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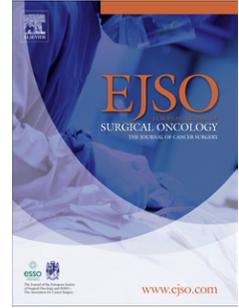
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Original article

Optimising surgical accuracy in palpable breast cancer with intra-operative breast ultrasound - feasibility and surgeons' learning curve

Short title: Intraoperative breast ultrasound training

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N. M. A. Krekel^a, A. M. F. Lopes Cardozo^b, S. Muller^c, E. Bergers^d, S. Meijer^a, M. P. van den Tol^a.

^aDepartment of Surgical Oncology, VU University Medical Centre, De Boelelaan 1117, 1081 HV Amsterdam, the Netherlands

^bDepartment of Surgery, Medical Centre Alkmaar, Wilhelminalaan 12, 1815 JD Alkmaar, the Netherlands

^cDepartment of Surgery, Red Cross Hospital Beverwijk, Vondellaan 3, 1942 LE Beverwijk, the Netherlands

^dDepartment of Radiology, VU University Medical Centre, De Boelelaan 1117, 1081 HV Amsterdam, the Netherlands

Email:

NMA Krekel – n.krekel@vumc.nl; AMF Lopes Cardozo - a.m.f.lopes.cardozo@mca.nl; S Muller – smuller@rkz.nl; E Bergers – e.bergers@vumc.nl; S Meijer – s.meijer@vumc.nl; MP van den Tol – mp.vandentol@vumc.nl

Corresponding author:

N. M. A. Krekel, M.D.

Department of Surgical Oncology

VU University Medical Centre

De Boelelaan 1117, Room 7F-020

1081 HV Amsterdam, the Netherlands

Email: n.krekel@vumc.nl

Tel: +31-20-4444400

Fax: +31-20-4444512

Abstract

Aims: To evaluate if intra-operative guidance with ultrasonography (US) could improve surgical accuracy of palpable breast cancer excision, and to evaluate the performance of surgeons during training for US-guided excision.

Materials and methods: Thirty female patients undergoing breast-conserving surgery for palpable T1-T2 invasive breast cancer were recruited. Three individual breast surgeons, assisted by US, targeted and excised the tumours. The main objective was to obtain adequate resection margins with optimal resection volumes. The specimen volume, tumour diameter and histological margin status were recorded. The specimen volume was divided by the optimal resection volume, defined as the spherical tumour volume plus a 1.0-cm margin. The resulting calculated resection ratio (CRR) indicated the amount of excess tissue resected.

Results: All tumours were correctly identified during surgery, 29 of 30 tumours (96.7%) were removed with adequately negative margins, and one tumour was removed with focally positive margins. The median CRR was 1.0 (range, 0.4 – 2.8), implying optimal excision volume. For all breast surgeons, CRR improved during the training period. By the 8th procedure, all surgeons showed proficiency in performing intra-operative breast US.

Conclusion: Surgeons can easily learn the skills needed to perform intra-operative US for palpable breast tumour excision. The technique is non-invasive, simple, safe and effective for obtaining adequate resection margins. Within the first two cases, resections reached optimal volumes, thereby, presumably resulting in improved cosmetic outcomes. In a multicentre, randomised, clinical trial, intra-operative US guidance for palpable breast tumours will be evaluated for oncological and cosmetic outcomes.

Keywords: Intra-operative ultrasonography; ultrasound; breast-conserving surgery; surgical training; learning curve; pitfalls.

Abbreviations: BCS, breast-conserving surgery; US, ultrasonography / ultrasound; DCIS, ductal carcinoma in situ; CRR, calculated resection ratio; SPSS, Statistical Package for the Social Sciences.

Synopsis:

This study evaluates the performance of surgeons during training for ultrasound-guided excision of palpable T1-T2 invasive breast cancer. Our findings reveal that surgeons can rapidly master intra-operative US, which is non-invasive, simple, safe and effective for obtaining adequate resection margins and excision volumes.

Introduction

The surgical treatment of breast cancer has undergone considerable evolution over the past decades. Breast-conserving surgery (BCS) has been accepted as an equally viable option as mastectomy for the management of early-stage breast cancer, and the sentinel node procedure has replaced axillary dissection in the majority of patients. [1,2] The current focus is on improving the surgical accuracy of BCS, which includes a higher rate of margin clearance with smaller excision volume, thereby improving patient satisfaction and cosmetic outcome. [3-8] To this end, advances have been made in image-guided breast surgery for nonpalpable breast cancer, and several studies have shown that the use of ultrasonography (US) for intra-operative tumour localisation results in the most accurate surgical excision. [9-14]

In daily practice, the excision of palpable breast cancer is guided by palpation. The adequacy of this procedure is based on pre-operative imaging techniques and the experience and tactile abilities of the surgeon. However, palpation of the tumour mass during this “blind” procedure can be problematic, especially in dense breasts. Indeed, in our previous retrospective study, 22.5% of all palpation-guided tumour-excisions presented with tumour-involved surgical margins. [5] Other studies have also reported a high incidence of positive margins after initial excision, ranging from 20 to 60%. [15-17] Moreover, it has been shown that many surgeons tend to overexcise volumes of normal tissue in an effort to obtain adequate margins. Actually, it was shown that the median excision volume of all palpation-guided tumour excisions is over two times to large. [5] Intra-operative guidance with US may therefore improve surgical accuracy of palpable breast cancer excision as well, being helpful for intra-operative tumour localisation, orientation, direction of planes of excision, and assessment of surgical margins.

In the hospital setting, US generally is performed by a radiologist. However, problems can arise in the planning and arrangement of a radiologist’s presence in the operating theatre. Therefore, surgeons have become interested in performing intra-operative US themselves.

Unfortunately, most surgeons have little experience with US, and a major obstacle to the use of US among surgeons is the difficulty in learning how to use it.

Preceding a randomised, controlled trial, a hands-on training period was initiated for surgeons to perform US-guided BCS for palpable breast cancer. [18] The main objectives were to obtain adequate, clear resection margins and remove as little healthy breast tissue as possible. In this article, we present the surgical accuracy of the procedure, as well as the practice-based learning experience, its difficulties, and the potential pitfalls that could suggest strategies for the training and improvement of the US procedure.

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Patients and Methods

Patient selection

Between May 1, 2010, and September 25, 2010, 30 female patients were recruited for this study. All women were evaluated in the outpatient clinic, and the formal workup included physical examination, diagnostic breast and axilla US, mammography, and fine-needle aspiration or core biopsy. Patients were chosen for this study when they had a palpable, US-visible, biopsy-supported, invasive carcinoma of the breast, stage T1 or T2. Patients with pre-operatively diagnosed primary or associated DCIS, multifocal disease, a history of neo-adjuvant therapy or previous surgical treatment or radiotherapy of the affected breast were excluded. Research Ethics Board approval was obtained from all hospitals. Informed consent was obtained from all patients.

Surgeons

Three dedicated breast surgeons participated in this training period. Procedures on patients 1 through 10 were performed by breast surgeon I, who had several years experience in radiologist-assisted US-guided excision of nonpalpable breast tumours. Breast surgeons II and III had no prior experience with intra-operative breast US. Procedures on patients 11 through 20 were performed by surgeon II, and procedures on patients 21 through 30 were performed by surgeon III. Surgeon I closely supervised all surgical procedures.

Prior to surgery

A close working relationship with the radiology department was required to ensure appropriate patient selection and evaluation for this clinical training phase. The surgeons carried out US under the direct supervision of a breast radiologist. The localisation of the

carcinoma, the margins (defined as regular or irregular), the size (length, width, and anterior-posterior diameter), and the distances to the skin and to the fascia were documented.

Surgical procedure

Surgeons used a 14-MHz US probe connected to a portable US system (Toshiba Viamo portable ultrasound system, Japan). The probe was covered with a sterile glove and plastic sheath filled with sterile acoustic gel. The patient was positioned supine with the ipsilateral arm raised beside the head. The surgeon carefully localised the tumour in the breast by palpation and US imaging. To visualise the tumour at its largest diameter, the US probe was moved in short, strokelike motions, perpendicular to the long axis of the transducer. The breast tissue was positioned in such a way that the lesion was located as close to the skin surface as possible. The breast was fixed in that position throughout the procedure by hand or with tape. The tumour diameter (transverse versus vertical), the lesion-to-skin distance and the lesion-to-fascia distance were measured in millimeters, and compared to the digital pre-operative US images, which could be retrieved on the same US system at any time. Thereafter, the tumour was positioned on the lateral borders of the screen to precisely mark the tumour margins on the skin. This process was repeated in the cranial-caudal plane. The skin marks were connected and used to determine the incision line (Fig. 1a). After making the incision, the skin over the lesion was dissected from the subcutaneous tissue, with the goal of obtaining an “optimal” 1-cm margin of healthy breast tissue around the tumour. The extent of dissection was determined using the skin marks and the US, which further assisted the surgeon with the excision. To achieve adequate margins, US was applied repeatedly in or around the wound from different angles while continuously monitoring the location and depth of the tumour and ensuring the maintenance of adequate resection margins. Right-angle scanning allowed the surgeon to modify the dissection if the margins seemed too close to the

lesion. The plane of dissection was determined by the presence of air between the specimen and normal breast tissue, which was clearly visible on the US image, thereby ensuring that the tumour remained surrounded by an appropriate margin of normal breast tissue (Fig. 1b). The adequacy of the deep margin between the breast and the pectoral fascia was determined by placing the US transducer perpendicular to the tumour and parallel to the chest wall (Fig. 1c). Finally, a spherical lump of breast tissue was excised. Cavity shavings were not performed; specimen radiography was not used. After excision, the specimen was examined with US *ex vivo* to determine whether the tumour was completely excised (Fig. 1d). If the margin appeared inadequate, additional breast parenchyma could be excised at that site. The specimen was oriented by marking sutures such that positive resection margins could be identified and re-excised if necessary.

Data

Preoperative data included patient age, tumour localisation, tumour stage, and tumour type. The duration of the excision (i.e., time from the mammary incision to wound closure), US-findings, and difficulties or pitfalls encountered during the surgical procedure were reported. After tumour excision, the specimen was weighed, and the volume was measured by using fluid displacement, which is considered the “gold standard” for volume measurement. [19] The tumour diameter, histological resection margin status, and length of the smallest clear margin were recorded from the pathology reports. Margins were categorised as negative (no tumour at the surgical resection margin), focally positive (an area of ≤ 4 mm with tumour at the surgical resection margin), or positive (grossly discernible tumour > 4 mm at the surgical resection margin). [20-22] In cases with positive margins, re-excision or even mastectomy would be indicated, while focally positive margins would require either additional surgery or external beam radiotherapy with a directed boost to the tumour bed.

The calculated resection ratio

To determine the excess tissue resection, the calculated resection ratio (CRR) was defined, whereby the specimen volume was compared to the “optimal” specimen volume. The optimal specimen volume was defined as the spherical tumour volume plus an arbitrarily chosen “optimal” 1-cm tumour-free resection margin. The tumour diameter was used to calculate the optimal specimen volume for each tumour using the following mathematical formula: $4/3\pi(r+1.0 \text{ cm})^3$. The CRR was calculated by dividing the specimen volume by the optimal specimen volume. In other words, in a perfect excision, the specimen volume would be equal to the optimal specimen volume, and the CRR would be 1.0. If the specimen volume is twice the size of the optimal specimen volume, then the CRR would be 2.0. [5,12]

Data analysis

All data were analysed by using the Statistical Package for the Social Sciences (SPSS statistical software, Version 15.0; SPSS, Inc., Chicago, IL, USA). Scatterplots were generated from time points versus the excision volume and CRR. Scatterplots were explored to see whether linear regression analysis was a valid method. Spearman’s correlation coefficients of time points versus the excision volume and CRR were applied.

Results

Patient and tumour characteristics (Table 1)

A total of 30 female patients were included in this study. The mean patient age was 53 (range, 33-79) years. Fifteen tumours (50.0%) were localised in the left breast. Twenty-eight of 30 (93.3%) tumours were invasive ductal carcinomas, which frequently presented with a minimal additional intraductal component (50.0%). An extensive tumour-associated ductal carcinoma in situ (DCIS) was unexpectedly present in two cases (6.7%).

Intra-operative findings

All tumours were readily identified by US during the surgery. Most invasive ductal carcinomas were characterised by heterogeneous areas of low echogenicity, and showed posterior shadowing that was adequately recognised before and during surgery. Although most tumours were well defined with regular margins (Fig. 2a), some tumours presented features that were less easily identified by US: irregularly demarcated margins, angular margins, or hypoechoic spiculations. One tumour presented with a well-recognised hematoma, and in two cases a well defined cyst was located near the tumour (Fig. 2b).

Intra-operative re-excision was not performed. The average duration of the procedure ranged from 5 to 26 minutes, with a mean duration of 14 minutes. It must be noted that the additional time needed for US -imaging prior to the incision and for specimen scanning after the excision (estimated, up to 5 minutes) was not included in the reported procedure duration.

Postoperative findings

Twenty-nine tumours (96.7%) were removed with adequate, tumour-free surgical margins. The median smallest margin length of uninvolved breast tissue was 0.3 (range, 0.1–1.0) cm. In one patient, a 24-mm highly spiculated infiltrating ductal carcinoma was excised with

focally invasive margin involvement; unexpectedly, several foci of DCIS were found as well, presenting 1-mm inferior to the inked margins. Because of intraductal disease, a re-excision was performed with a negative histologic finding.

The median specimen weight and volume were 30.5 (range, 12.0–138.0) grams, and 29.0 (10.0–130.0) cm³, respectively. The median CRR was 1.0 (range, 0.4–2.8). Table 2 describes the results on the margin statuses, resection volumes, and CRRs for the individual surgeons. There were no significant differences between the performances for the individual surgeons ($P > 0.05$). Fig. 3 shows the improvement of excision volume and CRR over time for each of the breast surgeons. In the beginning of the training period, the surgeons tended to overexcise the tumour. However, the volumes and CRRs became smaller after several surgical procedures, resulting in overall optimal-volume resections. Spearman's correlation coefficients of time points versus excision volumes and CRRs were not significant ($P > 0.05$). Within eight procedures, all breast surgeons achieved a level of competency and confidence such that they could readily incorporate the US techniques in the operating theatre. Post-operative complications within 30 days that required intervention were not reported.

Difficulties and pitfalls

Initially, the most difficult part of the procedure was to translate the US image to the tumour position in the breast. According to the procedure, the US probe is placed perpendicular to the tumour position, and one must be careful to continue dissection in that direction. Also, the breast tissue should continuously be fixed in one position by hand or with tape, particularly when tumours are located in the outer quadrant.

Most importantly, experience is required to identify poorly defined, irregular or angular tumour margins and inconspicuous spiculations. Moreover, unexpected additional intraductal disease can often not be detected by US. [10,23-25]

One technical pitfall was that the US-cover sheath should perfectly fit around the US probe, because the interference of air within a large sheath may cause an indistinct US image.

Furthermore, the 7-cm probe was too large to be placed within some wounds. The overlying skin had to be repositioned over the tumour, or the transducer had to be manipulated to guide the excision. Visibility markedly improved by using normal saline within the wound, thereby eliminating disturbing air artifacts.

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Discussion

Margin status

BCS has gained wide acceptance as the treatment of choice for breast cancer. So far, surgeons have striven to ensure a complete excision of the carcinoma; tumour-positive margins are associated with an increased risk of locoregional recurrence, thus requiring re-intervention. [15,20-22] In this hands-on training period of surgeon-performed intra-operative US for palpable invasive breast cancer, free margins were obtained in all the patients but one. In retrospect, these inadequate resection margins could probably not have been avoided, with or without US; the tumour had infiltrating spiculations that were nonpalpable and not clearly visible with US. Moreover, this tumour unexpectedly presented with extensive DCIS. Approximately half of all tumours presented with pre-operatively missed DCIS, which corresponds well with previously reported data. [5,10,12] Still, only one specimen showed surgical margins with DCIS. Therefore, the possible presence of tumour-associated DCIS does not justify excessively large resections to prevent intraductal margin involvement in daily practice, and will therefore not have implications for the use of intra-operative US. Previous studies have reported a high incidence of positive margins after initial palpation-guided excision, ranging from 20-60%. [5,15-17] Therefore, US-guided surgery seems promising for obtaining adequate, clear resection margins.

Resection volumes and calculated resection ratio's

BCS should be an oncologically effective, as well as cosmetically acceptable treatment. The cosmetic outcome after BCS is strongly related to the patient's well-being. [3,6] However, a number of studies have shown that the cosmetic results following BCS are unacceptable in as many as 40% of patients. Resection of a large volume of breast tissue is the key determinant. Specifically, a lump size exceeding 85 cm³ results in a significantly higher rate of cosmetic

failures. [4,7,8] A practical guideline during surgery is to achieve a safe and cosmetically acceptable resection margin of 5-10 mm. [15,20,22]

In the present study, the median resection volume was 29.0 cm³. The excision volumes exceeded 85 cm³ in four patients (13.3%), of whom three were treated early in the experience of surgeon III. The fourth patient presented with a cyst near the tumour, which also required excision and resulted in a large excision volume and CRR. The median CRR in the training period was 1.0, which implies that the median specimen volume was equal to the optimal specimen volume. Our previous study showed that the median CRR of all palpation-guided tumour excisions was 2.2. [5] Therefore, the results of this learning period seem promising for obtaining adequate tissue volumes as well.

Learning curve

US-guided BCS is a rather new technique for surgeons, who require a combination of knowledge and judgment of US images, and must be able to translate the US images into the technical ability of tumour excision. Performance during the training phase varied among surgeons. Breast surgeon I showed the fastest progress, probably because of a higher level of US expertise. Surgeons II and III, who had little experience with US, initially felt uncomfortable in switching off their tactile perceptions to rely on the US images. Indeed, one difficulty in learning US-guided BCS is that tactile perception is limited. Tactile abilities instead must be turned into visible judgments and translated from the US screen into a three-dimensional orientation inside the breast. Still, the surgeons easily familiarised themselves with the technique and rapidly mastered basic US skills. One should be aware that the surgeons were not required to distinguish benign from malignant lesions; the surgeons' aims were to target the breast tumour intra-operatively with US and to excise with precision by delineating the breast volume.

The benefits of intra-operative US-guided breast tumour localisation and excision have been consistently reported; US is accurate, simple, not time-consuming, and comfortable for the patient, and it carries a minimal risk of procedure-related complications. [9-14] The increasingly more important role of breast US in the intra-operative evaluation of breast cancer calls for efforts from surgeons to perform US-guided breast procedures, particularly in settings where dedicated radiologists are not readily available at all times. Although doubts have been addressed regarding the ability of surgeons to perform breast US, previous studies have shown a high accuracy of breast US performed by surgeons. [10,11,26-29] These findings support the conclusion that, with appropriate instruction and experience, breast surgeons can attain a level of competency that will enable them to perform US-guided BCS for palpable, and probably even impalpable, breast cancer.

Limitations of the study

Several limitations to this study need to be acknowledged. Although the surgeons performed well, there were only 3 subjects, and one of them had previously participated in radiologist-performed US-guided excisions. Additionally, none of the patients had presented with invasive lobular carcinoma. It may be more difficult to define margins of lobular breast cancer, and further work is required to evaluate the efficacy of US-guided excision of palpable lobular carcinomas. To calculate the optimal excision volumes, optimal resection margins of 1.0 cm were arbitrarily chosen. Although local recurrence and overall survival have proven to be unrelated to a tumour-free resection margin wider than 1 mm, a 1.0 cm margin is technically more feasible. [15,20-22] Moreover, to allow easy calculations, the formulas for the prediction of these volumes were based on the assumption that tumours are spherical, while in actuality, they may vary in shape. Furthermore, the exact data on the time needed for US-imaging prior to the incision and for specimen scanning after the excision are

failing, and future studies should analyse the time of the whole procedure. Lastly, this study was not controlled, and there was no evaluation of cosmetic outcome. The results of the multicentre, randomised clinical trial on US guided surgery for palpable breast cancer are, therefore, awaited.

Conclusions

It seems highly beneficial for surgeons to learn the skills needed to perform US-guided excision of palpable breast tumours. Intra-operative US allows real-time localisation of the breast carcinoma and subsequent planning of surgical margins, thereby presumably resulting in a more accurate tumour excision. The described technique is easy, straightforward, noninvasive, and not time consuming, and it may be learned in a relatively short time. In a multicentre, randomised, clinical trial, intra-operative US guidance for palpable breast tumours will be evaluated for margin clearance, excision volume, CRR, cosmetic outcomes and quality of life. The results will be compared with traditional palpation-guided surgery (Trial Registration Number: NTR2579). [18]

Conflict of interest statement:

The authors report no conflicts of interest.

Role of the funding source:

The Dutch Pink Ribbon Foundation provided funding for this trial. The Osinga-Kluis Foundation provided funding for a Toshiba Viamo portable ultrasound system. Toshiba Medical Systems Corporation provided two extra Viamo portable ultrasound systems for use during the study period.

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References

1. Fisher B, Anderson S, Bryant J, et al.: Twenty-year follow-up of a randomized trial comparing total mastectomy, lumpectomy, and lumpectomy plus irradiation for the treatment of invasive breast cancer. *N Engl J Med* 2002; 347:1233-1241.
2. Giuliano AE, Hunt KK, Ballman KV, et al.: Axillary dissection vs no axillary dissection in women with invasive breast cancer and sentinel node metastasis: a randomized clinical trial. *JAMA* 2011; 305:569-575.
3. Al-Ghazal SK, Fallowfield L, Blamey RW: Does cosmetic outcome from treatment of primary breast cancer influence psychosocial morbidity? *Eur J Surg Oncol* 1999; 25:571-573.
4. Cochrane RA, Valasiadou P, Wilson ARM, et al.: Cosmesis and satisfaction after breast-conserving surgery correlates with the percentage of breast volume excised. *Br J Surg* 2003; 90:1505-1509.
5. Krekel N.M.A., Zonderhuis B.M., Muller S., et al.: Excessive resections in breast-conserving surgery: A retrospective multicentre study. *Breast J* 2011; 17(5).
6. Sneeuw KC, Aaronson NK, Yarnold JR, et al.: Cosmetic and functional outcomes of breast conserving treatment for early stage breast cancer. 2. Relationship with psychosocial functioning. *Radiother Oncol* 1992; 25:160-166.

7. Taylor ME, Perez CA, Halverson KJ, et al.: Factors influencing cosmetic results after conservation therapy for breast cancer. *Int J Radiat Oncol Biol Phys* 1995; 31:753-764.
8. 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. *Radiother Oncol* 2000; 55:219-232.
9. Fortunato L, Penteriani R, Farina M, et al.: Intraoperative ultrasound is an effective and preferable technique to localize non-palpable breast tumors. *Eur J Surg Oncol* 2008; 34:1289-1292.
10. Haid A, Knauer M, Dunzinger S, et al.: Intra-operative sonography: a valuable aid during breast-conserving surgery for occult breast cancer. *Ann Surg Oncol* 2007; 14:3090-3101.
11. Harlow SP, Krag DN, Ames SE, Weaver DL: Intraoperative ultrasound localization to guide surgical excision of nonpalpable breast carcinoma. *J Am Coll Surg* 1999; 189:241-246.
12. Krekel NMA, Zonderhuis BM, Stockmann HBAC, et al.: A comparison of three methods for nonpalpable breast cancer excision. *Eur J Surg Oncol* 2011; 37:109-115.
13. Moore MM, Whitney LA, Cerilli L, et al.: Intraoperative ultrasound is associated with clear lumpectomy margins for palpable infiltrating ductal breast cancer. *Ann Surg* 2001; 233:761-768.

14. Rahusen FD, Bremers AJA, Fabry HFJ, et al.: Ultrasound-guided lumpectomy of nonpalpable breast cancer versus wire-guided resection: a randomized clinical trial. *Ann Surg Oncol* 2002; 9:994-998.
15. Park CC, Mitsumori M, Nixon A, et al.: Outcome at 8 years after breast-conserving surgery and radiation therapy for invasive breast cancer: influence of margin status and systemic therapy on local recurrence. *J Clin Oncol* 2000; 18:1668-1675.
16. Pleijhuis RG, Graafland M, de Vries J, et al.: Obtaining adequate surgical margins in breast-conserving therapy for patients with early-stage breast cancer: current modalities and future directions. *Ann Surg Oncol* 2009; 16:2717-2730.
17. Waljee JF, Hu ES, Newman LA, Alderman AK: Predictors of re-excision among women undergoing breast-conserving surgery for cancer. *Ann Surg Oncol* 2008; 15:1297-1303.
18. Krekel N, Zonderhuis B, Schreurs H, et al.: Ultrasound-guided breast-sparing surgery to improve cosmetic outcomes and quality of life A prospective multicentre randomised controlled clinical trial comparing ultrasound-guided surgery to traditional palpation-guided surgery (COBALT trial). *BMC Surg* 2011; 11:8.
19. Yip J, Mouratova N, Jeffery R, et al.: Accurate Assessment of Breast Volume: A Study Comparing the Volumetric Gold Standard (Direct Water Displacement Measurement of Mastectomy Specimen) With a 3D Laser Scanning Technique. *Ann Plast Surg* 2011.

20. Kaufmann M, Morrow M, von Minckwitz G, Harris JR: Locoregional treatment of primary breast cancer: consensus recommendations from an International Expert Panel. *Cancer* 2010; 116:1184-1191.
21. Morrow M: Trends in the surgical treatment of breast cancer. *Breast J* 2010; 16 Suppl 1:S17-S19.
22. Singletary SE: Surgical margins in patients with early-stage breast cancer treated with breast conservation therapy. *Am J Surg* 2002; 184:383-393.
23. Stavros AT, Thickman D, Rapp CL, et al.: Solid breast nodules: use of sonography to distinguish between benign and malignant lesions. *Radiology* 1995; 196:123-134.
24. Georgian-Smith D, Taylor KJ, Madjar H, et al.: Sonography of palpable breast cancer. *J Clin Ultrasound* 2000; 28:211-216.
25. Ohlinger R, Heyer H, Thomas A, et al.: Non-palpable breast lesions in asymptomatic women: diagnostic value of initial ultrasonography and comparison with mammography. *Anticancer Res* 2006; 26:3943-3955.
26. Donaldson LA, Cliff A, Gardiner L, et al.: Surgeon-controlled ultrasound-guided core biopsies in the breast--a prospective study and a new use for surgeons in the clinic. *Eur J Surg Oncol* 2003; 29:139-142.
27. Fine RE, Staren ED: Updates in breast ultrasound. *Surg Clin North Am* 2004; 84:1001-10vi.

28. Holmes DR, Silverstein MJ: A minimally invasive breast biopsy clinic: an innovative way to teach breast fellows how to perform breast ultrasound and ultrasound-guided breast procedures. *Am J Surg* 2006; 192:439-443.
29. Staren ED, Knudson MM, Rozycki GS, et al.: An evaluation of the American College of Surgeons' ultrasound education program. *Am J Surg* 2006; 191:489-496.

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Fig. 1a Medial tumour localisation. The tumour margins were precisely marked on the skin, and the skin marks were connected.

Fig. 1b US visible plane of dissection (arrow); the distance from the tumour to the plane of dissection indicates that an appropriate margin is obtained.

Fig. 1c The adequacy of the deep margin was determined by placing the US transducer perpendicular to the tumour and parallel to the chest wall.

Fig. 1d Immediately after excision, the specimen was examined with US ex vivo to determine complete tumour excision.

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Fig. 2a US image of a palpable malignant tumour in the upper inner quadrant of the right breast shows a well-defined hypoechoic mass (A), lobulated margins (B), and duct extension (C). Histologic findings were mixed infiltrating ductal carcinoma and ductal carcinoma in situ (DCIS); tumour diameter 2.30 cm. The tumour was excised with adequately negative resection margins, and the length of the smallest tumour-free margin was 0.4 cm. The specimen volume was 40 cm³, and the CRR was 1.01.

Fig. 2b US image of a palpable malignant tumour in the lower outer quadrant of the left breast shows a heterogeneous hypoechoic texture (A), irregular, indistinct, and angular margins (B), hypoechoic spiculations (C), and a small cyst (D). Histologic findings were mixed infiltrating ductal carcinoma and ductal carcinoma in situ (DCIS); tumour diameter 1.50 cm. The tumour was excised with adequately negative resection margins, and the length of the smallest tumour-free margin was 0.3 cm. The specimen volume was 25 cm³, and the CRR was 0.5.

Fig. 3 Learning curves of excision volume and CRR over time for each of the breast surgeons.

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TABLE 1 Patient and tumour characteristics

Tumour localisation	No. of patients	%
Upper outer quadrant	15	50.0
Upper inner quadrant	4	13.3
Lower outer quadrant	5	16.7
Lower inner quadrant	2	6.7
Central	4	13.3
Mean tumour diameter in cm (range)	2.1	(0.8-4.0)
Tumour stage	No. of patients	%
T1	14	46.7
T2	16	53.3
Tumour type	No. of patients	%
Invasive ductal carcinoma	11	36.7
Invasive ductal carcinoma with DCIS	17	56.7
Invasive papillary carcinoma	1	3.3
Invasive adenosquamous carcinoma	1	3.3
Axillary surgery	No. of patients	%
Sentinel lymph node biopsy	24	80.0
Axillary lymph node dissection	6	20.0

TABLE 2 Results for margin clearance, excision volumes and CRR for surgeons I, II, and III

	Surgeon I	Surgeon II	Surgeon III	Total
Tumour-free resection margins (N, (%))	10 (100.0)	9 (90.0)	10 (100.0)	29 (97.7)
Weight (grams) (median, (range))	31.0 (16.0 – 94.0)	34.5 (12.0 – 75.0)	27.0 (12.0 – 138.0)	30.5 (12.0 – 138.0)
Excision volume (cm³) (median, (range))	34.0 (15.0 – 100.0)	34.0 (10.0 – 75.0)	25.0 (10.0 - 130.0)	29.0 (10.0 – 130.0)
CRR (median, (range))	1.0 (0.5 – 1.6)	0.8 (0.4 – 2.2)	1.1 (0.4 – 2.8)	1.0 (0.4 – 2.8)

CRR Calculated Resection Ratio, indicating the excess tissue resection

Conflict of interest

The authors report no conflicts of interest.

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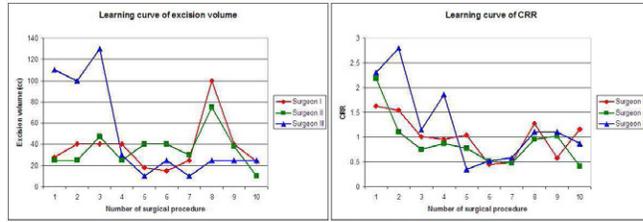
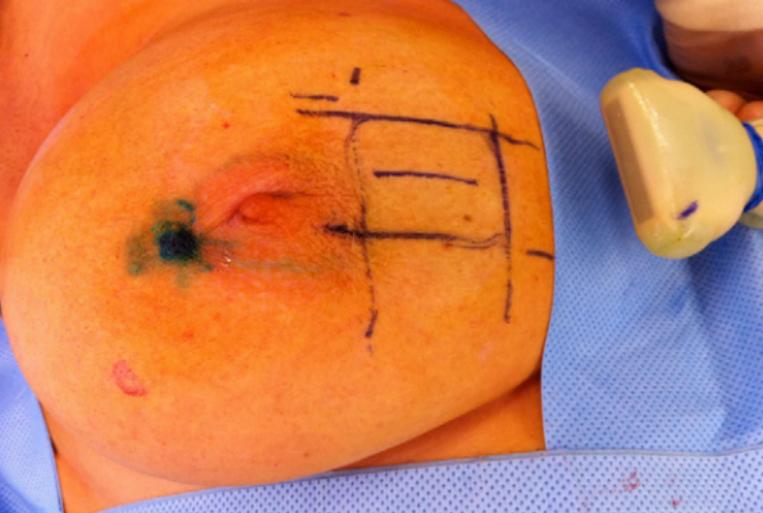
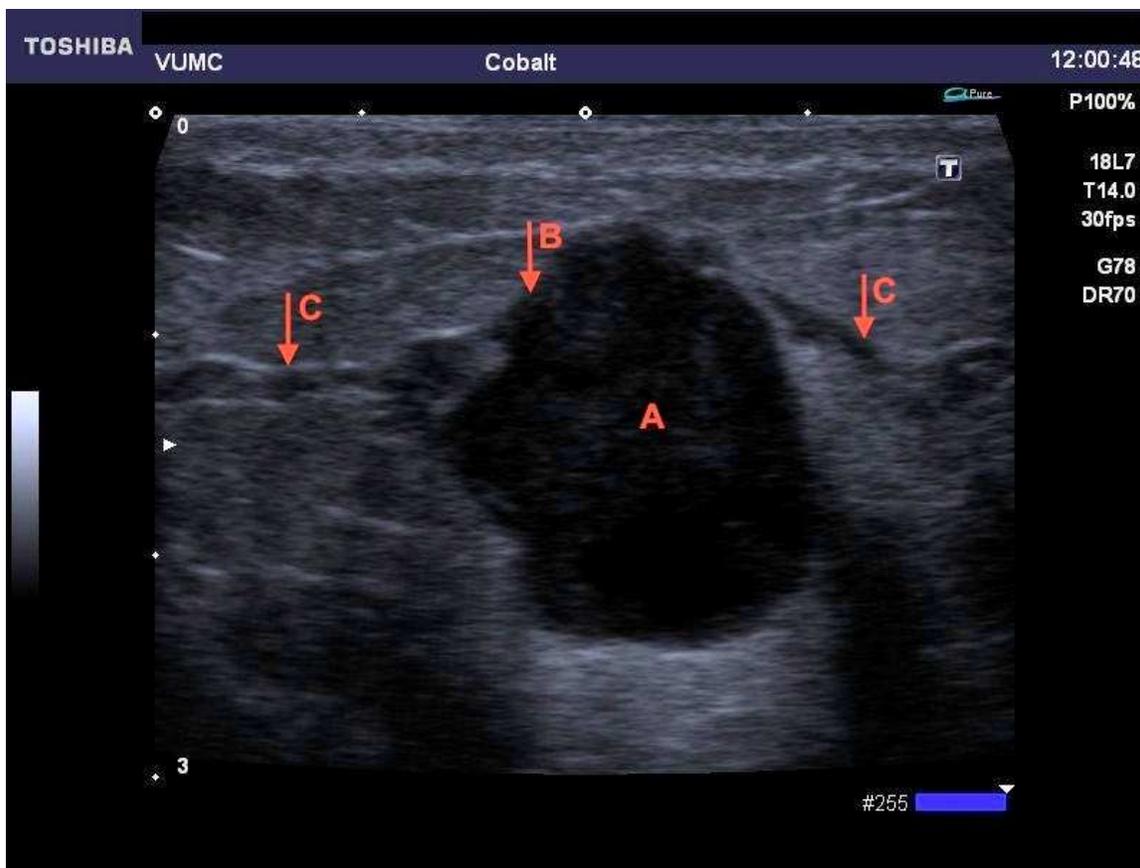


Fig. 3

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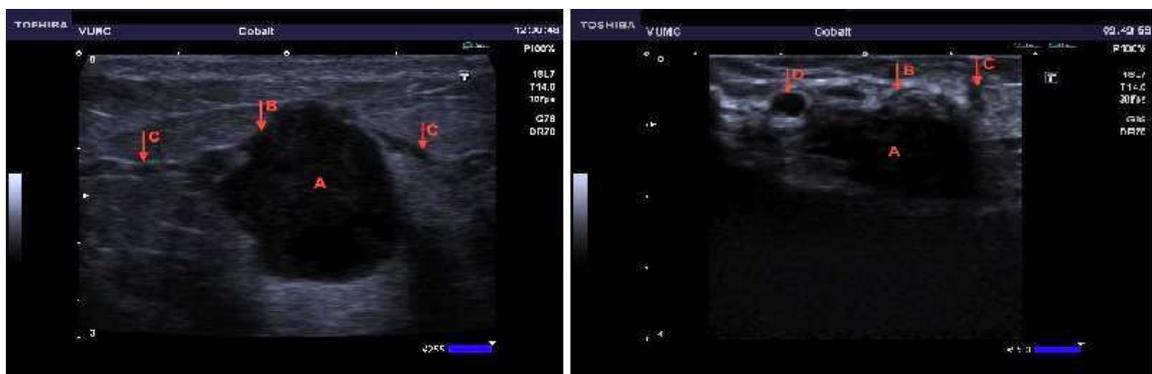


Fig. 2 a,b
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