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Intraoperative Ultrasound Facilitates Surgery for Early Breast Cancer

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Background: Mammogram-directed wire localization for nonpalpable cancer requires surgeon's time and coordination and some patient discomfort. Up to half of these nonpalpable lesions can be visualized by ultrasound. Use of intraoperative ultrasound streamlines the process of image-guided surgery.

Methods: We prospectively visualized 69 nonpalpable breast cancers between January 1998 and July 2001. Ultrasound localization was performed in the operating room immediately before definitive surgery. Breast cancers were localized using either blue dye or a guide wire.

Results: Ultrasound correctly localized all lesions at surgery. Negative margins for invasive carcinoma were found in 97% (67 of 69) of patients. Re-excisions were performed in only 6% (4 of 69) of patients. Overall negative margins were found in 90% (62 of 69) of patients. Most positive margins (71%) were due to the presence of noncalcified ductal carcinoma in situ. Mastectomy was necessary in 4% of patients, usually due to multifocal invasive carcinoma.

Conclusions: Increased familiarity with ultrasound has allowed the surgeon to localize breast cancer in the operating room, improving the process of image-guided surgery. Ultrasound localization is accurate, time efficient, technically feasible, and easier for the patient. The re-excision rate is very low and is similar to that for mammographic localization. Intraoperative ultrasound localization should be considered whenever a breast cancer needs image-guided excision.

Key Words: Breast cancer—Ultrasound—Nonpalpable—Image guidance—Intraoperative—Localization.

The broad use of screening mammography has delivered increased numbers of nonpalpable breast cancers to the breast surgeon.[1] Therapy of these early breast cancers requires accurate and complete excision of these small primary lesions. Image guidance is necessary to identify the location and extent of these nonpalpable and barely palpable tumors. The standard method of image guidance has been wire localization with mammography to visualize the lesion.[2] 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.

Ultrasound has been recognized as an alternative method of image guidance for some of these procedures.[3,4] Ultrasound can also be used to localize breast cancer in the OR by the breast surgeon.[5–7] There are theoretical and practical advantages of intraoperative ultrasound localization. These include ease of scheduling, less discomfort for the patient, less time required for the entire procedure, and overall cost savings.

Use of intraoperative ultrasound may streamline the process of image-guided surgery. We present a consecutive series of breast cancer patients whose cancer was successfully localized during surgery with ultrasound by the breast surgeon.

METHODS

We treated 250 consecutive breast cancer patients between January 1998 and July 2001. Of these, 126

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(50%) presented with nonpalpable lesions. In addition to physical examination, each of these nonpalpable patients was examined before surgery with ultrasound, either in the radiology department or in the surgeon's office, to determine whether the lesion was visible with ultrasound. Of the nonpalpable lesions, 47 were visible on ultrasound.

In addition to those with nonpalpable lesions, there were 30 patients with complaints of a palpable lesion that required image guidance for surgical excision. These patients had lesions that were either vague or barely palpable, or the original palpable lesion was not associated with the eventual location of the carcinoma. Of these patients, 20 underwent ultrasound localization and 10 underwent mammographic localization.

In all, image guidance was provided by ultrasound in 44% (69 of 156) and by mammography in 56% (87 of 156) of patients. The group of 69 patients who underwent intraoperative ultrasound localization is the focus of this report. The age range was 39 to 83 years, with 45% between the ages of 50 and 69 years and 22% younger than 50 years.

Ninety percent (62 of 69) of patients with ultrasound-guided examination had a preoperative needle biopsy confirming carcinoma. There were 55 fine-needle and 7 core needle biopsies. In addition, seven patients (4%) had a Breast Imaging Reporting and Data System class 4 or 5 mammogram revealing a lesion <1 cm in size. These few patients had ultrasound-guided surgical excision as both their diagnostic and therapeutic breast procedures.

In most cases, ultrasound was used to image both the preoperative diagnostic needle biopsy and the therapeutic localization at surgery. Five patients had a diagnostic stereotactic core biopsy before the initial visit to the surgeon. Because these lesions were visible on ultrasound, these patients also underwent ultrasound-guided therapeutic localization at surgery.

Intraoperative ultrasound used a 7.5-MHz linear array transducer with either a midsized wheeled unit or a hand-carried portable unit brought into the OR for each of the 69 patients. Either blue dye injection (n = 54) or guide-wire placement (n = 15) was used for the localization method in the OR.

When blue dye was used, a very small amount of either methylene blue or isosulfan blue dye was injected around the lesion just before the surgical preparation and draping of the patient. This small amount of dye (.1 mL) was placed on four sides of the lesion. The last location blue dye was placed was just below the skin, in the ultrasound window between the transducer and the lesion (Fig. 1).

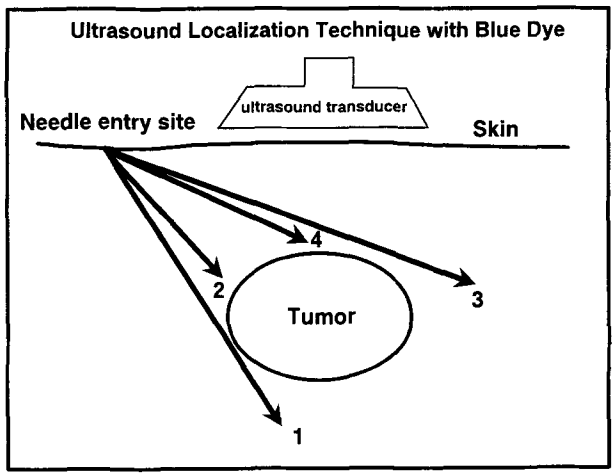

FIG. 1. Ultrasound localization technique with blue dye.

When a guide wire was placed by using ultrasound guidance, it was placed to one side of the lesion, according to the surgeon's preference, often deep to the lesion. The guide wire used in these patients had the benefit of encircling the lesion (Vivant Medical, Inc., Palo Alto, CA).

Regardless of the localizing method, the skin overlying the lesion was marked with a marking pen to further orient the surgeon. Breast cancer was found in each case of ultrasound localization on the initial specimen (100% accuracy). Patient and tumor data are listed in Table 1.

Frozen sections were performed in seven patients without a preoperative diagnosis, as discussed previously. Sentinel node procedures were completed in 76% of patients with invasive carcinoma. The remaining patients had no axillary surgery. In addition to standard pathologic information, margins were carefully identified, inked, and examined, yielding measurements of closest margin to both invasive and in situ carcinoma. Each specimen was marked in three tissue locations with sutures and clips for specimen mammography and pathologic orientation. Statistics were analyzed with SPSS for Windows software, version 8.0.0 (SPSS™ Inc., Chicago, IL).

RESULTS

Image guidance was used for surgery in 62% (156 of 250) of consecutive breast cancer patients over the time period. Intraoperative ultrasound was able to visualize 69 (44%) of 156 lesions with image-guided localization, whereas the remaining 87 patients had cancers seen only on mammography. Both ultrasound and mammographic

TABLE 1. *Ultrasound-guided excision tumor characteristics*

Characteristic	Data
Histology (n)	
IDC	50
IDCc EIC	7
ILC	5
DCIS	1
Special forms	6
Tumor size (n)	
T1a + T1b	17
T1c	42
T2	10
Grade, n (%)	
1	32 (47%)
2	23 (33%)
3	14 (20%)
Estrogen receptor positive, n (%)	
Yes	50 (73%)
No	8 (12%)
Her2/neu, n (%)	
Yes	13 (19%)
No	43 (62%)
Node status, n (%)	
Negative nodes	41 (59%)
Positive node	15 (22%)
Single positive node	7/15 (47%)
No axillary surgery	14 (20%)

IDC, invasive ductal carcinoma; IDCc EIC, invasive ductal carcinoma with extensive ductal carcinoma-in-situ; ILC, invasive lobular carcinoma; DCIS, ductal carcinoma in-situ.

localization correctly identified all target lesions at the initial surgery (there were no missed lesions).

The histological type of breast cancer was quite different between the two methods of localization. Mammographic localization identified almost equal amounts of invasive (46 of 87; 53%) and pure in situ (41 of 87; 47%) carcinoma. However, ultrasound identified only one patient with pure ductal carcinoma-in-situ (DCIS) (1 of 69; 1.5%); the remaining 98.5% all had invasive disease. This was a significant difference between the two methods of image-guided identification ($P < .001$) and is similar to findings in other reports.[8]

All ultrasound-guided targets (n = 69) were accurately identified, yielding a 100% positive predictive value for localization. There were no false-positive localizations. Satisfactory margins for invasive carcinoma (defined as no re-excision necessary) were found in 97% (67 of 69) of patients. The closest invasive margin was at least 1.0 cm in 29% (20 of 69) of patients and in 74% (51 of 69) was at least 5 mm (Table 2).

However, noncalcified DCIS was found in 11(16%) of ultrasound-guided patients. None of these in situ lesions had prominent calcifications, nor was the DCIS visible by ultrasound. This ductal process extended beyond the imaged invasive lesion and was the cause of three more positive margins; it caused a decrease to 62% (43 of 69) of patients with at least a 5-mm margin.

TABLE 2. *Margin status after intraoperative ultrasound-guided excision*

Margin status	Closest invasive margin	Closest margin (including DCIS)
Positive Margin (re-excised)	2 (3%)	4 (6%)
Focal positive (not re-excised)	2 (3%)	3 (4%)
At least 1 mm	65 (94%)	62 (90%)
At least 2 mm	62 (90%)	54 (78%)
At least 5 mm	51 (74%)	43 (62%)
At least 10 mm	20 (29%)	18 (26%)

DCIS, ductal carcinoma-in-situ.

The re-excision rate for all ultrasound-guided procedures was 6% (4 of 69) (Table 2). Two of these patients had invasive disease at the surgical margin, and two had DCIS. There were three additional patients who had focal carcinoma at a margin and did not have further surgery. One elderly woman who had clear margins of her 12-mm invasive carcinoma refused excision for an associated focus of in situ carcinoma at one margin. A second patient, who underwent a primary mastectomy for multifocal disease, had a focus of invasive carcinoma at the mastectomy pectoral muscle margin. A third patient had a very small focus of invasive carcinoma close to a subcutaneous skin margin and was accepted for treatment with radiotherapy without further surgery.

Mastectomy was necessary in 4% (3 of 69) of patients. All three patients had multifocal invasive disease as the reason for mastectomy. One had a primary mastectomy, but two required secondary mastectomies because of unknown multifocal disease at the time of image-guided excision.

The mean follow-up was 25 months (range, 8–55 months). 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. During the time of follow-up, no patient had local or systemic recurrence.

DISCUSSION

The widespread use of screening mammography has had a tremendous effect on the average size of breast cancer, with half the cases smaller than 15 mm.[9] As a direct result, the frequency of nonpalpable breast cancer in our practice has doubled from 28% to 56% in the last 10 years. In addition, the use of needle biopsy delivers the preoperative diagnosis of breast cancer of most nonpalpable lesions, which results in more-efficient first surgical procedures.[10] Our recent experience finds breast

cancer in two out of every three operations for nonpalpable breast lesions (Fig. 2).

With increasing numbers of nonpalpable breast cancers, improvement in the efficiency of imaged-guided surgery is welcome. Current standard mammographic wire localization is usually performed by a radiologist immediately before the surgical procedure. Limitations of this process are many. Scheduling patients both in radiology and then in surgery may be difficult. Time delays in radiology are common, pushing back the operating schedule. The mammographic suite is used during the localizing procedure, limiting the number of routine imaging procedures performed by the radiologist. Patients must endure a radiological localizing procedure, which may be uncomfortable. Thereafter, they must wait one or more hours with a wire protruding from the breast. Even after the localizing wire is in place, unexpected surgical events may also delay patients. 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.

The development of smaller mobile and portable ultrasound units has made it possible for surgeons to regularly use this imaging device both in their office and in the OR. With experience, surgeons have shown abilities with ultrasound that are comparable to radiologists'.[11–14] The ease of visualization of many breast cancers by ultrasound presents an opportunity for surgeons to perform their own image-guidance procedures. This results in a multitude of efficiencies for both patient and surgeon.

This study found that 44% of image-guided breast cancers were visible by ultrasound. The number of visible lesions is dependent on the characteristics of the tumor itself. Small stellate or circular lesions are often well seen by ultrasound. Calcifications are not imaged well by ultrasound, thus making mammographic localization the procedure of choice for calcifications. However, hematomas from recent stereotactic core biopsies for calcifications can be seen by ultrasound. Smith et al.[15] have localized calcifications by using the poststereotactic core biopsy hematoma as the ultrasound target. This method might allow some calcifications to be indirectly visible with ultrasound.

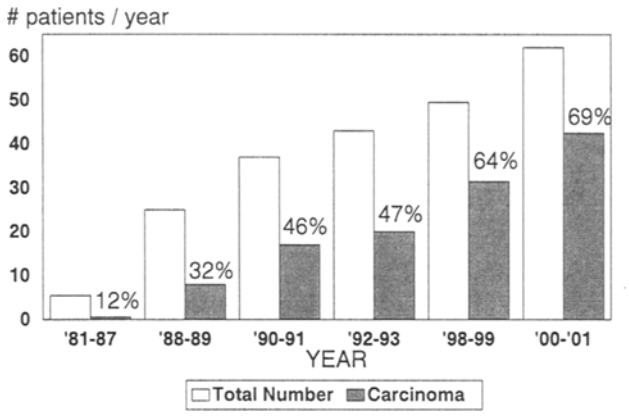

FIG. 2. Image-guided surgery excision results in 467 patients over 20 years.

There are a variety of techniques to localize breast cancer with ultrasound in the OR.[13] Some techniques involve continuous use of the ultrasound transducer during the operation. Here the surgeon examines with ultrasound, dissects using "line of sight," then re-examines with ultrasound.[15] Others use the ultrasound to place a guide wire or other marking device to guide the procedure. This is most similar to standard mammographic localization and was the method of this study. Still others simply use ultrasound to mark the skin overlying the lesion; thereafter they operate at the marked site.[16] This gives only a skin surface orientation, which may shift in the patient with pendulous breasts.

We used two methods of marking the lesion within the breast: blue dye or a guide wire. Both methods worked equally well in our experience. Guide-wire placement closely approximates the standard mammographic wire localizing technique, which would be familiar to most surgeons. Instead of going to radiology, the patient is brought directly to the OR, given sedation, and examined with ultrasound. Once the lesion is identified, lidocaine is infiltrated along the path used to place the guide wire.

The guide wire is then positioned just to one side of the lesion. If necessary, more than one guide wire can be placed to bracket the lesion. The skin overlying the lesion is then marked after it is visualized with ultrasound. After the guide wire is placed, the surgical technique is similar to standard wire localization. Each procedure requires a specimen mammogram.

In 15 of the patients in this study, we used an encircling guide wire for localization.[17] The metal wire is seen well by ultrasound and is placed under (deep to) the target lesion. As the wire is deployed, it encircles the lesion, creating a 2.0-cm loop around the neoplasm. The wire loop creates a palpable marker for the surgeon. The outer introducing sheath is withdrawn, and the patient is prepared and draped for the procedure.

Most patients in this study underwent blue dye ultrasound localization. One 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 (Fig. 1). This injection is not the same as peritumoral injection for sentinel node mapping. One potential problem occurs when too much dye is placed in any one area so that the blue spreads within the breast. If more than .1 mL is placed in any one location, diffusion of the blue dye can make localization more difficult. In addition to injecting at four locations around the lesion, a small amount of blue dye is placed in the subcutaneous window between the transducer and the cancer, just below the skin, to help find the general location of the lesion.

As in guide wire placement, a marking pen can be used on the skin overlying the cancer to identify where the blue dye is located within the breast. This is most important with pendulous or large breasts. After the blue dye is found at surgery, a wide excision is accomplished without further use of the ultrasound transducer. The disadvantage of blue dye is that there is no guide wire to see or feel. Because most of these lesions have some invasive component, the lesions are often palpable as they are approached within the breast. This also helps guide the procedure. Surgical dissection relies on visual clues and the surgeon's orientation.

One "ultrasound pearl" is that ultrasound makes a breast lesion appear closer to the skin than is actually found at surgery. While the lesion is visualized with ultrasound, 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.

Regardless of the method used, all ultrasound-guided surgical specimens should be sent for specimen mammography. Sutures and clips are placed on the lesion before specimen mammography. Besides documenting that the lesion was removed, the specimen mammogram is a guide for further resection of visibly close margins.

With comfort and familiarity, ultrasound becomes a very useful tool for the surgeon to identify breast cancer. The ultrasound localization in the OR takes very little time. Because these patients have had a prior ultrasound examination, the previous ultrasound picture should be available in the OR. Direct comparison can be made between what is seen in the OR and what the lesion looked like in the office. Even if several core biopsy specimens have already been taken, the lesion almost always looks exactly like it did in the office.

Positive excision margins after ultrasound guidance were due either to the presence of noncalcified DCIS or to multifocal invasive carcinoma. In each case, these pathologic findings were not predictable before surgery by imaging or during surgery by the surgeon. Regardless of the type of imaging guidance, patients with these findings will be at increased risk for a positive margin. This is a function of their pathology and not the imaging modality. Patients with noncalcified DCIS and multifocal disease are also at increased risk for mastectomy. However, the vast majority of breast cancers are unifocal and, if visible with ultrasound, will benefit from the improved efficiency of ultrasound guidance.

The goal of intraoperative ultrasound localization is to accurately identify the lesion and facilitate surgical excision with a clear margin. The re-excision rate for these 69 patients was only 6% (n = 4), with only half re-excised for invasive disease. This is comparable to other series of ultrasound localization,[8,13,15,18,19] as shown in Table 3. This re-excision rate is unlikely to be improved until we have methods to better identify noncalcified DCIS.

Because calcifications are not seen with ultrasound, localization with ultrasound is much more apt to find invasive carcinoma than in situ carcinoma. We found that 46% of mammographic localization revealed pure in situ disease, whereas <2% of ultrasound-guided procedures revealed pure in situ carcinoma ($P < .001$). Because in situ carcinoma is more likely to be associated with positive margins, whenever the preoperative needle biopsy shows DCIS, a wider excision might be planned.

Three fourths of these patients (52 of 69) underwent sentinel node surgery simultaneously with their ultrasound-guided breast procedure. Because our routine is to use the

TABLE 3. *Intraoperative ultrasound-guided excision of breast cancer*

Author	No. Cases	No. Cancers	No. Misses	Re-excisions	Recurrence
Rahusen[8]	20	20	0	2/20 (10%)	NA
Harlow[13]	62	62	0	3/62 (5%)	NA
Smith[15]	81	25	0	2/25 (8%)	2/25
Snider[18]	29	22	0	4/22 (18%)	NA
Paramo[19]	15	3	0	0/3 (0%)	NA
Kaufman[a]	69	69	0	4/69 (6%)	0/69

NA, not available.
[a] Current study, mean follow-up 25 months (range, 8–55 months).

subareolar approach for sentinel node identification, the blue dye with ultrasound localization did not interfere with the axillary surgery. One fourth of the patients did not have any axillary surgery. These were small lesions that could be predicted to have less than a 5% chance of positive nodes.[20] After thorough discussion with these patients, no axillary surgery was performed.

There are several benefits of intraoperative ultrasound localization. The most advantageous point of ultrasound localization is that it improves surgical scheduling without losing accuracy. The surgeon, the patient, and the OR staff all appreciate the efficiency of ultrasound localization. The surgeon has complete control of the timing of surgery. Far longer than 30 minutes of OR time is added to give the time needed for localization. Often, the localization is completed within 10 minutes.

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. The patient arrives to the OR calm and relaxed. The OR staff appreciate ultrasound localization because they can predict their OR schedule more accurately. Orderlies are not waiting for patients who are "almost ready," and patients do not have to arrive 4 hours before their operation. Financially, there are no charges for the radiologist, the radiology localization room, or several films. Charges are generated by the surgeon who localizes the lesion and for the ultrasound use. Overall, it saves surgical time, patient inconvenience, and money.

CONCLUSIONS

Increased familiarity with ultrasound has allowed the surgeon to localize breast cancer in the OR, improving the process of image-guided surgery. Ultrasound localization is accurate, time efficient, technically feasible, and easier for the patient. The re-excision rate is very low and is similar to that with standard mammographic localization. The presence of extensive in situ carcinoma or multifocal disease identifies patients at higher risk for positive margins. Intraoperative ultrasound localization should be considered whenever a breast cancer requires image-guided excision.

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