December 2017

Negative predictive value of ultrasound in predicting tumor-free margins in specimen sonography

Saira Naz
Aga Khan University, Saira.naz@aku.edu

Saima Hafeez,
Aga Khan University

Zainab Hussain
Aga Khan University, zainab.hussain@aku.edu

Kiran Hilal
Aga Khan University, kiran.hilal@aku.edu

ORIGINAL ARTICLE

Negative Predictive Value of Ultrasound in Predicting Tumor-Free Margins in Specimen Sonography

Saira Naz, Saima Hafeez, Zainab Hussain and Kiran Hilal

ABSTRACT

Objective: To evaluate the success of ultrasound in post-excision specimen visualization, and negative predictive value of ultrasound for estimation of tumor-free margins using histopathology as the gold standard.

Study Design: Cross-sectional analytical study.

Place and Duration of Study: The Aga Khan University Hospital, Karachi, Pakistan, from May 2010 till January 2013.

Methodology: Sonography of all breast nodules was done before and after exicision by two female radiologists with at least five years clinical experience. All surgeries were performed by the same referring breast surgeons. All nodules were non-palpable and had histopathology as well as specimen sonography performed at AKUH. Subjects were excluded, if histopathology was not available, post-procedure sonogram not done or done in another hospital and nodules that were not seen on ultrasound. After needle localization in 47 patients using ultrasound and in 7 patients using mammogram was done, sonogram was conducted in all 54 lesions. These were then assessed by ultrasound for detection of lesion and tumor-free margins in malignant lesion. Post-excision ultrasound was performed for the evaluation of lesion whether visualized or absent with localizing needle *in situ*, lesion dimensions, depth measurement between the superior margin of the lesion and its edge.

Results: All 54 lesions were present on post-exicison scan, out of which 28 were documented as malignant and 26 as benign. Ultrasound declared all specimens as tumor-free. On histopathology, two lesions were documented as having tumor-positive margins and were proven to be invasive lobular carcinoma. Therefore, the negative predictive value of the specimen sonography for margin detection was 26/28 (92.8%).

Conclusion: Ultrasound of the excised breast tumor specimen is a simple and reliable technique for confirmation of the tumor-free margins in non-palpable breast lesions.

Key Words: *Breast. Tumors. Specimen sonography. Ultrasound (US). Negative predictive value.*

INTRODUCTION

Breast sonogram and mammography is gaining significant popularity rapidly due to its early detection of breast lesions, particularly of the impalpable variety.[1] Therefore, interventional sonology is being comfortably affected by both the radiologists and surgeons for impalpable breast lesions.

Post-excision scanning of resected specimen is essential for warranting successful surgical removal of non-palpable breast masses. Radiography of the specimen remains the standard of care.[2,3] It reveals confinement, particularly in those masses which are hardly visible on mammogram but clearly evaluated on ultrasound. This, however, is not the case with specimen sonography as small, superficial and indistinct mammogram lesions can be well visualized. After evaluation of the literature review, the authors found that few studies have addressed this technique, and none addressed the sensitivity of specimen sonography for evaluating lesion margins.[4-6]

There is an increasing number of sonographically-guided needle localizations of impalpable breast masses. High performance levels of recent sonography machinery available in the present day practice, prompted the author to review the experience retrospectively, in evaluating breast specimens by sonography. The main objectives of this study were to determine the reliability of specimen sonography for visualization of excised breast lesions, and the accuracy of this technique for the prediction of tumor-free margin.

METHODOLOGY

That was a retrospective cross-sectional study with non-probability purposive sampling technique, conducted in the Radiology Department, The Aga Khan University Hospital, Karachi (AKUH), from May 2010 till January 2013. As the data collection consisted only of chart review, waiver from the ethical review committee was obtained. Data from clinical files were collected in all patients having lesions on preoperative ultrasound but were not palpable on examination as well as patients who underwent mammogram-guided needle localization. Excision of masses was performed by the referring breast surgeons. However, excised breast specimen

Department of Radiology, The Aga Khan University Hospital, Karachi.

Correspondence: Dr. Zainab Hussain, Assistant Professor, 19A Askari-I Apartments, Ch. Khaliq-uz-Zaman Road, Clifton, Karachi.
E-mail: zainab.hussain@aku.edu

Received: May 18, 2015; Accepted: November 5, 2017.

were assessed on ultrasound by two experienced radiologists for detection of the lesion and evaluating tumor margins. All excised impalpable breast masses with proven histopathology and patients who had post-excision ultrasound of specimen performed at AKUH were included in the study. Those subjects were excluded, if any mass without histopathology, post-excision scan not performed or performed outside AKUH and of lesions that were not identified on ultrasound.

Post-excision ultrasounds were performed for the evaluation of presence or absence of the lesion with localizing needle, dimensions of the tumor, dimension of the normal breast tissue between the tumor and edge of the specimen. All ultrasounds of breast specimen were performed using Toshiba (Xario and Aplio 400) machines using high frequency probes of 10-14-MHz in AKUH Radiology Department, both pre- and post-operatively. Post-excision scans were carried out within an hour of excision by the radiologists in breast imaging, and the above enlisted variables were documented. If the distance between the tumor and its surgical margin was ≤0.2 cm, then it was termed as positive; and was considered negative, if the edge was ≥0.2 cm. These measurements were settled upon in accordance with the surgeons and histopathology.

The analysis was performed on SPSS version 19.0. Frequencies with percentages were described for the categorical variables and mean with standard deviations was described for continuous variables. Negative predictive value of ultrasound was also evaluated for tumour-free margins. The formula for calculation of negative predictive value was taken as true negatives/ true negatives + false negatives.

RESULTS

All patients (Table I) were 21 to 61 years old (mean age = 39.56 ±6.2 years). Ultrasound of the specimens were done of all 54 patients after needle localization; of which, 47 (87%) were done sonologically while 7 (12.9%) were performed on mammogram. Specimen sonogram recognized all 54 (100%) tumors. All of the lesions measured less than 20 mm in size as the size of the lesions ranged between 10-18 mm. Out of 54 specimens, 28 (52%) were malignant and 26 (48%) were benign. Among the malignant lesions, 23 (82%) were ductal carcinoma *in situ* and five (18%) were invasive lobular carcinoma. Benign looking lesions were localized and excised since the primary surgeon was dubious regarding their etiology diagnosed on imaging. No preoperative percutaneous biopsy was performed in any of the masses in this study. In 26 benign lesions, margins evaluation was not done on histopathology.

Table I: Summary of results.

Age	21-61, mean (39.56) ± 6.2
Benign lesions	26 (48%)
Malignant lesions	28 (52%)
Lesions with tumor-free margins on US	28
Lesions with tumor-free margins on H/P	26
Negative predictive value of ultrasound (true negatives / true negatives + false negatives)	92.8%

On specimen sonography, all specimens were categorised as tumor-free. However, two of them had margin involvement and were proven to be invasive lobular carcinoma later on histopathology. As ultrasound had depicted all specimens as tumor negative; therefore, only the negative predictive value of the specimen sonography for margin detection was calculated in a 2x2 table. Hence, the ability of ultrasound to correctly label tumor-free margins in a specimen (negative predictive value) was 26/28 x 100 (92.8%S) taking histopathology as criterion.

All the 54 Kopans needles placed preoperatively were seen in the postoperative specimen. No wire was missing, thereby confirming that the lesion in question had been adequately excised.

DISCUSSION

Preoperative needle localization under ultrasound guidance is used in non-palpable masses which are adequately visualized on ultrasound. It is used as a substitute to stereotactic-guided localization, easily

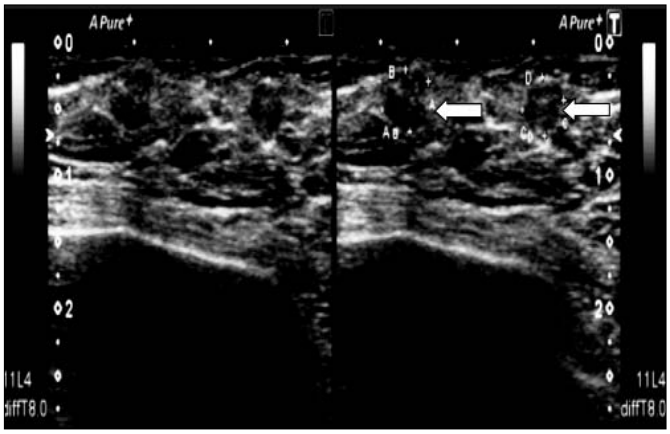

Figure 1a: Showing sonograhic image of 2 lesions prior to needle localization.

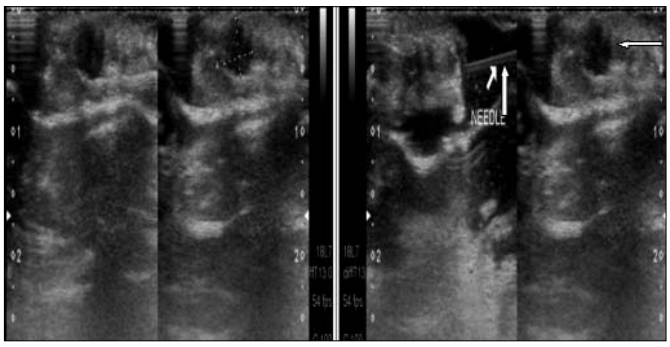

Figure 1b: Showing specimen sonography, a vertical arrow indicating a wire within the specimen and lesion. The lesions identified with horizontal arrows.

available, less expensive and less time consuming. In this study, 87% lesions were localized sonographically; therefore, it was logical to evaluate the role of ultrasound in specimen evaluation.[6-8]

According to some authors, specimen sonography is done by placement of specimen in a cellophane bag[9], or in a container filled with a small amount of saline.[10] The author used saline immersion technique in all of the cases.

High resolution transducer was utilized in this study, which permitted adequate imaging of superficial nodules even with the first few millimeter of the specimen in contact with the transducer. The specimen was rescanned after flipping it over, which proved to be helpful in visualizing normal appearance of parenchyma between the tumor and the specimen margin. In this study, ultrasound detected 54 targeted lesions (100%) within the specimen. However, in a study by Guerrieri *et al.*[10] the detection of the targeted lesion by the ultrasound was 95.4%. The high detection rate in this study is most likely due to use of saline immersion technique.

The same ultrasound machine was utilized for evaluation of pre- and post-excision scans of the tumors as variation in the instruments based on physics and machine factors, such as compounding and harmonics can alter the image appearance. It is of prime importance in smaller nodules or indistinct parenchymal lesions. Effective outcome of technique is not related to the presence or absence of needle within the nodule; yet it seemed appropriate to ask the surgeon to retain the hook wire in place inside the nodule as locating the nodule and evaluation of its margins is convenient by following the hook-wire, particularly in a big specimen. As in our study, all specimens had wire in place.

Following needle localization for lumpectomy, the key difficulty is failure to remove the target, which in other studies happens in □3% of cases.[11-13] In this series, none of the needle localization procedures were unsuccessful. Excellent results in this study and such positive results might be secondary to two factors. Primarily, in this study non-palpable nodules were localized rather than microcalcification using ultrasound as success rate is severely compromised with microcalcification.[14] Secondly, ultrasound guidance allows real time placement of the hook-wire through the mass; while mammographic guidance allows locating the needle close enough the lesion but without traversing it, in a number of cases.[15-18] No negative results were observed in this study as only seven specimens were localized under mammographic guidance and all of them were visible on ultrasound as well. However mammographic guidance was performed instead of ultrasound when micro-calcifications were targeted within a nodule. The present results suggest that ultrasound of the specimen is an alternate method of specimen imaging in cases of non-fatty breast, and if the lesion is evident on sonogram.

Evaluation of the margin was also carried out in this study using ultrasound of the specimen. The reasons attributing to the false negative results in this study were ill defined margins and obscuration of the posterior margins by the acoustic shadowing of the lesion, which is commonly seen in cases of invasive lobular carcinomas. In this study, tumor-free margins were claimed in 92.8% of the cases which is similar to the studies conducted by Newman, *et al.* and Georgian, *et al.* showing clear histologic margins in 82.6% and 92%, respectively.[18,19]

However, as all the margins were termed negative on the ultrasound scan, only the negative predictive value could be calculated for the malignant lesions. Margin evaluation is not performed in benign lesions; and hence, these results apply to the malignant lesions only.

The impact of specimen radiography in margin evaluation was not a part of this study.

The radiologist, carrying out needle localization and the post-excision specimen scan, should be the same person to minimalize the probability of inaccuracy.

CONCLUSION

In this study, specimen sonography was found be a simple and reliable procedure for confirmation of tumor-free boundaries in a non-palpable malignant breast tumor visualized on ultrasound.

REFERENCES

1. Homer MJ, Berlin L. Radiography of the surgical breast biopsy specimen. *AJR* 1998; **171**:1197-9.
2. D'Orsi CJ. Management of the breast specimen. *Radiology* 1995; **194**:297-302.
3. Fornage BD, Ross MI, Singletary SE, Paulus DD. Localization of impalpable breast masses: value of sonography in the operating room and scanning of excised specimens. *AJR* 1994; **163**:569-73.
4. Staradub VL, Rademaker AW, Morrow M. Factors influencing outcomes for breast conservation therapy of mammographically detected malignancies. *J Am Coll Surg* 2003; **196**:518-24.
5. Jackman RJ, Marzoni FA Jr. Needle-localized breast biopsy: why do we fail? *Radiology* 1997; **204**:677-84.
6. Homer MJ, Smith TJ, Safaii H. Prebiopsy needle localization: methods, problems, and expected results. *Radiol Clin North Am* 1992; **30**:139-53.
7. Liberman L, Goodstine SL, Dershaw DD. One operation after percutaneous diagnosis of nonpalpable breast cancer: frequency and associated factors. *AJR* 2002; **178**:673-79.
8. Margolis NE, Morley C, Lotfi P, Shaylor SD, Palestrant S, Moy L, *et al.* Update on imaging of the postsurgical breast. *Radiographics* 2014. **34**:642-60.

9. Brenner RJ, Bassett LW, Fajardo LL. Stereotactic core-needle breast biopsy: a multi-institutional prospective trial. *Radiology* 2001; **218**:866-72.

10. Guerrieri-Gonzaga A, Botteri E, Rotmensz N, Bassi F, Intra M, Serrano D, *et al.* Ductal intraepithelial neoplasia: postsurgical outcome for 1,267 women cared for in one single institution over 10 years. *Oncologist* 2009; **14**:201-12.

11. Piper M, Peled AW, Price ER, Foster RD, Esserman LJ, Sbitany H. Mammographic changes after oncoplastic reduction mammoplasty. *Ann Plast Surg* 2015 [Epub ahead of print].

12. Whipp EC, Halliwell M. Magnetic resonance imaging appearances in the postoperative breast: the clinical target volume-tumor and its relationship to the chest wall. *Int J Radiat Oncol Biol Phys* 2008; **72**:49-57.

13. Hirose M, Hashizume T, Seino N, Kubota H, Nobusawa H, Gokan T. Atlas of breast magnetic resonance imaging. *Curr Probl Diagn Radiol* 2007; **36**:51-65.

14. Leoni M, Sadacharan R, Louis D, Falcini F, Rabinowitz C, Cisbani L, *et al.* Variation among local health units in follow-up care of breast cancer patients in Emilia-Romagna, Italy. *Tumori* 2013; **99**:30-4.

15. Olson JA Jr, Morris EA, Van Zee KJ. Magnetic resonance imaging facilitates breast conservation for occult breast cancer. *Ann Surg Oncol* 2000; **7**:411-5.

16. Vicini FA, Goldstein NS, Kestin LL. Pathologic and technical considerations in the treatment of ductal carcinoma *in situ* of the breast with lumpectomy and radiation therapy. *Ann Oncol* 1999; **10**:883-90.

17. Stargen ED, O'Neil TP. Breast ultrasound. *Surg Clin North Am* 1998; **78**:219-36.

18. Newman PG, Rozycki GS. The history of ultrasound. *Surg Clin North Am* 1998; **78**:179-96.

19. Georgian-Smith D, Taylor KJW, Madjar H. Sonography of palpable breast cancer. *J Clin Ultrasound* 2000; **28**:211-6.