

# Sonographic features of invasive ductal breast carcinomas predictive of malignancy grade

Kanika Gupta, Meenakshisundaram Kumaresan<sup>1</sup>, Bhuvaneshwari Venkatesan, Tushar Chandra<sup>2</sup>, Aruna Patil<sup>3</sup>, Maya Menon<sup>4</sup>

Departments of Radiodiagnosis, <sup>1</sup>Pathology, <sup>3</sup>Community Medicine, <sup>4</sup>Obstetrics and Gynecology, ESI Medical College and PGIMSR, Chennai, Tamil Nadu, India, <sup>2</sup>Department of Radiology, University of Central Florida, Orlando, USA

**Correspondence:** Dr. Kanika Gupta, Department of Radiodiagnosis, ESI Medical College and PGIMSR, K K Nagar, Chennai - 600 078, Tamil Nadu, India. E-mail: hikanika@gmail.com

## Abstract

**Context:** Assessment of individual sonographic features provides vital clues about the biological behavior of breast masses and can assist in determining histological grade of malignancy and thereby prognosis. **Aims:** Assessment of individual sonographic features of biopsy proven invasive ductal breast carcinomas as predictors of malignancy grade. **Settings and Design:** A retrospective analysis of sonographic findings of 103 biopsy proven invasive ductal breast carcinomas. **Materials and Methods:** Tumor characteristics on gray-scale ultrasound and color flow were assessed using American College of Radiology (ACR) Breast Imaging Reporting and Data System (BI-RADS) Atlas Fifth Edition. The sonographic findings of masses were individually correlated with their histopathologic grades. **Statistical Analysis Used:** Chi square test, ordinal regression, and Goodman and Kruskal tau test. **Results:** Breast mass showing reversal/lack of diastolic flow has a high probability of belonging to histological high grade tumor ( $\beta$  1.566,  $P$  0.0001). The masses with abrupt interface boundary are more likely grade 3 ( $\beta$  1.524,  $P$  0.001) in comparison to masses with echogenic halos. The suspicious calcifications present in and outside the mass is a finding associated with histologically high grade tumors. The invasive ductal carcinomas (IDCs) with complex solid and cystic echotexture are more likely to be of high histological grade ( $\beta$  1.146,  $P$  0.04) as compared to masses with hypoechoic echotexture. **Conclusions:** Certain ultrasound features are associated with tumor grade on histopathology. If the radiologist is cognizant of these sonographic features, ultrasound can be a potent modality for predicting histopathological grade of IDCs of the breast, especially in settings where advanced tests such as receptor and molecular analyses are limited.

**Key words:** BI-RADS; breast malignancy; histological grade; invasive ductal carcinoma; ultrasound

## Introduction

Ultrasound is used as a first line modality of imaging for breast masses in patients less than 35 years and as an adjunct to mammography in older patients.<sup>[1-4]</sup> The purpose of this study was to investigate whether high resolution ultrasound

is able to predict the likelihood of histological grade of invasive ductal breast carcinomas. This study aims to find out which sonographic features based on American College of Radiology (ACR) Breast Imaging Reporting and Data System (BI-RADS) Atlas Fifth Edition help in predicting

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

**For reprints contact:** reprints@medknow.com

**Cite this article as:** Gupta K, Kumaresan M, Venkatesan B, Chandra T, Patil A, Menon M. Sonographic features of invasive ductal breast carcinomas predictive of malignancy grade. Indian J Radiol Imaging 2018;28:123-31.

### Access this article online

#### Quick Response Code:



**Website:**  
www.ijri.org

**DOI:**  
10.4103/ijri.IJRI\_257\_17

the histological grade of tumor.<sup>[5]</sup> This information may be useful to pick up high risk patients for nodal metastasis on ultrasound. To our knowledge, no report has correlated gray scale and vascularity findings in invasive ductal breast carcinomas that were analyzed according to BI-RADS Fifth Edition with histological grades.

### Materials and Methods

This study was conducted using a retrospective case record review design. A total of 394 solid breast masses were evaluated by ultrasound in the department of radiodiagnosis from May 2013 to September 2016. Out of these, we identified 103 biopsy proven invasive ductal breast carcinomas [Figure 1]. Each of these masses was assessed based on sonographic findings and color flow as per ACR BI-RADS Atlas Fifth Edition.<sup>[5]</sup> The study was approved by the institutional review board and ethics committee of the institution. The study group comprised of patients which were positive for invasive ductal carcinoma (IDC) of breast on core needle biopsy and had both sonographic images and histopathological data available. The age of the patients ranged from 31 years to 78 years.

#### Sonographic analysis

Ultrasound examination of breast masses was done on a Philips ultrasound machine unit (HD7/Clearvue 650) using linear, high frequency (3–12 MHz), and curvilinear (2–5 MHz) transducers. Each breast mass was assessed and given a BI-RADS grade based on its sonographic features as per ACR BI-RADS Atlas Fifth Edition by two radiologists with experience of 10 or more years.<sup>[5]</sup> Each

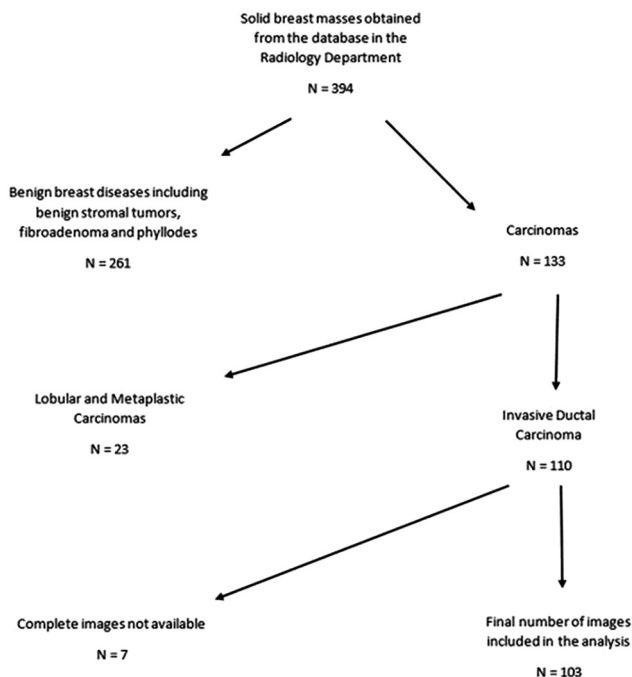
mass was characterized on sonography based on its shape, orientation, margin, echo pattern, posterior features, calcifications, presence of associated features if any, and color flow [Table 1]. “Lesion boundary” though has been eliminated in the ACR BI-RADS Atlas Fifth Edition, was additionally used in this study to describe the breast mass, since review of literature suggested a significant association between boundary zone and low/high grades of tumor.

#### Histopathological analysis

The histopathological study of each breast mass was performed by the department of pathology in our institution. The biopsy specimens were received in 10% buffered formalin. All specimens were routinely processed

**Table 1: Descriptors on ultrasound for characterization of each solid mass<sup>[5]</sup>**

Sonographic feature	Sonographic descriptor
Shape	Oval
	Round
	Irregular
Orientation	Parallel
	Not parallel
Margin	Circumscribed
	Not circumscribed
	Indistinct
Echo pattern	Angular
	Micro lobulated
	Spiculated
	Anechoic
Posterior features	Hyperechoic
	Complex cystic and solid
	Hypoechoic
	Isoechoic
	Heterogeneous
	No posterior features
Calcifications	Enhancement
	Shadowing
	Combined pattern
	Absence of suspicious calcifications
Associated features	Presence of suspicious calcifications
	Calcifications in a mass
	Intraductal calcifications
	No features
	Architectural distortion
	Duct changes
Vascularity	Skin changes
	Thickening
	Retraction
	Edema
	Internal vascularity absent
	Internal vascularity present with no reversal/inversion of diastolic flow
	Internal hypervascularity present with reversal/inversion of diastolic flow



**Figure 1: Sample included in the study analysis**

using graded alcohols, cleared in xylene and embedded in paraffin wax and 4–6 micron thickness sections were cut. All sections were stained with hematoxylin and eosin stain. The histopathological grading was performed with modified Bloom Richardsons' scoring for grading invasive ductal breast carcinomas.<sup>[6,7]</sup> Three factors were taken into consideration—gland formation, nuclear features, and mitotic activity. A score of 1–3 was given to each factor and then each score was added to give a final total score ranging from 3 to 9. The total score was used to determine the grade [Table 2]. Cancers with score of 3–5 were graded as 1, cancers with a score of 6–7 were graded as 2 and cancers with a score of 8–9 were graded as 3.

**Table 2: Scoring system for histological grading of invasive ductal carcinoma (IDC)-breast**

Bloom Richardsons' score	Grade
3-5	1
6-7	2
8-9	3

### Statistical analysis

The results for qualitative data was presented in frequency and percentage. Chi-square test was used to find association between histological grades of IDC (dependent parameter) and their sonographic features (independent parameters) [Table 3]. Ordinal regression was used to predict the contribution of each independent parameter to arrive at the final histological grade, which happens to be the dependent parameter in our study [Table 4]. Ordinal regression is a multivariate statistical analytical method which is applied for ordinal dependent variables, in our case the histological grade of IDC. It is more advantageous than logistic and multinomial regression as it treats the dependent variable as an ordinal variable and gives estimates of regression coefficients. The regression coefficients have to be interpreted as the chance of moving from the lowest grade of IDC to the highest grade with shift in the category of the ultrasound finding from the lowest to the highest in the predictability of histological grade.

**Table 3: Distribution of histological grade by sonographic feature category**

Ultrasound characteristics	Histological grade on biopsy				P
	1 n (%)	2 n (%)	3 n (%)	Total n (%)	
Shape					
Oval	3 (7.1%)	7 (19.4%)	4 (16%)	14 (13.6%)	0.006**
Round	1 (2.4%)	7 (19.4%)	0%	8 (7.8%)	
Irregular	38 (90.5%)	22 (61.1%)	21 (84%)	81 (78.6%)	
Margin					
Circumscribed	5 (11.9%)	3 (8.3%)	3 (12%)	11 (10.7%)	0.79
Indistinct	16 (38.1%)	17 (47.2%)	9 (36%)	42 (40.8%)	
Angular	1 (2.4%)	3 (8.3%)	1 (4%)	5 (4.9%)	
Microlobulated	11 (26.2%)	7 (19.4%)	9 (36%)	27 (26.2%)	
Spiculated	9 (21.4%)	6 (16.7%)	3 (12%)	18 (17.5%)	
Echo pattern					
Complex cystic and solid	1 (2.4%)	4 (11.1%)	3 (12%)	8 (7.8%)	0.236
Hypoechoic	41 (97.6%)	32 (88.9%)	22 (88%)	95 (92.2%)	
PAF					
No features	16 (38.1%)	15 (41.7%)	9 (36%)	40 (38.8%)	0.488
Enhancement	13 (31%)	9 (25%)	11 (44%)	33 (33%)	
Shadowing	10 (23.8%)	6 (16.7%)	4 (16%)	20 (19.4%)	
Combined pattern	3 (7.1%)	6 (16.7%)	1 (4%)	10 (9.7%)	
Suspicious calcification					
Absent	25 (59.5%)	25 (69.4%)	15 (60%)	65 (65%)	0.385
Intra mass calcification	15 (35.7%)	8 (22.2%)	7 (28%)	30 (29.1%)	
Intramass and Intra ductal	1 (2.4%)	0.00%	2 (8%)	3 (2.9%)	
Intra ductal calcification	1 (2.4%)	3 (8.3%)	1 (4%)	5 (4.9%)	
Doppler					
Absence of internal vascularity	20 (47.6%)	19 (52.8%)	8 (32%)	47 (45.6%)	0.0001***
Internal vascularity present with no reversal/inversion of diastole	21 (50%)	8 (22.2%)	6 (24%)	35 (34%)	
Internal vascularity present with reversal/inversion of diastole	1 (2.4%)	9 (25%)	11 (44%)	21 (20.4%)	
Boundary					
Echogenic halo	37 (88.1%)	20 (55.6%)	10 (40%)	67 (65%)	0.0001***
Abrupt interface	5 (11.9%)	16 (44.4%)	15 (60%)	36 (35%)	

NS: Not Significant, \*\*\*Highly significant. \*Pearson  $\chi^2$  test was used

**Table 4: Estimation of sonographic characteristics of the mass with histological grade using ordinal regression**

Parameters	Patient characteristics	Estimate	P	95% CI LB	95% CI UB
Echo pattern	Complex solid and cystic	1.146	0.04*	0.052	2.24
	Hypoechoic	0a	-	-	-
Suspicious calcification	Intraductal	-0.101	0.884	-1.452	1.25
	Intramass + intraductal	1.847	0.039*	0.091	3.602
	Intramass	0.406	0.266	-0.31	1.122
	Absence of suspicious calcifications	0a	-	-	-
Doppler	Internal vascularity with reversal/lack of diastolic flow present	1.566	0.001**	0.768	2.364
	Internal vascularity with reversal/lack of diastolic flow absent	0.603	0.129	-0.175	1.38
	Absence of Doppler features	0a	-	-	-
Boundary	Abrupt interface	1.524	0.001**	0.816	2.232
	Echogenic halo	0a	-	-	-

Link function: Complementary Log-log. aThis parameter is set to zero because it is redundant. 95% CI LB - 95% confidence interval lower bound. 95% CI UB - 95% confidence interval upper bound

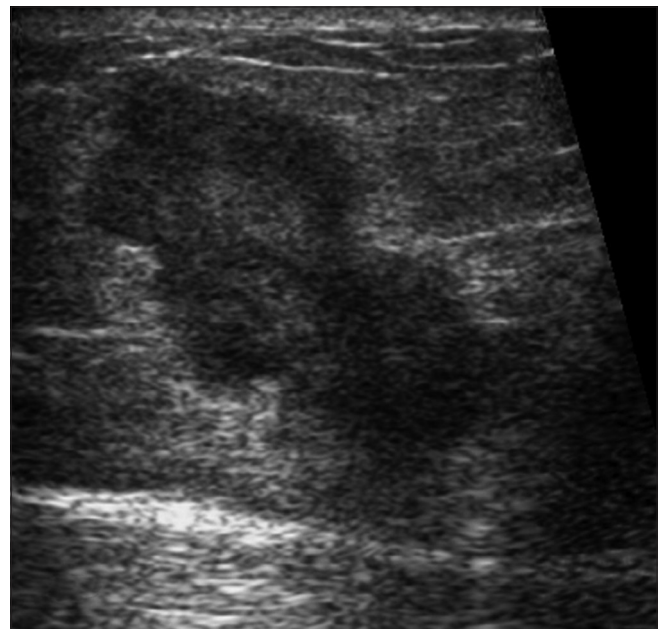
The statistical analysis was done using SPSS 21.0 in our study. The significance level was used at  $P \leq 0.05$ .

## Results

The analysis included 103 invasive ductal breast carcinomas diagnosed on core biopsy in 101 patients (100 females and 1 male). Bilateral cancer was present in two patients. The bivariate analysis of the sonological characteristics of masses with histological grading is shown in Table 3. Multivariate ordinal regression analysis and the regression coefficients with 95% confidence intervals are depicted in Table 4.

**Echopattern:** Based on the prior studies, most malignant masses are hypoechoic with some showing complex solid cystic mass with heterogeneous echotexture.<sup>[3,4]</sup> In our study, 95 (92.2%) masses were hypoechoic and eight (7.8%) masses had complex solid cystic mass with heterogeneous echotexture [Table 3; Figures 2 and 3]. No masses had hyperechoic, isoechoic, or anechoic echotexture. The ordinal regression results in our study revealed that complex solid cystic IDCs with heterogeneous echotexture have greater chance of having histological grade 3 as compared to masses having hypoechoic echotexture ( $\beta$  1.146,  $P$  0.04) [Table 4; Figure 4].

**Vascularity:** Fifty six (54.4%) masses out of 103 depicted one or more suspicious features of malignancy on color flow: internal hypervascularity with tortuous and irregular vessels, central distribution, presence of penetrating artery [Figure 5A] [Table 3]. Out of 56 masses showing internal vascularity, 21 (20.4%) masses depicted presence of reversal/lack of diastolic flow—a unique vascular finding [Figure 5B and C] [Table 3]. All 21 masses which depicted presence of reversal/lack of diastolic flow were correlated with their histological grades [Figure 5B and C]. 11 (52%) masses belonged to histological grade 3, 9 (43%) belonged to histological grade 2, and only 1 (5%) mass having reversal/lack of diastolic flow belonged to histological grade 1. A strong association of reversal/lack



**Figure 2:** A 47-year-old female with right breast mass—gray scale ultrasound image demonstrating sonographic features of hypoechoic echotexture and surrounding echogenic halo. This mass was proven to be grade 1 invasive ductal carcinoma (IDC) on histopathology

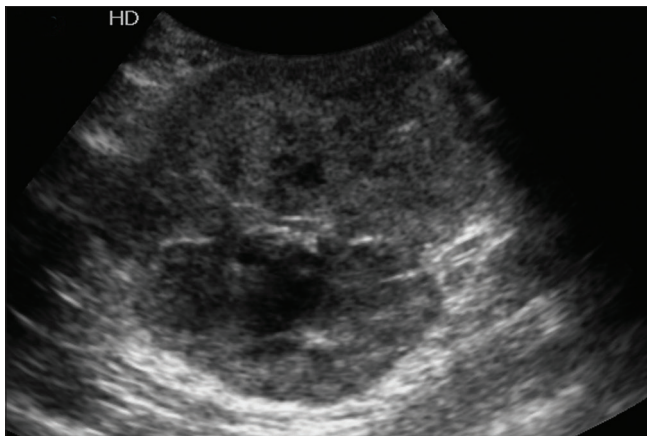
of diastolic flow with high histological grade of tumor was noted ( $P$  0.0001) [Table 3]. Ordinal regression statistics depicted that masses with reversal/lack of diastolic flow had a greater chance of belonging to histological grade 3 tumor as compared to masses without it ( $\beta$  1.566,  $P$  0.001) [Table 4].

**Boundary:** An echogenic halo boundary zone is a prominent feature to suggest malignancy in a breast mass and was seen in 67 (65%) masses in our study. Thirty six (35%) masses had abrupt interface with surrounding breast parenchyma. We assessed the occurrence of both boundary zones in histological grade 3 tumors and found that 15 (60%) masses had abrupt interface and 10 (40%) masses had echogenic halos [Table 3]. In histological grade 1 IDCs, 37 (88%) masses had echogenic halos, and five (12%) masses had abrupt interfaces [Figures 2 and 6]. Ordinal regression

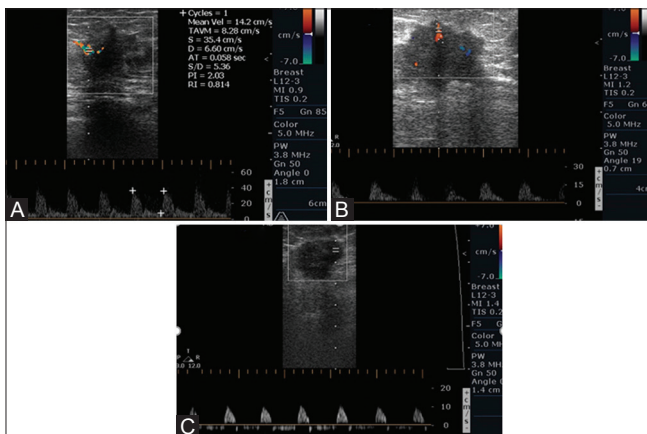
results suggested that mass had a greater chance of belonging to histological grade 3 when boundary zone was “abrupt interface instead of echogenic halo” ( $\beta$  1.524,  $P$  0.001) [Table 4; Figure 7].

**Calcifications:** In this study suspicious calcifications suggestive of malignancy were present in only 38 (36.9%) masses, located inside the breast mass and/or inside the dilated duct/s adjacent to it [Table 3]. IDCs which had calcifications present both within the mass and ducts showed a greater chance of having grade 3 tumor as compared to masses without it ( $\beta$  1.847,  $P$  0.039) [Table 4; Figure 8].

**Margin:** Indistinct margin was seen in 42 (40.8%) IDCs making it the commonest margin in our study, followed



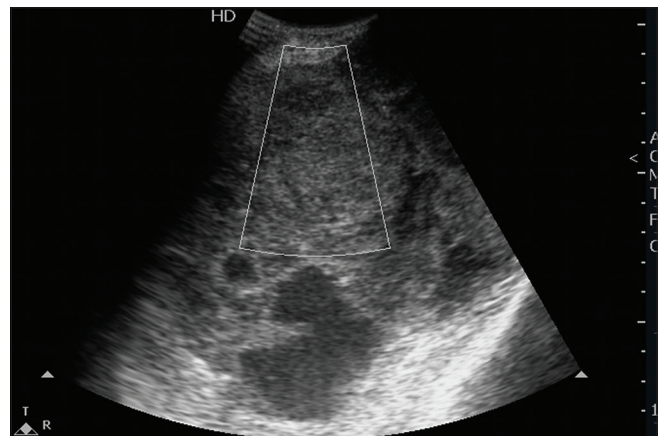
**Figure 3:** A 75-year-old female with right breast mass—gray scale ultrasound image demonstrating sonographic features of complex echogenicity with solid and cystic spaces. This mass proved to be grade 3 invasive ductal carcinoma (IDC) on histopathology



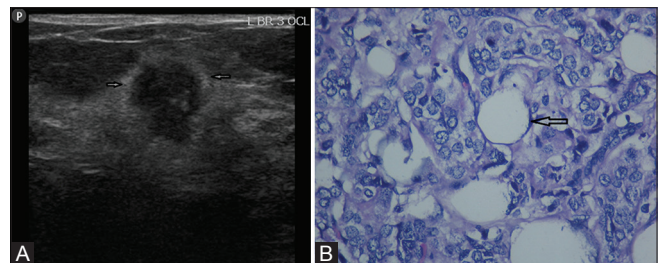
**Figure 5 (A-C):** Color Doppler features. (A) A 57-year-old female with right breast mass showing high resistance spectral pattern with absence of reversal/lack of diastolic flow. This mass proved to be grade 1 invasive ductal carcinoma (IDC) on histopathology. (B) A 39-year-old female patient with right breast mass showing reversal of diastolic flow. This mass proved to be grade 2 IDC on histopathology. (C) A 33-year-old female patient with left breast mass showing lack of diastolic flow. This mass was proven to be grade 3 IDC on histopathology

by microlobulated margins in 27 (26.2%) and spiculated margins in 18 (17.5%) masses. Spiculated margins were present in 21.4% of histological grade 1 IDCs, 16.7% of grade 2, and 12% of grade 3 IDCs [Table 3]. The histological grade 3 tumors had indistinct margins in 9 (36%), microlobulated margins in 9 (36%), circumscribed margins in 3 (12%), spiculated margins in 3 (12%), and angular margins in 1 (6%) mass [Table 3]. Ordinal regression results, however, suggested that margin of a mass did not contribute significantly to the prediction of histological grade in this study.

**Shape:** Irregular shape of a mass is a suspicious feature of malignancy, as was also observed in our study. Of all IDCs, 81 (78.6%) masses had irregular shapes, followed by oval shape in 14 (13.6%) and round shape in 8 (7.8%) masses [Table 3]. The histological grade 1 IDCs had irregular shape in 81 (90%) masses on ultrasound. The shape of the mass depicted statistically significant association with histological grade of tumor ( $P$  0.006) [Table 3]; however, ordinal regression results showed that shape does not predict the histological grade of IDC ( $P$  0.119) [Table 4].



**Figure 4:** Mass in left breast of a 50-year-old female showing complex echogenicity, abrupt interface and intra mass calcifications. This mass proved to be histological grade 3 invasive ductal carcinoma (IDC)



**Figure 6 (A and B):** A 38-year-old female patient with left breast mass. (A) Gray scale ultrasound image demonstrating sonographic features of echogenic halo (arrows) surrounding the hypoechoic mass. (B) Histological sections revealed composition of cells arranged in tubules (arrow) with minimal nuclear pleomorphism and less mitotic activity (less than 7 per 10 hpf) proving to be grade 1 IDC. 400x, Hematoxylin and Eosin stain

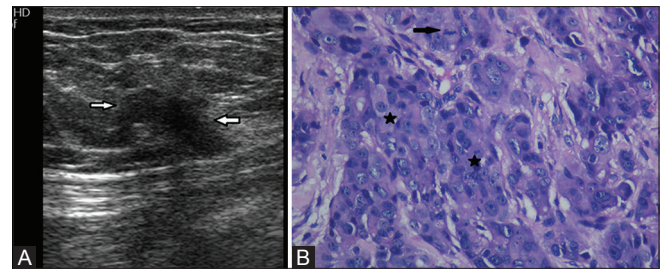
**Posterior features:** The most common posterior feature in our study was masses showing neither posterior enhancement nor posterior shadowing, seen in 40 (38.8%) IDCs. The posterior enhancement was present in 33 (32%) masses and posterior shadowing (either alone or in combination with enhancement) in 30 (29.8%) masses ( $P 0.488$ ) [Table 3]. Review of literature suggested an association of posterior enhancement with high-grade tumor and posterior shadowing with low-grade tumor; however, we found no statistically significant association between posterior features and grade of tumor ( $P 0.63$ , Table 5).

**Orientation:** The orientation of a breast mass perpendicular to the longitudinal plane of the breast is a very important diagnostic sign of malignancy. In our study, 65 (63.1%) masses had antiparallel orientation with no statistically significant distribution noted to suggest any association with grades of malignancy [Table 5].

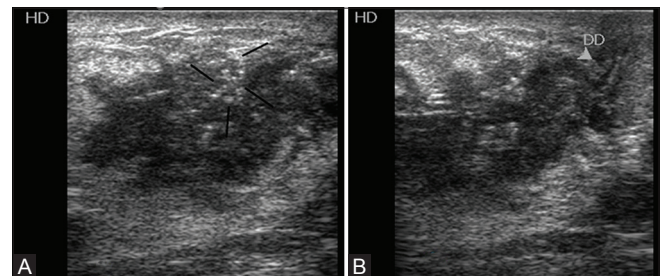
## Discussion

Ultrasound is a safe and widely available imaging modality for diagnostic evaluation of breast lesions, in addition to mammography.<sup>[2,3]</sup> Primarily, breast ultrasound has been used to differentiate benign and malignant lesions.<sup>[4,8]</sup> However, many studies have also looked at utilizing the tissue information available with ultrasound to differentiate various grades of malignancy in breast carcinomas.<sup>[9-11]</sup> BI-RADS lexicon use facilitates quality assurance, communication, research, and patient care.<sup>[4,5,8]</sup> In the present study, we used the latest (Fifth) Edition of ACR BI-RADS Atlas to individually assess ultrasound descriptors of breast masses for prediction of histological grade of IDC.<sup>[5]</sup> The role of vascularity within the mass was also assessed.<sup>[12-14]</sup> This study depicted a strong association of presence of reversal/lack of diastolic flow with histologically high grades of IDCs [Figure 9]. Features of masses on ultrasound as abrupt interface of tumor, complex solid cystic mass with heterogeneous echotexture, and presence of suspicious calcifications located intraductally and within the mass were shown to have a mild to moderate association with histologically high grades of IDCs.

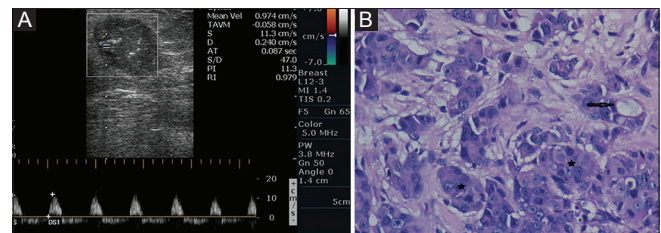
The management of breast malignancies and its prognosis is guided largely by its histological grade. The prognosis of a breast malignancy depends largely on the histological grade and biological markers as estrogen receptor, progesterone receptor, and human epithelial growth factor receptor.<sup>[15-18]</sup> In many countries, advanced modalities and tests such as receptor analyses are not widely available and therefore ultrasound is often the primary modality of imaging of a breast mass. The detection of cancer is the primary goal of breast imaging. Several prior studies have established that the major ultrasound features characterizing a malignant mass include hypoechoic or complex echotexture of the



**Figure 7 (A and B):** A 47-year-old female patient with left breast mass. (A) Gray scale ultrasound image demonstrating sonographic features of abrupt interface surrounding the hypoechoic mass. (B) Histological sections revealed composition of cells arranged in sheets (asterisk) with nuclear pleomorphism and increased mitotic activity (arrow) more than 15 per hpf proving to be grade 3 IDC. 400x, Hematoxylin and Eosin stain



**Figure 8 (A and B):** A 34-year-old female patient with right breast mass—gray scale ultrasound image demonstrating sonographic features of presence of intra-mass calcifications (lines in A) and ductal dilatation (DD) with intra ductal calcifications (B). This mass was proven to be grade 3 invasive ductal carcinoma (IDC) on histopathology



**Figure 9 (A and B):** A 55-year-old female patient with right breast mass. (A) Spectral Doppler image demonstrating presence of reversal of diastolic flow. (B) Histological sections showing composition of cells arranged in tubules (arrow) and in sheets (asterisk) with nuclear pleomorphism and mitotic activity between 8 and 14 per 10 hpf proving to be grade 2 invasive ductal carcinoma (IDC). 400x, Hematoxylin and Eosin stain

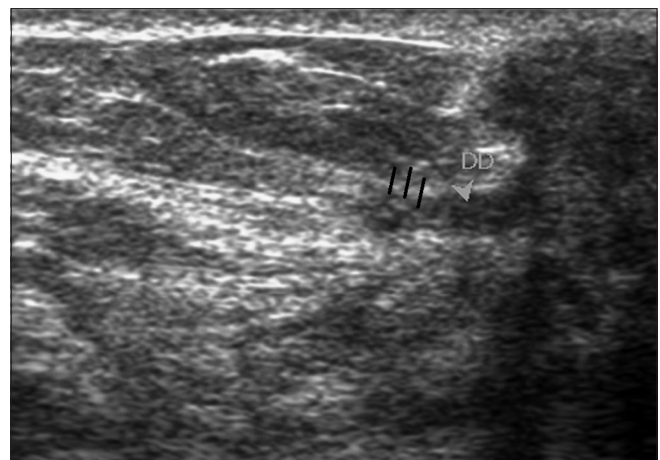
mass, irregular shape, and antiparallel orientation.<sup>[3,11,17]</sup> Additionally, if we also describe the sonographic features of the mass that suggest high aggressiveness of that malignant lesion, that information can be very useful to the referring surgeon in management of the patient. This particular information can be specifically used to identify the high-risk patient for lymph node metastasis.<sup>[19,20]</sup> Previous studies have indicated that there is evidence of ultrasound features and pathological tumor grade correlation in breast malignancies.<sup>[9-11,15-17]</sup> Some prior studies found that sonographic features of posterior enhancement and well circumscribed margins of a mass are features commonly

found in high grade breast tumors and posterior shadowing was seen commonly in low grade tumor.<sup>[11,15,16]</sup> Subsequent to the introduction of ACR BI-RADS lexicon for breast ultrasound in 2003, few studies correlated BIRADS Third and Fourth Editions' features with histological grade and found that histological grade 3 tumors having more commonly non circumscribed/micro-lobulated margins, abrupt boundary, and posterior enhancement.<sup>[9-11,21]</sup> Linear or pleomorphic calcifications were reported commonly in high-grade tumors.<sup>[11]</sup> Masses with spiculated margins, echogenic halos, and posterior acoustic shadowing were commonly low-grade histologically.<sup>[9-11]</sup> This study found a strong association between abrupt interface boundary and high grade IDC ( $P 0.0001$ ). Mild to strong association has already been made between abrupt interface boundary and high-grade tumor in several studies.<sup>[9,11,17]</sup> A highly proliferative lesion will be aggressive, hence will not give time to the host cells to induce a desmoplastic reaction. A low-grade tumor has low mitotic rate, hence has time to promote a desmoplastic reaction resulting in complex interaction with host cells, dense fibrosis, and echogenic halo in low-grade tumors. Though more commonly seen in low-grade tumors, echogenic halo surrounding a breast mass is a specific sign of malignancy. 88.1% of histological grade 1 tumors in this study had echogenic halos [Table 3]. A mild to moderate association was noted between complex solid cystic mass with heterogeneous echotexture and histological grade 3 malignancy. This finding is possibly related to presence of necrotic areas, low fibrous, and more cellular contents in complex masses. An association between hyperechoic echogenicity with low-grade tumors and complex echogenicities with high-grade tumors has been noted in the past studies.<sup>[9,11,17]</sup> The margins of a mass in an important feature to differentiate malignant and benign masses and is known to be somewhat effective in predicting the histological grade in previous studies, having reported an association of spiculated margins with low-grade tumors.<sup>[9,17,18]</sup> This study supported this postulation since 83% of masses with spiculated margins were grade 1 or grade 2 [Table 3]. The shape of a breast mass, though a strong indicator of a malignant mass; however, were largely ineffective in predicting high grade of malignancy. The posterior

features of malignant mass was another descriptor used in our study. The posterior acoustic properties of a mass are based on multiple factors as cellular structure, stromal reaction, and number of histological interfaces between fibrous and cellular components. Various studies in literature report that posterior acoustic enhancement is associated with high-grade tumors and posterior acoustic shadowing with low-grade tumors.<sup>[10,15,17,18]</sup> In this study, we found that posterior shadowing was more commonly seen in low-grade tumors; however, no association between posterior enhancement and high-grade of tumor was noted. The direct comparison of our results with the previous results is however difficult since the earlier studies used different descriptors of margins (including ACR BI-RADS Atlas Third and Fourth Editions)<sup>[8,15,16]</sup> and our study is based on ACR BI-RADS Atlas Fifth Edition.<sup>[5]</sup> The presence/absence of calcifications and their location was also studied in correlation with various grades of tumors. The presence of calcifications with suspicious morphology is generally known to raise the risk of breast malignancy by 13–78%.<sup>[5]</sup> Microcalcification within or outside a mass is reported to be associated with high-grade tumors.<sup>[11,22]</sup> Sonography, however, is a suboptimal modality of imaging for depiction of suspicious calcifications within a mass. In this study, suspicious calcifications were detected on ultrasound in 37% of cases, located either within the mass or intraductally. This study suggested a mild association between presence of intraductal calcifications on ultrasound and histological grade 3 of tumors [Table 4; Figure 10]. The association of calcifications, sonographically, or mammographically, were predictors of extensive intraductal component (EIC) present, thus having a worse correlation with pathology. Another modality of imaging as MRI is warranted in masses with associated calcifications to rule out intraductal spread of IDC as MRI is more sensitive for its detection than sonography.<sup>[22]</sup>

**Table 5: Degree of strength of sonographic features in relation to histological grades**

S. no	Sonographic features	$\tau$	$P$
1	Margin	0.012	0.772
2	Echotexture	0.028	0.239
3	Boundary	0.176	0.068
4	Shape	0.077	0.003**
5	Orientation	0.005	0.781
6	PAF	0.014	0.636
7	Suspicious calcification	0.014	0.633
8	Doppler	0.081	0.002**



**Figure 10:** A 40-year-old female patient with left breast mass—gray scale ultrasound image demonstrating sonographic features of ductal dilatation (DD) and intraductal calcifications (marked by lines) on ultrasound

The color flow findings when used in association with gray-scale features can provide useful information in differentiating benign and malignant breast masses.<sup>[12-14,21]</sup> ACR BI-RADS Atlas Fifth Edition used three descriptors of color flow to describe the vascularity of mass: absent, internal vascularity, and vascularity in rim.<sup>[5]</sup> Features as internal vascularity with irregular vessels and a central distribution, with or without an observable penetrating artery, high RI greater than 0.8 and Pulsatility index greater than 0.4 are suggestive signs of malignancy on color Doppler.<sup>[12-14]</sup> The presence of reversal/lack of diastolic flow is known to be a specific (specificity up to 99% and positive predictive value up to 97%) sign of malignancy.<sup>[12]</sup> In this study, the presence of reversal/lack of diastolic flow was the strongest predictor to suggest histologically high grade of tumor ( $\tau 0.081$ ,  $P 0.002$ ) [Table 5]. A larger previous study of 826 breast lesions found that though infrequently seen (14% in their study), sign of inversion/lack of diastolic flow when present, was suggestive of high aggressiveness of lesion.<sup>[12]</sup> Our study found a strong association between reversal/lack of diastolic flow and histological high grades of tumor ( $P 0.0001$ ) [Table 3]. The presence of reversal/lack of diastolic flow was infrequently seen in our study (20.4%), and found significant association with histologically high grade of IDCs ( $\beta 1.566$ ,  $P 0.001$ ) [Table 4].

There are a few limitations in our study. Due to retrospective nature, analysis was based on some selected images of the case rather than evaluating the masses in real-time. A possible source of bias in the study is that the radiologists were aware that the study comprises of only biopsy proven breast masses and this may have affected their observation of ultrasound features. We tried to minimize bias by selecting all biopsy proven cases of IDC within a given time frame. Another limitation of our study is a relatively small sample size. Despite these limitations, our study provides valuable information about sonographic features of breast masses that correlate with high malignancy grade. Further work with larger studies is needed to elucidate the full potential of sonography for predicting the histological grade of tumor.

## Conclusion

In conclusion, our study confirms that histological grades of invasive ductal breast carcinomas determine differences in ultrasound imaging. The masses with complex solid cystic mass with heterogeneous echotexture, abrupt interfaces, calcifications and/or presence of reversal/lack of diastolic flow may suggest high grade of tumors. The finding of reversal/lack of diastolic flow in a breast mass was the strongest predictor of high grade of tumor in our study and warrants early lymph nodal sampling.

## Financial support and sponsorship

Nil.

## Conflicts of interest

There are no conflicts of interest.

## References

- Osako T, Takahashi K, Iwase T, Iijima K, Miyagi Y, Nishimura S, *et al.* Diagnostic ultrasonography and mammography for invasive and noninvasive breast cancer in women aged 30 to 39 years. *Breast Cancer* 2007;14:229-33.
- McCavert M, O'Donnell ME, Aroori S, Badger SA, Sharif MA, Crothers JG, *et al.* Ultrasound is a useful adjunct to mammography in the assessment of breast tumours in all patients. *Int J Clin Pract* 2009;63:1589-94.
- Paulinelli RR, Freitas-Júnior R, Moreira MA, Moraes VA, Bernardes-Júnior JR, Vidal Cda S, *et al.* Risk of malignancy in solid breast nodules according to their sonographic features. *J Ultrasound Med* 2005;24:635-41.
- Costantini M, Belli P, Lombardi R, Franceschini G, Mulè A, Bonomo L. Characterization of solid breast masses: Use of the sonographic breast imaging reporting and data system lexicon. *J Ultrasound Med* 2006;25:649-59.
- Rao AA, Feneis J, Lalonde C, Ojeda-Fournier H. A Pictorial Review of Changes in the BI-RADS Fifth Edition. *Radiographics* 2016;36:623-39.
- Scarff RW, Torloni H. Histological typing of breast tumors. International histological classification of tumours, Vol. 2. World Health Organization, Geneva; 1968. p. 13-20.
- Bloom HJ, Richardson WW. Histological grading and prognosis in breast cancer. *Br J Cancer* 1957;11:359-77.
- Levy L, Suissa M, Chiche JF, Teman G, Martin B. BIRADS ultrasonography. *Eur J Radiol* 2007;61:202-11.
- Aho M, Irshad A, Ackerman SJ, Lewis M, Leddy R, Pope TL, *et al.* Correlation of sonographic features of invasive ductal mammary carcinoma with age, tumor grade, and hormone-receptor status. *J Clin Ultrasound* 2013;41:10-7.
- Blaichman J, Marcus JC, Alsaadi T, El-Khoury M, Meterissian S, Mesurolle B. Sonographic appearance of invasive ductal carcinoma of the breast according to histologic grade. *AJR Am J Roentgenol* 2012;199:W402-8.
- Kim SH, Seo BK, Lee J, Kim SJ, Cho KR, Lee KY, *et al.* Correlation of ultrasound findings with histology, tumor grade, and biological markers in breast cancer. *Acta Oncol* 2008;47:1531-8.
- del Cura JL, Elizagaray E, Zabala R, Legórburu A, Grande D. The use of unenhanced Doppler sonography in the evaluation of solid breast lesions. *AJR Am J Roentgenol* 2005;184:1788-94.
- Schroeder RJ, Bostanjoglo M, Rademaker J, Maeurer J, Felix R. Role of power Doppler techniques and ultrasound contrast enhancement in the differential diagnosis of focal breast lesions. *Eur Radiol* 2003;13:68-79.
- Stanzani D, Chala LF, Barros ND, Cerri GG, Chammas MC. Can Doppler or contrast-enhanced ultrasound analysis add diagnostically important information about the nature of breast lesions? *Clinics (Sao Paulo)* 2014;69:87-92.
- Rotstein AH, Neerhut PK. Ultrasound characteristics of histologically proven grade 3 invasive ductal breast carcinoma. *Australas Radiol* 2005;49:476-9.
- Lamb PM, Perry NM, Vinnicombe SJ, Wells CA. Correlation between ultrasound characteristics, mammographic findings and histological grade in patients with invasive ductal carcinoma of the breast. *Clin Radiol* 2000;55:40-4.
- Costantini M, Belli P, Bui E, Asunis AM, Ferra E, Bitti GT. Association between sonographic appearances of breast cancers and their histopathologic features and biomarkers. *J Clin Ultrasound* 2016;44:26-33.



18. Irshad A, Leddy R, Pisano E, Baker N, Lewis M, Ackerman S, *et al.* Assessing the role of ultrasound in predicting the biological behavior of breast cancer. *AJR Am J Roentgenol* 2013;200:284-90.
19. Elverici E, Zengin B, Nurdan Barca A, Didem Yilmaz P, Alimli A, Araz L. Interobserver and Intraobserver Agreement of Sonographic BIRADS Lexicon in the Assessment of Breast Masses. *Iran J Radiol* 2013;10:122-7.
20. Kijima Y, Yoshinaka H, Koriyama C, Funasako Y, Natsugoe S, Aikou T. Ultrasound examination is useful for prediction of histologic type in invasive ductal carcinoma of the breast. *Ultrasound Med Biol* 2008;34:517-24.
21. Horvath E, Cuitiño MJ, Pinochet MA, Sanhueza PS. Color Doppler in the study of the breast: How do we perform it? *Revista Chilena de Radiología* 17.
22. Shin HJ, Kim HH, Huh MO, Kim MJ, Yi A, Kim H, *et al.* Correlation between mammographic and sonographic findings and prognostic factors in patients with node-negative invasive breast cancer. *Br J Radiol* 2011;84:19-30.