Original Study

Surgeon-led Intraoperative Ultrasound Localization for Nonpalpable Breast Cancers: Results of 5 Years of Practice

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Abstract

Non-palpable breast cancers require marking prior to breast conserving surgery. We report 5 years of data where the lesions are localized by the surgeon with ultrasound intraoperatively. In 95 patients, the cancer was identified 100% of the time, and the positive margin rate was comparable. The use of the technique both has benefits to the patient and reduces reliance on the radiology department.

Background: The uptake of breast screening has led to a rise in the number of nonpalpable breast cancer diagnoses. Breast conserving therapy (BCT) is the treatment of choice for early breast cancer, and this requires localization of the lesion. Commonly detection is achieved by wire-guided localization in the radiology department. This technique has complications and requires utilization of a radiologist. Intraoperative ultrasound (IOUS) has been shown to be a safe alternative, but there is little data on its use. The aim of this study is to report the use of surgeon-led IOUS over the past 5 years, assessing the ability to detect lesions and the re-excision rate for involved margins. **Patients and Methods:** A retrospective observational study was performed on consecutive patients undergoing IOUS-marked BCT between 2014 and 2018. The technique is described, and patients' records were reviewed to assess the histologic specimen reports and need for subsequent re-excision. **Results:** Ninety-five IOUS BCT operations were performed. Every cancer was identified by IOUS and removed. Fourteen margins were positive and required re-excision. Of these, only 2 contained residual tumor. **Conclusion:** This is the first data from the United Kingdom for IOUS skin marking without wire localization. IOUS is a safe method of localization in BCT. It offers advantages both to the patient and the unit as it reduces pressure on the radiology department.

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Introduction

One in 7 women in the United Kingdom (UK) will be diagnosed with breast cancer in their lifetime.[1] With the implementation of the breast screening program, which in the UK invites all women from the age of 47 for 3 yearly screening mammograms,[2] the number of screen-detected and nonpalpable breast cancers has risen to nearly 50% of diagnosed breast cancers.[3] Breast conserving therapy (BCT), comprised of wide local excision surgery combined with chest wall radiotherapy and additional adjuvant treatments, has been shown in multiple large randomized control trials to produce comparative disease-free and overall survival to mastectomy[4-9] and is now standard treatment for early breast cancer.

The main objective of BCT is to remove the breast cancer with a clear margin, while maintaining an aesthetic quality to the breast. Margin clearance is one of the most important factors in preventing local reoccurrence, and therefore, if the margins of the removed specimen are positive, the patient requires further excision or mastectomy.[10] The incidence of re-excision of margins in the literature varies from less than 10% to over 40%,[11-14] whereas UK data presents the rate of re-excision at around 20%.[15] The comparison of re-excision rates in BCT is difficult as different centers use different criteria for margin positivity. The Society of Surgical Oncology (SSO) and American Society for Radiation Oncology (ASTRO) in 2014 produced a consensus where they proposed margins were clear if there was 'no ink on the tumour.'[16] In 2015, the Association of Breast Surgery (ABS) published their consensus guideline where 1-mm clearance for both invasive tumor and ductal carcinoma in-situ (DCIS) was acceptable.[17] Following publication of a meta-analysis

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in 2016, SSO and ASTRO altered their guidance to a 2-mm clearance for DCIS.[18] The National Institute for Health and Care Excellence (NICE) recommended in 2018 that where margins for invasive cancer or DCIS are within 2-mm, discussion should be had and a joint decision taken with the patient for re-excision.[19] This lack of consensus in management continues within the UK, with sites using differing guidelines in treating their patients.[20]

As these tumors are impalpable, localization prior to surgery is imperative. In the majority, this has been achieved by wire-guided localization (WGL); however, this has disadvantages including: discomfort to the patient, migration of the wire, technical difficulties in placing the wire, and the need to coordinate the radiology and operating departments.[21] Other techniques available include radio-guided surgery in the form of radio-guided occult lesion localization and the use of ultrasound.[22]

Ultrasound skin marking can be performed in the radiology department by breast radiologists prior to theater. More recently, there has been growing worldwide adoption of intraoperative ultrasound scanning (IOUS) either by a radiologist[23-25] or the surgeon themselves.[26-36]

There still remains limited data on surgeon-performed IOUS in BCT surgery overall and no data from the UK. The aim is to review one surgeon's (AS) past 5 years surgery of using IOUS to assess its use in excising breast cancer and rate of re-excisions.

Patients and Methods

A retrospective review was conducted of consecutive patients undergoing BCT with IOUS between 2014 and 2018. Patients were identified from the operation logs. Their preoperative imaging and initial clinic letter were reviewed, along with the operation note and subsequent histology. All included patients had been discussed at a multidisciplinary meeting and been deemed suitable for ultrasound skin marking. At our institution for all other surgeons, these patients would be marked preoperatively in the radiology department prior to transfer to theater.

In the clinic following the multidisciplinary meeting where the patient is counseled and consented for the surgery, the lesion would be scanned by the operating surgeon to ensure it was visible.

In theatre, once anesthetized and in the correct operating position with the arm abducted, the same Sonosite M-Turbo 13MHz probe was used to locate the cancer. First, in a transverse method, the probe would be moved until the cancer was in the center and the ends of the probe marked. Then the same process was repeated in a cranial-caudal direction. Where the lines intersected is the location of the tumor. The location is then clarified by gently placing the probe in the center of the cross and identifying the tumor centrally, noting the depth and size of the lesion. Incision markings and a map of the area of planned excision is then drawn. The patient is prepped and draped, and an incision made as planned. Tissue resection continues to the pectoral fascia. If there is concern about location during the operation, the probe is placed into a sterile cover and the lesion re-identified from within the incision. Once removed, orientation sutures are placed, and the specimen is macroscopically examined by the surgeon. If it is felt any margins are involved, a cavity shave can be performed. Otherwise, the specimen is sent to the pathologist, and the majority of patients are discharged the same day.

The margins accepted in our institution are 1 mm for invasive cancers and 2 mm for DCIS. Where there was multifocal disease, the size of the tumor was based on the combined coverage. Only patients with an invasive cancer at histology were included.

Table 1 Patient Characteristics for BCT with IOUS

	IOUS BCT Operations (n = 95)
Age, y	
Average	59
Range	32-84
ASA	
1	17
2	67
3	11
4	0
Tumor size, mm	
Preoperative average	14
Preoperative range	4-34
Histologic average (including DCIS)	20
Histologic range (including DCIS)	4-58
Histology	
NST	81
Invasive lobular	9
Mucinous	3
Tubular	2
Grade	
1	27
2	46
3	22
Receptors	
Estrogen-positive	85
HER2-positive	10
Screen-detected	53
Neoadjuvant chemotherapy	6
Margin re-excision	14

Abbreviations: ASA = American Society of Anesthesiologists; BCT = breast conserving therapy; DCIS = ductal carcinoma in situ; HER2 = human epidermal growth factor receptor 2; IOUS = intraoperative ultrasound; NST = no special type.

Results

Within 5 years, BCT with IOUS was performed by the same surgeon (A.S.) in 95 operations (94 patients). All patients were female, with an average age of 59 years (range, 32-84 years). The average tumor size including DCIS was 19.8 mm. One patient underwent a bilateral procedure. In one case, the surgery was performed for a local recurrence 10 years after original surgery. Fifty-three (55.8%) patients were screen-detected cancers, and 6 (6.3%) had undergone neoadjuvant chemotherapy, with 1 experiencing a complete response. Table 1 summarizes the findings.

Table 2 Patient Characteristics for Re-excision Operations

	Re-excision Operations (n = 14)
Age, y	
Average	61
Range	44-68
Tumor size, mm	
Preoperative average	13
Preoperative range	6-24
Histologic average (including DCIS)	26
Histologic range (including DCIS)	11-37
Histology	
NST	12
Invasive lobular	0
Mucinous	1
Tubular	1
Grade	
1	2
2	4
3	8
Screen-detected	11 (79%)
Neoadjuvant chemotherapy	2
WLE histology	
Contained DCIS	9 (64%)
Significant DCIS	7 (50%)
Shave histology	
Contained tumor	2 (14%)

Abbreviations: DCIS = ductal carcinoma in situ; NST = no special type; WLE = wide local excision.

Every cancer was identified by IOUS and removed. Fourteen patients underwent margin re-excision. Of these, only 2 had cancer or DCIS in the re-excised margin. One of these patients required a second margin excision to attain completely free margin status. Fifty percent of the patients who underwent re-excision had significant DCIS ($\geq$ 50% size of the invasive tumor). Two had undergone neoadjuvant chemotherapy, and histologically, 1 case was of a mucinous tumor and 1 of tubular histology. The average size of the tumors (including DCIS) requiring margin re-excision was 19 mm. Table 2 summarizes the findings.

Discussion

The results from this study are comparable to other publications of surgeon-led IOUS. Table 3 compares the re-excision rates to other studies reporting greater than 50 cases. As illustrated in Table 3, the variable definitions of involved margins make direct comparison of results difficult. The basis of the ultrasound technique for skin marking is identical across all the studies. Some studies use ultrasound after the specimen has been removed to try and assess the margins intraoperatively to reduce the need for reoperation.[24,28,31,33,35,36] The average re-excision rates in this subset were 9%.

In 2 of the studies, intraoperative frozen sections were taken.[34,35] This facility allowed the surgeon to knowingly excise involved margins during the primary surgery. Both studies reported their results of re-excision if the frozen section was positive and required further tissue to be excised.

In our study, 14% of cases required re-excision of margins. Risk factors for margin involvement or tumor threatening the margins are well-described. These include the presence of DCIS,[37] as this often is not visible on preoperative imaging or IOUS and cannot be palpated. Neoadjuvant chemotherapy and lobular histology[38,39] along with a larger tumor size[40] have all been shown to increase the risk of involved margins.

Six cases in this study had been treated by neoadjuvent chemotherapy. This preoperative treatment can shrink the tumor size to allow BCT where it previously may not have been suitable, and can also produce a complete response. The use of IOUS in patients who have received neoadjuvent chemotherapy has been shown to have the same outcomes as WGL in this subset of patients, with less tissue needing to be removed and re-excision rates of between 9% and 12%.[41,42]

The use of IOUS has been compared with WGL in a large meta-analysis.[43] IOUS was found to reduce the involved surgical margin rates in nonpalpable breast cancer. This study concluded that IOUS was a safe option in treatment of breast cancer but warned that there were no large scale randomized control trials to provide robust level 1 evidence. There is no published review evidence comparing IOUS with radio-guided occult lesion localization.

IOUS has also been used as an adjunct in placing markers or wires to aid resection of breast tissue. In a study from the UK,[3] IOUS was used to either surface mark or insert wires or clips prior to resection. Using these methods, there was a 12% re-excision rate, all of which were lobular cancers. A similar study from the United States used IOUS to insert localizing wires and mark the skin; here, the re-excision rate was 9%.[44]

It is not only in nonpalpable cancers that IOUS has been found to be of benefit. The Cosmetic Outcome of the Breast After Lumpectomy Treatment (COBALT) trial, a multicenter randomized controlled trial, compared the results of excision of palpable tumors through palpation alone or in conjunction with IOUS.[45] Where IOUS was used, there was significantly reduced margin involvement and less tissue mass was excised, helping improve cosmetic outcome.

The use of ultrasound by surgeons in theater is not a new concept. Vascular surgeons have used IOUS for decades in their treatment of varicose veins,[46] pseudoaneurysms, and inserting inferior vena cava filters.[47] Liver surgeons utilize ultrasound when resecting primary and metastatic tumors of the liver,[48] and anesthetic colleagues have, for a long time, used ultrasound to aid vascular cannulation and in nerve blocks.[49]

This is the first report of the use of IOUS without the insertion of wires in the UK. The advantages to the patient of IOUS, aside from its improved clear margin rate, is that it saves the uncomfortable and occasionally prolonged process of having a wire inserted. Compared with preoperative ultrasound marking by a radiologist, IOUS is performed with the patient in the operating position, minimizing the risk of the tumor moving from under the skin marking in the transfer to the theater room. The patient's journey is improved, as on their day of surgery they do not have to be transported around the hospital to the radiology department. Furthermore, IOUS

Table 3 Publications of Surgeon-led IOUS

Author	Year	Country	Number of Breast Cancers	Number of Cancers Missed at Operation	Re-excision Rate, %	Definition of Positive Margin
Harlow[24]	1999	USA	62	0	5[a]	Inked margin
Fortunato[28]	2002	Italy	60	0	3	1 mm
Ngo[30]	2007	France	70	1	4	1 mm
Haid[31]	2007	Austria	262	0	24-13[b]	Not specified
Barentsz[32]	2012	Netherlands	120	0	13	Inked margin
Ramos[33]	2013	Spain	223	1	4	2 mm
Chi-Chang Yu[34]	2013	Taiwan	381	0	10[c]	2 mm
Thanasittichai[35]	2016	Thailand	86	0	5[c]	1 mm
Eggemann[36]	2016	Germany	90	0	12	Not specified
This study	2019	UK	95	0	14	1 mm invasive cancer
						2 mm DCIS

Abbreviations: DCIS = ductal carcinoma in situ; IOUS = intraoperative ultrasound.
[a]Radiologist marked initial 20 cases.
[b]Improved when a pathologist was present intraoperatively.
[c]Used frozen sections intraoperatively.

marking by the surgeon negates the reliance on the radiology department, not only freeing the radiologist to provide other services, but in a time where there is a shortage of breast radiologists, ensures that the surgery can proceed without the need of a radiologist.

A limitation to this study is that the mass of tissue excised is not reported, although this is not imperative to the initial aims of reporting IOUS as a safe technique in excising breast cancer and assessing re-excision rates. Tissue mass removed is an important factor in maintaining breast esthetics, and the use of IOUS has been shown to decrease excised tissue mass.[50] Surgeon-led IOUS also requires that the surgeon be trained and confident in using ultrasound for breast lesions. As previously described, the use of ultrasound in other specialities of surgery and medicine is widely used and accepted. This technique offers both patient and the service advantages. The teaching of ultrasound to breast surgical trainees should be encouraged and increased to increase skill and allow surgeons to be able to offer IOUS to their patients.

This study, the first in the UK with a large number of patients undergoing BCT with IOUS, shows surgeon-delivered IOUS to be safe. There was no need for the insertion of wires or clips intraoperatively. All lesions were identified and removed. The re-excision rate for involved margins of 14% was in keeping with other reports of IOUS and improved on the UK average of 20% in BCT by other methods.[15] There are real benefits to the patient, their journey through the hospital, and the use of resources within the radiology department. Looking forward to the future, ultrasound needs to be incorporated into training much more to allow this service to be delivered. Further research into the effect of IOUS on tissue mass excision, need for specimen x-rays, and its role in palpable tumors is being undertaken.

Clinical Practice Points

- This study presents 5 years of data on surgeon-delivered intraoperative ultrasound localization in non-palpable breast cancer. This is a practice which has been adopted in Europe but is not commonplace in the UK.
- The findings show the practice to be safe, with 100% cancer detection and the ability to deliver outcomes comparable to both other techniques and the literature of similar practice with regards to re-excision rates.
- The use of this practice in the UK is feasible and has benefits to the patient and institution.
- Training in the use of ultrasound within breast surgery should be encouraged in order to produce surgeons who can offer this method to their patients.

Disclosure

The authors have stated that they have no conflicts of interest.

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