

# Ultrasound for postoperative surveillance after mastectomy in patients with breast cancer

## A retrospective study

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### Abstract

This study aimed to evaluate the clinical usefulness of postoperative surveillance by ultrasound (PSU) in patients after breast cancer surgery.

In this retrospective study, 324 patients with breast cancer after mastectomy were included between January 2006 and December 2008. The final-positive lesions (FPL) were diagnosed according to the results of cytopathology, clinical and imaging examinations. The outcome evaluations included the sensitivity (SS), specificity (SC), ultrasound accuracy for FPL (UAFPL), and positive predictive value (PPV) after the mastectomy.

A total of 5117 ultrasound examinations were conducted for all those patients to the December 2016. After mastectomy, the SS, SC, UAFPL, and PPV were as follows: mastectomy bed (SS, 100.0%; SC, 99.7%; UAFPL, 99.7%; and PPV, 36.0%), contralateral breast (SS, 100.0%; SC, 99.0%; UAFPL, 99.0%; and PPV, 25.4%), ipsilateral axillary or supraclavicular (SS, 91.7%; SC, 99.4%; UAFPL, 99.4%; and PPV, 25.6%), and contralateral axilla or supraclavicular lymph nodes (SS, 100.0%; SC, 99.9%; UAFPL, 99.9%; and PPV, 33.3%).

In summary, we demonstrated that applied PSU can detect the malignant lesions in the breast regional area with high sensitivity, specificity and accuracy.

**Abbreviations:** BC = breast cancer, CM = contralateral malignancy, FPL = final-positive lesions, LRR = locoregional recurrence, LUE = locoregional ultrasound examinations, PPV = positive predictive, PSU = postoperative surveillance by ultrasound, SC = specificity, SS = sensitivity, UAFPL = ultrasound accuracy for FPL.

**Keywords:** breast cancer, mastectomy, postoperative surveillance, ultrasound

## 1. Introduction

Breast cancer (BC) is one of the most common cancers among the women population all over the world.<sup>[1]</sup> It is also the one of the leading causes of death among those population.<sup>[1–3]</sup> Advances in early diagnosis and BC treatment, a combination of surgery, chemotherapy, and radiation therapy, in the past decades have resulted in prolonged survival in patients with BC.<sup>[4–10]</sup> However,

the major problem for the BC management is still its local-regional recurrence and distant metastasis in BC patients who have previously undergone surgery.<sup>[11–16]</sup> It has been reported that early detection of its recurrence can not only help to control the disease and its treatment, but also can help to improve the survival for BC patients after surgery.<sup>[17–18]</sup>

In 2006, the American Society of Clinical Oncology updated the BC follow-up and management guidelines, and recommended an annual mammography for the follow-up in patients with BC.<sup>[19–22]</sup> Although this guideline did not recommend ultrasound examination as the postoperative follow-up, several studies still reported that ultrasound examination is a very helpful way in the early detection of BC recurrence.<sup>[17,23]</sup> However, only few studies specifically focused on the ultrasound detection of patients with BC after mastectomy.<sup>[23]</sup>

Currently, limited data of postoperative surveillance by ultrasound (PSU) in such particular patients among Chinese population are available. Thus, in this study, we aimed to assess the clinical usefulness of PSU for the detection in patients with BC after mastectomy.

## 2. Methods

In this retrospective study, 324 patients with breast cancer after mastectomy were included. It was formally approved by the Medical Ethical Committee of Inner Mongolia Forestry General Hospital, and The Second Affiliated Hospital of Mudanjiang Medical University. The informed consent was obtained from all patients. It was conducted at Inner Mongolia Forestry General Hospital, and The Second Affiliated Hospital of Mudanjiang

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Medical University from January 2006 to December 2008. Patients were excluded if they lost to ultrasound follow-up less than 3 year, and patients received breast conservation surgery. In addition, patients who already had recurrent diseases or distant metastases were also excluded.

A total of 5117 PSU examinations were conducted for all those patients to the December 2016. It was conducted by six experienced radiologists in breast examination using a Siemens ATL 5000 (Philips, Best, Netherlands) with linear probe 13 MHz. PSU was conducted every 6 months, and mammography was performed each year. PSU was performed at the mastectomy bed, contralateral breast, and also bilateral axillary and supraclavicular after mastectomy surgery. Mammography was performed at the contralateral breast. Additionally, we also applied ultrasound guided fine needle aspiration biopsy if the suspicious axillary, or supraclavicular or lesions were found in the mastectomy bed.

In this study, we assessed the sensitivity (SS), specificity (SC), ultrasound accuracy for final-positive lesions (UAFPL), and positive predictive value (PPV) in patients with BC after the mastectomy.

Locoregional recurrence (LRR) was defined as recurrence in the mastectomy bed, or bilateral axillary and supraclavicular after mastectomy. Contralateral malignancy (CM) was defined as recurrence occurred in the contralateral normal breast. Ultrasound positive was defined as lesions suspicious for the recurrences of LRR and CM. Distant metastasis was defined as the cancer was found in other parts of the body, except the regional breast areas. It was diagnosis confirmed according to the cytopathology, and the clinical examinations. In addition, true-positive, false positive, false-negative, and true-negative were also defined based on the final positive and ultrasound positive results.

All outcome data were analyzed by the SAS software (version 8.1; SAS Institute, Inc., Cary, NC). Chi-square tests were used to analyze the categorical data, and *t* test or Mann–Whitney *U* test were used to analyze the continuous data with relative risks and 95% confidence intervals. Kaplan–Meier analysis was used to analyze the survival data. The statistical significance level was set at  $P < .05$ .

### 3. Results

In total, 432 patients were screened. Of them, 108 patients were excluded, because they lost to ultrasound follow-up less than 3 years ( $n=41$ ), received breast conservation surgery ( $n=37$ ), recurrent disease ( $n=17$ ), and distant metastases ( $n=13$ ). Thus, 324 patients were included in this study finally. A total of 5117 ultrasound examinations were applied for all those 324 patients to the December 2016.

The characteristics of study population are listed in Table 1. The mean age of all included patients was ( $45.9 \pm 11.2$ ) years. All patients were Chinese and Han ethnicity. The mean tumor size was ( $20.7 \pm 3.3$ )mm, and duration of follow-up were ( $97.1 \pm 21.5$ ). The histopathology included invasive ductal cancer ( $n=269$ ), invasive lobular cancer ( $n=11$ ), ductal cancer in situ ( $n=19$ ), lobular cancer in situ ( $n=5$ ), mucinous cancer ( $n=7$ ), medullary cancer ( $n=6$ ), carbriform cancer ( $n=4$ ), and papillary cancer ( $n=3$ ). The stage of T category consisted of Tis ( $n=24$ ), T1 ( $n=175$ ), T2 ( $n=121$ ), and T3 ( $n=4$ ), and stage of N category were N0 ( $n=201$ ), N1 ( $n=77$ ), N2 ( $n=29$ ), and N3 ( $n=17$ ).

Ninety-four ultrasound positive lesions in 71 patients were found in this study (Table 2). The results of locations and the final

**Table 1**

**Characteristics of study population.**

Characteristics	Value
Mean age, years	45.9 (11.2)
Race (Asian–Chinese)	324 (100.0)
Ethnicity (Han)	324 (100.0)
Occupation	
Employed	267 (82.4)
Unemployed	57 (17.6)
Marital status	
Married	275 (84.9)
Single	49 (15.1)
Tumor size, mm	20.7 (3.3)
Duration of follow-up (months)	97.1 (21.5)
Histopathology	
Invasive ductal cancer	269 (83.0)
Invasive lobular cancer	11 (3.4)
Ductal cancer in situ	19 (5.9)
Lobular cancer in situ	5 (1.5)
Mucinous cancer	7 (2.2)
Medullary cancer	6 (1.9)
Carbriform cancer	4 (1.2)
Papillary cancer	3 (0.9)
Stage of T category	
Tis	24 (7.5)
T1	175 (54.0)
T2	121 (37.3)
T3	4 (1.2)
Stage of N category	
N0	201 (62.0)
N1	77 (23.8)
N2	29 (9.0)
N3	17 (5.2)

Data are present as mean  $\pm$  standard deviation or number (%).

N=lymph node involvement, T=size.

diagnose of ultrasound surveillance with positive lesions are presented in Table 2. Of those, 25 were malignant lesions, and 69 were benign lesions.

The results of ultrasound surveillance for final-positive lesions (FPL) after surgery are summarized in Table 3. The SS, SC, UAFPL, and PPV included mastectomy bed (SS, 100.0%; SC, 99.7%; UAFPL, 99.7%; and PPV, 36.0%), contralateral breast (SS, 100.0%; SC, 99.0%; UAFPL, 99.0%; and PPV, 25.4%), ipsilateral axillary or supraclavicular (SS, 91.7%; SC, 99.4%; UAFPL, 99.4%; and PPV, 25.6%), and contralateral axilla or supraclavicular lymph nodes (SS, 100.0%; SC, 99.9%; UAFPL, 99.9%; and PPV, 33.3%).

**Table 2**

**Results of locations and the final diagnosis of ultrasound surveillance with positive lesions.**

Location	No. of ultrasound positive lesions (n=94)	Malignant (n=25)	Benign (n=69)
Mastectomy bed	21 (22.3)	8 (32.0)	13 (18.9)
Contralateral breast	45 (47.9)	11 (44.0)	34 (49.3)
Ipsilateral axillary or supraclavicular fossa	24 (25.5)	5 (20.0)	19 (27.5)
Contralateral axilla or supraclavicular lymph nodes	4 (4.3)	1 (4.0)	3 (4.3)

**Table 3****The outcomes of ultrasound examinations for final-positive lesions after surgery.**

Location	True-positive	False-positive	True-negative	False-negative	Sensitivity, %	Specificity, %	UAFPL, %	PPV, %
Mastectomy bed	9	16	5092	0	100.0	99.7	99.7	36.0
Contralateral breast	18	53	5046	0	100.0	99.0	99.0	25.4
Ipsilateral axillary or supraclavicular fossa	11	32	5073	1	91.7	99.4	99.4	25.6
Contralateral axilla or supraclavicular lymph nodes	2	4	5111	0	100.0	99.9	99.9	33.3

PPV = positive predictive value, UAFPL = ultrasound accuracy for final-positive lesions.

#### 4. Discussion

Several previous studies have explored the value of ultrasound surveillance for BC patients after surgery. One study investigated the efficacy of locoregional ultrasound examinations (LUE) for the detection of recurrence in asymptomatic patients who underwent mastectomy and the impact of LUE on prognosis.<sup>[17]</sup> It found that LUE was helpful for the early detection in BC recurrence in patients with BC after mastectomy, and it may result in a better prognosis for patients.<sup>[17]</sup> The other study assessed the diagnostic performance of ultrasound examinations for the malignant lesion detection in patients with postoperative BC, and evaluated its clinical value in such kinds of patients.<sup>[24]</sup> It concluded that postoperative ultrasound examinations for detection of malignant lesions in patients with BC had a high sensitivity.<sup>[24]</sup> Thus, it can be used as a predictor of distant metastasis in patients received mastectomy, but not for patients with breast conservation surgery.<sup>[24]</sup> Another study explored the detection of lymph node recurrence in BC patients after surgery.<sup>[23]</sup> Its results demonstrated that ipsilateral lymph node recurrence is a distant metastasis predictor, and its assessment during ultrasound surveillance in BC patients is also useful for early detection of lymph node recurrence in asymptomatic patients.<sup>[23]</sup>

The results of our study are consistent with the previous studies.<sup>[17,24]</sup> Although several studies have focused on the impact of PSU in patients with BC, no studies specifically focused on such issue among Chinese female population with BC. In this study, we evaluated the clinical usefulness of PSU in patients after BC surgery. We found that PSU can be used for the detection of the malignant lesions in patients of BC after surgery with high SS, SC, and UAFPL.

This study has 2 limitations. First, this study only included Chinese Han ethnicity population, and it may be not affect to the other ethnicities in China. Second, we just included patients with BC who received the mastectomy, but not the breast conservation surgery, so we are not sure if it still works in patients with BC who received breast conservation surgery.

#### 5. Conclusions

The results of this study demonstrated that PSU can be used for detection of the malignant lesions in the breast regional area of Chinese patients with BC.

#### References

- Forouzanfar MH, Foreman KJ, Delossantos AM, et al. Breast and cervical cancer in 187 countries between 1980 and 2010: a systematic analysis. *Lancet* 2011;378:1461–84.
- Xu F, Zhang C, Cui J, et al. The prognostic value and potential drug target of phosphatase and tensin homolog in breast cancer patients: a meta-analysis. *Medicine (Baltimore)* 2017;96:e8000.
- Zhang J, Huang Y, Wang C, et al. Efficacy and safety of endocrine monotherapy as first-line treatment for hormone-sensitive advanced breast cancer: a network meta-analysis. *Medicine (Baltimore)* 2017;96:e7846.
- Sato M, Shirakami G, Fukuda K. Comparison of general anesthesia and monitored anesthesia care in patients undergoing breast cancer surgery using a combination of ultrasound-guided thoracic paravertebral block and local infiltration anesthesia: a retrospective study. *J Anesth* 2016;30:244–51.
- de Abreu Junior GF, Pitta GB, Araújo M, et al. Ultrasonographic changes in the axillary vein of patients with lymphedema after mastectomy. *Rev Col Bras Cir* 2015;42:81–92.
- Rietjens M, Villa G, Toesca A, et al. Appropriate use of magnetic resonance imaging and ultrasound to detect early silicone gel breast implant rupture in postmastectomy reconstruction. *Plast Reconstr Surg* 2014;134:e13–20.
- Zhang B, Dong JN, Sun P, et al. Effect of therapeutic care for treating fatigue in patients with breast cancer receiving chemotherapy. *Medicine (Baltimore)* 2017;96:e7750.
- Zhang Q, Zhao GS, Yuan XL, et al. Tumor necrosis factor alpha-238G/A polymorphism and risk of breast cancer: an update by meta-analysis. *Medicine (Baltimore)* 2017;96:e7442.
- Berry DA, Cronin KA, Plevritis SK, et al. Effect of screening and adjuvant therapy on mortality from breast cancer. *N Engl J Med* 2005;353:1784–92.
- Lu WL, Jansen L, Post WJ, et al. Impact on survival of early detection of isolated breast recurrences after the primary treatment for breast cancer: a meta-analysis. *Breast Cancer Res Treat* 2009;114:403–12.
- Pace MM, Sharma B, Anderson-Dam J, et al. Ultrasound-guided thoracic paravertebral blockade: a retrospective study of the incidence of complications. *Anesth Analg* 2016;122:1186–91.
- Neal CH, Yilmaz ZN, Noroozian M, et al. Imaging of breast cancer-related changes after surgical therapy. *AJR Am J Roentgenol* 2014;202:262–72.
- Flowers CI, Mooney BP, Drukteinis JS. Clinical and imaging surveillance following breast cancer diagnosis. *Am Soc Clin Oncol Educ Book* 2012;59–64.
- Nagashima T, Sakakibara M, Kadowaki M, et al. Response rate to neoadjuvant chemotherapy measured on imaging predicts early recurrence and death in breast cancer patients with lymph node involvements. *Acta Radiol* 2011;52:241–6.
- Taghian A, Jeong JH, Mamounas E, et al. Patterns of locoregional failure in patients with operable breast cancer treated by mastectomy and adjuvant chemotherapy with or without tamoxifen and without radiotherapy: results from five National Surgical Adjuvant Breast and Bowel Project randomized clinical trials. *J Clin Oncol* 2004;22:4247–54.
- Anderson SJ, Wapnir I, Dignam JJ, et al. Prognosis after ipsilateral breast tumor recurrence and locoregional recurrences in patients treated by breast-conserving therapy in five National Surgical Adjuvant Breast and Bowel Project protocols of node-negative breast cancer. *J Clin Oncol* 2009;27:2466–73.
- Kim HJ, Kwak JY, Choi JW, et al. Impact of US surveillance on detection of clinically occult locoregional recurrence after mastectomy for breast cancer. *Ann Surg Oncol* 2010;17:2670–6.
- Houssami N, Ciatto S, Martinelli F, et al. Early detection of second breast cancers improves prognosis in breast cancer survivors. *Ann Oncol* 2009;20:1505–10.

- [19] Khatcheressian JL, Wolff AC, Smith TJ, et al. American Society of Clinical Oncology 2006 update of the breast cancer follow-up and management guidelines in the adjuvant setting. *J Clin Oncol* 2006; 24:5091–7.
- [20] Gunia SR, Merrigan TL, Poulton TB, et al. Evaluation of appropriate short-term mammographic surveillance in patients who undergo breast-conserving Surgery (BCS). *Ann Surg Oncol* 2012;19:3139–43.
- [21] Lewis JL, Tartert PI. The value of mammography within 1 year of conservative surgery for breast cancer. *Ann Surg Oncol* 2012;19:3218–22.
- [22] Massaccesi M, Digesù C, Macchia G, et al. Mammography before post-operative radiotherapy in conservatively managed breast cancer patients: is it useful? *Br J Radiol* 1017;85:e682–5.
- [23] Moon HJ, Kim MJ, Kim EK, et al. US surveillance of regional lymph node recurrence after breast cancer surgery. *Radiology* 2009; 252:673–81.
- [24] Suh YJ, Kim MJ, Kim EK, et al. Value of ultrasound for postoperative surveillance of Asian patients with history of breast cancer surgery: a single-center study. *Ann Surg Oncol* 2013;20:3461–8.