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Analysis of sonographic features for the differentiation of benign and malignant breast tumors of different sizes

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KEYWORDS: breast tumor; tumor size; margin; sonography

ABSTRACT

Objective *To analyze the value of various sonographic features in differentiating benign from malignant breast tumors of different sizes to improve the diagnostic accuracy in small lesions.*

Methods *The sonographic features of 1203 histologically confirmed solid breast lesions were prospectively documented with respect to anteroposterior (AP) diameter/width ratio, shape, margin, echogenicity, echotexture, posterior echo and bilateral refraction sign. The sensitivity, specificity and accuracy of breast ultrasound were calculated for lesions grouped according to size (≤ 1, 1.1–2 and > 2 cm). Univariate and multiple logistic regression analyses including calculation of odds ratios for single sonographic features were used to analyze the significance of the different diagnostic features.*

Results *The accuracy of breast sonography in differentiating between benign and malignant tumors ≤ 1, 1.1–2 and > 2 cm in size was 75.6%, 86.4% and 88.4%, respectively. Univariate analysis demonstrated that all sonographic features were significant in tumors ≥ 1.1 cm. Shape, margin, echogenicity and echotexture were the significant factors in those tumors ≤ 1 cm. Multiple logistic regression analysis demonstrated that margin, shape, posterior echo and echogenicity were the significant factors for differential diagnosis in tumors > 2 cm. Echogenicity, margin, shape, bilateral refraction sign and echotexture were the significant factors for tumors 1.1–2 cm. On multiple regression analysis, margin was the only significant factor for tumors ≤ 1 cm.*

Conclusion *Tumor margin is the most important sonographic feature in evaluating breast lesions in any size group. With the combination of significant factors and emphasis on specific features according to size of lesion, the diagnostic accuracy of ultrasound for the differential diagnosis of malignant and benign tumors may be improved. Copyright © 2003 ISUOG. Published by John Wiley & Sons, Ltd.*

INTRODUCTION

Sonographic examination of the breast is a well-established adjunct to mammography, especially in patients with dense breasts or those with palpable breast lesions[1]. With the demonstration of specific sonographic features, the accuracy of diagnosing palpable breast lesions is as high as 95%[2]. Although sonography is an excellent tool for detecting and evaluating breast lesions, it is still not widely accepted as a screening modality due to its poor detection rate of microcalcifications and lower accuracy for non-palpable carcinomas[3]. Even with well-established sonographic features of benign and malignant breast lesions, the specificity remains low due to overlapping features, particularly in small lesions.

Breast lesions usually exhibit variable sonographic characteristics due to differences in histological type, histological grading and tissue components within the tumors. Smaller breast cancers tend to be of lower histological grade, have fewer desmoplastic changes, be less necrotic and have less aggressive adjacent tissue invasion[4–7]. In order to establish which sonographic features will differentiate benign from malignant breast lesions of different sizes it is essential to understand the diagnostic value of these features. In this study, we aimed to identify which individual and combined sonographic features have the greatest diagnostic accuracy for the differentiation between benign and malignant tissue in small lesions.

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METHODS

Between 1996 and 1998, 1203 Chinese females with palpable breast tumors who had undergone sonographic examination to confirm the presence of solid lesions were included in the study. Histological diagnoses were made following excision biopsy or core needle biopsy in all the lesions. As there is a lack of uniformity in observers' use of descriptive terms for solid breast masses[8], only the ultrasound reports obtained by one of the authors (S.C.C.) were included in this prospective study, thus eliminating interobserver variability. The ultrasound machines used were the Aloka SSD-2000 or SSD-5500 system (Aloka, Tokyo, Japan) with a 7.5- or 10.0-MHz linear array transducer with water bath. In general, a screening ultrasound examination of both breasts was performed followed by a targeted scan of the abnormal area. Sonographic features were prospectively recorded in a computer database and included anteroposterior (AP)/width ratio, shape, margin, internal echogenicity, internal echotexture, posterior acoustic phenomena and the presence of bilateral refraction signs. The classifications and definitions of sonographic features were consistent with those used by others[9]. Briefly, AP/width ratio was defined as the ratio of the height of the lesion to the width of the lesion, and subdivided as being ≤ 0.7 or > 0.7. Shape was classified as round, oval, lobulated or irregular. Margin was classified as smooth or irregular. The internal echogenicity was categorized as hyper-, iso- or hypoechogenic. The internal echotexture distribution was categorized as being uniform or non-uniform. Posterior acoustic phenomena included enhancement, neutral and shadowing. The bilateral refraction sign was recorded as present or absent.

Statistics

The tumor descriptors were classified into benign or malignant tumors in this study. The data were statistically analyzed in groups of different tumor size according to greatest diameter measured by ultrasound. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and accuracy for combinations of the dichotomized sonographic features were calculated. The odds and odds ratio of individual sonographic features and the basis for the odds of malignancy were analyzed separately in different size groups with the Chi-square test. The *P*-value was considered significant when < 0.05. Multiple logistic regression analysis was performed for combinations of the sonographic features. All the statistical analyses in this study were carried out

Table 1 Ultrasound diagnosis of breast tumors of various sizes

Parameter	*All cases* (n = *1203)*	*≤ 1 cm* (n = *135)*	*1.1–2 cm* (n = *567)*	*> 2 cm* (n = *501)*
Benign tumors (*n*)	812	96	411	305
Malignant tumors (*n*)	391	39	156	196
Sensitivity (%)	79.3	43.6	73.1	91.3
Specificity (%)	89.3	88.5	91.5	86.6
PPV (%)	78.1	60.7	76.5	81.4
NPV (%)	90.0	79.4	90.0	94.0
Accuracy rate (%)	86.0	75.6	86.4	88.4

NPV, negative predictive value; PPV, positive predictive value.

Table 2 Sonographic features of benign and malignant tumors > 2 cm in size

Features	*Benign* (n = *305)* (n *(%))*	*Malignant* (n = *196)* (n *(%))*	*Odds for cancer*	*Odds ratio*	P
AP/width ratio					
≤ 0.7	267 (87.5)	135 (68.9)	0.51	1.0	
> 0.7	38 (12.5)	61 (31.1)	1.61	3.2	< 0.001
Shape					
Oval/lobulated	277 (90.8)	30 (15.3)	0.11	1.0	
Irregular	28 (9.2)	166 (84.7)	5.93	53.9	< 0.001
Margin					
Smooth	271 (88.9)	24 (12.2)	0.09	1.0	
Irregular	34 (11.1)	172 (87.8)	5.03	55.9	< 0.001
Internal echogenicity					
Isoechogenic	281 (92.1%)	69 (35.2)	0.25	1.0	
Hypoechogenic	24 (7.9%)	127 (64.8)	5.29	21.2	< 0.001
Internal echotexture					
Uniform	257 (84.3)	28 (14.3)	0.11	1.0	
Non-uniform	48 (15.7)	168 (85.7)	3.50	31.8	< 0.001
Posterior echo					
Neutral	294 (96.4)	74 (37.8)	0.25	1.0	
Shadowing	11 (3.6)	122 (62.2)	11.00	49.0	< 0.001
Bilateral refraction sign					
Yes	186 (61.0)	21 (10.7)	0.11	1.0	
Absent	119 (39.0)	175 (89.3)	1.47	13.4	< 0.001

AP, anteroposterior.

Table 3 Sonographic features of benign and malignant tumors 1.1–2 cm in size

Features	*Benign (n = 411) (n (%))*	*Malignant (n = 156) (n (%))*	*Odds for cancer*	*Odds ratio*	P
AP/width ratio					
≤ 0.7	353 (85.9)	88 (56.4)	0.25	1.0	
> 0.7	58 (14.1)	68 (43.6)	1.17	4.7	< 0.001
Shape					
Oval/lobulated	383 (93.2)	55 (35.3)	0.14	1.0	
Irregular	28 (6.8)	101 (64.7)	3.61	25.8	< 0.001
Margin					
Smooth	382 (92.9)	48 (30.8)	0.11	1.0	
Irregular	29 (7.1)	108 (69.2)	3.72	33.8	< 0.001
Internal echogenicity					
Isoechogenic	359 (87.3)	55 (35.3)	0.15	1.0	
Hypoechogenic	52 (12.7)	101 (64.7)	1.94	12.9	< 0.001
Internal echotexture					
Uniform	360 (87.6)	49 (31.4)	0.14	1.0	
Non-uniform	51 (12.4)	107 (68.6)	2.10	15.0	< 0.001
Posterior echo					
Neutral	399 (97.1)	91 (58.3)	0.23	1.0	
Shadowing	12 (2.9)	65 (41.7)	5.42	23.7	< 0.001
Bilateral refraction sign					
Yes	155 (37.7)	14 (9.0)	0.09	1.0	
Absent	256 (62.3)	142 (91.0)	0.55	6.1	< 0.001

AP, anteroposterior.

Table 4 Sonographic features of benign and malignant tumors ≤ 1 cm in size

Features	*Benign (n = 96) (n (%))*	*Malignant (n = 39) (n (%))*	*Odds for cancer*	*Odds ratio*	P
AP/width ratio					
≤ 0.7	59 (61.5)	20 (51.3)	0.34	1.0	
> 0.7	37 (38.5)	19 (48.7)	0.51	1.5	0.277
Shape					
Oval/lobulated	87 (90.6)	28 (71.8)	0.32	1.0	
Irregular	9 (9.4)	11 (28.2)	1.22	3.8	0.005
Margin					
Smooth	89 (92.7)	25 (64.1)	0.28	1.0	
Irregular	7 (7.3)	14 (35.9)	2.00	7.1	< 0.001
Internal echogenicity					
Isoechogenic	74 (77.1)	19 (48.7)	0.26	1.0	
Hypoechogenic	22 (22.9)	20 (51.3)	0.91	3.5	0.001
Internal echotexture					
Uniform	86 (89.6)	29 (74.4)	0.34	1.0	
Non-uniform	10 (10.4)	10 (25.6)	1.00	2.9	0.024
Posterior echo					
Neutral	91 (94.8)	34 (87.2)	0.37	1.0	
Shadowing	5 (5.2)	5 (12.8)	1.00	2.0	0.126
Bilateral refraction sign					
Yes	19 (19.8)	5 (12.8)	0.26	1.0	
Absent	77 (80.2)	34 (87.2)	0.44	1.7	0.337

AP, anteroposterior.

using SPSS for Windows software (SPSS Inc., Chicago, IL, USA).

RESULTS

The median age of the 559 patients with benign tumors was 36 (range, 14–83) years and of the 391 patients with malignant tumors was 46 (range, 26–83) years. Among the 1203 histologically confirmed breast lesions, 135 lesions were ≤ 1 cm, 567 were 1.1–2 cm and 501 were > 2 cm. The histological types of malignant tumors were infiltrating ductal carcinomas in 312 patients, 16 invasive lobular carcinomas, 14 medullary carcinomas, 29

Table 5 Multiple logistic regression analysis of the sonographic features of breast tumors of different sizes

	≤ 1 cm		*1.1–2 cm*		*> 2 cm*	
Features	*Odds ratio (95% CI)*	P	*Odds ratio (95% CI)*	P	*Odds ratio (95% CI)*	P
AP/width ratio (> 0.7)	1.173 (0.504–2.731)	0.711	1.550 (0.860–2.795)	0.145	1.138 (0.540–2.398)	0.735
Shape (Irregular)	0.861 (0.192–3.870)	0.846	2.645 (1.014–6.903)	0.047	3.607 (1.383–9.409)	0.009
Margin (Irregular)	25.00 (2.219–284.9)	0.009	2.751 (1.015–5.357)	0.014	4.271 (1.395–13.071)	0.011
Internal echogenicity (Hypoechogenic)	2.670 (1.003–7.110)	0.050	2.874 (1.559–5.298)	0.001	2.556 (1.205–5.420)	0.014
Internal echotexture (Non-uniform)	0.204 (0.021–1.957)	0.168	2.348 (1.117–4.935)	0.024	1.713 (0.672–4.369)	0.260
Posterior echo (Shadowing)	0.335 (0.051–2.213)	0.256	1.422 (0.580–3.487)	0.441	2.718 (1.120–6.594)	0.027
Bilateral refraction sign (Absent)	1.096 (0.351–3.418)	0.875	2.397 (1.215–4.730)	0.012	1.362 (0.612–3.034)	0.449

AP, anteroposterior.

intraductal carcinomas and 20 others. The benign tumors included 649 fibroadenomas, 97 fibrocystic changes and 66 others.

The sensitivity, specificity, PPV, NPV and accuracy of breast ultrasound in differentiating benign from malignant tumors in the groups of different tumor size are shown in Table 1. The overall sensitivity, specificity and accuracy were 79.3%, 89.3% and 86.0%, respectively. The diagnostic accuracy in tumors of ≤ 1, 1.1–2 and > 2 cm was 75.6%, 86.4% and 88.4%, respectively. From the results we observed that sensitivity, PPV, NPV and accuracy were directly proportional to tumor size, while specificity did not show a significant difference. For tumors ≤ 1 cm the sensitivity, specificity and accuracy were 43.6%, 88.5% and 75.6%, respectively.

All sonographic features were significant in differentiating benign from malignant breast lesions in the size groups 1.1–2 and > 2 cm. The odds and odds ratio of malignancy are shown in Tables 2 and 3. For those tumors ≤ 1 cm, margin, shape, internal echogenicity and internal echotexture were statistically significant in decreasing order (Table 4). On multiple logistic regression analysis the values of sonographic features in terms of their ability to distinguish between benign and malignant breast tumors of different sizes differed from those on univariate analysis (Table 5). The margin, shape, internal echogenicity and posterior echo were the significant diagnostic features for tumors > 2 cm. For tumors 1.1–2 cm in size, shape, margin, internal echogenicity, internal echotexture and bilateral refraction sign were the significant criteria. Margin was the only statistically significant feature for those tumors ≤ 1 cm.

DISCUSSION

Breast sonography has equivalent diagnostic ability to mammography for palpable lesions[10], but its sensitivity and accuracy are limited in small or non-palpable tumors and microcalcifications[11]. This reason accounts for sonography not being considered to be as good as mammography in earlier reports[12]. However, sonography has been shown to be superior to mammography in the demonstration of tumor margin, especially in those cases in which the lesion is obscured within the dense breast tissue[13]. Most Chinese women have relatively small and dense breasts[14], and the median age of breast cancer patients is 47 years which is 8 years younger than in Western women[15]. Practically, we choose sonography as the primary work-up tool in the clinic instead of mammographic examination. A breast cancer-screening program for the high-risk population in Taiwan has also demonstrated that breast sonography has the same ability as X-ray mammography in detecting non-palpable breast carcinomas[16], which is consistent with the results of others[17–19]. Gordon and Goldenberg diagnosed 44 breast cancers in 1575 non-palpable solid lesions that were non-visible by mammography and treatment planning was altered accordingly[20]. Moon *et al.* reported that sonography identified multifocal cancers in 28/201 (14%) patients in whom there was no mammographic or clinical suspicion of malignancy, and therapeutic decisions were thus altered[21]. For small or non-palpable tumors, ultrasound-guided fine needle aspiration[22], needle biopsy[23], core needle biopsy[24] or excision[25,26] are as sensitive and specific as mammography-guided biopsy. All these studies clearly demonstrated that sonography can depict small or non-palpable lesions but the accuracy of diagnosis for malignancy was low.

As the diagnostic accuracy of sonography is acceptable in tumors ≥ 1.1 cm but not in smaller tumors, it is essential to identify the distinguishing sonographic features in small tumors. Shape, margin, internal echogenicity, echotexture distribution, posterior echo and bilateral refraction sign have been shown to be valuable in the differential diagnosis of benign and malignant breast tumors[8]. A heterogeneous, hypoechogenic mass with an irregular margin and posterior acoustic shadowing is characteristic of invasive lobular carcinoma[6]. High-grade tumors are likely to demonstrate posterior acoustic enhancement and well-defined margins[7]. A jagged margin was the major feature in a study on the differential diagnosis of typical and atypical medullary carcinoma[27]. All the reports revealed that the sonographic features were attributable to the different histological types or grades although considerable overlap existed.

Although there were slight differences noted when the lesions were divided by size, no specific trends could be established in the study of Cole-Beuglet *et al.*[28]. Instead the majority of the tumors in both groups (≤ 2 cm; > 2 cm) exhibited an irregular contour, weak echogenicity and strong to intermediate attenuation. The boundary echoes were usually intermediate in brightness anteriorly and weak to absent posteriorly. Only the lesion shapes were variable. Skaane and Engedal found that the irregular contour was the most important feature of impalpable tumor with high odds ratio of 63.0 and central posterior shadowing was the major feature of palpable tumor with an odds ratio 102.3[5]. In our series all the sonographic features were significant predictors for malignancy in tumors > 1 cm by univariate analysis. The odds and odds ratio of malignancy in decreasing order are irregular margin, irregular shape, posterior acoustic shadowing, non-uniform echotexture, hypoechogenicity, absence of bilateral refraction sign and AP/width ratio > 0.7 (Table 2). For tumors ≤ 1 cm, the irregular margin, irregular shape, hypoechogenicity and non-uniform echotexture were the most significant factors in univariate analysis. However, multiple logistic regression analysis demonstrated that the shape, margin, internal echotexture and posterior echo were the significant factors in differentiating between benign and malignant tumors > 2 cm. Margin was the only significant differentiating factor in the tumors ≤ 1 cm (Table 5). Such findings are consistent with Skaane and Engedal's conclusion that margin was the most important factor in differential diagnosis of impalpable tumors[5].

Echogenicity has not been considered an important factor in differentiation because of a lack of a standardized definition of hypoechogenicity between observers[8]. In the present study, the echogenicity was an independent and important feature for differentiation in large tumors but not in small tumors. Nearly half of the small, malignant tumors were isoechogenic, leading to a loss in predicting power of differentiation in tumors ≤ 1 cm.

Central posterior shadowing is a common feature suggesting malignancy and is much more frequently present in low-grade malignancy[28,29]. The cause of posterior shadowing is the heterogeneous character of tumors[30]. In our study, posterior shadowing was seen in 62.2% of breast cancers > 2 cm and in only 12.8% of those ≤ 1 cm. This difference may be explained by the fact that there was less heterogeneous tissue in the small breast cancers.

The feature of bilateral refraction sign is an acoustic phenomenon that mostly occurs in benign breast tumors. Smooth margins cause a reduction of reflecting echoes by diffraction of the sound wave that touches the margin of the sound boundary[31]. Similar to our results, bilateral refraction sign is not common in most breast cancers due to the presence of an irregular or jagged margin. In benign cases, the larger tumors had a significantly higher percentage of bilateral refraction sign than the smaller tumors (61.0% for tumors > 2 cm, 37.7% for tumors 1.1–2 cm and 19.8% for tumors ≤ 1 cm). Using multiple logistic regression analysis, the refraction sign was a significant factor in differential diagnosis only in those tumors 1.1–2 cm in size.

The AP/width ratio has been used as a good parameter for the differentiation of benign and malignant breast tumors[23]; tumors with greater AP/width ratio are suspected to be malignant. In the present study, the AP/width ratio was found to be significant for the tumors ≥ 1.1 cm, but was not significant in tumors ≤ 1 cm by using the odds and odds ratio analyses. They had no significant predicting power of malignancy by multiple logistic regression analysis.

The echotexture was significantly different between benign and malignant breast tumors of any size. Unfortunately the subjective nature of this feature can lead to misclassification and it had no significant predicting power by multiple logistic regression analysis in small tumors.

Interobserver variability and variation in the sonographic diagnostic features chosen by the operators will lead to inconsistent results, and so the more sonographic features chosen for differentiation the higher the accuracy and NPV will be. However, the interpretation of results becomes more complicated with more criteria. With the consideration of frequency, reliability and interobserver agreement, it is ideal to select three or four sonographic features in combination in order to improve the accuracy[32]. Rahbar *et al.* selected shape, margin and AP/width ratio as the optimal criteria[4] and Skaane and Engedal selected surrounding tissue, posterior echo and margin[5]. Based on our study, we believe that different sizes of tumors may have different sonographic features due to morphological and histological differences. By using a number of different statistical methods we found that margin, shape, posterior echo and echogenicity were the useful factors for tumors > 2 cm. Margin and echogenicity were the significant factors for small tumors. Of the sonographic features, margin is conclusively the most reliable in the differentiation of benign and malignant tumors of any size and it is the only significant factor for tumors ≤ 1 cm. In conclusion, the significant sonographic diagnostic features vary in tumors of differing sizes. Understanding the sonographic features and choosing the optimal combination, especially one involving margin contour, will improve the accuracy of diagnosis in small breast tumors.

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