OPEN

PRS GLOBAL OPEN

ORIGINAL ARTICLE
Breast

Histologic Examination of Mastectomy Scars during Breast Reconstruction: A Systematic Review

Ori Berger, MD
Ran Talisman, MD

Background: Breast reconstruction is a standard procedure in postmastectomy plastic surgery. The necessity of routine histological examinations for mastectomy scars during delayed reconstruction remains a topic of debate. We evaluated the need for histological examination of scars during delayed breast reconstruction.
Methods: We conducted a systematic review using PubMed, TDnet, and Cochrane Central in August 2023. Inclusion criteria involved delayed breast reconstruction with histological scar analysis and malignancy reporting. Exclusion criteria encompassed noncancerous breast diseases, prophylactic mastectomies, articles lacking relevant information, case reports, technique descriptions, and reviews. We independently assessed articles. Differences in recurrence rates were determined using a Z-test for proportions. A linear regression model explored the relationship between reconstruction timing and pathological results. The number needed to treat was calculated based on the literature. The Wilcoxon test was used to compare mean reconstruction times and postreconstruction follow-up between groups.
Results: Our analysis covered 11 retrospective observational studies published between 2003 and 2018, including 3754 mastectomy scars. The malignancy recurrence rate was 0.19%, consistent with previous reports, with a number needed to treat of 144.93–188.68 patients. The timing of breast reconstruction postmastectomy averaged 19.9 months, without statistically significant association between reconstruction timing and recurrence rates. Postreconstruction follow-up periods ranged from 60 to 87 months. The postreconstruction adverse outcomes ratio was 2.21%.
Conclusions: Assessing the necessity of histological examination in breast reconstruction is complex. Based on the literature and this study, we do not recommend routine histological examination of mastectomy scars during delayed reconstruction. A selective approach based on risk factors may be beneficial, warranting further research. *(Plast Reconstr Surg Glob Open 2024; 12:e5847; doi: 10.1097/GOX.0000000000005847; Published online 24 May 2024.)*

INTRODUCTION

Breast reconstruction following mastectomy has become a standard practice in plastic surgery.[1] An ongoing debate wages about whether it is necessary to perform histologic examinations on mastectomy scars during delayed breast reconstruction.

On one side of the debate, proponents like Granick et al[2] advocate for routine histological examination of all excised mastectomy scars, citing four cases intended for late reconstructive surgery. In one of these, a pathological examination has identified adenocarcinoma in the absence of abnormal clinical findings. This perspective highlights the potential for histological analysis to uncover otherwise undetectable recurrences, suggesting that thorough examination is crucial for patient safety.

Conversely, some argue that the low rates of positive pathology make routine histological examination unnecessary.[3–5] They advocate for relying on comprehensive clinical examinations and appropriate imaging techniques as sufficient methods for detecting local recurrence. This view is supported by studies indicating that local recurrence within mastectomy scars is not only rare but also typically evident upon clinical examination,[4,6] thereby questioning the value of routine histopathologic analysis.

From The Plastic Surgery Unit, Barzilai University Hospital Medical Center, Ashkelon, Israel.

Received for publication February 24, 2024; accepted April 8, 2024.

DOI: 10.1097/GOX.0000000000005847

Disclosure statements are at the end of this article, following the correspondence information.

Related Digital Media are available in the full-text version of the article on www.PRSGlobalOpen.com.

The literature reveals that local recurrence after mastectomy occurs in a small percentage of patients, with a portion of these recurrences manifesting within the skin and subcutaneous tissue of the mastectomy scar itself.[7–11] Despite the rarity of such occurrences, the possibility of in-scar recurrence presents a clinical challenge, raising questions about the threshold for significance that would necessitate histologic processing.

Patients undergoing delayed breast reconstruction exhibit heterogeneity, with reconstructions performed at various time points, sometimes after radiotherapy or immediate first-stage reconstruction.[12] This diversity, along with the absence of signs or symptoms in some patients, complicates the decision-making process regarding histological examination of mastectomy scars.

Given the ongoing debate and the conflicting results from various studies,[3] this systematic literature review aims to critically evaluate the necessity of routine histological examination of mastectomy scars during breast reconstruction, seeking to contribute to the resolution of this important clinical question.

Takeaways

Question: Does routine histological examination of mastectomy scars during delayed breast reconstruction contribute to patient outcomes?

Findings: Our systematic review encompassed 11 retrospective observational studies, revealing a low recurrence rate of 0.19% in mastectomy scars during delayed reconstruction. No statistically significant association was found between reconstruction timing and positive pathological results. However, a notable 2.32% postreconstruction adverse outcomes ratio was observed.

Meaning: Routine histological examination of mastectomy scars during delayed breast reconstruction may not be necessary, considering the low recurrence rate and unclear cost-effectiveness.

METHODS

In August 2023, we conducted a literature search according to PRISMA guidelines, across various databases, including PubMed, TDnet (which aggregates articles from OVID, Clinical Key, and Unpaywall), and Cochrane Central, using the search query "mastectomy scar" AND "breast reconstruction" AND "histology." We imposed no restrictions on publication dates or language. We identified six more relevant articles by using PubMed's "similar articles" tool and uncovered three additional publications by reviewing the reference lists of selected articles. We then evaluated the relevance of article titles and abstracts, removing any duplicate records through manual screening.

Our inclusion criteria encompassed articles discussing late breast reconstruction, providing histological analysis of scars, and reporting the number of scars diagnosed with malignancy. We excluded articles related to noncancerous breast diseases or prophylactic mastectomies, those lacking information on reconstruction or histological scar analysis, case reports and series, publications describing a technique, as well as review articles that merely cited previous studies. The authors independently assessed all selected articles according to the specified criteria. Any disagreements regarding inclusion were resolved through joint decision-making. All studies were grouped into one cohort for data synthesis. When synthesizing the data, we noted which studies were included in each outcome calculation.

Data collected included evidence strength; the number of patients; the number of scars diagnosed with malignancy, as a number and as a ratio from the total number of patients; the timing of reconstruction in months, in range and as a mean; prereconstruction history of radiotherapy or chemotherapy; type of malignancy diagnosed; cost of pathological examination in US dollars; duration of follow-up after reconstruction in months, as a range and a mean; recurrence outcomes; and year of publication.

As mentioned, the estimated expected rate of recurrence in the mastectomy scar ranges from 0.72% to 0.88%. To assess whether the recurrence rate in this systematic review significantly deviated from the expected rate, we conducted a Z-test for proportions. Additionally, a Wilcoxon rank-sum test was used to examine potential differences in mean reconstruction times and postreconstruction follow-up periods between the recurrence and no-recurrence groups. Furthermore, we used a linear regression model to investigate the association between the timing of reconstruction and the rate of positive pathological examinations, addressing the potential risk of confounding. The number needed to treat (NNT) was calculated by determining the absolute risk reduction (ARR), which is obtained by subtracting the observed recurrence rate in the mastectomy scar (positive histological ratio) from the expected recurrence rate derived from previous literature or estimates. This ARR is then used to determine how many patients need to be treated to prevent one additional recurrence.

RESULTS

In this review, we analyzed 11 retrospective observational studies published between 2003 and 2018 that met our inclusion criteria[1,3–6,12–17] (Fig. 1). (See **appendix, Supplemental Digital Content 1,** which displays a summary of the publications included in the review. **http://links.lww.com/PRSGO/D234**). Collectively, these studies examined 3754 mastectomy scars, identifying seven cases of breast malignancy recurrence, equating to a 0.19% recurrence rate. This figure is notably lower than the previously reported range of 0.72%–0.88%.[9–11] Statistical analysis yielded a Z-score of −0.6621, indicating the recurrence rate falls within the expected range (significance level 0.05, one-tailed Z-value threshold 1.645). The ARR varied from 0.53% to 0.69%, and the NNT was calculated to be between 145 and 189 patients.

The timing of breast reconstruction postmastectomy varied significantly, from 2 to 168 months, averaging at 19.9 months.[1,3,12–17] A comparison revealed that patients without recurrence underwent reconstruction sooner, at an average of 19.81 months, versus 39 months for those

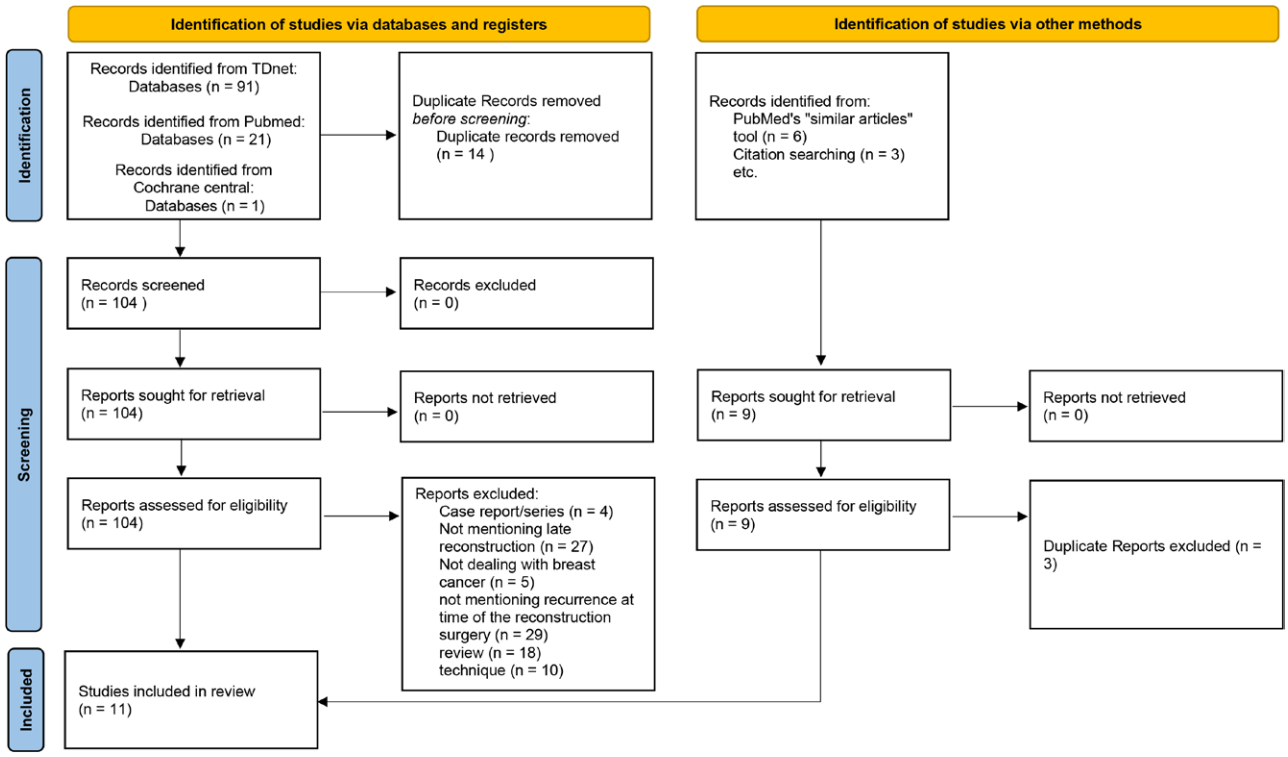

Fig. 1. PRISMA flow diagram of the review process.

with recurrence, a statistically significant difference (W = 26229, $P < 0.05$). However, a linear regression analysis found no significant association between mean reconstruction timing and the ratio of positive pathological examinations ($R^2 = 0.105$, $P = 0.226$).

Information regarding radiotherapy or chemotherapy before reconstruction is summarized in **Supplemental Digital Content 1** (**http://links.lww.com/PRSGO/D234**).[6,12,14,17] Follow-up durations postreconstruction averaged 60.88 months,[1,14,15] with a longer follow-up period observed in patients without recurrence (60.92 months) compared with those with recurrence (48.75 months), indicating a statistically significant difference (W = 4492, $P < 0.05$). Six patients (seven scars) experienced recurrence in their mastectomy scars.[1,6,15,17] Detailed information about the characteristics, histological diagnosis, and outcomes of the patients with recurrence is presented in Table 1. Adverse outcomes postreconstruction were reported in 83 patients (2.21%),[5,12–15] as detailed at **Supplemental Digital Content 1** (**http://links.lww.com/PRSGO/D234**). The costs associated with pathological examinations varied, with US institutions covering an average of $602 in some studies,[12,13] whereas patients in the Netherlands and the United Kingdom faced costs around US $65.[4,14]

In addition to the observational studies, we encountered two additional case reports and two case series.[2,18–20] The findings of these publications are described in Table 2.

DISCUSSION

In this study, the histological examination of mastectomy scars during delayed reconstruction revealed a recurrence rate of 0.19%, not significantly different from expected rates based on past literature.[7] The average time of delayed reconstruction was 19.9 months. Despite a difference in reconstruction timing between cases with recurrence at reconstruction and those without, no association was found between the ratio of positive pathological examination results and reconstruction timing. This aligns with comparable rates of locoregional breast cancer recurrence reported after immediate or delayed postmastectomy procedures.[21] Furthermore, the timing of local recurrence was not linked to the extent of reconstruction.[22]

Out of the reviewed studies, only three recommended a routine histological examination.[6,15,17] Conversely, other publications did not endorse routine evaluation, with all but one reporting a 0% recurrence rate at reconstruction. The other singular study opposing routine evaluation had a recurrence rate of 0.77%,[1] suggesting that discovering microscopic scar recurrence is rare, and consequently, the practical benefit of such histological assessments during delayed reconstruction remains uncertain and questionable.

The histological analysis of mastectomy scars in breast reconstruction is considered crucial for early detection of imperceptible recurrences or new neoplasms.[12] Omitting routine examination raises concerns about patient safety. However, it is essential to note that excised scar examination covers only a small part of the breast, potentially overlooking early malignancies in other areas. Recent findings suggest a lower local recurrence rate at the scar compared with the rest of the breast tissue.[7] Additionally, native breast skin, often

Table 1. Patients with Recurrence at Reconstruction among Included Publications

Publication	Age at Reconstruction (y)	Mastectomy Diagnosis	Interim Adjuvant Treatment	Operation Interval (Mo)	Reconstruction	Reconstruction Diagnosis	Postreconstruction Treatment	Postreconstruction Follow-up (Mo)	Outcome
Alam et al[1]	—	Invasive ductal carcinoma	—	—	—	Invasive ductal carcinoma	—	60	No recurrence
Zambacos et al[6]	36	Locally extensive carcinoma, nodal involvement	Chemotherapy and radiotherapy	24	Left latissimus dorsi and permanent tissue expander	Estrogen-receptor positive carcinoma in lymph-vascular spaces of the skin	Chemotherapy (Zoladex, Arimidex)	—	—
Warner et al[15]	49	Multifocal ductal carcinoma	Chemotherapy and radiotherapy	72	Latissimus dorsi myocutaneous flap and silicone implant	Adenocarcinoma at scar and axillary lymph node, consistent with the breast primary tumor	Anastrozole	60	No recurrence
Warner et al[15]	50	Bilateral multifocal breast carcinoma, axillary nodal involvement	Chemotherapy	24	Bilateral tissue expanders	Bilateral breast carcinoma	Radiotherapy; bilateral deep inferior epigastric perforator flap breast reconstruction 15 months later	48	No recurrence
Warner et al[15]	42	Infiltrating lobular carcinoma	Tamoxifen	36	Latissimus dorsi flap and silicone implant	Infiltrating lobular carcinoma	Two more local excisions, followed by Anastrozole treatment.	27	Metastasis-related fatality
Nahabedian et al[17]	—	Breast carcinoma	Radiotherapy	—	Transverse rectus abdominis musculocutaneous flap, and secondary revision procedure conducted 6 months later	Breast carcinoma	Appropriate oncologic management	—	—

Table 2. Additional Case Reports and Studies

Publication	Publication Year	Diagnosed Population	Reconstruction Time, Mean and Range, Mo	Radiation/Chemotherapy before Reconstruction	Diagnosis	Postreconstruction Follow-up, Mo	Postreconstruction Recurrence	Advocate Routine Histology
Granick et al[2]	1987	4	Patient 1–6; patient 2–12; patient 3–24; patient 4–132	Patient 2: chemotherapy; patient 3: radiation	Patient 1: clinically detected adenocarcinoma; patient 2: clinically detected adenocarcinoma; patient 3: intraductal and infiltrating adenocarcinoma; patient 4: clinically detected infiltrating adenocarcinoma.	Patient 2–12	None	+
Rayatt et al[18]	2007	2	Patient 1–84; patient 2–18	Patient 1: radiation	Carcinoma	Patient 1–35 months; patient 2–33 months	None	—
Hsieh et al[19]	2007	1	67	No	Lobular carcinoma	36 months	None	+
Sinha et al[20]	2004	1	144	Radiation	Adenocarcinoma	Not stated	None	+

excluded from routine examination during autologous delayed reconstruction,[14] could be a potential site for recurrence. Supporting this concern, 83 patients (or 2.21%) experienced recurrences not confined to the scar area or encountered metastasis. This underscores the need for a more tailored approach to ensure comprehensive patient safety.

Supporting this approach are factors such as the costs associated with routine pathologic analysis and the potential for false negatives. Addressing the financial implications of histological evaluation in patient care is crucial. The appropriate use of pathology not only contributes to significant cost savings in healthcare but also ensures patient well-being.[23] The cost of identifying one patient with scar recurrence through pathology ranges from $9414 to $113,643. This range is calculated by applying the NNT, which varies from 144.93 to 188.68 patients, by the mentioned minimal and maximal costs of pathological examinations.[4,12–14] The wide cost range for pathological examinations highlights the variability in pricing among institutions and the challenge in assessing the financial feasibility of routine examinations. These costs, strictly for the examination fees, do not account for any follow-up tests or treatments. This variability complicates the evaluation of routine examination practicality and demonstrates that cost-effectiveness varies by geographic location and hospital policy, influenced by local costs and practices.[24]

A more focused and selective approach to histological examination could aid in identifying patients at a higher risk of scar tissue recurrence.[4] Some experts recommend selective monitoring based on the likelihood of significant findings[25] or associated risk factors.[23] Differentiating based on known risk factors for local recurrence after mastectomy can provide additional justification for the cost-effectiveness of histological examination. These risk factors are typically disease-related and encompass factors such as tumor size (>2 cm), margins (<2 mm), increased grade and T score, extent of nodal involvement, histologic ductal carcinoma, fascia or extracapsular lymphovascular invasion, and chest wall involvement.[7,22,26] Additionally, the combination of ER/PR/HER2 negative, ER/PR negative, and HER2 positive receptor statuses has been associated with increased risk compared with other receptor status combinations.[26] Patient characteristics that elevate the risk include premenopausal status and young age.[26] Charting such an approach is beyond the scope of this article and requires further research.

To the best of our knowledge, this study represents the first systematic review on the subject. However, it has certain limitations, primarily stemming from the diverse presentation of findings and data in the various studies reviewed. Most of these studies are single-center and retrospective observational studies, introducing potential biases and the risk of inaccurate or missing data.

There may be a publication bias, as studies that did not observe any recurrence might not have deemed it relevant to report. Obtaining a more reliable denominator would require an extensive review of papers reporting series of reconstruction, introducing a different kind of bias, as it would be unclear whether there were any recurrences or

not. Despite these challenges, we consider the results of this study to provide the best denominator within these mentioned limitations.

Moreover, when studies mentioned histopathologic diagnoses, the information was often presented in general terms and lacked detailed specifics, such as tumor stage, biology, receptor positivity, and level of differentiation. These details are crucial as they can significantly impact recurrence rates and subsequent management. Although publications provided data on malignancy rates, they frequently lacked a thorough analysis of potential confounding factors, such as patient demographics, surgeon experience, or specific surgical techniques. Another complicating factor is the absence of mentioned pathological examination protocols, which can vary significantly between studies and influence the ratio of positive examinations. All this limits the ability to draw conclusions regarding the correct way of action. Large-scale, higher-quality studies could potentially provide more definitive evidence regarding the characteristics of higher risk patients and whether histological examination of mastectomy scars is necessary for all or only a subset of patients.

Our findings, in concordance with what has been previously reported in the literature, underscore the complexities involved in assessing the importance of histologic examination of mastectomy scars during delayed breast reconstruction. The low recurrence rate, the higher postreconstruction adverse outcomes, the likelihood of recurrence in other areas of the breast, and the unclear cost-effectiveness of the examination all raise doubts about the necessity for routine histological examination. In the current era of multimodality therapy, diverse tools are available to address residual oncological tissue effectively. Therefore, we believe that routine histological examination of the mastectomy scar is unnecessary in delayed breast reconstruction.

CONCLUSIONS

In summary, our systematic review has shown that the rate of malignancy recurrence in delayed breast reconstruction is 0.19%, aligning with expected rates. No significant association was found between reconstruction timing and positive pathological results. Furthermore, a 2.21% negative outcome ratio postreconstruction was observed. Given these findings, alongside the questionable effectiveness and significant cost implications of routine scar examinations, we strongly advise against the routine pathological examination of mastectomy scars during delayed reconstruction, advocating instead for a more individualized approach that considers risk factors for recurrence in such a heterogenous population. Further research is warranted to refine this recommendation.

Ori Berger, MD
Ha-Histadrut Street 2
Ashkelon, Israel
E-mail: droriberger@gmail.com

DISCLOSURE

The authors have no financial interest to declare in relation to the content of this article.

REFERENCES

1. Alam M, Kiely C, Shah SH, et al. Mastectomy scar histopathology of limited clinical value. *Ann Plast Surg.* 2006;57:374–375.
2. Granick MS, Bragdon RW, Hanna DC. Recurrent breast carcinoma at the time of breast reconstruction. *Ann Plast Surg.* 1987;18:69–70.
3. Agostini T, Mori A, Dini M. Contribution to histologic analysis of mastectomy scars following breast reconstruction. *Plast Reconstr Surg.* 2009;124:2197–2198.
4. Momeni A, Tran P, Dunlap J, et al. Is routine histological examination of mastectomy scars justified? An analysis of 619 scars. *J Plast Reconstr Aesthet Surg.* 2013;66:182–186.
5. Soldin MG, Grob M, Dawson A, et al. Routine histological examination of the mastectomy scar at the time of breast reconstruction: important oncological surveillance? *Br J Plast Surg.* 2004;57:143–145.
6. Zambacos GJ, Wilson PA, Miminas D, et al. Routine histological examination of the mastectomy scar at the time of breast reconstruction. *Br J Plast Surg.* 2005;58:122.
7. Kaidar-Person O, Poortmans P, Offersen BV, et al. Spatial location of local recurrences after mastectomy: a systematic review. *Breast Cancer Res Treat.* 2020;183:263–273.
8. Joo JH, Ki Y, Kim W, et al. Pattern of local recurrence after mastectomy and reconstruction in breast cancer patients: a systematic review. *Gland Surg.* 2021;10:2037–2046.
9. Johnson CH, van Heerden JA, Donohue JH, et al. Oncological aspects of immediate breast reconstruction following mastectomy for malignancy. *Arch Surg.* 1989;124:819–23; discussion 823.
10. Stanec Z, Žic R, Budi S, et al. Skin and nipple-areola complex sparing mastectomy in breast cancer patients: 15-year experience. *Ann Plast Surg.* 2014;73:485–491.
11. Noone RB, Frazier TG, Noone GC, et al. Recurrence of breast carcinoma following immediate reconstruction: a 13-year review. *Plast Reconstr Surg.* 1994;93:96–106; discussion 107.
12. Fishman JE, Pang JHY, Dabbs D, et al. Utility and cost effectiveness of routine, histologic evaluation of the mastectomy scar in two-stage, implant-based reconstruction during expander-to-implant exchange. *Plast Reconstr Surg.* 2018;142:836e–839e.
13. Fishman JE, Pang JH, De La Cruz C. Impact and cost-analysis of routine mastectomy scar surveillance in two stage implant-based reconstruction. *Plast Reconstr Surg Glob Open.* 2018;6(4 Suppl):78–79.
14. Woerdeman LAE, Kortmann JBJ, Hage JJ. Routine histologic examination of 728 mastectomy scars: did it benefit our patients? *Plast Reconstr Surg.* 2006;118:1288–1292.
15. Warner RM, Wallace DL, Ferran NA, et al. Mastectomy scars following breast reconstruction: should routine histologic analysis be performed? *Plast Reconstr Surg.* 2009;123:1141–1147.
16. Mathen V, Khan S, O'Brien M, et al. Routine histological examination of the mastectomy scar at the time of breast reconstruction. *J Plast Reconstr Aesthet Surg.* 2006;59:1248–1249.
17. Nahabedian MY. Routine histologic examination of 728 mastectomy scars: did it benefit our patients? *Plast Reconstr Surg.* 2007;120:353.
18. Rayatt SS, Goon PKY, Green SN, et al. Intraoperative findings of cancer in delayed breast reconstruction: a dilemma? *Aesthetic Plast Surg.* 2004;28:399–400.
19. Hsieh F, Malata CM. Incidental lobular carcinoma scar recurrence at delayed breast reconstruction 6 years after mastectomy. *Int J Surg.* 2008;6:e83–e85.
20. Sinha M, Gupta S, Hogg F. A case for sending mastectomy scars for routine histopathology. *Plast Reconstr Surg.* 2007;120:1085–1086.
21. Bargon CA, Young-Afat DA, Ikinci M, et al. Breast cancer recurrence after immediate and delayed postmastectomy breast reconstruction—a systematic review and meta-analysis. *Cancer.* 2022;128:3449–3469.

22. Dillekås H, Demicheli R, Ardoino I, et al. The recurrence pattern following delayed breast reconstruction after mastectomy for breast cancer suggests a systemic effect of surgery on occult dormant micrometastases. *Breast Cancer Res Treat*. 2016;158:169–178.
23. Fisher M, Burshtein AL, Burshtein JG, et al. Pathology examination of breast reduction specimens: dispelling the myth. *Plast Reconst Surg Global Open*. 2020;8:e3256.
24. Raab SS. The cost-effectiveness of routine histologic examination. *Am J Clin Pathol*. 1998;110:391–396.
25. Fisher M, Alba B, Bhuiya T, et al. Routine pathologic evaluation of plastic surgery specimens: are we wasting time and money? *Plast Reconstr Surg*. 2018;141:812–816.
26. Van Der Leij F, Elkhuizen PHM, Bartelink H, et al. Predictive factors for local recurrence in breast cancer. *Semin Radiat Oncol*. 2012;22:100–107.