Received: 24 February 2019 | Revised: 15 August 2019 | Accepted: 16 August 2019

DOI: 10.1111/tbj.13575

SHORT COMMUNICATION

The Breast Journal WILEY

Intraoperative sonography for nonpalpable breast lesions: Additional indications for a consolidate technique

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Abstract

This prospective study evaluated the intraoperative ultrasound scan (IUSS) for nonpalpable breast lesions' detection. A total of 108 consecutive female patients underwent surgery using IUSS: Frozen sections demonstrated clear margins in 95.5% of neoplastic patients. Only four (4.5%) patients underwent local re-excision in the same operation. IUSS demonstrated to be quick, accurate, useful, effective, and safe for the intraoperative management of neoplastic nonpalpable breast lesions when performed by a surgeon who has undergone US training, particularly for people in whom alternative approaches can show some limitations due to contraindications or because of scheduling constraints, costs, and patient discomfort.

KEYWORDS

breast cancer, intraoperative study, nonpalpable breast lesion, ultrasound

1 | INTRODUCTION

Ultrasound (US) and mammography represent the standard imaging modalities for breast lesions, with magnetic resonance imaging used only in selected cases. Secondary prevention programs and technical advancement of diagnostic imaging increased the percentage of tumors discovered in an early stage and relatively small in size. As a consequence, an increase in the number of nonpalpable lesions has been observed and surgeons need adequate tools for such lesions.

Actually, nonpalpable breast lesions are managed by preoperative localization with wire, magnetic or radiofrequency tags, radioactive seeds, or radioguided occult lesion localization (ROLL). Intraoperative ultrasound scan (IUSS) was reported firstly in 1996[1]: Its main purposes in breast surgery are localization of nonpalpable lesions and excision with minimal sacrifice of surrounding healthy tissue. On the other hand, ROLL is based on both preoperative interventional imaging and intraoperative radioguided detection of an occult neoplastic lesion using radiopharmaceuticals.[2] Recently, Alamdaran et al[3] evaluated also a combination of IUSS and ROLL for localizing nonpalpable breast lesions, but subcutaneous and intraductal lesions were not "recommended" for ROLL.[3]

The aim of our study was to evaluate IUSS alone in this set of patients to assess accuracy of tumor identification and excision; additionally, correlations between preoperative imaging, IUSS, and pathological examination were also analyzed.

2 | PATIENTS AND METHODS

One hundred and eight consecutive women affected by nonpalpable breast lesions and referred to Breast Unit of our University Hospital were prospectively enrolled from May 2008 to May 2018: All gave written informed consent; the local ethics committee approved the study. Exclusion criteria were presence of multiple lesions, breast abscess, history of breast ipsilateral surgery, and ectopic breast.[4] All patients underwent physical examination, preoperative

TABLE 1 Characteristics of the 89/108 neoplastic and 19/108 non-neoplastic patients

Histology	Pathological tumor size range (mm)	Breast Localization						Radiologic (mammography and US) findings			Postoperative margins (mm)	Metastases spreading during follow-up period
		SLQ	SQJ	SMQ	ILQ	IMQ	R	Nonpalpable mass	Nonpalpable mass and calcification	Architectural distortion and calcification		
IDC (65 pts)	7-18	27	13	8	7	4	6	33	29	3	CM (65 pts)	DM (2 pts)
ILC (12 pts)	6-12	5	3	1	1	1	1	6	5	1	CM (11 pts) MFI (1 pt)	DM (2 pts)
IDC with DCIS (8 pts)	5-9	4	3	0	0	1	0	1	4	3	CM (6 pts) MFI (2 pts)	/
DCIS (4 pts)	5-8	1	1	0	1	0	1	1	2	1	CM (3 pts) MFI (1 pt)	/
Fibrocystic mastopathy (12 pts)	5-18	5	3	2	1	1	0	12	0	0	/	/
Florid adenosis (5 pts)	7-13	2	1	1	1	0	0	5	0	0	/	/
Fibroadenoma (2 pts)	9-12	0	0	0	1	1	0	2	0	0	/	/

Abbreviations: CM, clear margins (ie, >1 mm from the inked margin); DCIS, intraductal carcinoma or ductal carcinoma in situ; DM, distant metastases; IDC, infiltrating ductal carcinoma; ILC, infiltrating lobular carcinoma; ILQ, inferolateral quadrant; IMQ, inferomedial quadrant; MFI, margin focally infiltrated (ie, ≤1 mm from the inked margin); Pt, patient; R, retroareolar; SLQ, superolateral quadrant; SMQ, superomedial quadrant; SQJ, superolateral to superomedial quadrants junction.

mammography, and sonography (by breast imaging dedicated radiologists), within 4-6 weeks before surgery. Tumor locations were annotated on presurgery images specifying the quadrant. US-guided fine-needle aspiration cytology or core biopsy was performed in all patients when appropriate and justified surgical procedure. No patient underwent neo-adjuvant chemotherapy. Ultrasound scanner (*Esaote Caris Plus Ultrasound System*) equipped with a 7.5-12 MHz linear transducer was used for IUSS. All surgical breast procedures were performed by two senior surgeons (MGF and FF), and IUSS was always executed by the same senior surgeon (FF) in the operation room, with the US probe covered a sterile sheath and the patient under general anesthesia. The surgeon was constantly guided by images and report of preoperative investigation. US was used to measure the diameters of lesions and their distance from the skin; in both positions, two ends of the transducer were marked: Surgical incision was performed within these four points. No wire guide or clips were used; postexcision US imaging confirmed the removal of the lesions in all patients. In all cases, intraoperative and definitive histology assessment was done. Margins were also evaluated by the pathologist, and considered positive either ≤1 mm (defined as "focal") or >1 mm (as "diffuse"). Axillary surgical exploration and sentinel lymph node (SLN) biopsy were performed when appropriate using blue dye alone. Patients undergoing axillary surgery were treated according to institutional protocols, which specify procedural recommendations in this setting. Patients were discharged 1-5 days after surgery; afterward they were followed up (Table 1).

Continuous variables were expressed as a mean with standard deviation and qualitative data as absolute frequencies. Student's *t* test was used to analyze the differences between the preoperative, intraoperative, and histologic size of lesions. Values of $P < .05$ were considered statistically significant.

3 | RESULTS

Our study group was made up of 108 females aged 60.3 ± 12.8 years (range, 32-82). Median body mass index (BMI) was 22.8 ± 2.8 (range, 19.3-27.9), and most frequent brassiere cup size was 90B (40 cases, 37%). Breast lesions were located in the superolateral quadrant (44 cases, 40.7%), superolateral to superomedial quadrants junction (24, 22.2%), superomedial quadrant (12, 11.1%), inferolateral quadrant (12, 11.1%), inferomedial quadrant (8, 7.6%), and retroareolar region (8, 7.6%) (Figure 1).

Mean preoperative breast lesion sizes, at US and mammography investigation, were 10.7 ± 4.3 mm (range, 5-21) and 11.1 ± 5.4 mm (range, 5-23), respectively ($P = .8097$); their correlation was statistically significant ($R^2 = 0.8791$; $P < .0001$). In 48 patients, clusters of microcalcifications were found; namely lesions appeared as mass alone, mass with calcifications, and architectural distortion with calcifications in 60, 40, and eight patients, respectively. Fine-needle aspiration cytology/core biopsy was positive for malignancy in 44 patients, but in the remaining 64 cases it was not helpful.

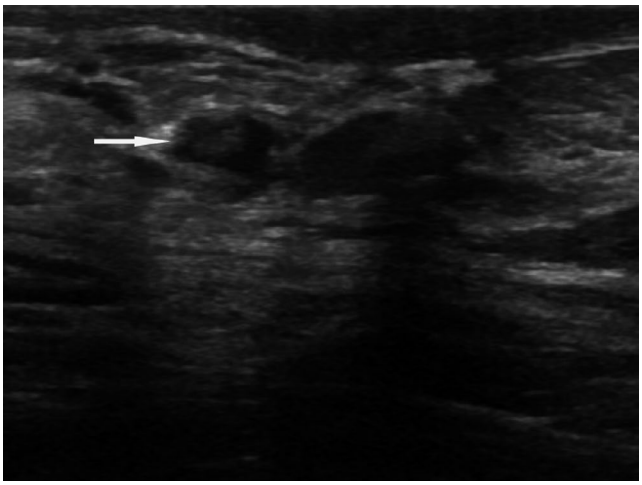

FIGURE 1 Patient (72-y-old, female) with history of left breast carcinoma, treated with surgery, chemotherapy, and whole-breast radiation therapy in 1999. In 2014, mammography and echography of the contralateral breast, performed for prevention purposes, revealed the presence of suspicious calcifications in the retroareolar region of her right breast. IUSS (*Esaote Caris Plus Ultrasound System* with 7.5-12 MHz linear transducer) showed a subcentimetric retroareolar hypoechoic breast lesion (arrow, 2× image zoom) with irregular margins and nonuniform echogenicity. Final histology was conclusive for triple negative DCIS

All nonpalpable breast lesions were successfully localized by IUSS. The length of time to scan, locate, and confirm the target lesion and mark transducer location was 7 ± 2.35 minutes; there was no need to relocate lesions. Clear margins were obtained in 85/89 neoplastic patients (95.5%), and the excision margin ranged from 2 to 21 mm. In the remaining four positive cases, margins were "focally" infiltrated (ie, ≤1 mm from the inked margin), which required local re-excision (all of them appeared as microcalcifications only at radiologic preoperative imaging). Histology revealed infiltrating ductal carcinoma (IDC) alone in 65, infiltrating lobular carcinoma (ILC) in 12, IDC with an intraductal carcinoma or ductal carcinoma in situ (DCIS) in 8, and DCIS alone in four cases. The 48 patients harboring cluster of microcalcifications were part of the neoplastic patients. In the remaining 19 non-neoplastic patients, the most frequent histologic diagnosis was fibrocystic mastopathy (12 cases) followed by florid adenosis (five cases) and fibroadenoma (two cases). Mean pathological size was 10.3 ± 3.9 mm (range, 5-18; $P = .6037$ vs preoperative mammography; $P = .7412$ vs preoperative US). Correlation between preoperative breast lesion sizes at mammography and pathological sizes was significant ($R^2 = 0.8052$; $P < .0001$); moreover, also preoperative breast lesion sizes at US and pathologic sizes correlated significantly ($R^2 = 0.7812$; $P < .0001$). SLN was negative in 57 cases (64%), whereas 32 patients underwent axillary lymph node dissection (36%; in 20/32 lymph node metastases were found). Postoperative complications of slight entity (10.1%) were observed in only nine patients (6 seromas and 3 hematomas). No late complications were recorded. At a mean follow-up of 18.5 months, overall survival and

disease-free survival rates were 100% and 96.3%, respectively; four patient developed distant metastases.

4 | DISCUSSION

Methods commonly used to guide surgical excision of nonpalpable breast lesions include preoperative wire localization (PWL), carbon injections, radiofrequency tags, radioisotope techniques, radioactive seeds, and paramagnetic seeds, the latter being displayable by both mammography and US.[5] However, all of them have some disadvantages, including scheduling constraints, costs, and patient discomfort. Recently, Chang et al[6] evaluated hydrogel clips to facilitate IUSS-guided lumpectomies and found that this technique could be a cost-effective alternative to PWL in patients who are candidates for clip placement. On the other hand, calcifications represent a major concern in the use of IUSS, since they cause imaging problems for IUSS, heading for overtreatment or positive margins.[7]

IUSS represents a non-invasive and time-saving method,[8] but requires adequate training. Several experiences have reported good results in terms of sensitivity, negative neoplastic margins, and percentage of patients undergoing re-excision, demonstrating that IUSS is safe and effective, reducing patient anxiety and discomfort due to supplementary examinations or insertion of a guide wire and saving time and money for hospitals.[8-10]

Snider and Morrison compared the use of IUSS and PWL obtaining an equivalent amount of disease-free margin for both, even if this goal was reached removing a smaller mean volume of tissue with IUSS (IUSS, 62.6 cm^3; PWL, 81.1 cm^3).[11] In the study of Rahusen et al,[12] US-guided excision seemed to be superior to wire-guided excision for margin clearance (P = .007).[12] Recently, Karadeniz Cakmak et al[13] evaluated positively IUSS for margin status, re-excision rate, tissue sacrifice, and cost-time analysis.

Initial studies evaluating ROLL suggested its superiority to wire localization and the large experience reported by the European Institute of Oncology in Milan supported its role in breast surgery.[14] However, recently, Aguilar et al[15] analyzed 816 patients with nonpalpable breast lesions undergoing ROLL, but in 42/816 (5.1%) it was not successful because of the following reasons: The radiotracer was not injected sufficiently close to the lesion (n = 22), the radiotracer was administered inside the ducts or in a lymphatic vessel, diffusing in the breast (n = 20), the scintigraphy revealed no radioactivity, and the procedure had to be repeated (n = 2)[15]; in particular, because of radiopharmaceutical spreading and subsequent larger excised tissue volume, subcutaneous and intraductal lesions were not "recommended" for ROLL[3]: Our experience regarding mainly ductal/intraductal breast carcinomas permits to state that IUSS technique can be preferred in such cases, overcoming these ROLL limitations and establishing additional indications for IUSS in breast surgery. Namely, since ROLL technique is performed using radiopharmaceutical administration, IUSS approach can be preferred when ROLL is contraindicated or when patients refuse to undergo wire/tag/seed placement. Finally, the short length time of IUSS procedure reported in our study justifies its application in terms of cost-effectiveness.

There are some limitations to this study. This is a single-center study, which does not report the use of additional techniques: We did not seek to compare additional techniques as control group, but rather aimed to describe our experience using IUSS alone. All our patients underwent mammography and echography and were biopsied, but in cases with no ultrasound findings it is difficult to perform US-guided procedures and this could represent a potential limitation of IUSS technique application. It would be desirable a clear breakdown of imaging characteristics among different lesions, but on the basis of the imaging modalities nowadays available it is impossible, since in a clinical real life scenario it is not uncommon to deal with lesions with features not specific for benign or malignant behavior.

In our experience, sensitivity of US-guided perioperative localization has reached 100%, in line with the recent review of Colakovic et al[16] Margins were clear in the 95.5% of neoplastic patients. Only few patients underwent local re-excision in the same operation. As a result, IUSS is a non-invasive, accurate, and useful method for the intraoperative localization of neoplastic nonpalpable breast lesions and permits to excise them easily and in a nonstressful manner for the patient, particularly when alternative approaches can show the above described limitations.

CONFLICT OF INTEREST

The authors have no disclosures in relation to this manuscript.

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How to cite this article: Fama' F, Di Maria A, Cicciu' M, et al. Intraoperative sonography for nonpalpable breast lesions: Additional indications for a consolidate technique. *Breast J*. 2019;00:1–5. https://doi.org/10.1111/tbj.13575