Power Doppler and gray-scale sonography standardized by BI-RADS for the differentiation of benign postoperative lesion and local recurrence after breast-conserving therapy

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Received June 17, 2011; Accepted August 4, 2011

DOI: 10.3892/or.2011.1445

Abstract. The diagnosis of ipsilateral breast tumor recurrence (IBTR) after breast-conserving therapy is of great interest to breast physicians. The present study compared the utility of gray-scale sonography standardized by a breast imaging reporting and data system (BI-RADS) and power Doppler sonography for differentiating between benign scar formation and IBTR after breast-conserving therapy. Gray-scale sonography detected 83 solid breast lesions classified as BI-RADS categories 3-5 in 272 patients after breast-conserving therapy, and these lesions were entered into the study (53 lesions as category 3, probably benign; 30 lesions as categories 4-5, suspected malignancy). Power Doppler sonography revealed intratumoral flow in 19 of 83 solid breast lesions. BI-RADS category 3 was accepted as probably benign and BI-RADS categories 4-5 were considered as suspicious for breast tumor recurrence in the gray-scale ultrasound criteria. Positive and negative intratumoral flow were employed as suspicious for breast tumor recurrence and probably benign, respectively, in the power Doppler sonography criteria. Sensitivity was higher for power Doppler sonography (94.7±10.0%) than for gray-scale sonography (57.9±22.2%). Specificity was also higher for power Doppler sonography (98.4±3.0%) than for gray-scale sonography (70.3±0.6%). These results suggest that power Doppler sonography can complement gray-scale sonography standardized by BI-RADS in differentiating between IBTR and benign scar lesions.

Introduction

In the mid-1980s, the National Surgical Adjuvant Breast and Bowel Project (NSABP) B-06 trial demonstrated no difference in survival between mastectomy versus lumpectomy followed by radiation (1). Recently, breast-conserving therapy (BCT), defined as lumpectomy followed by whole-breast irradiation, has become the most common therapeutic option for breast cancer (2-4). Approximately 10-15% of patients undergoing BCT for operable breast cancer develop locoregional recurrence within 10 years (5-7). Patients with ipsilateral breast tumor recurrence (IBTR) without simultaneous distant metastases are considered as good candidates for salvage mastectomy (8,9) or repeat BCT (8,10). However, IBTR is considered to represent one predictor of systemic recurrence and breast cancer-related death after BCT (11). The diagnosis of IBTR after BCT is thus of great interest to breast physicians. BCT is less radical and has a more favorable psychological impact on patients, but frequently results in postoperative changes (12-18). Such changes may include both IBTR and benign situations such as scarring, reparative changes, accumulation of exudate or liquid, post-irradiation mastitis and fibrosis (12-18). The value of both mammography and ultrasonography after BCT is limited, as scars tend to be indistinguishable from IBTR (16,17). According to Balu-Maestro *et al* (15), ultrasonography was markedly more sensitive than mammography for detecting benign abnormalities after BCT (ultrasonography, 95.7%; mammography, 72.3%). However, ultrasound-guided biopsy is reportedly indispensable for positive diagnosis, due to the imaging similarities between benign changes and IBTR (13,15).

Several clinical trials have shown that color Doppler sonography (CDS) or power Doppler sonography (PDS) can successfully distinguish between benign and malignant breast tumors (19-21). The American College of Radiology developed a breast imaging reporting and data system (BI-RADS) lexicon for breast sonography to standardize the characterization of breast lesions (22). Several studies have reported that scoring findings from breast ultrasonography based on the criteria used for BI-RADS allowed highly accurate differentiation of benign structures from malignant breast tumor (23-25). The present study compared the accuracy of PDS and gray-scale sonography standardized by BI-RADS for differentiating scar formation and IBTR after BCT.

Materials and methods

The records in our ultrasound section were reviewed for 272 women with early breast cancer treated using BCT between

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Key words: breast-conserving therapy, local recurrence, breast cancer, ultrasonography, Doppler ultrasound

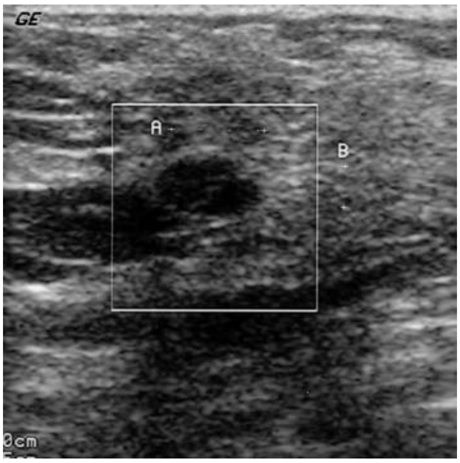

Figure 1. Gray-scale ultrasound image of a septate lesion, showing lobulated shape, smooth margins, thin septation, more parallel orientation, anechoic content and posterior enhancement characteristic of a cluster of small cysts: BI-RADS category 3.

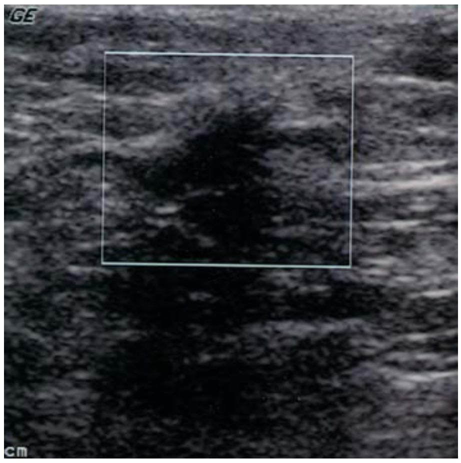

Figure 3. Gray-scale ultrasound image of a solid hypoechoic lesion, showing polymorphic shape, indistinct margin with some spiculae, uncertain orientation, heterogeneous matrix: BI-RADS category 4 (shown histologically to represent benign scar formation). Doppler flow signal was absent in the lesion.

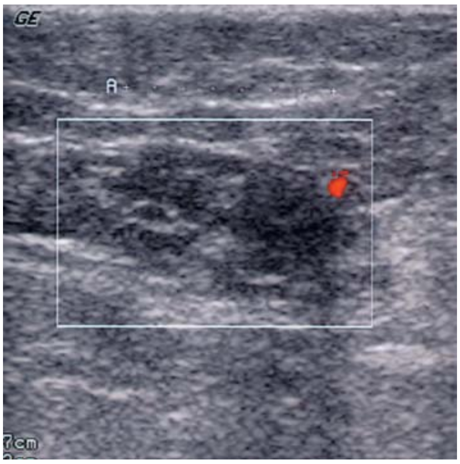

Figure 2. Gray-scale ultrasound image of a solid lesion, showing mild lobulation, smooth margins, homogeneous hypoechoic matrix, parallel orientation and slight posterior enhancement: BI-RADS category 3 (diagnosed as benign scar formation based on no growth in size during 2 years of follow-up). Doppler flow signal was negative.

Figure 4. Gray-scale ultrasound image of a solid hypoechoic lesion, showing polymorphic shape, indistinct, spiculated margin, non-parallel orientation and marked posterior shadowing, making it highly suspicions for malignancy: BI-RADS category 5 (shown histologically to represent benign scar formation). Power Doppler sonography depicted no intratumoral flow signal.

January 2000 and November 2010. For the follow-up schedule after BCT, bilateral sonography of the breasts and axilla was performed every 6 months for the first 8 years and annually thereafter. Tissue examinations were recommended if ultrasonography depicted malignant features or intratumoral flow in the breast mass lesion according to our breast medical section rules. All cases of IBTR (19 lesions in 16 patients) and 12 benign postoperative changes (1 fibroadenoma and 11 instances of necrotic tissue) were diagnosed by core needle biopsy. The remaining 52 scars and 36 cysts showed negative results from aspiration cytology and/or no growth in size over more than 2 years on follow-up ultrasound studies. Contralateral breast tumor recurrences (11 patients) were not included in this study. All study protocols were performed in accordance with the regulations of the local Ethics Committee.

Gray-scale sonography and BI-RADS category. A LOGIQ 700 MR system (GE Healthcare, Milwaukee, WI, USA) equipped with a 7.5- to 11.0-MHz probe for gray-scale imaging and a 5-MHz probe for Doppler mode imaging was used. For our ultrasound section protocol, gray-scale images were recorded in both radial and transverse planes. Additional gray-scale images were obtained in some cases to better depict the lesion. Sonography (both gray-scale and Doppler) was performed by an experienced radiologist (K.K.) who performs more than 1,000 ultrasound examinations each year. The radiologist stored ultrasound images on magneto-optical disc during the routine examination. Two radiologists (A.N. and Y.O.) with 21-25 years of experience in breast imaging reviewed the stored images for this investigation. Reviewers interpreted gray-scale ultrasound images displayed on the ultrasound unit monitor. Interobserver inconsistencies were resolved by consensus decision.

The lesion was characterized using BI-RADS ultrasound descriptors of mass margin, shape, orientation, matrix echogenicity and homogeneity and attenuation. For each of these

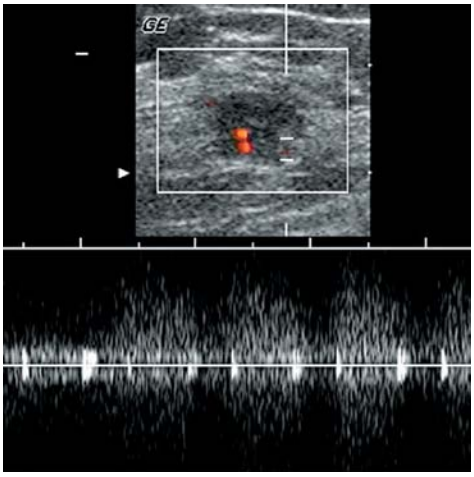

Figure 5. A Doppler ultrasound true-positive result in a 68-year-old woman with recurrent invasive ductal carcinoma. Gray-scale ultrasound showed a BI-RADS category 3 solid lesion, but intratumoral flow was positive. Doppler spectral analyses revealed a pulsatile waveform.

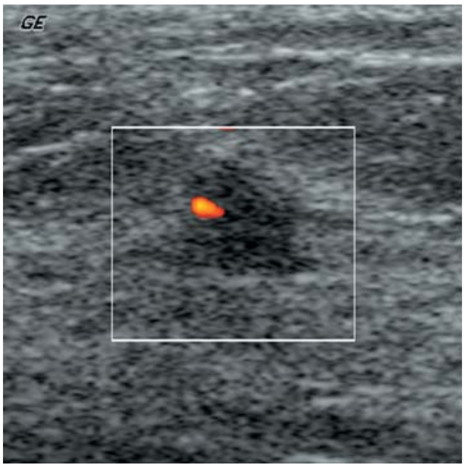

Figure 6. A Doppler ultrasound false-positive result in a 36-year-old woman. Although gray-scale sonography showed a BI-RADS category 3 solid lesion (mild lobulation, smooth margin, homogeneous hypoechoic matrix and parallel orientation), power Doppler sonography revealed intratumoral flow signals. Core needle biopsy confirmed fibroadenoma.

descriptor categories from the ultrasound BI-RADS lexicon, the rater was limited to selecting the one feature descriptor that was most appropriate. Category 1 was selected if no isolated lesion was found on ultrasound. Category 2 (simple cyst) was selected if the shape of the lesion was round, oval or gently lobulated, the margin was circumscribed, echogenicity was anechoic and acoustic enhancement was seen. Category 3 (complicated cyst) was selected in the presence of homogeneous low-level internal echoes throughout a cystic lesion with all the other features of a simple cyst or if clusters of small cysts were evident (Fig. 1). Solid lesions presenting no sonographic features of malignancy were classified as category 3 (Fig. 2, probably benign). Category 4 (Fig. 3) or 5 (Fig. 4) was selected for solid masses that were irregular in shape and for which margins dominated the other features, suggesting malignancy. Category 5 lesions have a greater likelihood of malignancy than category 4 lesions.

Table I. Correlation between gray-scale ultrasound findings and final diagnoses.

BI-RADS	IBTR	Non-IBTR	P-value
Category 4, 5	11	19	
Category 3	8	45	0.025
Total	19	64	

The number of lesions is shown. Data were analyzed using the χ^2 test. IBTR, ipsilateral breast tumor recurrence.

Power Doppler sonography. For our ultrasound section protocol, Doppler gain was adjusted to the highest value at which the image was not affected by color artifacts, and the color-coded area was restricted as much as possible to maximize color sensitivity. The pulse repetition frequency and bandpass filter were selected to optimize the detection of weak signals. The records of routine Doppler ultrasound findings by the ultrasound operator were used for the present retrospective analyses. The breast tumor was rated as having an intratumoral flow signal if spectral analyses detected a pulsatile waveform from at least one intratumoral color signal (Fig. 5).

Analysis of data. Although, complicated cyst or solid breast mass findings (BI-RADS categories 3-5) were evaluated, apparent benign findings (BI-RADS categories 1-2) were excluded from the present study. Gray-scale ultrasound (BI-RADS categories 3-5) and PDS findings were compared with final diagnoses to determine the sensitivity and specificity for IBTR. BI-RADS category 3 was accepted as probably benign and BI-RADS categories 4-5 were considered suspicious for IBTR in the gray-scale ultrasound criteria. Positive intratumoral flow and negative intratumoral flow were employed as suspicious for IBTR and probably benign in the PDS criteria, respectively.

SPSS version 10.0 software (SPSS, Chicago, IL, USA) was used to assess statistical significance, with the level of significance at the 5% level in two-sided tests. Fisher's exact test and the χ^2 test were used for comparing categorical data.

Results

Gray-scale sonography classified 189 subjects as BI-RADS category 1, with no isolated lesion. The remaining 83 subjects had 119 cysts or solid lesions found by gray-scale sonography (category 2, 36 lesions; category 3, 53 lesions; category 4, 18 lesions; category 5, 12 lesions). Gray-scale sonography and PDS findings are compared with final diagnoses (tissue examination and/or long-term follow-up study) in Tables I and II, respectively. Significant differences were seen between final diagnoses and both gray-scale sonography (χ^2 test, P=0.025) and PDS findings (Fisher's exact test, P<0.001). Sensitivity was higher for PDS (94.7±10.0%) than for gray-scale sonography (57.9±22.2%). Specificity was also higher for PDS (98.4±3.0%) than for gray-scale sonography (70.3±0.6%). Only one case each of false-positive and false-negative results were

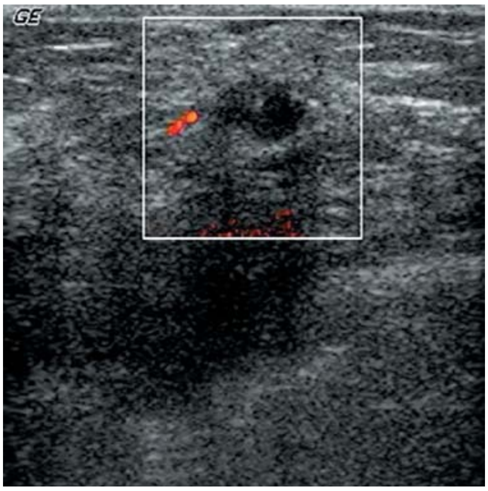

Figure 7. A Doppler ultrasound false-negative result in a 57-year-old woman. Gray-scale sonography depicted a BI-RADS category 3 solid lesion with negative flow signal on power Doppler sonography (shown histologically to represent invasive ductal carcinoma after biopsy because of growth in size identified 9 months later).

Table II. Correlation between power Doppler ultrasound findings and final diagnoses.

Doppler flow signal	IBTR	Non-IBTR	P-value
Positive	18	1	
Negative	1	63	<0.001
Total	19	64	

The number of the lesions is shown. Data were analyzed using Fisher's exact method. IBTR, ipsilateral breast tumor recurrence.

observed with PDS (Figs. 6 and 7) (Table II). PDS depicted intratumoral flow in 7 of 8 IBTRs with BI-RADS category 3 and contributed to the higher sensitivity (Fig. 5). Conversely, PDS demonstrated no flow signal in any benign postoperative changes (Figs. 3 and 4) other the false-positive case (Fig. 6).

Discussion

Gray-scale sonography has become an essential medical tool in the detection and differentiation of breast tumor (22-30), showing higher sensitivity for breast tumor compared to mammography before surgery (gray-scale sonography, 88%; mammography, 69%) (31). Balu-Maestro *et al* (15) found that gray-scale sonography was more sensitive than mammography for detecting benign lesions after BCT, but showed almost equal ability to detect IBTR (radiography, 95.5%; sonography, 90.0%). Gray-scale sonography is thus accepted as showing equivalent ability to detect breast tumor as mammography. Surgery and irradiation harden the breast tissue. Gray-scale sonography is considered more useful than mammography, particularly after BCT, as mammography is difficult to perform in cases where breast tissue has become difficult to compress. Gray-scale sonography using the BI-RADS lexicon can accurately differentiate between benign and malignant breast tumor (23-25). However, our application of the standardized BI-RADS lexicon to gray-scale sonography in the present study showed insufficient accuracy in differentiating IBTR from benign conditions. Balu-Maestro *et al* (15) also suggested that gray-scale sonography shows limitations in that posterior attenuation of the scar may simulate cancer or mask a malignancy or mass of scar tissue. Some investigators have considered ultrasound-guided biopsy as indispensable for positive diagnosis, given the imaging similarities between benign and IBTR (13,15).

Malignant breast tumor shows color flow signals at a higher rate than benign tumor (19-21). Some investigators have reported that the tumor vascularity revealed by PDS or CDS correlates with the rate of lymph node involvement (32,33). Nodal involvement has been identified by PDS or CDS in 50-73% of cases with positive intratumoral flow and 10-27% of cases with negative intratumoral flow (32,33). Furthermore, Holcombe reported that breast cancer with hypervascularity revealed by CDS tend to be of higher histological grade than lower vascularity breast cancer (32). These results imply the possibility that detection of intratumoral flow by PDS or CDS offers an indicator of tumor ability to spread. Positive intratumoral flow on CDS provided 61-72.7% sensitivity and 22.2-95% specificity for predicting breast malignancy (19-21). These results for CDS in differentiating the breast tumor are insufficient to justify practical application, as benign tumors also often show intratumoral flow on CDS (19-21). Gokalp *et al* (34) combined BI-RADS gray-scale sonography and PDS findings to differentiate malignant and benign breast tumors. The sensitivity and specificity of gray-scale sonography in differentiating breast tumor were 100.0 and 58.2%, respectively, while the combined findings offered 100.0% sensitivity and 57.7% specificity (34). They concluded that PDS has no contribution to make to BI-RADS gray-scale sonography in terms of preoperative condition (34). Contrary to expectations given the outcomes described by Gokalp *et al* (34), PDS showed higher accuracy than BI-RADS gray-scale sonography in differentiating between IBTR and benign condition in the present investigation. The favorable outcomes in this study mainly depended on the low frequency of intratumoral flow in benign postoperative changes and the high frequency of flow in IBTR. Conversely, the low specificity of CDS/PDS for differentiating between benign and malignant lesions mainly depends on the relatively high frequency of intratumoral flow in benign lesions (19-21). Scar lesions after BCT show flow on CDS/PDS at a lower frequency (16.7% according to Tranquart *et al* (35), 1.6% in our study) compared to preoperative benign lesions, such as fibroadenoma (30.2-77.8%) (19-21). On the other hand, Tranquart *et al* and the present study revealed a high frequency of positive flow in IBTR on CDS/PDS (35). However, the value of contrast-enhanced Doppler sonography in differentiating between benign lesions and IBTR has also been investigated, since the ability of pre-contrast CDS to differentiate between benign lesions and IBTR was poor due to a low positive intratumoral flow rate in IBTR. The reason for inconsistencies in positive intratumoral flow rates between the previous reports may be due to differences in subjects and ultrasound systems between investigations (12,35). In a study to evaluate the benefit of echo contrast-enhanced Doppler sonography in differentiating benign lesions from IBTR after BCT, CDS showed vascularity in 50% (5 of 10 lesions) of IBTR in a baseline pre-contrast-enhanced study. Contrast-enhanced CDS then revealed a significant increase in tumor vascularity in all 10 IBTRs, but in only one of the 28 benign scars (12). The sensitivity of CDS/PDS to vessels is improving with advances in technology and techniques, and further studies are needed to confirm the necessity of contrast-enhancement for CDS/PDS in a large study population.

Doppler spectral parameters calculated from spectral Doppler tracings have been reported as useful in differentiating between malignant and benign lesions before therapy for breast tumors (36-38). Mesaki *et al* (38) reported that sensitivity to malignant breast tumor by acceleration time index, a Doppler spectral parameter, was 79.4%, while Hollerweger *et al* (37) reported resistive index, another spectral parameter, showed 55% sensitivity. Unfortunately, Doppler spectral parameters were not available in the present study, as the requisite calculations were not performed for the study population. Calculation of Doppler spectral parameters is extremely time-intensive, although technological advances may resolve this issue and make the automatic calculation of Doppler spectral parameters more feasible in the future. Further investigations to reveal which Doppler spectral parameters can best contribute to the diagnosis of IBTR will no doubt attract the interest of many breast physicians in the future.

In conclusion, our findings suggest that PDS can differentiate IBTR from benign scar lesions with higher accuracy than gray-scale sonography standardized by the BI-RADS lexicon. Ultrasound techniques consisting of gray-scale mode, CDS/PDS and other optional measures, such as contrast-enhancement and calculation of Doppler spectral parameters, are still evolving. Further investigations to determine the roles of these various ultrasound techniques in diagnosing breast tumor are needed.

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