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The Importance of Intraoperative Ultrasound Guidance to Achieve Negative Margins for Palpable and Nonpalpable Breast Cancer

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Background

- Breast-conserving surgery (BCS) plus adjuvant radiotherapy has become the alternative treatment to mastectomy for early-stage breast cancer
  - with evidence from randomized controlled trials reporting equivalent survival *
- Residual tumor is the most significant risk factor for local recurrence after BCS
- Approximately 20 to 40% of patients have positive margins after partial mastectomy and require a second operation for margin clearance∞
- Re- excision is the preferred choice to achieve negative surgical margins

*Fisher B, Anderson S, Bryant J, Margolese RG, Deutsch M, Fisher ER, 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.
*Veronesi U, Cascinelli N, Mariani L, Greco M, Saccozzi R, Luini A, et al. Twenty-year follow-up of a randomized study comparing breast-conserving surgery with radical mastectomy for early breast cancer. N Engl J Med 2002;347:1227.
∞Wilke LG, Czechura T, Wang C, et al. Repeat surgery after breast conservation for the treatment of stage 0 to II breast carcinoma: a report from the National Cancer Data Base, 2004-2010. JAMA Surg 2014;149:1296-305.
∞McCahill LE, Single RM, Aiello Bowles EJ, et al. Variability in reexcision following breast conservation surgery. JAMA 2012;307:467-75.

Background

- Intraoperative ultrasound guided (IUG) - BCS is being increasingly embraced by breast surgeons worldwide
- The goals of BCS are to provide the survival equivalent of mastectomy, a low rate of recurrence and a cosmetically acceptable breast after excision
- The major advantage of BCS is to allow patients preserve their breast without sacrificing oncologic outcome which requires complete surgical removal of the tumor with negative surgical margins*

*Wilke LG, Czechura T, Wang C, Lapin B. Repeat Surgery After Breast Conservation for the Treatment of Stage 0 to II Breast Carcinoma: A Report From the National Cancer Data Base, 2004-2010. AMA Surg. 2014 Dec;149(12):1296-305.

Background

- Real-time sonographic localization provides tumor free margins with low excision volumes and decreases the rate of reoperations
- Originally, US guidance has been proposed for nonpalpable tumors ∞
- However, its beneficial effect for palpable conterparts also merit consideration according to current literature ✔

∞Ramos M, Díaz JC, Ramos T, Ruano R, Aparicio M. Ultrasound-guided excision combined with intraoperative assessment of gross macroscopic margins decreases the rate of reoperations for non-palpable invasive breast cancer. Breast. 2013;22(4):520-4.
✔ Yu CC, Chiang KC, Kuo WL, Shen SC. Low re-excision rate for positive margins in patients treated with ultrasound-guided breast-conserving surgery. Breast. 2013;22(5):698-702.
✔Angarita FA, Nadler A, Zerhouni S, Escallon J. Perioperative measures to optimize margin clearance in breast conserving surgery. Surg Oncol. 2014;23(2):81-91.

Background

- Since 2005, breast US is being routinely performed preoperatively for breast lesions at our institution
- Real time surgeon performed intraoperative US guided BCS is the preferred method of surgical choice in all patients with palpable and nonpalpable breast cancer

Objectives

- Primary
  - To compare the efficacy of IUG-BCS for palpable and nonpalpable breast cancer with respect to margin status, re-excision rate, tumor free tissue sacrifice and cost-time analysis
- Secondary
  - To analyze the relationship between intraoperative assessment of gross macroscopic and ultrasonographic margins and frozen section analysis with final histopathologic results

Patients and Methods

- 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, and analysis of the results as regards margins were evaluated, and the requirement for synchronous or metachronous re-excision was evaluated for palpable and nonpalpable tumors

Statistical Analysis

- All statistical analyses were carried out using SPSS software, version 13.0 (SPSS Inc., Chicago, IL, USA).
- To assess the association between the documented variables and the existence of a positive margin, categorical variables were compared by Pearson's chi-square test and continuous variables were assessed using t test.
- A P value equal to or less than 0.05 was considered statistically significant

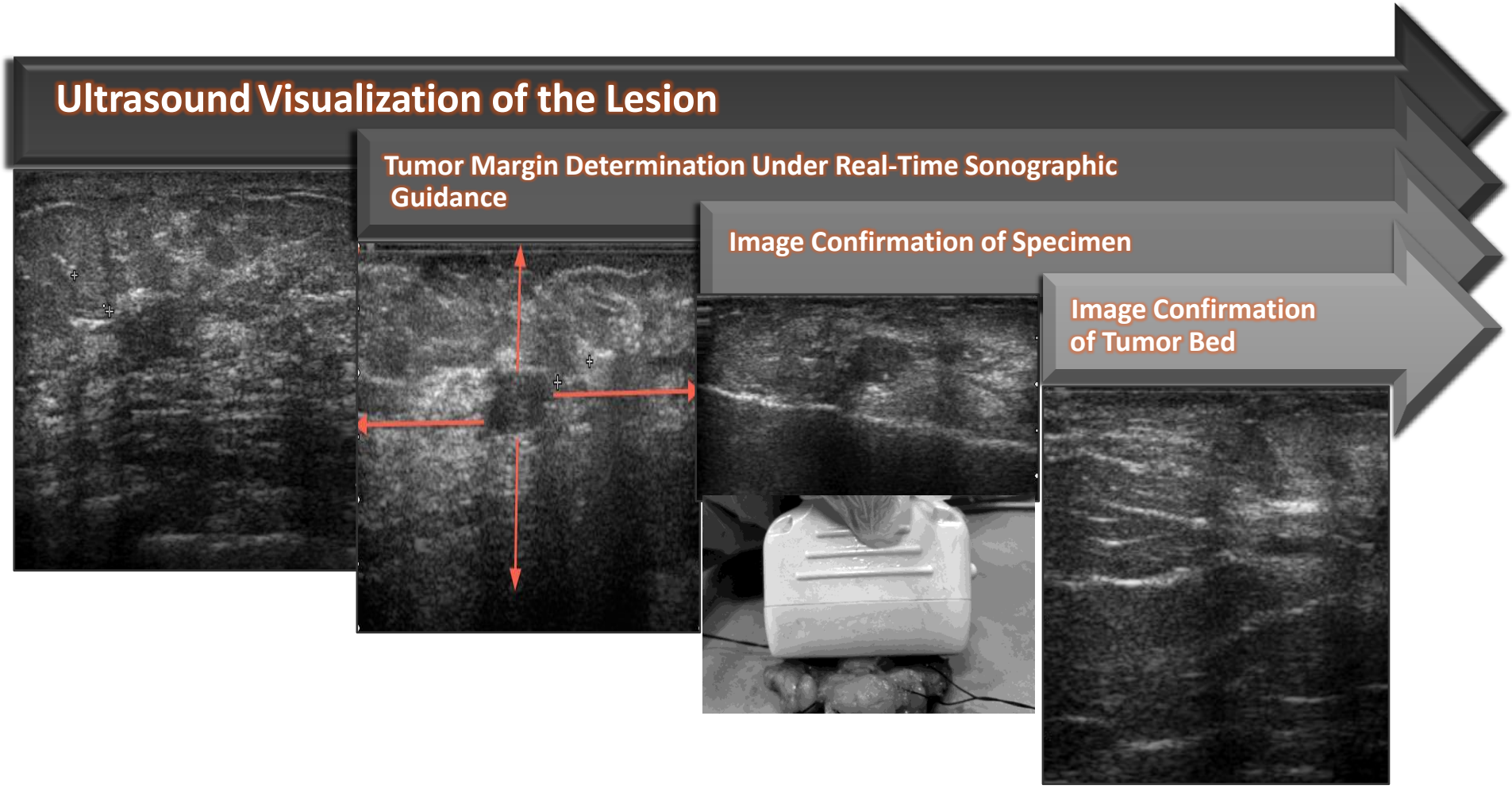
Patients

- **Patients**
  - A total of 259 patients with the diagnosis of in situ or invasive carcinoma had IUG-BCS by a single surgeon at BEUN breast unit between 2011-2015

Methods

- **Methods**
  - IUG tumor localization and BCS
  - Sonographic and macroscopic assessment of the surgical margins by surgeon
  - Frozen section analysis of 6 margins from each specimen
  - Cavity shaved margins from tumor bed for permanent section analysis

Intraoperative Tumor Localization Protocol



Patients and Tumor Characteristics

n=(259)	Palpable tm. (n=117) 45.1%	Nonpalpable tm. (n=142) 54.9%
Age (mean ±sd) (range=25-92 y.)	54.5±3.7	50.6±7.5
Tumor size (mean ±sd, cm.)	2.6±1.4	1.7±0.7
Histology		
DCIS	%15	%17
IDC	%75	%76
ILC	%6	%4
Others	%4	%3
Grade		
I	%25	%42
II	%51	%36
III	%24	%22
Menopausal status		
Premenopausal	42%	44%
Postmenopausal	58%	56%
BMI	29±2	25±3

Results of IUG-BCS			
	Palpable tm.	Nonpalpable tm.	Total
Accuracy of excision	100% (117/117)	100% (142/142)	100% (259/259)
Sonographically negative margins verified by frozen section	91.4% (107/117)	92.2% (131/142)	91.9% (238/259)
Identification of involved margin via specimen sonography	90% (9/10)	100 % (11/11)	95.2% (20/21)
Overall positive margin rate determined by frozen section analysis	2.8% (20/702)	1.9% (16/852)	2.3% (36/1554)
Reoperation requirement	2.5% (3/117)	2.1% (3/142)	2.3% (6/259)

Results

- The overall positive margin rate determined by frozen section analysis was 2.3% (36/1559)
- 68,2% (15/22) of patients with the diagnosis of positive margin by frozen section analysis proved to have significant degrees of pure DCIS or mixed invasive ductal carcinoma with DCIS at final histopathologic evaluation

Results

- A second operation was required only in six cases
  - 3 patients (2.1%) with nonpalpable
  - 3 patients (2.5%) with palpable tumors
- for either determination of close margins or multifocality at cavity shaved margins
- without residual cancer on pathological examination of the reoperative specimens
- The calculated resection ratio and cost-time analysis was found to be similar for palpable and nonpalpable tumors

Discussion

- In BCS, US satisfies the requirements for diagnosis and assisted treatment of breast cancer
- US has been extensively used in the fields of preoperative evaluation, procedure-guided diagnostics, intraoperative tumor localization, and intraoperative margin assessment
- Hence, as a study objective, we focused on breast cancer patients treated with BCS who underwent US for intraoperative tumor localization

Discussion

Review of literature on intraoperative use of ultrasound for identifying and excising primary invasive breast cancer (more than 50 cases).

Source	No. cancers	Not found	Re-excisions %	Local recurrence
Harlow et al.	65	0	4.8	n.d.
Kaufmann et al.	101	0	9	0/100
Ngo et al.	70	1	4.2	n.d.
Haid et al.	299	0	19	1/299
Ramos et al.	225	1	4.0	0/225

Harlow SP, Krag DN, Ames SE, Weaver DL. Intraoperative ultrasound localiza- tion to guide surgical excision of nonpalpable breast carcinoma. ACS 1999;189(3):241-6.
Kaufman CS, Jacobson L, Bachman B, Kaufman LB. Intraoperative ultrasonog- raphy guidance is accurate and efficient according to results in 100 breast cancer patients. American Journal of Surgery 2003;186(4):378-82.
Ngô C, Pollet AG, Laperrelle J, et al. Intraoperative ultrasound localization of nonpalpable breast cancers. Annals of Surgical Oncology 2007;14(9):2485-9.
Haid A, Knauer M, Dunzinger S, et al. Intra-operative sonography: a valuable aid during breast-conserving surgery for occult breast cancer. Annals of Surgical Oncology 2007;14(11):3090-101.
Ramos M, Díaz JC , Ramos T, Ruano R, Aparicio M, et al.Ultrasound-guided excision combined with intraoperative assessment of gross macroscopic margins decreases the rate of reoperations for non-palpable invasive breast cancer. The Breast 2013;22:520-524

Discussion

- The results of the presented study show that intraoperative continuous use of ultrasonography provides significant surgical accuracy of either palpable or nonpalpable breast cancer
- The proportion of adequate clear resection margins was high; more than 90% of women had tumour-free resection margins confirmed by frozen section analysis

Discussion

- Accordingly, the improved margin clearance achieved with ultrasound guidance lowered the need for either a re-excision, or mastectomy
- Moreover, cavity shavings from tumor bed for permanent section analysis as the standard of the procedure decreased the need of re-operations to 2.3%.
- Avoidance of further treatment has the potential to reduce adverse effects on cosmesis, psychological distress, and health costs

Discussion

- US-guided surgery resulted in significantly smaller specimen volumes and less resection of healthy breast tissue relative to the excessive specimen volumes seen in women who underwent palpation-guided surgery in literature *
- A reduction in specimen volume could lead to improved cosmetic outcomes, thereby increasing patients' satisfaction, quality of life and decreasing costs

*Krekel NM, Haloua MH, Lopes Cardozo AM, et al. Intraoperative ultrasound guidance for palpable breast cancer excision (COBALT trial): a multicentre, randomised controlled trial. Lancet Oncol. 2013;14(1):48-54.

Discussion

- The considerable improvements in surgical accuracy provided by US-guided BCS might only be questioned by the fact that the proportion of tumor-free margins was less in case of additional DCIS
- In our study, DCIS was determined in 15 out of 22 patients (68.2%) with positive margins
  - 8 patients with nonpalpable tm.
  - 7 patients with palpable tm.

Discussion

- US-guided BCS can substantially improve a surgeon's performance
- One of the most crucial issue is that surgeons should gain competence in the use of US,
  - to design preoperative planning
  - to avoid the need for a radiologist to be present at surgery
  - to perform continuous intraoperative scanning
  - to enhance hand-eye coordination by personal performance of US-guided surgery
- The required expertise to perform US-guided BCS has been recommended as up to eight procedures *
- In our opinion, skilled surgeons can gain adequate expertise after a training period under the supervision of an expert up to a least ten procedures with both palpable and nonpalpable lesions

*Krekel NM, Lopes Cardozo AM, Muller S, et al. Optimising surgical accuracy in palpable breast cancer with intra-operative breast ultrasound: feasibility and surgeons' learning curve.Eur J Surg Oncol 2011; 37: 1044–50.

Discussion

- Cavity shaved margins
- In literature, cavity shaving has been reported to halve the rates of positive margins and reexcision among patients with BCS
- According to the design of our study protocol routine cavity shaving was performed to all cases
  - This approach decreased the need of reexcisions in only 10% of our patients
  - This discordance is also attributed to the beneficial effect of intraoperative US guidance that enables to real-time visualize and evaluate margin status
  - Thus cavity margins is more tumor free than expected

Chagpar AB, Killelea BK, Tsangaris TN, Butler M, et al. A Randomized, Controlled Trial of Cavity Shave Margins in Breast Cancer. N Engl J Med. 2015 May 30.

Conclusion

- Our study demonstrated that US-guided BCS for either palpable or nonpalpable breast carcinomas facilitates negative margins
  - without much need to secondary interventions
  - with less healthy tissue sacrifice
  - with satisfactory cosmetic results
  - with lower costs

Conclusion

- IUG-BCS is an invaluable and effective modality for both palpable and nonpalpable breast cancer in obtaining clear surgical margins with optimum resection volumes and reducing re-operations
- Sonographic and frozen section assessment of the specimen margins together with shaving cavity margins of the tumor bed for permanent analysis could be a feasible method for minimizing the requirement for reoperations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Thank you