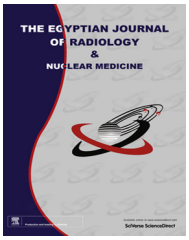
The Egyptian Journal of Radiology and Nuclear Medicine (2013) **44**, 411–415

Egyptian Society of Radiology and Nuclear Medicine

The Egyptian Journal of Radiology and Nuclear Medicine

www.elsevier.com/locate/ejrnm
www.sciencedirect.com



ORIGINAL ARTICLE

Intraoperative ultrasound localization of nonpalpable breast cancers: A valuable aid during breast-conserving surgery

Hesham El Sheikh [a,*], **Nabil Yassin Abdulaziz** [b]

[a] *Department of Diagnostic Radiology – Benha University, Egypt*
[b] *Department of General Surgery – Al Azhar University, Egypt*

Received 18 December 2012; accepted 19 January 2013
Available online 16 February 2013

KEYWORDS

Breast cancer;
Ultrasound;
Nonpalpable;
Intraoperative;
Localization

Abstract *Objective:* To evaluate the usefulness of intra-operative ultrasonography (US) for localization of nonpalpable breast cancer that could be visualized with preoperative US.
Patients and methods: We prospectively assessed 57 nonpalpable sonographically detected and biopsy-proved breast cancers in 57 patients. US localization of breast cancers was performed in the OR by the radiologist immediately before definitive surgery using either injection of blue dye or placement of a guide wire after marking of the skin overlying the lesion with a marking pen. Tumor identification, the correlation with tumor diameter on preoperative US, analysis of resection margins, and the need to perform surgical re-excision were analyzed.
Results: US correctly localized all lesions at surgery. Re-excision due to positive resection margins was necessary in four patients (7%) including three patients with ductal carcinoma-in situ (DCIS) and one patient with invasive disease at the surgical margin. Mastectomy was necessary in one patient (1.7%) due to multifocal invasive carcinoma. Thus, the re-excision rate was 8.7% (5 of 57).
Conclusion: US in the operating room is an attractive alternative guiding tool of localizing nonpalpable breast cancers that have been seen on preoperative US improving the process of image-guided surgery.

1. Introduction

The widespread use of screening mammography has delivered increased numbers of nonpalpable breast cancers to the breast surgeon and the use of needle biopsy delivers the preoperative diagnosis of breast cancer of most nonpalpable lesions, which results in more-efficient first surgical procedures (1,2). Therapy of these early breast cancers requires accurate and complete excision of these small primary lesions. Image guidance is nec-

* Corresponding author. Tel.: +20 966598181340.
Peer review under responsibility of Egyptian Society of Radiology and Nuclear Medicine.

ELSEVIER Production and hosting by Elsevier

0378-603X © 2013 Egyptian Society of Radiology and Nuclear Medicine. Production and hosting by Elsevier B.V.
Open access under CC BY-NC-ND license. http://dx.doi.org/10.1016/j.ejrnm.2013.01.007

essary to identify the location and extent of these nonpalpable tumors. The standard method of image guidance has been wire localization with mammography to visualize the lesion (3). This requires an imaging procedure in radiology and then travel to the operating room (OR). This process presents a variety of inefficiencies that may occur between those two sites. By the time the patients arrive on the operating table, the localizing wire may have been moved or displaced, impairing the accuracy of the surgical procedure. In addition, scheduling patients both in radiology and then in surgery may be difficult. Another disadvantage of the wire placement is that the patient has to undergo an extra intervention before surgery. Wire placement is an unpleasant procedure and heightens the patient's anxiety related to the surgical intervention (2).

It is, therefore, not surprising that alternative methods for tumor localization, such as US have been investigated. Recent studies found that intra-operative sonography can be a reliable and helpful tool in OR, not only for tumor localization of nonpalpable breast cancers, but also for orientation during tumor excision (2,4).

Accordingly, we designed our study to evaluate the usefulness of intra-operative US for the localization of nonpalpable breast cancer.

2. Patients and methods

This prospective study was conducted from June 2009 to August 2012 for 57 patients with 57 nonpalpable sonographically detected and biopsy-proved breast cancers who underwent intraoperative US-guided localization for the breast cancers in the OR before definitive surgery. The age range was 39–83 years, with 45% between the ages of 50 and 69 years and 22% younger than 50 years.

All patients underwent focused breast US of the area of interest in the radiology department by an experienced radiologist prior to surgery using a high-resolution 5–9 MHz linear array transducer of (Medison SONOACE 6000 C unit). Breast US provided specific information regarding the tumor location and extent, the tumor depth from the skin and distance from pectoralis muscle, the presence of ductal extension, and the presence of multifocal or satellite lesions (Fig. 1).

The US-guided localization procedure was explained to the patient in detail. After informed consent had been obtained, patients were assigned to the surgical treatment.

The patient was brought to the OR, given sedation, and examined with US by the same radiologist and the same US machine used in pre-operative assessment in the radiology department which was brought into the OR for each of the 57 patients. Once the lesion is identified, direct comparison was made between what was seen in the OR and what the lesion looked like in the previous preoperative US picture.

Before US-guided localization, the skin overlying the lesion was marked with a marking pen to further orient the surgeon. The surgical incision and planned volume of the breast tissue, skin, and fascia-pectoralis muscle to be removed were drawn on the skin of the breast (Fig. 2).

Intraoperative US-guided localization was performed by the radiologist using either blue dye injection ($n = 43$) or guide-wire placement ($n = 14$). When blue dye was used, a very small amount (1 ml) of methylene blue dye was injected around the lesion just before the surgical preparation of the

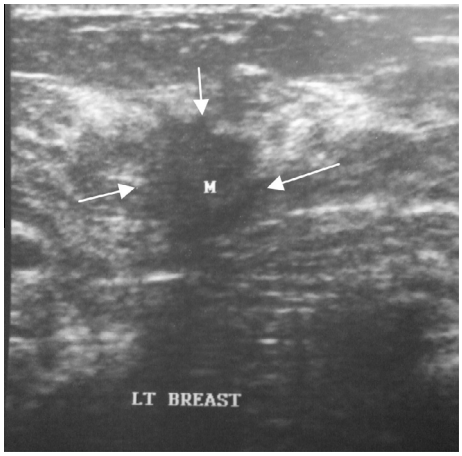


Fig. 1 Preoperative US of breast cancer. M: infiltrating ductal carcinoma of the left breast (arrows) characterized as hypoechoic heterogenous lesion with angulated margins and the lesion shows posterior shadowing.

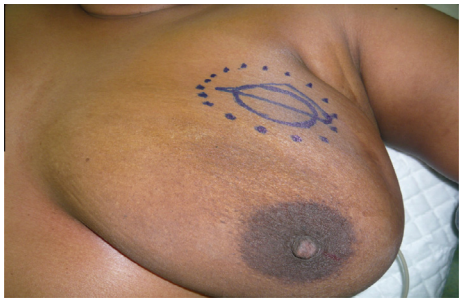


Fig. 2 Markings drawn on the skin of the breast overlying the lesion in the OR immediately before surgery. The surgical incision and planned volume of the breast tissue, skin, and fascia-pectoralis muscle to be removed were drawn on the skin of this patient's breast. The central drawn circle identifies the underlying US location of the tumor; the continuous line outlines the ellipse of the skin to be resected; and the interrupted circumferential line defines the volume of the breast tissue to be excised.

patient. The dye was placed on four sides of the lesion. The last location blue dye was placed just below the skin, in the US window between the transducer and the lesion to help find the general location of the lesion (Fig. 3). After the blue dye is found at surgery, a wide excision is accomplished without further use of the US transducer. When using a guide wire (Vivant Medical, Inc., Palo Alto, CA), it was placed by using US guidance to one side of the lesion according to the surgeon's preference ($n = 8$) or more than one guide wire can be placed to bracket the lesion ($n = 6$).

All US-guided resected specimens were checked with US in the OR and the US probe used was held in a sterile plastic sheath (Fig. 4). Besides documenting that the lesion was removed, the specimen US was a guide for further resection of visibly close margins.

In addition to standard pathologic information, margins were carefully identified, inked, and examined. The pathologic status of the margins from the initial surgical excision speci-

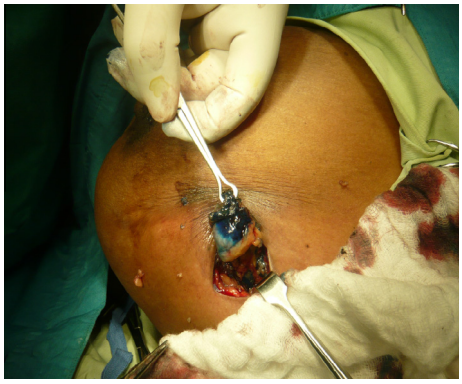


Fig. 3 The lesion during surgical excision identified by the injected blue dye.

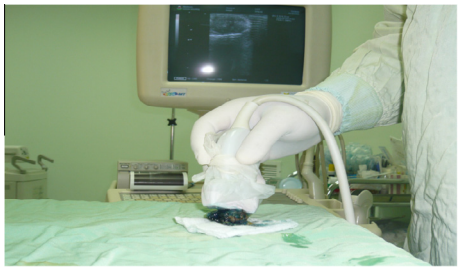


Fig. 4 In the operating room, the surgical specimen is checked with US for adequate margins.

men and any further excisions, either at the first operation or later procedures, was recorded. The distance from the tumor to the closest margin of excision was also determined. Resections were described as being inadequate when microscopic tumor involvement of the (inked) resection border was present. A microscopically adequate margin was defined as $\geqslant$10 mm (4).

The mean follow-up was 25 months (range, 8–38 months). The patients underwent physical examination and mammogram of the affected breast every 6 months for the first 2 years. Thereafter, the same examinations occurred every year.

3. Results

US localization in the OR took very little time (10–20 min). The correlation with preoperative diagnostic US for tumor dimensions was satisfactory. The sizes of the masses measured on the US ranged from 0.7 to 2.6 cm (mean ± SD, 1.2 ± 0.5 cm).

Sonography of the freshly excised specimen in the OR showed the absence of the lesion in the specimen in two cases prompted immediate re-excision which was successful. Thus, US localization correctly identified all target lesions at the initial surgery and breast cancer was found in each case of US localization on the initial specimen (100% accuracy).

Re-excision due to positive resection margins was necessary in four patients (7%) including three patients with ductal carcinoma-in situ (DCIS) and one with invasive disease at the surgical margin. In addition, mastectomy was necessary in one patient (1.7%) due to multifocal invasive carcinoma unknown at the time of US-guided excision. Thus, five patients required surgical re-excision and the re-excision rate for all US-guided procedures was 8.7% (5 of 57).

Table 1 Patient and tumor characteristics.

Characteristic	Value and percentage
No. patients	57
Age, mean (range) (y)	39–83
Breast-conserving therapy	57
Tumor diameter, mean (SD) (cm)	0.7–2.6 cm, 1.2 ± 0.5
Accurate localization of breast cancer	57 (100%)
Margins for invasive carcinoma	
Satisfactory	53 (93%)
Unsatisfactory	4 (7%)
Surgical re-excision for carcinoma	5 (8.7%)
Positive resection margin	4 (7%)
Multifocal invasive cancer (mastectomy)	1 (1.7%)
Tumor type on US examination	
Ductal carcinoma-in situ (DCIS)	2 (3.5%)
Invasive carcinoma	55 (96.5%)
Tumor type on pathological examination	
Ductal carcinoma-in situ (DCIS)	12 (21%)
Invasive carcinoma	45 (79%)

On pathologic examination, there were 12 patients (21%) with DCIS and the remaining 45 patients (79%) all had invasive disease. US identified only two patients with DCIS (2 of 57; 3.5%); the remaining 55 patients (96.5%) all had invasive disease. Thus, DCIS could not be visible by US in 10 patients (10 of 57; 17.5%) and five of these in situ lesions had prominent calcifications (calcified DCIS). Patient and tumor characteristics are listed in Table 1.

4. Discussion

There are a variety of techniques to localize breast cancer with US in the OR. Some techniques involve continuous use of the US transducer during the operation (5). Others use the US to inject blue dye or to place a guide wire or other marking device to guide the procedure. This is most similar to the standard mammographic localization (2,4). Still others simply use US to mark the skin overlying the lesion; thereafter they operate at the marked site (6). This gives only a skin surface orientation, which may shift in the patient with pendulous breasts. In our study, we used two methods to localize breast cancer with US in the OR: injection of blue dye or placement of a guide wire around the lesion. However, before US-guided localization by either method, we used US in OR to mark the skin overlying the lesion with a marking pen to further orient the surgeon. The surgical incision and planned volume of the breast tissue, skin, and fascia-pectoralis muscle to be removed were drawn on the skin of the breast (Fig. 2). When using blue dye injection, a marking pen can identify where the blue dye is located within the breast. This is most important with pendulous or large breasts.

The advantage of using blue dye is that it is readily available (for the sentinel node procedure). A small amount of dye is placed around the lesion, making it very visible. The disadvantage of blue dye is that there is no guide wire to see or

feel and surgical dissection relies on visual clues and the surgeon's orientation. One potential problem occurs when too much dye (more than 1 ml) is placed in any one area so that the blue dye spreads within the breast and can make localization more difficult (2). In spite of these limitations of using blue dye, most patients in our study underwent US localization using blue dye (no = 43) and we found that US localization correctly identified all target lesions at the initial surgery. This conforms to Cary et al., (2). The goal of intraoperative US localization is to accurately identify the lesion and facilitate surgical excision with a clear margin. Tumors resected with involved margins have an increase in the local recurrence rate, thus re-excision for positive margins is indicated (7). In our study, re-excisions were required for positive margins for only four patients (7%) and mastectomy was necessary in one patient (1.7%). Thus, five patients required surgical re-excision and the re-excision rate for all US-guided procedures was 8.7% (5 of 57) which is comparable to other series of US localization (5,8–10).

The pathologic findings in the five patients required re-excisions in our study included calcified DCIS in two patients, noncalcified DCIS in one patient, invasive disease at the surgical margin in one patient (these patients underwent re-excision) and multifocal invasive carcinoma in one patient (underwent mastectomy). Thus, DCIS was the pathologic findings in the three of the five patients required re-excisions and multifocal invasive carcinoma in one patient. This conforms to Cary et al. (2) who found that regardless of the type of imaging guidance, patients with DCIS and multifocal invasive cancer will be at increased risk for a positive margin and at increased risk for re-excision or mastectomy. These findings were not predictable before surgery by US. This may be explained by ability of US to detect invasive carcinoma more than DCIS particularly the calcified type because calcifications are not seen with US and the ductal process extends beyond the imaged invasive lesion (2). Therefore, whenever the preoperative needle biopsy shows DCIS, a wider excision might be planned. In addition, the vast majority of breast cancers is unifocal and, if visible with US, will benefit from the improved efficiency of US guidance.

One could theorize that real-time imaging with US during the operation allows for a more accurate determination of a margin around the tumor and that, therefore, specimen size will be smaller. This is important not only for the success rate of the procedure, but also for cosmetic outcome in breast-conserving treatment (11). Frans et al., (4) haveconfirmed this hypothesis. However, to achieve these objectives in our study we checked all US-guided resected specimens with US in the OR and showed the absence of the lesion in the specimen in two cases prompted immediate re-excision which was successful. Besides documenting that the lesion was removed, the specimen US was able to delineate a margin around a nonpalpable breast cancer, which made adequate resection possible without the unnecessary sacrifice of the healthy breast tissue. Thus sonography of the specimen can indicate within seconds whether the excision has been successful.

One "US pearl" is that US makes a breast lesion appear closer to the skin than is actually found at surgery. While the lesion is visualized with US, there is direct pressure on the subcutaneous tissue and breast, essentially compressing the distance from the skin to the lesion. Then, during surgical exposure of the lesion, the skin is retracted up and away from the lesion. This magnifies the operative distance from the skin to the lesion, making the surgical distance to the lesion greater than expected.

There are several benefits of intraoperative US localization. The most advantageous point is that it improves surgical scheduling without losing accuracy. The patient arrives to the OR calm and relaxed and patients do not have to arrive 4 h before their operation. The surgeon has complete control of the timing of surgery. Far longer than 30 min of OR time is added to give the time needed for localization. Often, as in our study the localization is completed within 10 min because we made direct comparison between the preoperative and intraoperative US pictures for the lesion. In addition, patients find it more comfortable to avoid a needle procedure just before their surgery. No repeat wire readjustments, no dislodged wires, and no vasovagal episodes occur for the patient. Financially, there are no charges for the radiology localization room or several films. Charges are generated by the radiologist who localizes the lesion and for the US use. Overall, it saves surgical time, patient inconvenience, and money. Therefore, the surgeon, the patient, and the OR staff all appreciate the efficiency of US localization.

5. Conclusion

US proved to be a reliable and a very useful tool to localize non-palpable breast cancer in the OR, improving the process of image-guided surgery. US localization is accurate, time efficient, and technically feasible. It simplifies organizational work and spares the patients' discomfort of preoperative needle localization. Therefore, intraoperative US localization should be considered whenever a breast cancer requires image-guided excision.

References

(1) Tabár L, Dean PB, Kaufman CS, Duffy SW, Chen HH. A new era in the diagnosis of breast cancer. Surg Oncol Clin North Am 2000;9:233–77.
(2) Kaufman S Cary, Jacobson Leslie, Bachman Barbara, Lauren Kaufman BS. Intraoperative ultrasound facilitates surgery for early breast cancer. Ann Surg Oncol 2002;9:988–93.
(3) Homer JM, Smith TJ, Safaii H. Prebiopsy needle localization: methods, problems and expected results. Radiol Clin North Am 1992;30:139–53.
(4) Rahusen Frans D, Bremers Andre JA, Fabry Hans FJ, Taets van Amerongen AHM, Boom Rob PA, Meijer S. Ultrasound-guided lumpectomy of nonpalpable breast cancer versus wire-guided resection: a randomized clinical trial. Ann Surg Oncol 2002;9:994–8.
(5) Smith LF, Rubio IT, Henry-Tillman R, Korourian S, Klimberg VS. Intraoperative ultrasound-guided breast biopsy. Am J Surg 2000;180:419–23.
(6) Wilson M, Boggis CR, Mansel RE, Harland RNL. Non-invasive ultrasound localization of impalpable breast lesions. Clin Radiol 1993;47:337–8.
(7) Mokbel K, Ahmed M, Nash A, Sacks N. Re-excision operations in nonpalpable breast cancer. J Surg Oncol 1995;58:225–8.
(8) Harlow SP, Krag DN, Ames SE, et al. Intraoperative ultrasound localization to guide surgical excision of nonpalpable breast carcinoma. J Am Coll Surg 1999;189:241–6.

(9) Paramo JC, Landeros M, McPhee MD, Mesko TW. Intraoperative ultrasound-guided excision of nonpalpable breast lesions. Breast J 1999;5:389–94.
(10) Snider HC, Morrison DG. Intraoperative ultrasound localization of nonpalpable breast lesions. Ann Surg Oncol 1999;6:308–14.
(11) Vrieling C, Collette L, Fourquet A, et al. The influence of patient, tumor and treatment factors on the cosmetic results after breast-conserving therapy in the EORTC 'boost vs. no boost' trial. EORTC radiotherapy and breast cancer cooperative groups. Radiother Oncol 2000;55:219–32.