactions at week 6	Grade 1: 2, Grade 2: 1
Breast swelling (patient report) at week 2	None reported
at week 6	None reported
Technique used	Tangential field-in-field techniques, with deep inspiration breath-hold for left-sided treatments

Photographic documentation was conducted to visually assess and compare skin reactions. The images obtained using a standardized method involving a gray card to ensure uniform lighting and color accuracy supported the clinical evaluations by providing clear evidence of skin reaction progression or resolution during the follow-up period.

Table 2 Evaluation of the acute skin toxicity after radiotherapy

Skin toxicity (RTOG)	2nd week		6th week	
	n	%	n	%
Grade I	7	11.6	2	3.3
Grade II	1	1.6	1	1.6
Grade III	–	–	–	–

RTOG: Radiation Therapy Oncology Group

DISCUSSION

This study represents one of the first evaluations of the FAST-Forward radiotherapy protocol in a Turkish cohort, focusing primarily on early skin reactions. Ultrahypofractionation has emerged as a novel strategy for the management of early-stage breast cancer. However, concerns regarding skin toxicity and cosmetic outcomes have hindered its widespread adoption in clinical practice. In this study, we report the prevalence of skin reactions among Turkish breast cancer patients who received radiotherapy using the FAST-Forward scheme. Our findings indicated that the incidence of skin reactions in this patient population was relatively low.

Breast radiotherapy fractionation has been the subject of extensive research over the past 30 years. The current international standard involves moderate hypofractionation, which entails administering 15 or 16 fractions over a period of three weeks, with total doses ranging from 40 to 42.5 Gy.[3,6] Recent UK studies have concentrated on five-fraction breast radiotherapy, demonstrating its safety, efficacy, and streamlined treatment approach.[2,4]

Skin toxicity is a major issue for patients with breast cancer undergoing radiotherapy, and it can affect their quality of life and adherence to treatment. Acute skin toxicity is commonly experienced by these patients, and various factors such as beam energy, field separation, breast size, and radiation delivery techniques can influence the severity of the reaction.[7]

Many factors have been identified that determine skin toxicity. Anthropometric measurements and breast volume have been demonstrated to correlate with the risk of skin toxicity, emphasizing the significance of individualized treatment planning.[8]

To mitigate skin side effects, the use of moisturizing creams and prophylactic topical treatments has been shown to be effective in patients receiving radiotherapy for breast cancer.[9] Furthermore, the prophylactic use of mometasone furoate during radiotherapy may reduce acute skin toxicity compared to placebo, as evidenced by a reduction in itching, irritation, and burning sensations.[10]

As it is known, erythema, hyperpigmentation, dry or moist desquamation, and edema are the most common acute skin side effects of conventional radiotherapy. Our findings align with previous research suggesting a lower incidence of severe skin reactions with

hypofractionated schedules compared to conventional fractionated radiotherapy.[1] Studies have highlighted the benefits of hypofractionated schedules in reducing the duration of treatment while maintaining efficacy and lowering the incidence of severe skin reactions.

The FAST-Forward trial demonstrated that a regimen of 26 Gy delivered in five fractions over one week achieves efficacy comparable to a traditional 40 Gy in 15 fractions schedule, thus supporting the adoption of hypofractionated schedules. Furthermore, this approach has been shown to be well-tolerated among different age groups, including elderly patients, thereby validating its use across a broad demographic spectrum.[11]

The use of modern radiotherapy techniques such as Volumetric Modulated Arc Therapy (VMAT) has also contributed to favorable cosmetic outcomes and lower toxicity levels, underscoring the advancements in radiation therapy technology that benefit patient quality of life.[12] In our study, although all of our patients were treated with the tangential field-in-field technique, acute skin reactions were tolerable. Therefore, the effect of the techniques on skin reactions needs further evaluation.

In addition to the tolerability of the hypofractionated regimens, a meta-analysis explored the broader implications of hypofractionated radiotherapy on patient outcomes including local recurrence, relapse-free survival, overall survival, and cosmetic outcomes. This study demonstrated that hypofractionated regimens do not compromise treatment effectiveness compared to conventional schedules and may reduce the incidence of severe adverse reactions such as acute skin toxicity.[1] Regarding local control and overall survival, our results will also be presented after long-term follow-up.

The safety and feasibility of delivering simultaneous integrated boost (SIB) were demonstrated by Zanoguera et al.[13] in their recent study. According to this study, despite the increased radiation dose up to 30 Gy over 5 fractions in a single week, no severe toxicities were observed. Only mild, transient dermatological effects such as dermatitis and hyperpigmentation occurred, which mostly resolved by the six-month follow-up. These results suggest that SIB can effectively replace sequential boosts, thus enhancing patient compliance and comfort by minimizing treatment time and logistical burdens. This is crucial as it supports our results and further corroborates the viability of SIB in clinical settings, emphasizing the potential to maintain treatment efficacy while reducing the burden on patients.

The role of patient-specific factors in influencing treatment outcomes cannot be ignored. Studies have highlighted how radiation schedules and individual patient characteristics, such as body mass index (BMI), smoking status, and breast size, significantly affect skin toxicity.[7,8] These findings emphasize the importance of personalized treatment planning to optimize therapeutic outcomes and minimize adverse effects.

Our study adds to the evidence supporting the efficacy of the FAST-Forward protocol in managing breast cancer, presenting a viable option that balances treatment effectiveness with patient quality of life. The minimal early skin reactions observed in our cohort, coupled with the manageable levels of acute skin toxicity reported in comparable studies, confirmed the potential of this protocol to improve the therapeutic experience of patients. Our study has several limitations. First, we only evaluated the FAST-Forward cohort and could not conduct comparisons with other therapeutic methods. Additionally, the sample size was inadequate for deriving sweeping inferences. Finally, the duration of follow-up was relatively brief to obtain comprehensive findings.

CONCLUSION

As a conclusion, our study supports the integration of the FAST-Forward protocol into clinical practice in Turkey, representing a significant advancement in breast cancer radiotherapy. By tailoring treatments to individual patient characteristics and utilizing modern radiotherapy technologies, this approach promises not only effective disease control but also an enhanced quality of life for patients. This early assessment of toxicity confirms the practical use of the FAST-Forward protocol without compromising any toxicity results.

Ethics Committee Approval: The study was approved by the Koc University Ethics Committee (no: 2024.212.IRB2.098, date: 30/05/2024).

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