The Impact of a Postmastectomy Chest Wall Scar Boost on Local Recurrence-free Survival in High-risk Patients

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Abstract

Data regarding the use of a scar boost following postmastectomy radiation are limited. In this study, 140 patients with invasive breast cancer treated with mastectomy and postmastectomy radiation were analyzed. In this cohort, the use of a scar boost did not translate into a local recurrence-free survival benefit even among patients with high-risk features.

Introduction: A scar boost following postmastectomy radiation to a total dose of > 50 Gy can be considered in cases of invasive breast cancer with high-risk features including advanced tumor stage, lymphovascular space invasion (LVSI), and positive margins. The purpose of this study was to determine the impact of a scar boost on 5-year local recurrence-free survival (LRFS). **Materials and Methods:** We retrospectively analyzed 140 patients with invasive breast cancer treated with mastectomy and postmastectomy radiation at a single institution between 2007 and 2016. Patients received 50 to 50.4 Gy to the chest wall and the majority of scar boosts were 9 to 10 Gy. LRFS was examined using the Kaplan-Meier method and univariable Cox regression. **Results:** A total of 140 patients met inclusion criteria with a median follow-up time of 48 months. Ninety-four (67.1%) patients did receive a scar boost and 46 (32.9%) patients did not. On subset analysis of patients with LVSI or positive margins, 5-year LRFS was 79.3% in patients treated with scar boost compared with 71.1% in patients without a scar boost ($P = .537$). In patients with T3 or T4 disease, 5-year LRFS was 80.9% in those who received scar boost and 71.6% in patients who did not ($P = .967$). The use of a scar boost was not associated with a significant improvement in LRFS on Cox regression (hazard ratio, 0.83; 95% confidence interval, 0.37-1.84; $P = .654$). **Conclusion:** Use of a scar boost following postmastectomy radiation decreased the absolute percentages of local recurrences in patients with high-risk features; however, this did not translate into a statistically significant benefit.

Clinical Breast Cancer, Vol. 19, No. 5, 363-9
Keywords: Chest wall, Local recurrence, Postmastectomy, Radiation, Scar boost

Introduction

A scar boost following postmastectomy radiation to a total dose of > 50 Gy can be considered in cases of invasive breast cancer with high-risk features such as advanced tumor stage, lymphovascular space invasion (LVSI), and positive margins.[1] However, the data supporting a chest wall scar boost are limited, and its use has not been evaluated in prospective randomized trials. The 2001 American Society for Clinical Oncology guidelines for the use of postmastectomy radiation therapy stated there was insufficient evidence to make recommendations about the use of a scar boost, and no recommendation for the use of a scar boost is included in the most recent American Society for Clinical Oncology guidelines.[2] The American College of Radiology Appropriateness Criteria on postmastectomy radiation states that a central chest wall boost may be appropriate as indicated by risk of residual microscopic disease relative to the radiation dose achieved with chest wall irradiation.[3]

A survey of practice patterns among radiation oncologists specializing in breast cancer demonstrated that 55% of these physicians routinely use a boost to the chest wall following post-

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Submitted: Feb 4, 2019; Revised: Apr 5, 2019; Accepted: Apr 15, 2019; Epub: May 2, 2019

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1526-8209/$ - see frontmatter
https://doi.org/10.1016/j.clbc.2019.04.010

mastectomy radiation, 18% prescribe a boost depending on margin status, and 27% do not use a boost at all.[4] In another survey of practicing radiation oncologists in academics and private practice, 77% of respondents reported they routinely use a boost following post-mastectomy radiation, and important factors for the use of a boost were inflammatory breast cancer, positive margins, close margins, and T4 tumors.[5]

Additionally, the use of neoadjuvant chemotherapy may impact the risk of local recurrence after postmastectomy radiation, and the role of postmastectomy radiation after neoadjuvant chemotherapy is currently being investigated. As such, the need for additional dose in the form of a chest wall scar boost may be even less with the increasing use of systemic therapy. The purpose of this study was to determine factors associated with the use of a postmastectomy chest wall scar boost at a single institution and determine differences in 5-year local recurrence-free survival (LRFS) based on the use of a chest wall scar boost.

Materials and Methods

We obtained institutional review board approval to retrospectively analyze 140 patients with invasive breast cancer treated with mastectomy and postmastectomy radiation at a single institution between 2007 and 2016. Patients received 50 to 50.4 Gy to the chest wall using 3-dimensional conformal radiation with tangent fields following mastectomy. Radiation was delivered with 5 mm of tissue equivalent superflab bolus placed over the chest wall for half of the treatment. The majority of scar boosts were 9 to 10 Gy. Boosts were delivered using 6 to 10 megaelectron volts, and the target typically included the scar with a 2-cm circumferential margin. Five mm of bolus material was placed over the treatment field for the delivery of the boost.

Data collected included age at diagnosis, race, body mass index, clinical stage prior to neoadjuvant chemotherapy, receptor status (estrogen receptor, progesterone receptor, and human epidermal growth factor receptor 2 [HER2]/neu receptor positivity), surgical margin status, presence of LVSI, total radiation dose received, dose fractionation, receipt of breast reconstruction (immediate or delayed), and chemotherapy treatment details. Demographic, clinical, and treatment details were compared via the χ^2 test between patients who received a scar boost and those that did not.

Univariable logistic regression was used to determine factors associated with the use of a scar boost. Follow-up was based from the initial date of breast cancer diagnosis. Local recurrence was defined as tumor recurrence in the chest wall. Univariable Cox regression was used to determine covariables associated with LRFS among all patients. LRFS was defined as elapsed time from the date of diagnosis to earliest occurrence of local recurrence or death from any cause. LRFS curves comparing patients treated with and without a scar boost were generated using the Kaplan-Meier method and compared via the log-rank test. All analysis was performed using SPSS version 20 (IBM Inc, Armonk, NY).

Results

A total of 140 patients met inclusion criteria, including 46 (32.9%) patients who did not receive a scar boost and 94 (67.1%) patients who did receive a scar boost. The local recurrence rate for the entire cohort was 12%, and the median follow-up time was 48 months (range, 9-134 months). Sixty-one (43.6%) patients were alive and not lost to follow-up at 60 months. Local recurrence rates were 10.5%, 8.3%, 13.7%, and 28.2% for stage I, stage II, stage III, and stage IV, respectively. Fifty-two percent of patients received neoadjuvant chemotherapy, and 69.3% of patients received adjuvant chemotherapy. A summary of demographic and clinical characteristics of patients is found in Table 1. Characteristics between treatment groups were not significantly different although the percentage of patients with positive margins was slightly higher in the scar boost treatment group.

On univariable logistic regression, patients with T2 (odds ratio [OR], 2.86; 95% confidence interval [CI], 1.07-7.62) and T4 (OR, 3.57; 95% CI, 1.22-10.4; $P = .02$) disease were more likely to receive a scar boost compared with patients with T1-staged disease. There was a trend towards increase in the use of a boost among patients with T3 disease (OR, 3.05; 95% CI, 0.94-9.93; $P = .064$). There was also a trend towards increased likelihood of receiving a scar boost among patients with stage III disease (OR, 2.93; 95% CI, 0.97-8.87; $P = .058$). Fifteen (10.7%) patients underwent breast reconstruction. Reasons for not undergoing reconstruction included personal preference or comorbidities that prohibited this procedure. A scar boost was only used in 1 patient who underwent immediate breast reconstruction as compared with being used in 6 (6.4%) patients who had delayed reconstruction. Neither immediate reconstruction nor delayed reconstruction was significantly associated with the use of a scar boost on univariable Cox regression. Age, race, positive LVSI, positive margins, and molecular subgroup were not significantly associated with the use of a scar boost. Univariable logistic regression for factors associated with the use of a scar boost is shown in Table 2.

The receipt of a scar boost was not associated with a significant improvement in LRFS on univariable Cox regression as compared with no scar boost (hazard ratio [HR], 0.83; 95% CI, 0.37-1.84; $P = .654$) as shown in Table 3. Triple negative disease was associated with worse LRFS (OR, 3.03; 95% CI, 1.31-7.02; $P = .010$). Because there was only one variable identified with a significant association with LRFS, a multivariable Cox regression was not subsequently performed.

To determine the interplay of different risk factors for LRFS, several subset analyses were performed. On subset analysis of patients with LVSI or positive margins, 5-year LRFS was 79.3% in patients treated with scar boost compared with 71.1% in patients without a scar boost ($P = .537$). In patients with T3 or T4 disease, 5-year LRFS was 80.9% in those who received scar boost and 71.6% in patients who did not ($P = .967$). In an additional subset analysis of patients with triple-negative disease, 5-year LRFS was 54.9% in patients that received a scar boost versus 50.5% in patients that did not ($P = .570$). Among patients who received neoadjuvant chemotherapy, 5-year LRFS was 84.4% for those that received a scar boost compared with 78.0% who did not ($P = .763$). For patients who did not receive neoadjuvant chemotherapy, 5-year LRFS was 84.2% for patients who received a boost and 72.8% for patients who did not ($P = .803$). LRFS curves are shown in Figure 1.

Discussion

In the current analysis, 94 (67.1%) patients received a chest wall scar boost, and 46 (32.9%) patients did not. Higher tumor stage was associated with an increased use of a scar boost. On subgroup analyses, LRFS was higher among patients with LVSI or positive

Table 1 Demographic and Clinical Characteristics of Patients

	No Scar Boost, n = 46 (%)	Scar Boost, n = 94 (%)	*P* Value
Age, y			.551
<40	8 (17.4)	14 (14.9)	
>40	38 (82.6)	80 (85.1)	
Body Mass Index			.997
Normal	9 (19.6)	19 (20.2)	
Overweight	14 (30.4)	29 (30.9)	
Obese	18 (39.1)	35 (37.2)	
Morbidly obese	5 (10.9)	11 (11.7)	
Race			.329
White	17 (37.0)	24 (25.5)	
Black	28 (60.8)	69 (73.4)	
Other	1 (2.2)	1 (1.1)	
Stage Grouping			.136
I/II	29 (62.8)	46 (48.8)	
III/IV	17 (37.2)	48 (51.2)	
Molecular Grouping			.777
Luminal A/B	23 (50.0)	46 (49.0)	
$HER2^{+}$	9 (19.6)	24 (25.5)	
Triple negative	14 (30.4)	24 (25.5)	
Lymphovascular Space Invasion			
Negative	30 (65.2)	72 (76.6)	.155
Positive	16 (34.8)	22 (23.4)	
Positive Margin			
No	43 (93.5)	84 (89.4)	.431
Yes	3 (6.5)	10 (10.6)	
Neoadjuvant Chemotherapy			.584
No	23 (50.0)	43 (45.7)	
Yes	23 (50.0)	51 (54.3)	
Adjuvant Chemotherapy			.407
No	15 (32.6)	24 (25.5)	
Yes	31 (67.4)	70 (74.5)	
Immediate Reconstruction			
No	43 (93.5)	93 (98.9)	.063
Yes	3 (6.5)	1 (1.1)	
Delayed Reconstruction			
No	41 (89.1)	88 (93.6)	.325
Yes	5 (10.9%)	6 (6.4%)	

Abbreviation: HER2 = human epidermal growth factor receptor 2.

margins who received a scar boost as compared with those who did not. LRFS was also higher among patients with T3 and T4 disease as compared with those who did not and slightly higher among patients with TNBC who received a scar boost. These differences were not, however, statistically significant. Additionally, the use of scar boost was not significantly associated with an improvement in LRFS on univariable Cox regression among all patients.

Local-regional Failure after Mastectomy

Risk factors for local-regional failure after mastectomy include young age (< 35 years), nodal status, tumor size, lymphovascular invasion, multicentricity, number of lymph nodes removed, and biologically aggressive tumors including triple-negative breast cancer (TNBC).[6-10] In the Danish Breast Cancer Cooperative Group studies, the 18-year probability of locoregional recurrences (LRRs) with or without distant metastases was lower with radiation than without radiation, 14% versus 49% ($P < .001$), and the frequency of all sites of LRR was lower with radiation as compared with no radiation.[11] Chest wall failures were the most common type of LRR in both groups: 55% of patients who did not receive radiation and 70% of patients who did receive radiation had involvement of this site. Preventing local recurrence after the treatment of breast cancer in the postmastectomy setting is important because salvage treatment for locally recurrent disease has been shown to be associated

Table 2 Univariable Logistic Regression for Receipt of Scar Boost

	OR (95% CI)	*P* Value
Age, y		
<40	1	
>40	1.20 (0.46-3.11)	.703
Race		
White	1	
Black	1.72 (0.80-3.68)	.163
Other	0.71 (0.04-12.1)	.812
Body Mass Index		
Normal	1	
Overweight	0.98 (0.36-2.72)	.971
Obese	0.92 (0.35-2.44)	.869
Morbidly obese	1.04 (0.28-3.90)	.951
Tumor Stage		
1	1	
2	2.86 (1.07-7.62)	**.036**
3	3.05 (0.94-9.93)	.064
4	3.57 (1.22-10.4)	**.020**
Pathologic Tumor Stage		
1	1	.386
2	1.50 (0.60-3.71)	.883
3	1.10 (0.32-3.74)	.476
4	1.54 (0.47-5.00)	.678
Overall Stage		
I	1	
II	1.50 (0.51-4.39)	.459
III	2.93 (0.97-8.87)	.058
IV	0.68 (0.12-3.87)	.659
Lymphovascular Space Invasion		
No	1	
Yes	1.75 (0.81-3.78)	.157
Positive Margins		
Negative	1	
Positive	1.71 (0.45-6.53)	.435
Neoadjuvant Chemotherapy		
No	1	
Yes	1.22 (0.60-2.48)	.584
Adjuvant Chemotherapy		
No	1	
Yes	1.39 (0.64-3.02)	.408
Molecular Subgroup		
Luminal A/B	1	
$HER2^{+}$	1.28 (0.51-3.22)	.604
Triple negative	0.89 (0.38-2.07)	.778
Immediate Reconstruction		
No	1	
Yes	0.15 (0.01-1.87)	.103
Delayed Reconstruction		
No	1	
Yes	0.54 (0.12-1.87)	.331

Abbreviations: CI = confidence interval; HER2 = human epidermal growth factor receptor 2; OR = odds ratio.
The values that are shown in bold are those that are considered statistically significant with a value of less than 0.05.

with significant morbidity and in some cases, locally recurrent disease may not be successfully salvaged.[6,12] Additionally, local recurrence after treatment has been associated with a significantly higher risk of distant metastases and death.[13] A radiation boost to the lumpectomy cavity has been shown to provide an improvement in local recurrence rate after breast conserving surgery and radiation.[14,15] However, the benefit of additional dose in the form of a chest wall scar boost in the postmastectomy setting is not as clear.[4,5]

Evidence for a Chest Wall Boost

In the current study, we did not find a statistically significant benefit of the use of scar boost with regards to LRFS; however, the absolute numbers were higher among those groups of patients who received a scar boost as compared with those who did not. The smallest magnitude of difference was in the subset with TNBC. In a large retrospective series investigating the use of a chest wall boost in 582 patients, Panoff et al found that the addition of a postmastectomy chest wall boost greater than 50.4 Gy resulted in lower incidence of locoregional recurrence in patients with stage II to III breast cancer.[1] Although a benefit was seen among all patients who received higher doses, this retrospective study does not determine the magnitude of benefit in certain subsets of high-risk patients, including those with positive margins or those with TNBC. The authors concludes the higher rate of LRR in the low-dose group was likely owing to the high percentages of patients with inflammatory breast cancer, stage III disease, and TNBC in this study. In a series of 399 patients, Shah et al found that rates of chest wall recurrence and LRR were low (1.6%) including patients who did not receive a boost to the chest wall scar.[16] The authors concluded that a scar boost could safely be omitted in most patients and should be reserved for cases of close/positive margins or T4 disease.

Practice Patterns

We found that a chest wall scar boost was used at our institution in approximately 67% of cases. Survey data shows that the use of scar boost is variable, with use ranging from approximately 55% to 75% of postmastectomy cases.[4,5] Other data indicate that the use of scar boost may be physician- and institution-dependent, with some practices routinely using a scar boosts whereas others do not.[17-20] For example, in a study of 396 patients who underwent postmastectomy radiation, a chest wall scar boost was used in only 8% of cases.[21] In the current study, we found that the use of a scar boost appeared to be most influenced by tumor staging and to a lesser extent, overall disease staging. Additionally, we found that a scar boost was used infrequently in patients who had immediate breast

Table 3 Univariable Cox Regression for Local Recurrence-free Survival Among All Patients

	HR (95% CI)	*P* Value
Age, y		
<40	1	
>40	0.68 (0.30-1.58)	.374
Race		
White	1	
Black	1.07 (0.49-2.33)	.875
Other	1.70 (0.21-13.5)	.615
Body Mass Index		
Normal	1	
Overweight	0.60 (0.33-1.91)	.603
Obese	0.90 (0.37-2.17)	.821
Morbidly obese	0.15 (0.03-1.73)	.150
Tumor Stage		
1	1	
2	1.63 (0.594-4.50)	.342
3	1.04 (0.32-3.42)	.944
4	1.53 (0.55-4.29)	.416
Pathologic Tumor Stage		
1	1	
2	1.64 (0.67-4.03)	.281
3	1.46 (0.44-4.88)	.541
4	0.93 (0.30-2.90)	.901
Overall Stage		
I	1	
II	1.31 (0.36-4.76)	.686
III	1.63 (0.47-5.61)	.438
IV	0.53 (0.05-5.45)	.595
Lymphovascular Space Invasion		
No	1	
Yes	1.89 (0.92-3.90)	.085
Positive Margins		
No	1	
Yes	0.60 (0.18-2.01)	.410
Molecular Subgroup		
Luminal A/B	1	
$HER2^{+}$	1.11 (0.40-3.06)	.841
Triple negative	3.03 (1.31-7.02)	**.010**
Receipt of Scar Boost		
No	1	
Yes	0.83 (0.37-1.84)	.654

Abbreviations: CI = confidence interval; HER2 = human epidermal growth factor receptor 2; HR = hazard ratio.
The values that are shown in bold are those that are considered statistically significant with a value of less than 0.05.

reconstruction even though this was not statistically significant. Furthermore, expert opinion differs with regard to use of a scar boost, with some considering a boost in higher-risk patients and others not routinely using a boost.[22] An argument against a chest wall scar boost is that the scar itself may not correlate anatomically with the original site of disease and may not be the only site at risk of failure. Therefore, if one is to treat to a higher dose, then the whole chest wall should be included. Furthermore, the appropriate depth of a chest wall boost is unclear.

Neoadjuvant Chemotherapy

Postmastectomy radiation plays a role in the prevention of LRR in locally advanced breast cancer and has been shown to increase overall survival.[23-26] However, earlier trials investigating the role of postmastectomy radiation involved patients who did not receive neoadjuvant chemotherapy. In the modern era, response to neoadjuvant systemic therapy may potentially be used to select patients who may benefit most from postmastectomy radiation or patients for whom postmastectomy radiation can be omitted.[27] Retrospective data from the MD Anderson Cancer Center demonstrated that postmastectomy radiation provides a benefit for patients with clinical stage III disease and who achieve a pathologic complete response after neoadjuvant chemotherapy.[18,28] The National Surgical Adjuvant Breast and Bowel Project (NSABP) B-51/Radiation Therapy Oncology Group (RTOG) 1304 ongoing trial is evaluating the benefit of radiation in patients with clinical T1 to T3 N1 disease who have had a complete response in the axilla after neoadjuvant chemotherapy.[29] On this trial, a 12 to 14 Gy chest wall boost is permissible only in cases of close (≤ 2 mm) surgical margins on the mastectomy specimen for total doses of 62 or 64 Gy. The Alliance 011202 trial includes patients who have positive sentinel nodes after neoadjuvant chemotherapy. Patients will be randomized to completion axillary lymph node dissection and nodal radiation therapy or axillary radiation and nodal radiation therapy.[30] This trial mandates a chest wall scar boost.

In the current analysis, approximately one-half of patients received neoadjuvant chemotherapy, which may have had an impact of local recurrence rates. On subset analysis, we found no difference in the benefit of scar boost among patients who did not receive chemotherapy. Likewise, no significant benefit a scar boost was found among patients who did receive neoadjuvant chemotherapy. In addition to providing data about women for whom postmastectomy radiation may be omitted after neoadjuvant chemotherapy, the NSABP-51/RTOG 1304 and Alliance 0111202 trials may shed further light on patterns of failure and risk factors for local recurrence after neoadjuvant chemotherapy and whether additional dose in the form of a chest wall boost may be beneficial in this setting.

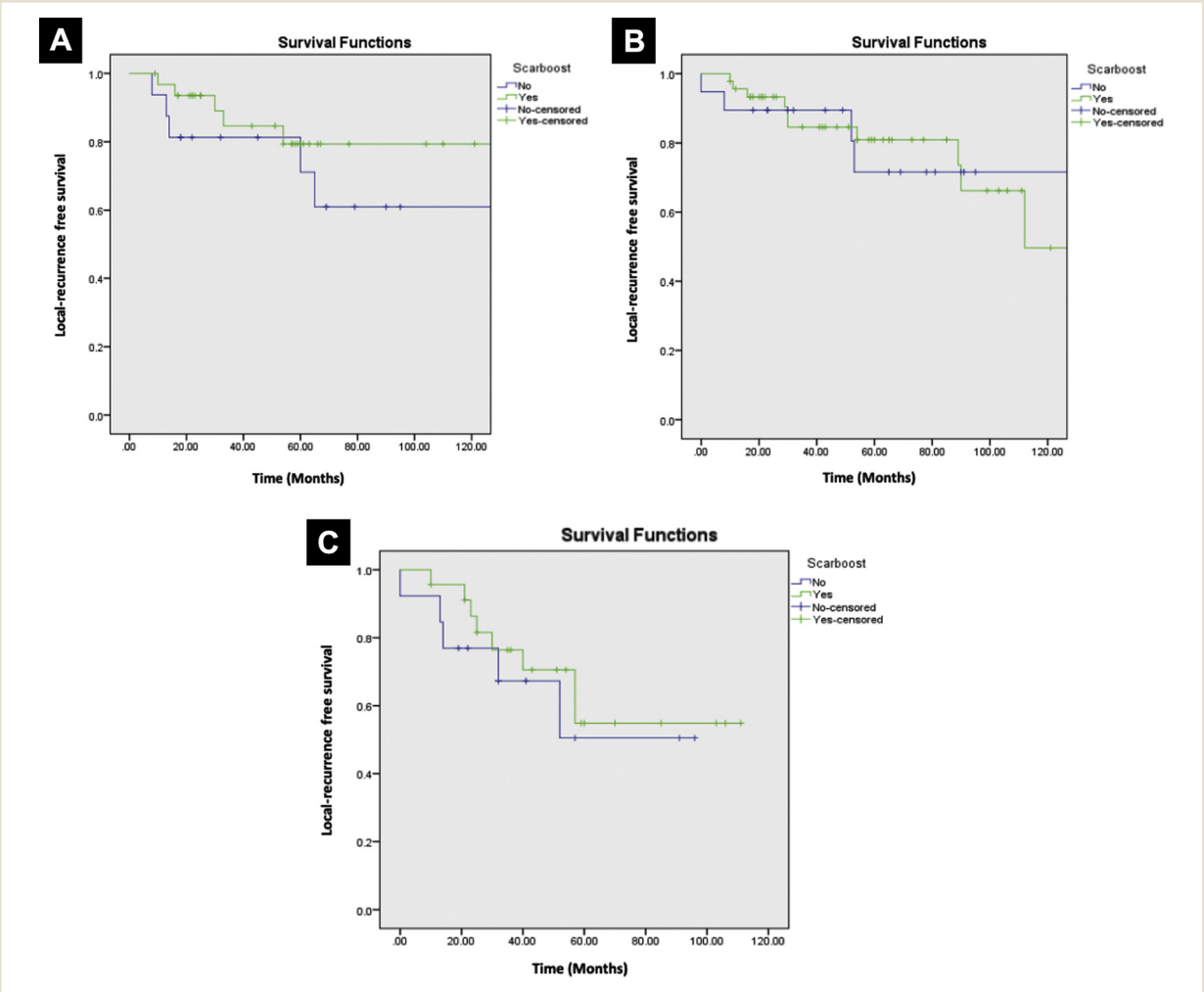
Toxicity

Rationale for omitting a chest wall boost includes the possibility of worse skin toxicity with additional dose. Predictors for skin toxicity among patients receiving postmastectomy radiation include black race, higher body mass index, younger age, and postmenopausal status.[31] Importantly, skin toxicity has been shown to increase the likelihood of treatment breaks or termination of treatment.[32] Less data about the specific impact of a scar boost on skin toxicity are available; however, further investigation is warranted in order to more accurately identify patients in which the benefit of a scar boost outweighs the risks.

Limitations

Limitations of this study include its retrospective nature. Additionally, there were a small number of total patients in the

Figure 1 Comparison of LRFS at 5 Years Between Patients Treated With and Without Postmastectomy Scar Boost. A, Patients With LVSI or Positive Margins; 5-year LRFS 79.3% Versus 71.1%; $P = .537$. B, Patients With T3 and T4 Disease; 5-year LRFS 80.9% Versus 71.6%; $P = .967$. C, Patients With Triple-Negative Disease; 5-year LRFS 54.9% Versus 50.5%; $P = .570$



Abbreviations: LRFS = Local Recurrence-free Survival; LVSI = Lymphovascular Space invasion.

cohort, and thus the study may not be powered to detect a statistically significant difference in local recurrence among treatment groups and likewise may not detect a difference among subgroups. Finally, the median follow-up time was 48 months, and it is plausible that a statistically significant difference based on the use of a chest wall scar boost could be detected with additional follow-up time.

Conclusion

Although the absolute percentage of local recurrences was higher among the patients with high-risk features who did not receive a scar boost in addition to postmastectomy chest wall irradiation compared with the high-risk patients who did, this did not translate into a statistically significant benefit with regards to LRFS. The smallest difference between patients who received a scar boost compared with those who did not was in the group of patients with TNBC. The majority of the patients received chemotherapy as a part of their treatment regimen, suggesting that in the setting of modern systemic therapy, additional radiation in the form of a scar boost may not provide a significant local recurrence or overall survival benefit and can be omitted to avoid additional toxicity. However, additional data from prospective trials involving the use of neoadjuvant chemotherapy may shed further light on the exact benefit of a postmastectomy chest wall boost in certain high-risk groups of patients.

Clinical Practice Points

- A scar boost following postmastectomy radiation is sometimes used in cases of invasive breast cancer with high-risk features.
- However, there are limited retrospective data and currently no prospective data supporting the use of a scar boost. Additionally, practice patterns among radiation oncologists regarding the use of a scar boost vary greatly. Furthermore, the use of neoadjuvant chemotherapy may impact the risk of local recurrence and

therefore decrease the need for higher doses of radiation in the form of a boost in this group of patients.
- Identifying patients who are at high risk for local recurrence may better guide radiation treatment following mastectomy.

Disclosure

The authors have stated that they have no conflicts of interest.

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