

Gray Scale and Power Doppler Sonographic Findings of Invasive Breast Cancer

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Purpose: The purpose of this study was to correlate power Doppler sonographic findings with histologic grade in patients with invasive breast cancer.

Materials and Methods: One hundred and ninety-one women (age range, 26 - 75 years; median age, 52 years) with breast masses evaluated with sonography and subsequently proven to be invasive ductal carcinoma not otherwise specified, composed our study population. Two radiologists quantified the lesion vascularity at power Doppler sonography and results obtained were correlated with histologic tumor grades.

Results: Of the 191 invasive ductal carcinomas, vascularity was seen in 97% (74 of 76) of high-grade tumors, 71% (65 of 92) of intermediate-grade tumors, and 26% (6 of 23) of low-grade tumors. Hypervascularity was seen in 63% (48 of 76) of high-grade tumors but in only 17% (16 of 92) of intermediate-grade tumors and not at all in low-grade tumors. Tumor vascularity at power Doppler sonography was significantly associated with a mass margin ($p < .001$) and acoustic transmission ($p < .001$) at gray scale sonography, and was found to be correlated with histologic grade ($r = 0.598$, $p < .001$).

Conclusion: Tumor vascularity at power Doppler sonography was correlated with histologic grade.

Index words: Breast neoplasms; Breast sonography; Power Doppler studies

INTRODUCTION

Sonography is used as an adjunct to mammography to help differentiate benign and malignant breast solid lesions. Malignant lesions often show spiculated margins, marked hypoechogenicity, a thick echogenic rim, and posterior acoustic shadowing at gray scale sonography and tend to produce more flow signals and to have

more irregularly shaped vessels at power Doppler sonography (1 - 5). However, a significant number of breast cancers do not present with these typical sonographic features, and thus, can be misclassified as probably benign, American College of Radiology Breast Imaging Reporting and Data System (BI-RADS) category 3 lesions (6). In a study of 162 solid breast nodules, one of three reviewers interpreted 4 (2.5%) circumscribed carcinomas as probably benign at gray scale sonography. In addition, no tumor vascularity was found in up to 38% of invasive breast cancers at color or power Doppler sonography (7, 8).

In breast cancer, relationships between sonographic findings and tumor components or histologic grades have been examined at gray scale sonography (1, 9 -

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11). To our knowledge, however, relations between the findings at gray scale and power Doppler sonography and histologic grade has not been reported in patients with invasive ductal carcinoma. Therefore, the purpose of this study was to correlate gray scale and power Doppler sonographic findings and histologic grades in patients with invasive breast cancer.

MATERIALS AND METHODS

Patients and Masses

Institutional Review Board (IRB) approval was obtained and informed consent was waived.

Between December 2002 and January 2004, 580 consecutive women (age range, 25 - 79 years; median age, 51 years) with breast masses detected clinically or mammographically and scheduled for sonography-guided needle biopsy (n = 479) or surgery (n = 101) were examined with gray-scale and power Doppler sonography. Sonography-guided needle biopsy or surgery in 580 women revealed 258 cancers (230 cases of invasive cancers and 28 cases of ductal carcinoma in situ) and 322 benign lesions. Of the 230 patients with invasive cancers, 191 patients (age range, 26 - 75 years; median age, 52 years) with invasive ductal carcinoma not otherwise specified composed our study population. When multiple cancers were reported on a pathologic report, only the lesion with the greatest diameter was included in the analysis.

Of the 191 patients with breast cancer, 99 (52%) presented with a palpable mass and nine presented with a bloody nipple discharge. On mammograms, breast cancers were seen as a mass in 79 cases, a mass with microcalcifications in 61 cases, an asymmetric density in 23 cases, and as an architecture distortion in four cases. No mammographic abnormality was found in 24 (13%) patients. Of the 191 patients, 21 (11%) had an entirely fatty breast (grade 1), 36 (19%) had scattered fibroglandular tissues in fatty breasts (grade 2), 72 (38%) had heterogeneously dense breasts (grade 3), and 62 (32%) had extremely dense breasts (grade 4) (12).

Sonographic Examinations

Sonographic examinations were performed by one of three experienced radiologists. A 10- or 12-MHz linear

array probe (HDI 3000 and HDI 5000; Advanced Technology Laboratories, Bothell, Wash) was used in 128 patients and a 13-MHz linear array probe (LOGIQ 700; GE Medical Systems, Milwaukee, WI) was used in 63 patients.

For gray scale sonography, targeted examinations were performed with patients in the supine position with the arms raised. Scanning was done in radial and antiradial planes as well as longitudinal and transverse planes. Examination took approximately 20 minutes (range, 15 - 35 minutes).

For power Doppler sonography, the transducer automatically shifted to 6- or 8-MHz in power Doppler interrogation mode. The following settings were used: transmission power, low; mechanical index, 0.7; and log compression, 55 dB. The color box was enlarged to include the lesion and a margin of normal breast tissue. Scanning planes were selected to provide optimal visualization of vascularity. Color sensitivities were set at a level where the background color was just suppressed and a small vessel could be detected. Power Doppler sonography gains ranged from 75% to 80%. Care was taken not to apply pressure with the probe, as this can obliterate small, low-pressure vessels associated with breast lesions. Power Doppler sonographic examinations took approximately 5 minutes (range, 2 - 10 minutes).

Image Evaluations

Sonographic images were analyzed prior to biopsy in consensus between two radiologists, including the radiologist who performed the sonography. Sonographic images were analyzed without mammographic information or histology results. These radiologists had 6-10 years of experience at performing and interpreting breast sonography.

For gray scale sonography, the size of the mass was measured at the greatest dimension. Lesions were described according to the shape as oval, round, or irregular; according to the orientation as parallel or not parallel; margins as circumscribed, microlobulated, angular, indistinct or spiculated; echogenicities as anechoic, hyperechoic, isoechoic, hypoechoic, or complex; acoustic transmissions as enhancement, normal, or shadowing; boundaries as absent or as echogenic haloes; and calcifications as absent or present (6). In addition, BI-RADS

final assessment categories were provided to indicate the probability of malignancy.

For power Doppler sonography, lesions vascularity was classified into three categories based on the estimated amount of color within a mass in two orthogonal planes, i.e., avascular, defined as without flow; hypovascular, defined as less than 10% color flow; and hypervascular, defined as greater than 10% color flow (5, 7). The shape of vessel was classified into regular or irregular. Irregular vessels were blood vessels that lacked the normal tapering, tortuous vessels, or vessels that penetrated the tumor radially (4).

Histology

All patients underwent surgery within 30 days of sonographic examinations. Needle localization was performed under sonography guidance for nonpalpable lesions. The histologic diameter of the lesions ranged from 0.4 to 5.9 cm (mean, 1.6 cm).

Histologic tumor grades were classified as low for 23 lesions (12%), intermediate for 92 lesions (48%), and high grade for 76 lesions (40%). In terms of histologic tumor grading, the Elston-Ellis method of tumor grading was used (13), in which a score of 1 - 3 was assigned for (a) tubule formation, (b) pleomorphism, and (c) mitotic count. The total score could range from 3 to 9, where a total of 3 - 5 represents grade 1, 6 or 7, grade 2, and 8 or 9, grade 3. Axillary lymph node involvement

was found in 55 (29%) patients. 95% (181 of 191) of the cases were interpreted by one pathologist without information on imaging findings.

Statistical Analysis

The imaging findings at gray scale sonography and lesion vascularity findings at power Doppler sonography were compared with histologic tumor grades. The Chi-squared test was used to investigate possible relations between each of the imaging findings at gray-scale sonography and the tumor vascularity at power Doppler sonography. Spearman's rank correlation coefficients were used to assess the correlation between the tumor vascularity at power Doppler sonography and histologic grades in patients with invasive ductal carcinoma. To investigate the size effect on tumor vascularity, breast cancers seen at sonography were separated arbitrary into two groups according to size: those 1.5 cm or smaller and those larger than 1.5 cm. Statistically significant correlations ($p < .05$) were considered substantial when the correlation coefficient (r value) was at least 0.700 (14). Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS version 10.0 for Windows, Chicago, Ill).

RESULTS

The mean lesion size at sonography was 1.7 cm

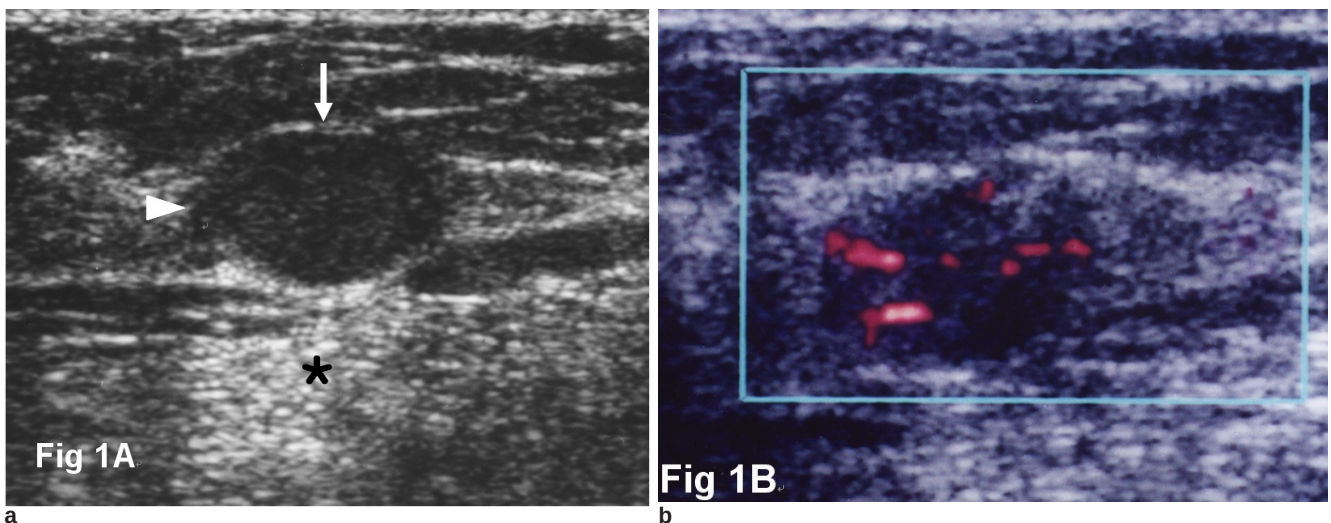


Fig. 1. High-grade invasive ductal carcinoma in a 44-year-old woman.

a. Radial gray scale sonogram shows a 1.2-cm ovoid hypoechoic mass (arrow) with a circumscribed margin and posterior acoustic enhancement (asterisk) in the area corresponding to nodular density at mammography. The final assessment was BI-RADS category 3, probably benign.

b. Radial power Doppler sonogram shows multiple vessels penetrating the lesion radially.

(range, 0.4 - 5.2 cm, median, 1.6 cm). Seventy-nine (41%) were 1.5 cm or smaller and 112 (59%) were larger than 1.5 cm. At gray scale sonography, an irregular shape (92%; n = 175), indistinct margin (64%; n = 122), and hypoechogenicity (91%; n = 174) were predominant findings, but an oval shape (1%; n = 2), circumscribed margin (2%; n = 3), and isoechogenicity (0.5%; n = 9) were also noted (Fig. 1, Fig. 2). Posterior acoustic enhancement was seen in 43 (23%) of the 191 cancers, and posterior acoustic shadowing in 58 (30%) cancers. A circumscribed margin was seen in 4% (three of 76) of high-grade tumors but not in intermediate-grade or low-grade tumors. A spiculated margin was seen in 57% (13 of 23) of low-grade tumors and 20% (18 of 92) of intermediate-grade and 7% (five of 76) of high-grade tumors. Posterior acoustic enhancement was seen in 33% (25 of 76) of high-grade tumors, in 20% (18 of 92) of intermediate-grade tumors and in no low-grade tumor. Posterior acoustic shadowing was seen in 61% (14 of 23) of low-grade, 35% (32 of 92) of intermediate-grade, and 16% (12 of 76) of high-grade tumors.

At power Doppler sonography, 45 (23%) of the 191 cancers were avascular, 82 (43%) were hypovascular and 64 (33%) were hypervascular (Fig. 1, Fig. 2 and Table 1). Hypervascularity was seen in all (3 of 3) of cancers with a circumscribed margin, 50% (13 of 26) of

cancers with a microlobulated margin, 29% (43 of 122) of cancers with an indistinct margin, and in 10% (four of 36) cancers with a spiculated margin. Hypervascularity was seen in 80% (34 of 43) of cancers with posterior acoustic enhancement, but in only 6% (3 of 58) of cancers with posterior acoustic shadowing. Of the eight gray scale sonographic imaging findings, only mass margins ($p < .001$) and acoustic transmission ($p < .001$) were significantly associated with tumor vascularity at power Doppler sonography regardless of tumor size. Of the 191 invasive ductal carcinomas, vascularity was seen in 97% (74 of 76) of high-grade tumors, 71% (65 of 92) of intermediate-grade tumors, and 26% (6 of 23) of low-grade tumors. Hypervascularity was seen in 63% (48 of 76) of high-grade tumors but in only 17%

Table 1. Vascularity of 191 Invasive Breast Cancers at Power Doppler Sonography

Vascularity	Low Grade (n=23)	Intermediate Grade (n=92)	High Grade (n=76)
< 1.5 cm			
Avascular	11	18	1
Hypovascular	3	25	7
Hypervascular	0	4	7
> 1.5 cm			
Avascular	6	8	1
Hypovascular	3	25	19
Hypervascular	0	12	41

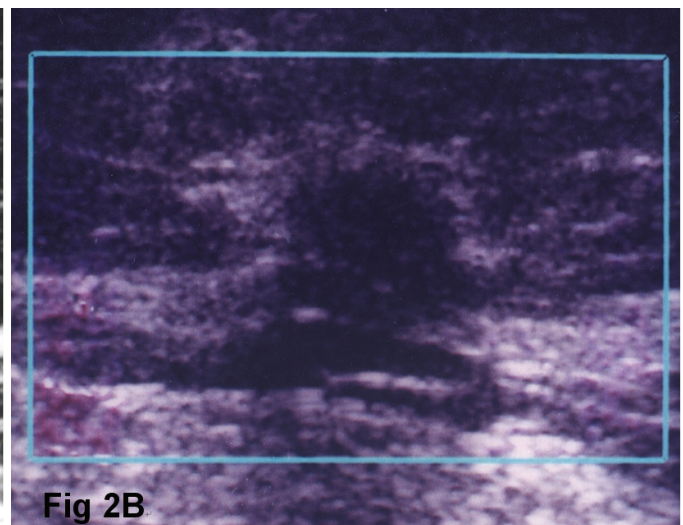
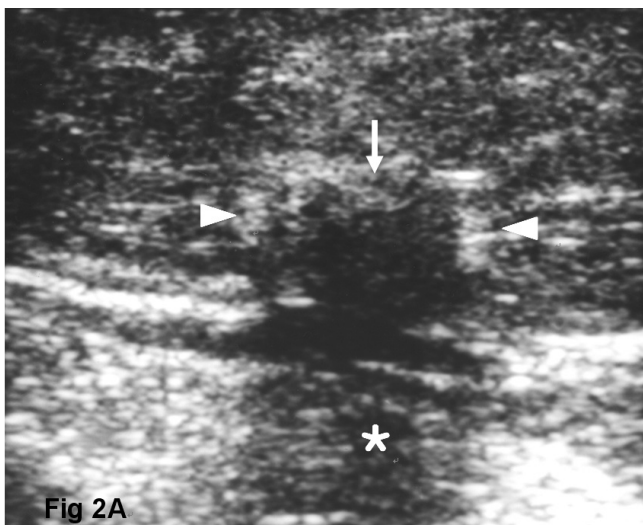


Fig. 2. Low-grade invasive ductal carcinoma in a 57-year-old woman.
a. Antiradial gray scale sonogram shows a 1.1-cm hypoechoic mass (arrow) with a spiculated margin, posterior acoustic shadowing (asterisk), and a thick echogenic halo (arrowheads) around the mass. The final assessment was BI-RADS category 5, highly suggestive of malignancy.
b. Antiradial power Doppler sonogram shows no vascular signal in the mass.

(16 of 92) of intermediate-grade tumors and not all in low-grade tumors. Tumor vascularity at power Doppler sonography was correlated with histologic grade regardless of tumor size ($r = 0.598$, $p < .001$). Statistically significant correlations were noted in both the cancers 1.5 cm or smaller ($r = 0.516$, $p = .006$) and larger than 1.5 cm ($r = 0.539$, $p = .004$).

With gray scale sonography, the final assessment of the 191 cancers was category 3 (probably benign) in three (2%), category 4 (suspicious) in 117 (61%), and category 5 (highly suggestive of malignancy) in 71 (37%). All three breast cancers misclassified as probably benign were high-grade tumors. Only one of the three was palpable. These three cases had typical findings of a benign breast mass, i.e., an oval shape ($n = 2$), a circumscribed margin ($n = 3$), and posterior acoustic enhancement ($n = 2$) (Figure 2). However, all three probably benign, category 3 lesions were hypervascularity at power Doppler sonography.

DISCUSSION

Previous studies (10, 11, 15) and the present study have demonstrated that the classical appearance of a malignant breast mass, i.e., a spiculated mass associated with posterior acoustic shadowing at gray scale sonography, is more typical of a low-grade tumor. High-grade tumors on the other hand, are more likely to demonstrate posterior acoustic enhancement, and a proportion have a circumscribed margin at gray scale sonography. In the present study, tumor vascularity at power Doppler sonography was significantly associated with mass margins ($p < .001$) and acoustic transmission types ($p < .001$) at gray scale sonography and to be correlated with histologic grade ($r = 0.598$, $p < .001$).

Previous studies that have examined the relation between sonographic characteristics and the pathological features of breast cancer have attributed particular importance to the presence of fibrous connective tissue in those cases that demonstrate posterior acoustic shadowing: the so-called 'desmoplastic reaction' (16 - 18). Conversely it has been suggested that tumors which demonstrate posterior acoustic enhancement are more cellular and contain more hyaluronic acid in the extracellular matrix (18) whereas high-grade tumors or typi-

cal medullary carcinomas tend to be more cellular and incite lymphoplasmacytic, rather than the fibroelastotic host responses incited by low-grade tumors and tubular carcinomas. Moreover, the combination of tumor neovascularity and inflammatory hyperemia makes most circumscribed carcinomas cancers appear hypervascular at power Doppler sonography, whereas the majority of spiculated cancers appear avascular (8, 19).

Our results suggest that high-grade invasive ductal carcinomas have imaging features that are similar to those of benign breast masses. In the present study, 3 (2%) of 191 invasive breast cancers were prospectively misclassified as probably benign at sonography based on benign findings, i.e., an oval shape, a circumscribed margin, isoechoogenicity, and posterior acoustic enhancement. Parker et al. (20) evaluated 124 solid breast nodules with sonography before core needle biopsy and determined a BI-RADS final assessment category to indicate the probability of malignancy and of the 54 BI-RADS category 3 lesions examined, one was found to be a 9-mm high-grade invasive ductal carcinoma. Anecdotal cases have been reported that power Doppler sonography reveals prominent tumor vessels in breast lesions otherwise considered being probably benign at gray scale sonography and mammography (5). In the present study, hypervascularity was seen in all three circumscribed cancers misclassified as probably benign, category 3 lesions at gray scale sonography. This finding indicates that further study is needed to determine whether power Doppler sonography has the potential to reduce false-negative rates at gray scale sonography.

Our study has several limitations that should be considered. First, we analyzed only cases with proven invasive breast cancer. Therefore, we did not have data on the specificity of gray scale or power Doppler sonography for the classification of solid breast masses. A prospective Doppler evaluation and tracking of all probably benign assessed lesions at gray scale sonography may be helpful. Second, we used a subjective semi-quantitative method for interpreting Doppler images, whereas the BI-RADS lexicon was used to interpretate gray scale images. It is difficult to compare our results with previous Doppler studies that used different techniques and diagnostic criteria (21 - 24). We make the point that successful Doppler-based assessments require

the standardizations of technique, evaluation, and analysis. Third, invasive tumor sizes in our study were larger than the mammographically detected cancers reported in the literature (25), which could have affected sonographic features and correlations with histologic grade.

In conclusion, typical breast cancers with a spiculated margin and posterior acoustic shadowing at gray scale sonography were rather low-grade tumors, whereas breast cancers with benign sonographic features were high-grade tumors. Tumor vascularity at power Doppler sonography was correlated with histologic grades.

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