Asian Journal of Surgery (2020) 43, 148–153

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.e-asianjournalsurgery.com

ORIGINAL ARTICLE

Breast cancer hormone receptor negativity, triple-negative type, mastectomy and not receiving adjuvant radiotherapy were associated with axillary recurrence after sentinel lymph node biopsy

Chikako Sekine [a,d,*], Satoko Nakano [a], Akemi Mibu [a], Masahiko Otsuka [b], Toshinori Oinuma [c], Hiroshi Takeyama [d]

[a] Department of Breast Surgery, Kawaguchi Municipal Medical Center, Saitama, Japan
[b] Department of Surgery, Kawaguchi Municipal Medical Center, Saitama, Japan
[c] Department of Pathology, Kawaguchi Municipal Medical Center, Saitama, Japan
[d] Department of Breast and Endocrine Surgery, Jikei University School of Medicine, Tokyo, Japan

Received 27 November 2018; received in revised form 31 January 2019; accepted 1 May 2019
Available online 30 May 2019

KEYWORDS
Adjuvant radiotherapy;
Axillary lymph node recurrence;
Early breast cancer;
Sentinel lymph node biopsy

Summary *Background:* Axillary lymph node dissection (ALND) can be avoided in selected patients with positive sentinel lymph nodes (SLNs). However, regional lymph node recurrence may occur after SLN biopsy (SLNB). This study aimed to identify the risk factors for axillary recurrence to ensure safe axillary surgery.
Methods: Between June 2004 and December 2017, a total of 1056 women underwent SLNB without ALND. Patient data were prospectively entered into the breast cancer database at Kawaguchi Municipal Medical Center. From October 2012, we did not perform ALND in patients with (a) 1 or 2 positive SLNs, (b) positive SLNs that were unmatted or did not show gross extra nodal extension, (c) a clinical tumor size $\leq$5 cm, and in (d) those who received adjuvant endocrine therapy or chemotherapy and radiotherapy. Subsequently, appropriate adjuvant systemic and/or radiation treatment was administered.
Results: Of the 1056 patients included, 996 had negative SLNs, 49 had positive SLNs, and 11 had undetectable SLNs. The identification rate for SLNs was 99.0%, and the median number of removed SLNs was 2. During the median 6.9-year follow-up period, 10 patients (1.0%) showed axillary recurrence without SLNs metastasis. Hormone receptor negativity ($p < 0.01$), triple-negative type (0.047), mastectomy (<0.01) and not receiving adjuvant radiotherapy (<0.01) were significantly related to axillary recurrence.
Conclusion: ALND can be safely avoided in selected patients with early breast cancer. Patients

* Corresponding author. 3-25-8, Nishishimbashi, Minato-ku, Tokyo, 105-8461, Japan.Fax: +81 3 5472 4140.
E-mail address: chikako.s@jikei.ac.jp (C. Sekine).

https://doi.org/10.1016/j.asjsur.2019.05.001

with hormone receptor-negative tumors, especially triple-negative breast cancer, patients who underwent mastectomy without ALND or those who did not receive adjuvant radiotherapy should be followed up carefully.

1. Introduction

Axillary staging is important in predicting the prognosis and local control of early breast cancer. Sentinel lymph node biopsy (SLNB) is a widely accepted method that avoids unnecessary axillary lymph node dissection (ALND).[1,2] The American College of Surgeons Oncology Group (ACOSOG) Z0011 trial suggested that SLNB alone is acceptable in certain patients despite the presence of sentinel lymph node (SLN) metastasis.[3] The 2014 guidelines of the American Society of Clinical Oncology (ASCO) recommend that women with one to two metastatic SLNs planning to undergo breast-conserving surgery along with whole-breast radiation should not undergo ALND.[1] Although in the ACOSOG Z0011 trial, patients were selected by surgical method, tumor size, the number of positive SLNs, and the planning of adjuvant therapy including whole-breast radiation therapy, the selection criteria did not include hormone receptor (HR) status and human epidermal growth factor receptor 2 (HER2) expression. On the other hand, regional lymph node recurrence was observed in some cases after SLNB without ALND. Therefore, the aim of this study was to identify the risk factors for axillary lymph node recurrence in patients who underwent SLNB without ALND.

2. Methods

Between June 2004 and December 2017, 1056 women underwent SLNB without ALND at Kawaguchi Municipal Medical Center; their data were prospectively entered into the breast cancer database of the center. From October 2012, we did not perform ALND for patients with (a) 1 or 2 positive SLNs, (b) positive SLNs that were unmatted or did not show gross extra nodal extension, (c) a clinical tumor size $\leq$ 5 cm, and in those (d) who received adjuvant endocrine therapy or chemotherapy and radiotherapy. Cases of mastectomy, lumpectomy with a positive margin and additional resection or boost radiotherapy, and bilateral cancer were also included.

The ACOSOG Z0011 criteria only included patients undergoing lumpectomy as opposing tangential field irradiation often treats low axillary nodes. For patients with positive SLNs who underwent lumpectomy, we expanded the irradiation area to the axillary field. In patients with positive SLNs who underwent mastectomy, we performed irradiation of the axillary field only. Radiation therapy to the chest wall was only performed for patients with high-risk disease, i.e., a pathological tumor size >5 cm or tumor invasion of the skin or chest wall. Clinically node-negative patients receiving neoadjuvant chemotherapy underwent SLNB prior to chemotherapy.

Adjuvant systemic therapy and/or radiation treatment was administered as per the National Comprehensive Cancer Network and the Japanese Breast Cancer Society Clinical Practice Guidelines and was based on the patients' pathological and clinical traits. The adjuvant therapy administered before and after publication of the Z0011 trial was the same in patients with the exception of using radiotherapy in patients with positive SLNs. We used only trastuzumab for adjuvant and neoadjuvant HER2-targeted therapy. Follow-up visits included a physical examination of the breast and regional lymph nodes twice per year and annual mammography and sonography. All patients were followed-up for 10 years after surgery.

SLNs were identified using a combination of technetium-99 m-labeled sulfur colloid and blue dye that was injected at the areola on the morning of the day of surgery. All blue nodes and hot nodes were collected for intraoperative histological investigation. All collected SLNs were bisected longitudinally. Half of each node was examined intraoperatively using hematoxylin and eosin (H&E) staining of frozen sections that represented the maximum cut surface. The other half was fixed in 10% buffered formalin for postoperative histological examination by H&E staining of paraffin-embedded sections.

Data on patients, tumor characteristics of patients with or without axillary recurrence, and the treatments of cases with axillary recurrence were reviewed. We used a log-rank test to compare characteristics among patients with invasive breast cancer. Cases with missing data or non-invasive cancer were excluded. All tests were two-sided, and *P*-values <0.05 were considered significant. All statistical analyses were performed using STATA statistical software (version 14; Stata Corp. College State, TX, USA).

3. Results

All patient and tumor characteristics are listed in Table 1. Between June 2004 and December 2017, a total of 1056 patients with clinically negative nodes underwent SLNB without ALND. Of these, 996 had negative and 49 had positive SLNs; in 11 patients, SLNs were not detected. A median of 2 (1—7) SLNs were removed, and the SLN-detection rate was 99.0%. The median age of the patients was 59 years (range, 21—88 years). The median invasive breast tumor size was 15 mm (range, 0.05—85 mm). In addition, 1.8% of the tumors were pathological T3 lesions, and 131 patients (12.5%) developed lymphatic vessel invasion. Regarding procedures, 691 (65.7%) patients underwent lumpectomy, of which 666 (96.4%) patients received whole

Table 1 Patient and tumor characteristics (N = 1056).

Age, years	
median (min, max)	59 (21, 88)
SLN, number	
median (min, max)	2.0 (0, 7)
SLN detection rate	99.0%
Tumor size, mm	
Median (min, max)	15 (0.05, 85)
In situ, n (%)	131 (12.4%)
<20 mm, n (%)	652 (61.7%)
20–50 mm, n (%)	241 (22.8%)
>50 mm, n (%)	17 (1.6%)
Missing data, n (%)	15 (1.4%)
Histological type, n (%)	
Ductal infiltration	817 (77.4%)
Lobular infiltration	36 (3.4%)
Other	57 (5.4%)
In situ	131 (12.4%)
Missing data	15 (1.4%)
Tumor grade, n (%)	
1	631 (59.8%)
2	149 (14.1%)
3	130 (12.3%)
In situ	131 (12.4%)
Missing data	15 (1.4%)
Lymphatic vessel invasion, n (%)	
Positive	134 (12.7%)
Negative	907 (85.9%)
Missing data	15 (1.4%)
Surgical method, n (%)	
Lumpectomy	696 (65.9%)
Mastectomy	345 (32.7%)
Missing data	15 (1.4%)

SLN, sentinel lymph node.

breast radiotherapy, 22 (3.2%) patients received whole breast and axillary radiotherapy, and 3 (0.4%) patients did not receive any radiotherapy. The other 339 (32.3%) patients underwent mastectomy, where 11 (3.2%) patients received radiotherapy for chest wall, 10 (2.9%) patients received only axillary radiotherapy and 318 patients did not receive any radiotherapy.

After a median follow-up of 82.7 months (range, 1–122 months), 10 patients (0.95%) showed axillary recurrence with no SLN metastasis. The median time to axillary lymph node recurrence was 23 months (range, 8–92 months). All 10 patients received adjuvant therapy (Table 2). By the last follow-up in December 2017, 7 patients were disease free and 3 patients showed distant metastasis.

After the diagnosis of axillary lymph node recurrence, all except for one patient received ALND and additional therapy. Since we started widening the inclusion criteria after the median follow-up of 31.0 months (October 2012), only one patient experienced axillary recurrence with no SLN metastasis. This patient had a triple-negative, 1.2 cm, invasive ductal carcinoma and received adjuvant chemotherapy with cyclophosphamide, adriamycin, and 5-fluorouracil. She developed axillary lymph node recurrence 8 months after surgery, while receiving adjuvant radiotherapy for breast cancer.

After excluding 130 cases of non-invasive cancer and those with missing data, univariate analysis showed that the surgery type, HR status, breast cancer subtype, and radiotherapy were significant predictive factors for axillary lymph node recurrence. However, patient age, the number of SLNs, tumor size, histological type, nuclear grade, lymphatic vessel invasion, SLN metastasis, and HER2 status were not correlated with axillary recurrence (Table 3).

4. Discussion

SLNB has allowed to avoid ALND morbidities, including arm lymphedema and neurologic injury, in patients with clinically node-negative breast cancer.[1,2,4] Since the ACOSOG Z0011 trial result was published,[3] the expansion of the selection criteria, allowing for the avoidance of ALND, may gain popularity in patients with breast cancer. However, false-negative SLNBs can occur even when a biopsy is performed by an experienced specialist and expanding the criteria to avoid ALND may lead to an increase in axillary recurrence rate. Therefore, it is important to identify the factors associated with axillary lymph node recurrence.

Table 2 Summary of axillary recurrence cases.

Case	Age (years)	Number of SLNs	Number of positive SLNs	LY	Tumor size, mm	HR	HER2	Adjuvant therapy	Time to recurrence (months)
1	75	2	0	0	35	+	−	ANA	13
2	42	2	0	0	55	−	−	CAF	10
3	58	4	0	1	18	−	+	CAT + T	31
4	65	1	0	0	25	+	+	CAF + T	15
5	61	2	0	0	6	−	+	AC + T	13
6	59	1	0	1	25	+	−	ANA	50
7	68	3	0	0	35	−	−	CAF	52
8	44	1	0	0	13	+	−	LPR + TAM	91
9	66	4	0	1	25	+	−	TAM	53
10	62	1	0	0	12	−	−	CAF	6

A: adriamycin; ANA: anastrozole; C: cyclophosphamide; F: 5-fluorouracil; HER2: human epidermal growth factor receptor 2; HR: hormone receptor; LPR: leuprorelin acetate; LY: lymphatic vessels invasion; SLN: sentinel lymph node; T: trastuzumab; TAM: tamoxifen.

Table 3 Axillary recurrence among invasive tumors, log-rank test (N = 900).

	N (%)	Axillary recurrence (n = 10)	No axillary recurrence (n = 890)	*P*-value
Age, years				0.47
<50	266 (29.6%)	2 (20%)	264 (29.7%)	
≥50	634 (70.4%)	8 (80%)	626 (70.3%)	
SLNs				0.55
≤2	634 (70.4%)	7 (70%)	627 (70.4%)	
>2	255 (28.3%)	3 (30%)	252 (28.3%)	
Missing data	11 (1.2%)	–	11 (1.2%)	
Tumor size, mm				0.059
≤20	642 (71.3%)	4 (40%)	638 (71.7%)	
>20, ≤50	238 (26.4%)	5 (50%)	233 (26.1%)	
>50	20 (2.2%)	1 (10%)	19 (2.1%)	
Histological type				0.57
Ductal infiltration	807 (89.7%)	10 (100%)	797 (89.6%)	
Lobular infiltration	36 (4.0%)	–	36 (4.0%)	
Other	57 (6.3%)	–	57 (6.4%)	
Nuclear grade				0.079
1	624 (69.3%)	4 (40%)	620 (70.0%)	
2	146 (16.2%)	4 (40%)	142 (16.0%)	
3	130 (14.4%)	2 (20%)	128 (14.4%)	
Lymphatic vessels invasion				0.11
Positive	131 (14.6%)	3 (30%)	128 (14.4%)	
Negative	769 (85.4%)	7 (70%)	762 (85.6%)	
Surgery				<0.01
Lumpectomy	613 (68.1%)	3 (30%)	610 (68.5%)	
Mastectomy	287 (31.9%)	7 (70%)	280 (31.5%)	
SLN metastasis				0.53
Negative	851 (94.6%)	10 (100%)	841 (94.5%)	
Positive	49 (5.4%)	–	49 (5.5%)	
HR				<0.01
Negative	157 (17.4%)	5 (50%)	152 (17.1%)	
Positive	734 (81.6%)	5 (50%)	729 (81.9%)	
Missing data	9 (1.0%)	–	11 (1.0%)	
HER2 receptor				0.073
Negative	785 (87.2%)	7 (70%)	778 (87.4%)	
Positive	106 (11.8%)	3 (30%)	103 (11.6%)	
Missing data	9 (1.0%)	–	10 (1.0%)	
Receptor status				0.047
HR+/HER2−	687 (77.1%)	4 (40%)	683 (76.7%)	
HR+/HER2+	47 (5.3%)	1 (10%)	46 (5.2%)	
HR−/HER2+	59 (6.6%)	2 (20%)	57 (6.4%)	
HR−/HER2−	98 (11.0%)	3 (30%)	95 (10.7%)	
Missing data	9 (1.0%)	–	9 (1.0%)	
Radiotherapy				<0.01
Yes	631 (70.1%)	3 (30%)	628 (70.1%)	
No	269 (29.9%)	7 (70%)	262 (29.4%)	

HER2: human epidermal growth factor receptor 2; HR: hormone receptor; SLN: sentinel lymph node.

According to previous studies, the axillary recurrence rate after SLNB without ALND was approximately 1.0%.[5–9] Consistent with these findings, our study showed a low axillary recurrence rate, even after expanding the criteria to avoid ALND (since October 2012). Although false negative SLNBs or skip metastasis in non-sentinel lymph nodes are considered as a cause of axillary recurrence, according to the ACOSOG Z0011 trial, these small amount of cancer cells are treated by adjuvant therapy and might not affect overall and disease-free survival.

In our study, the number of patients with positive SLNs who did not undergo ALND was small, and the follow-up period was short. However, several previous studies reported that axillary recurrence after SLNB without ALND tended to occur within 2 years of the surgery.[5,10] Furthermore, the median time to axillary recurrence in the

ACOSOG Z0010 trial was only 19.1 months.[4] Ogiya et al. reported that HR-positive tumors recurred later than HR-negative tumors.[11] However, in this study, the number of cases with axillary recurrence was too small to analyze the recurrence time relative to HR status.

In our cohort, we found that receptor status, especially HR negativity, but not HER2 status, was significantly related with axillary recurrence. Lymphatic vessel invasion, which was reported as a predictive factor of axillary lymph node recurrence, was not related to axillary recurrence.[3,11–13] According to previous studies, the patterns of recurrence and outcomes differ among breast cancer subtypes. HR-negative tumors are more likely to recur, even in patients receiving adjuvant therapy.[14–16] Voduc et al.[16] found that triple-negative tumors were associated with higher local recurrence rates and poorer overall survival rates than HR-positive tumors.

Based on previous studies, triple-negative tumors are less likely to invade lymphatic vessels and metastasize to lymph nodes, despite their high local recurrence rate and aggressive characteristics.[17–19] This contradiction has not been explained clearly, but one theory is the existence of hidden cancer cells, which could resist the administration of adjuvant therapy. Only a small number of cancer cells survive after surgery in patients who meet the criteria for avoiding ALND, and systemic adjuvant therapy can destroy these remaining cells. However, the development of axillary lymph node recurrence may indicate that adjuvant therapy has failed. Ugras et al.[17] suggested that this issue is due to the unavailability of targeted therapy (such as hormone or HER2-targeted therapy) for triple-negative tumors. Therefore, there was a certain rate that any adjuvant therapy is less effective. On the other hand, in the ACOSOG Z0011 trial, there was no difference in overall and disease-free survival between HR-positive and HR-negative patients,[3,5,20] but the number of patients with triple-negative tumors registered in the trial were small. Therefore, triple-negative tumors should not be excluded in the criteria for SLNB without ALND, and their progression should be carefully monitored.

We found that mastectomy was associated with axillary lymph node recurrence. Although patients with large tumors tend to undergo mastectomy and are more likely to have a poor prognosis, the tumor size was not significantly related to axillary recurrence. The only other difference between lumpectomy and mastectomy cases was the administration of radiotherapy, suggesting that radiotherapy, even standard tangential irradiation after surgery, can prevent cancer recurrence. Previous studies showed that the absence of radiation therapy after SLNB was significantly related with axillary recurrence in patients with breast cancer,[5,8,21] which supports our findings.

The use of axillary field radiation therapy in selected patients with early breast cancer is still controversial. In the ACOSOG Z0011 trial, the records on radiation therapy were available in only two-third of the patients. In addition, the records included high-tangent or third-field irradiation.[22] Mamtani et al.[23] found that post-mastectomy radiation therapy in patients with early-stage breast cancer who had axillary micro-metastasis or isolated tumor cells did not decrease the rate of axillary recurrence; the risk for axillary recurrence in these patients was considered as sufficiently low. Therefore, routine axillary field irradiation is not required in patients with negative SLNs who undergo mastectomy.

Although mastectomy was not included in the ACOSOG Z0011 criteria, in this study, we showed that patients with positive SLNs who underwent mastectomy can avoid ALND if they receive axillary field radiotherapy after surgery. If the first recurrence is only in the axillary lymph nodes, additional ALND and adjuvant therapy may be used for curative purposes. Regular follow-up of such patients is important to detect recurrence at an early stage and while it is localized to the lymph nodes.

Although our study identified several predictors for axillary lymph node recurrence, it has several limitations. First, we could not perform multivariate analysis for all analyzed parameters because the number of cases with recurrence was small. Second, the follow-up period was short, especially after expanding the selection criteria. However, several studies have reported that axillary recurrence after SLNB without ALND tended to occur within 2 years of the surgery.[6,10] Further large randomized trials should be performed to confirm the results of our cohort study.

5. Conclusion

ALND can be safely avoided in selected patients with early breast cancer despite the presence of SLN metastasis. HR-negative tumors, especially the triple-negative type, mastectomy, and not receiving radiotherapy are significant factors for axillary recurrence. Therefore, patients with these factors should be followed up carefully.

Conflicts of interest

The authors have no conflicts of interest to declare.

Acknowledgements

None.

References

1. Lyman GH, Giuliano AE, Somerfield MR, et al. American society of clinical Oncology guideline recommendations for sentinel lymph node biopsy in early stage breast cancer. *J Clin Oncol*. 2005;23:7703–7720.
2. Naik AM, Fey J, Gemignani M, et al. The risk of axillary relapse after sentinel lymph node biopsy for breast cancer is comparable with that of axillary lymph node dissection: a follow-up study of 4008 procedures. *Ann Surg*. 2004;240:462–468.
3. Giuliano AE, McCall L, Beitsch P, et al. Locoregional recurrence after sentinel lymph node dissection with or without axillary dissection in patients with sentinel lymph node metastases: the American College of Surgeons Oncology Group Z0011 randomized trial. *Ann Surg*. 2010;252:426–432.
4. Hunt KK, Ballman KV, McCall L, et al. Factors associated with local-regional recurrence after a negative sentinel node dissection: results of the ACOSOG Z0010 trial. *Ann Surg*. 2012; 256:428–436.

5. Giuliano AE, Ballman K, McCall L, et al. Locoregional recurrence after sentinel lymph node dissection with or without axillary dissection in patients with sentinel lymph node metastases: long-term follow-up from the American College of Surgeons Oncology Group (Alliance) ACOSOG Z0011 randomized trial. *Ann Surg*. 2016;264:413—420.
6. Poletti P, Fenaroli P, Milesi A, et al. Axillary recurrence in sentinel lymph node-negative breast cancer patients. *Ann Oncol*. 2008;19:1842—1846.
7. Kiluk JV, Ly QP, Meade T, et al. Axillary recurrence rate following negative sentinel node biopsy for invasive breast cancer: long-term follow-up. *Ann Surg Oncol*. 2011;18(Suppl 3):S339—S342.
8. van Wely BJ, Wildenberg FJH, Gobardhan P, et al. Axillary recurrence after sentinel lymph node biopsy: a multicenter analysis and follow-up of sentinel lymph node negative breast cancer patients. *Eur J Surg Oncol*. 2012;38:925—931.
9. Inoue T, Nishi T, Nakano Y, et al. Axillary lymph node recurrence after sentinel lymph node biopsy performed using a combination of indocyanine green fluorescence and the blue dye method in early breast cancer. *Breast Canc*. 2016;23:295—300.
10. Fisher B, Jeong JH, Anderson S, et al. Twenty-five-year follow-up of a randomized trial comparing radical mastectomy, total mastectomy, and total mastectomy followed by irradiation. *N Engl J Med*. 2002;347:567—575.
11. Metzger-Filho O, Sun Z, Viale G, et al. Patterns of recurrence and outcome according to breast cancer subtypes in lymph node-negative disease: results from international breast cancer study Group trials VIII and IX. *J Clin Oncol*. 2013;31:3083—3090.
12. Takei H, Kurosumi M, Yoshida T, et al. Axillary lymph node dissection can be avoided in women with breast cancer with intraoperative, false-negative sentinel lymph node biopsies. *Breast Canc*. 2010;17:9—16.
13. Lin PH, YEH MH, LIU LC, et al. Clinical and pathologic risk factors of tumor recurrence in patients with node-negative early breast cancer after mastectomy. *J Surg Oncol*. 2013;108:352—357.
14. Nguyen PL, Taghian AG, Katz MS, et al. Breast cancer subtype Approximated by estrogen receptor, progesterone receptor, and HER-2 is associated with local and distant recurrence after breast-conserving therapy. *J Clin Oncol*. 2008;26:2373—2378.
15. Lowery AJ, Kell MR, Glynn RW, et al. Locoregional recurrence after breast cancer surgery: a systematic review by receptor phenotype. *Breast Canc Res Treat*. 2012;133:831—841.
16. Voduc KD, Cheang MC, Tyldesley S, et al. Breast cancer subtypes and the risk of local and regional relapse. *J Clin Oncol*. 2010;28:1684—1691.
17. Ugras S, Stempel M, Patil A, Morrow M. Estrogen receptor, progesterone receptor, and HER2 status predict lymphovascular invasion and lymph node involvement. *Ann Surg Oncol*. 2014;21:3780—3786.
18. Crabb SJ, Cheang MC, Leung S, et al. Basal breast cancer molecular subtype predicts for lower incidence of axillary lymph node metastases in primary breast cancer. *Clin Breast Canc*. 2008;8:249—256.
19. Wiechmann L, Sampson M, Stempel M, et al. Presenting features of breast cancer differ by molecular subtype. *Ann Surg Oncol*. 2009;16:2705—2710.
20. Giuliano AE, Ballman K, McCall L, et al. Effect of axillary dissection vs No axillary dissection on 10-year overall survival among women with invasive breast cancer and sentinel node metastasis: the ACOSOG Z0011 (Alliance) randomized trial. *JAMA*. 2017;318:918—926.
21. Houvenaeghel G, Classe JM, Garbay JR, et al. Survival impact and predictive factors of axillary recurrence after sentinel biopsy. *Eur J Cancer*. 2016;58:73—82.
22. Jagsi R, Chadha M, Moni J, et al. Radiation field design in the ACOSOG Z0011 (Alliance) trial. *J Clin Oncol*. 2014;21:3600—3606.
23. Mamtani A, Patil S, Stempel M, Morrow M. Axillary micrometastases and isolated tumor cells are not an indication for past-mastectomy radiotherapy in stage 1 and 2 breast cancer. *Ann Surg Oncol*. 2017;24:2182—2188.