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Original article

Ultrasound-guided excision combined with intraoperative assessment of gross macroscopic margins decreases the rate of reoperations for non-palpable invasive breast cancer

Manuel Ramos [a,*], Juan Carlos Díaz [b], Teresa Ramos [a], Ricardo Ruano [c], Martín Aparicio [b], Magdalena Sancho [d], José María González-Orús [a]

[a] Department of Surgery, Breast Surgery Unit, Salamanca University Hospital, Paseo S.Vicente 82, 37002 Salamanca, Spain
[b] Department of Radiology, Breast Unit, Salamanca University Hospital, 37002 Salamanca, Spain
[c] Department of Nuclear Medicine, Breast Unit, Salamanca University Hospital, 37002 Salamanca, Spain
[d] Department of Pathology, Breast Unit, Salamanca University Hospital, 37002 Salamanca, Spain

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ABSTRACT

Aims: The standard technique for intraoperative tumour localization of clinically occult tumours is wire-guided localization (WGL). This, however, this has several disadvantages. The aim of the present work is to report our single-centre experience with intraoperative ultrasound-guided (IOUS) excision, performed by surgeons, combined with intraoperative assessment of macroscopic pathologic and ultrasound margins in non-palpable invasive cancers indicated for conservative breast therapy.
Patients and methods: Two-hundred and twenty-five non-palpable invasive breast cancers were subjected to excision with IOUS. The lesion was located in the operating room with a high-frequency ultrasound probe (8–12 MHz), which was then used to guide surgical removal. The specimen margins were estimated by ultrasonography and macroscopic pathologic examination. The sensitivity of IOUS and effectiveness in the characterization of the specimen margins were evaluated, assessing the need for reoperation.
Results: Pathologic tumour size was 12.0 ± 6.7 mm and 13 lesions (6.4 %) were <5 mm. The sensitivity of IOUS localization was 99.6% (224/225 cases). Only one cancer of less than 5 mm was not localized. The average weight of the specimens was 26.1 g. A second operation was required to remove margins in the 4% of cases (9/225). In 5 cases remains of *in situ* or invasive carcinoma were found. In two cases, conservative surgery was converted to mastectomy.
Conclusions: IOUS excision combined with the intraoperative assessment of the macroscopic margins of non-palpable breast cancers is a safe, useful, and efficient technique. We obtained an excellent characterization of tumour margins with moderate removal of breast tissue and consequently a lower number of reoperations were required and good cosmetic results were obtained. We believe that use of this technique in conservative breast cancer surgery should be recommended.

Introduction

Breast cancer screening programs with mammography have led to an increase in the diagnosis of suspicious small non-palpable lesions, which require a biopsy to confirm or rule out malignancy.[1] Core or needle biopsy guided by stereotaxia or ultrasonography have increased the accuracy of diagnosis and decreased the number of excisional biopsies in non-palpable tumours. Following the discovery of positive breast cancer results, an atypical lesion, or even a non-definitive result, surgery is mandatory. The standard technique for intraoperative tumour localization of clinically occult tumours is wire-guided localization (WGL). This is a time-consuming procedure; it requires an experienced radiologist, and is uncomfortable and usually stressful for the patient. It also depends on the surgeon's capacity to obtain a three-dimensional perspective from two projections, which WGL does not provide. A recent publication[2] has criticised its use because of a 20% positive margin rate in early-stage breast cancers, leading to significant number of tumour re-excisions in a second surgical procedure. One current trend in breast-conserving therapy for non-

* Corresponding author. Tel.: +34 923 219392; fax: +34 923 291178.
E-mail address: mramos@usal.es (M. Ramos).

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palpable breast lesions or invasive breast cancer is intraoperative ultrasound-guided excision (IOUS), examining the breast tissue before and during surgery, in many cases replacing WGL.[3–11] Microscopic evaluation of radial margins on permanent sections is the gold standard for assessing the adequacy of tumour excision. Positive surgical margins in the excision specimen predict local recurrence, such that an evaluation of surgical margins is essential for the correct local treatment of breast cancer. There is also evidence that the cosmetic result depends on the volume of breast excised and the number of reoperations performed.[12]

The aim of our study is to report the efficacy of IOUS excision combined with intraoperative macroscopic margin assessment, using ultrasound and a macroscopic pathological study, in reducing the need for a second operative procedure in non-palpable invasive cancers indicated for conservative breast therapy.

Patients and methods

Intraoperative ultrasound-guided excisions (IOUS) were begun in January 2007 at the Breast Unit of our University Hospital. We included all consecutive patients until December 2011 with non-palpable or vaguely palpable histologically proven primary invasive breast carcinoma. Most of the patients were from the Screening Program of the Regional Community of Castile & Leon. All underwent IOUS as an alternative to WGL if the non-palpable invasive breast cancer was clearly identified by ultrasound. The in situ primary ductal carcinomas were not included in the study because this type of cancer is mainly expressed via calcifications, which are not readily seen with ultrasound, and the patients receiving neo-adjuvant chemotherapy (NAC) admitted for conservative breast therapy were excluded from the study. In all cases, the diagnosis of invasive cancer was confirmed by the operative specimen.

Preoperative mammography and complementary ultrasonography were suitable in all patients. The initial ultrasound identification of the lesion was performed by an experienced radiologist, determining tumour size and the growth pattern, and acquiring core biopsies for diagnosis. Also, in difficult cases of localization and in the same procedure, the radiologist set a metallic marker (MReye Breast Localization Coil. Cook Incorporated. Bloomington, IN 47404, USA) inside or next to the lesion or the suspicious malignant area to facilitate intraoperative ultrasound identification.

Once inside the operating theatre, with the patient in the surgical position but prior to setting up a sterile field, the surgeon with the most ultrasound breast imaging experience examined the breast using a 6–12 MHz high-frequency linear array transducer (Falcon Ultrasound Scanner, B-K Medical Systems, MA 01960, USA). With the ultrasound, and based on the preoperative report, the lesion to be excised was located, and its projection marked on the skin to pinpoint the correct site of incision. The type of resection was lumpectomy (Fisher type), which was extended to the pectoralis fascia in the most peripherally located tumours or in cases of patients with small breasts. Skin removal was only performed in a few cases where the tumour was close to the skin. Together with the underlying subcutaneous tissue, the skin was generously dissected away and the lesion was identified again by ultrasound. During the procedure, with the ultrasound probe inside a sterilized plastic bag, repeated imagings were used to guide the surgeon and to examine the excised tissue for margin status.

The IOUS-excised specimen was oriented appropriately and marked three-dimensionally with sutures, assessing the margins by ultrasound. Then, the main tumour specimen and the re-excised specimen(s) were weighed and the margins were inked and an intraoperative study of the margins was carried out by gross macroscopic pathologic examination. The macroscopic sections were aligned based on the anatomical orientation and according to the closest margins on the ultrasound image. If the ultrasonographic or the gross pathology findings suggested that the margins were not clear or were close to the tumour ($\leq$3 mm), an intraoperative directed re-excision of the additional cavity margins was performed. The thickness of these margins was $\geq$3 mm and were reoriented with respect to the resection site and the edge next to the tumour cavity. The breast cavity limits were marked with titanium clips to facilitate radiotherapy planning and patient follow-up. The margin was considered histologically positive or very close to the lesion if the carcinoma, invasive or "in situ", lay at the margin or within the 2 mm on the inked border in the final pathological examination. In these cases, a reoperation was performed. The margin status was classified as negative if it was $\geq$2 mm.

Sentinel node biopsy was performed in all patients with invasive breast cancers. The combined technique (blue dye plus isotope) was the approach used for node staging.

The study was observational and non-randomized, with prospective acquisition of data from a clinical database compiled at our clinic. The clinicopathological data, successful lesion removal, specimen weight, and analysis of the results as regards margins were evaluated, and the need for re-excision on the same (synchronous) or on a different day (metachronous) was considered.

Results

From January 2007 to December 2011, 1069 breast cancers were treated consecutively at our institution. Four hundred and forty-six (42.1%) were non-palpable breast cancers and were candidates for conservative surgery. Patients were excluded from the study if they were in the following categories: tumour removal with WGL (96 cases); those who had received NAC (89 cases), and those diagnosed with ductal carcinomas in situ (DCIS) (36 cases). The remaining 225 cases (223 patients) included in this study underwent IOUS performed exclusively by surgeons.

The patient and tumour characteristics and the diagnostic and therapeutic processes used are summarized in Table 1. Mean age was 59.5 $\pm$ 11.1 years (range 29–90 years). All patients included were diagnosed preoperatively with invasive carcinoma. In 102 (45.3%), a metal marker was placed at the time of core needle biopsy. The median pathologic tumour size was 12.1 $\pm$ 5.7 mm and there were lesions $<$5 mm (6.4%).

Table 1
Patients and tumour characteristics.

	n = 225 cases (223 patients)
Age in years (mean $\pm$ sd) (range)	59.5 $\pm$ 11.1 (29–90)
$\leq$50 years (%)	54 (24.3%)
$>$50 years (%)	169 (75.7%)
Tumour diameter (mean $\pm$ sd) (mm)	12.1 $\pm$ 5.7
Diameter $\leq$ 5 mm (%)	14 (6.2%)
Histology	
Invasive ductal carcinoma	191 (84.9%)
Invasive lobular carcinoma	25 (11.1%)
Others	9 (4.0%)
Grade	
Highly differentiated	46 (20.4%)
Moderately differentiated	98 (43.6%)
Poorly differentiated	81 (36.0%)
Estrogen or progesterone receptor +	80%
UICC stage	
I	143 (63.6%)
II–III	82 (36.4%)