DOI:10.3969/j.issn.1005-202X.2016.10.001

医学影像物理

Radiological features of breast malignant and benign lesions

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Abstract: To compare radiological features of breast malignant and benign lesions in digitized mammograms. Digitized mammograms of 466 patients were randomly selected from Digital Database for Screening Mammography, University of South Florida. Radiological features of breast malignant and benign lesions were compared by specialized radiologists who had at least 5 years of experience in breast imaging. Two-sample *t* test revealed that the number of calcification in an area of 1 cm×1 cm was significantly larger in malignant mammograms than that in benign mammograms (P<0.001). The irregular or lobulated mass with spiculated margins rate was significantly higher in malignant mammograms than that in benign mammograms (P<0.000 1). An opposite result was found for the irregular or lobulated mass with circumscribed margins. Additionally, the oval or round mass with circumscribed margins presented a significantly higher rate in benign mammograms than that in malignant mammograms (P=0.001). However, the present data revealed that only the malignant mammograms exhibited the oval or round mass with spiculated margins. Architectural distortion rate was slight higher in malignant mammograms (5.2%) than that in benign mammograms (1.7%) (P=0.042). No significant difference was found in other radiological features. The findings in the study suggest that masses with spiculated margins or architectural distortion, and calcification cluster that the calcification number was more than 21 in an area of 1 cm×1 cm were predominant radiological features in malignant mammograms, while masses with circumscribed margins were predominant radiological features in benign mammograms.

Key words: breast; lesion; digitized mammogram; calcification; benign mammogram; malignant mammogram

Introduction

Breast cancer is a public health problem worldwide[1]. The World Health Organization estimates that more than 385 000 women worldwide die of breast cancer[2]. Clear evidence shows that early diagnosis and treatment of breast cancer can significantly increase the survival rate of patients[3]. Mammography is the most effective method for the detection of early breast cancer[4]. In practice, an average of 78% of breast cancers is detected by mammography screening[5-6]. Some studies show that radiologists do not detect all breast cancers that are retrospectively detected on mammograms[7]. Approximately 10%-30% of breast cancer cases are missed by radiologists, and half of missed breast cancers are retrospectively visible on mammograms[8-10]. Double reading and computer-assisted detection methods improve the performance of radiologists by improving the cancer detection[11-13]. The dedicated training in mammography through continuing medical education or the American College of Radiology Breast Imaging Reporting and Data System (BI-RADS) can also improve the performance of radiologists by increasing sensitivity and decreasing the size of detected cancers, without a loss of specificity[14-17]. The missed diagnosis of breast cancer in mammography is multifactor. The radiologists sometimes may fail to detect an abnormality. Once one is seen, the radiologists may dismiss it as a normal finding or may misclassify it as benign or probably benign. Therefore, it is important for radiologists to correctly differentiate radiological features of malignant, benign and normal mammograms, which can decrease the missed diagnosis in mammography. The study aims to compare the radiological features of breast malignant and benign

Received: 2016-03-12
Supported by Natural Science Foundation of Shandong Province (ZR2015HL095), Science and Technology Development Plan of Tan'an City(2015NS2159) and Taishan Medical University Doctor Foundation (20072009)
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lesions in digitized mammography.

1 Materials and methods

The database in the study consisted of 1 864 standard-view (mediolateral oblique and craniocaudal) mammograms obtained from 466 patients in the Digital Database for Screening Mammography (DDSM). The DDSM is a resource for use by the mammographic image analysis research community. The purposes of the database include the development of algorithms which can aid in the diagnosis and the development of teaching or training aids. The DDSM contains approximately 2 500 studies. Each study includes two images of each breast, along with some associated patient information (age at time of study, breast density rating of American college of radiology, subtlety rating for abnormalities, keyword description of American college of radiology for abnormalities) and image information (scanner, spatial resolution, etc). Images containing suspicious areas have associated pixel-level "ground truth" information about the locations and types of suspicious regions. The DDSM which has been extensively used by the research community is maintained at the University of South Florida to keep the database accessible on the web (http://marathon.csee.usf.edu/Mammography/Database.html).

In the dataset of the study, the mammograms from 233 patients (average age 62 years, median age 63 years, range 33 to 89 years) were malignant, and the other mammograms from 233 patients (average age 54 years, median age 53 years, range 31 to 89 years) were benign. Each patient had at least one lesion, but only the most apparent lesion was evaluated, and each lesion was assessed by using the BI-RADS. Among 233 malignant lesions, 11.2% (26 of 233) was BI-RADS category 3 (probably benign), and 53.2 % (124 of 233) was BI-RADS category 4 (suspicious abnormality), and 35.6% (83 of 233) was BI-RADS category 5 (highly suggestive of malignancy). Among 233 benign lesions, 4.7% (11 of 233) was BI-RADS category 2 (benign), and 7.7% (18 of 233) was BI-RADS category 3 (probably benign), and 87.6 % (204 of 233) was BI-RADS category 4 (suspicious abnormality). All mammograms were digitized to a pixel size of 0.043 5 mm × 0.043 5 mm (or 0.050 0 mm × 0.050 0 mm) and a 12-bit gray scale. Malignant mammogram cases were formed from screening exams in which cancer was proven by at least one pathology, while benign mammogram cases were formed from screening exams in which something suspicious was found, but was confirmed not to be malignant by pathology, ultrasound.

In order to study the mammogram cases, a software system which could display and process the standard-view mammogram images was developed. Reading was performed by using a monochrome liquid crystal display panel (RadioForce G20, EIZO NANAO Corporation, Japan) with a resolution of 1 200×1 600 pixels, and high luminance and contrast (the maximum luminance was 750 candelas per square meter, and the contrast was 900∶1). The standard-view full raw mammogram images were read by a specialized radiologist. The radiological features of breast lesions were different on the basis of different pathology categories[18-23]. In the study, each lesion was described in the following aspects: (a) clustered calcifications only which was defined as a region containing three or more calcifications in an area of 1 cm × 1 cm; (b) lucent-centered calcification only; (c) irregular or lobul-ated mass; (d) oval or round mass; (e) architectural disto-rtion; (f) asymmetric breast tissue only; (g) focal asym-metric density only. If the diagnosis did not accord with the description in the overlay file from DDSM, the case would be presented at a consensus meeting, and four specialized radiologists would decide the final diagnosis results. Each of specialized radiologists has at least 5 years of experience in breast imaging.

2 Statistical analysis

For the seven lesion category rates were calculated separately, the calculations were performed with statistical software (SPSS 19.0). To compare every lesion and margin category rate in the malignant and benign mammograms, the χ^2 test was applied in two-sided variant for 2×2 tables. The P (observed ≥expected or observed ≤expected) value was used, and $P\leq 0.05$ indicated statistically significant differences. Two-sample t test was used to evaluate the difference of calcification number in an area of 1 cm×1 cm between malignant and benign mammograms.

3 Results

3.1 Calcification feature comparison

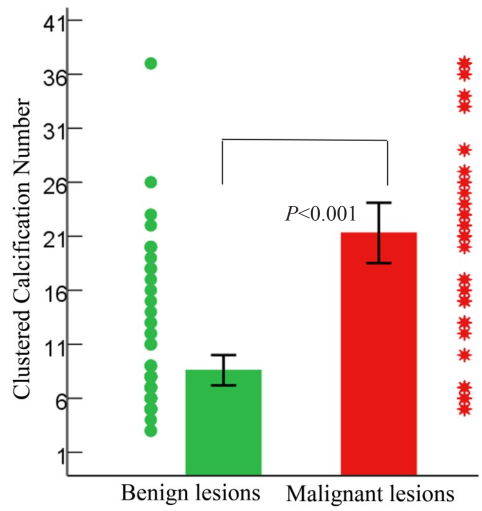
For 233 patients with malignant breast lesions, 24.0% (56 of 233) showed the calcification cluster was the only suspicious feature of mammogram. For 233 patients with benign breast lesions, 35.2% (82 of 233) showed the calcification cluster was the only suspicious feature of mammogram. The rate of calcification cluster only in benign mammograms was higher than that in malignant mammograms (P=0.008) (Tab.1).

Tab.1 Distribution of radiological features of malignant and benign lesions in mammograms (*n*)

Feature	Malignant	Benign	*P* value
Clustered calcifications only	56 (24.0%)	82 (35.2%)	0.008 0
Lucent-centered calcification only	0 (0.0%)	8 (3.4%)	0.004 0
Irregular or lobulated mass	141 (60.5%)	54 (23.2%)	<0.000 1
Oval or round mass	18 (7.7%)	85 (36.5%)	<0.000 1
Architectural distortion	12 (5.2%)	4 (1.7%)	0.042 0
Asymmetric breast tissue only	3 (1.3%)	0 (0.0%)	0.247 0
Focal asymmetric density only	3 (1.3%)	0 (0.0%)	0.247 0
Total	233 (100.0%)	233 (100.0%)	

In addition, two-sample t test revealed that the number of calcification in an area of 1 cm×1 cm was significantly smaller in benign mammograms than that in malignant mammograms, and that the average numbers of calcification in benign and malignant mammograms were respectively (9.7±6.4) and (21.8±10.2) (Fig.1).

Furthermore, calcification clusters were classified into following categories: amorphous distribution, pleomorphic distribution, punctate distribution, fine linear branching distribution, pleomorphic fine linear branching distribution (Fig.2).



The green dot denoted the benign calcification cluster, and the red asterisk denoted the malignant calcification cluster. The green bar denoted the average number of benign calcification in the cluster, and the red bar denoted the average number of malignant calcification in the cluster. The black coarse line denoted the standard error. P<0.001 indicated a significant difference.

Fig.1 Two-sample *t* test result of benign and malignant calcification clusters

The rate of pleomorphic distribution was respectively 58.9% and 75.6% in malignant and benign calcification clusters, which showed that the pleomorphic distribution was the dominant category, and that the rate in benign calcification was higher than that in malignant calcification (P=0.001) (Tab.2). In addition, lucent-centered calcifications were benign (Fig.2). Among 233 patients with benign breast lesions, 3.4% (8 of 233) showed that the lucent-centered calcification was the only suspicious feature in mammogram.

3.2 Irregular or lobulated mass feature comparison

The irregular or lobulated mass was frequently a malignant finding in the breast. However, the irregular or lobulated mass sometimes may be manifested as a benign lesion (Fig.3).

Among 233 patients with malignant breast lesions, 60.5% (141 of 233) showed the irregular or lobulate mass was the suspicious feature in mammography. Among 233 patients with benign breast lesions, 23.2% (54 of 233) showed the irregular or lobulate mass was the suspicious feature in mammography (Tab.1). The irregular or lobulate mass rate was higher in malignant mammograms than in benign mammograms (P<0.000 1). The spiculated mar-

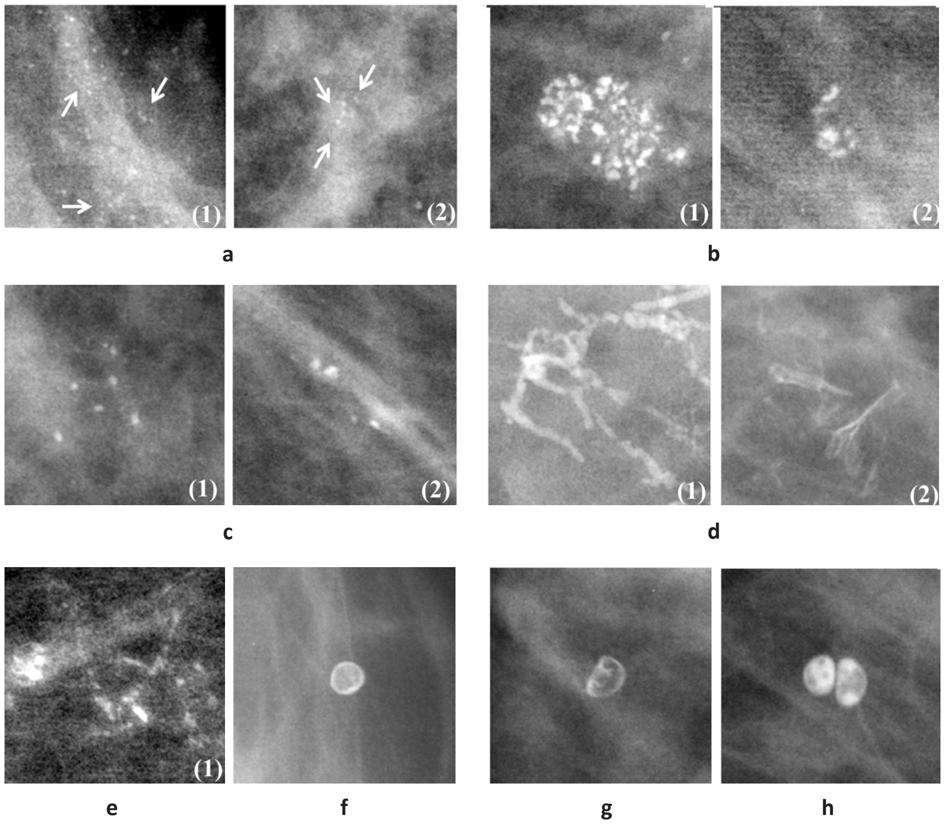


Fig.2a was amorphous distribution. The suspicious area in Fig.2a(1) detected on the basis of calcification cluster (arrows) only was from a 37-year-old woman (BI-RADS 3, subtlety 4, pathology malignant), and the suspicious area in Fig.2a(2) detected on the basis of calcification cluster (arrows) only was from an 84-year-old woman (BI-RADS 4, subtlety 2, pathology benign). Fig.2b was pleomorphic distribution. The suspicious area in Fig.2b(1) detected on the basis of calcification cluster only was from a 52-year-old woman (BI-RADS 5, subtlety 5, pathology malignant), and the suspicious area in Fig.2b(2) detected on the basis of calcification cluster only was from a 63-year-old woman (BI-RADS 4, subtlety 4, pathology benign). Fig.2c was punctate distribution. The suspicious area in Fig.2c(1) detected on the basis of calcification cluster only was from a 64-year-old woman (BI-RADS 5, subtlety 5, pathology malignant), and suspicious area in Fig.2c(2) detected on the basis of calcification cluster only in a 51-year-old woman (BI-RADS 4, subtlety 4, pathology benign). Fig.2d was fine linear branching distribution. The suspicious area in Fig.2d(1) detected on the basis of calcification cluster only was from a 54-year-old woman (BI-RADS 5, subtlety 5, pathology malignant), and the suspicious area in Fig.2d(2) detected on the basis of calcification cluster only was from a 70-year-old woman (BI-RADS 4, subtlety 4, pathology benign). Fig.2e was pleomo-rphic fine linear branching distribution, and the suspicious area detected on the basis of calcification cluster only was from a 77-year-old woman (BI-RADS 5, subtlety 4, pathology malignant). The suspicious area in Fig.2f detected on the basis of lucent-centered calcification only was from a 40-year-old woman (BI-RADS 2, subtlety 4, pathology benign). The suspicious area in Fig.2g detected on the basis of lucent-centered calcification only was from a 55-year-old woman (BI-RADS 2, subtlety 3, pathology benign). The suspicious area in Fig.2h detected on the basis of lucent-centered calcification only was from a 64-year-old woman (BI-RADS 2, subtlety 3, pathology benign).

Fig.2 Categories of calcification clusters of malignant and benign lesions

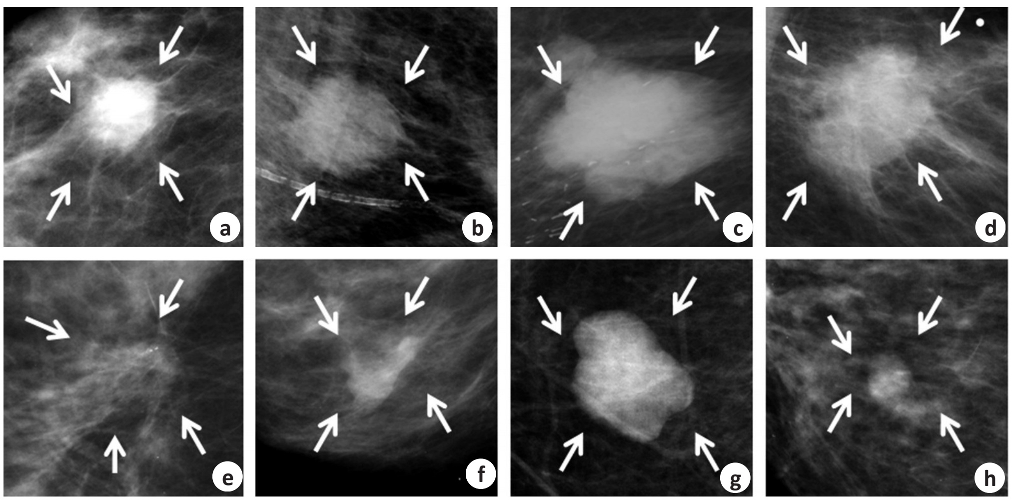
gin was a predominant margin feature of malignant irregular or lobulated mass, and the rate was higher in malignant mammograms than that in benign mammograms (P<0.000 1). The circumscribed margin was a predominant margin feature of benign irregular or lobulated mass, and the rate was higher in benign mammograms than that in malignant mammograms (P<0.000 1). The irregular or lobulated mass with obscured or ill-defined margins rate was higher in benign mammograms than that in malignant mammograms (P=0.042). For the irregular or lobulated mass with microlobulated margin, no statistically significant difference was found between benign and malignant mammograms (Tab.3).

Tab.2 Distribution of calcification cluster categories for malignant and benign lesions (*n*)

Category	Malignant	Benign	*P* value
Amorphous	4 (7.1%)	10 (12.2%)	0.103
Pleomorphic	33 (58.9%)	62 (75.6%)	0.001
Punctate	8 (14.3%)	8 (9.8%)	1.000
Fine linear branching	8 (14.3%)	2 (2.4%)	0.055
Pleomorphic fine linear branching	3 (5.4%)	0 (0.0%)	0.082
Total	56 (100.0%)	82 (100.0%)	

3.3 Oval or round mass feature comparison

Most of oval or round masses were benign lesions in mammogram. However, some oval or round masses also might be malignant (Fig.4). Among 233 patients with malignant breast lesions, 7.7% (18 of 233) showed the oval or round mass was the suspicious feature in mammogram. Among 233 patients with benign breast lesions, 36.5% (85 of 233) showed the oval or round mass was the suspicious feature in mammogram. Compared with malignant mammograms, the oval or round mass rate was significantly higher in benign



Suspicious area in Fig.3(a) detected on the basis of irregular mass with spiculated margins (arrows) was from a 59-year-old woman (BI-RADS 5, subtlety 5, pathology malignant). Suspicious area in Fig.3(b) detected on the basis of irregular mass with ill-defined margins (arrows) was from an 84-year-old woman (BI-RADS 4, subtlety 4, pathology malignant). Suspicious area in Fig.3(c) detected on the basis of lobulated mass with circumscribed margins (arrows) was from a 71-year-old woman (BI-RADS 5, subtlety 5, pathology malignant). Suspicious area Fig.3(d) detected on the basis of irregular mass with microlobulated margins (arrows) was from a 41-year-old woman (BI-RADS 5, subtlety 5, pathology malignant). Suspicious area in Fig.3(e) detected on the basis of architectural distortion mass with spiculated margins (arrows) was from a 46-year-old woman (BI-RADS 4, subtlety 5, pathology benign). Suspicious area in Fig.3(f) detected on the basis of oval mass with ill-defined margins (arrows) was from a 58-year-old woman (BI-RADS 4, subtlety 4, pathology benign). Suspicious area in Fig.3(g) detected on the basis of lobulated mass with circu-mscribed margins (arrows) was from a 41-year-old woman (BI-RADS 4, subtlety 5, pathology benign). Suspicious area in Fig.3(h) detected on the basis of lobulated mass with microlobulated margins (arrows) was from a 67-year-old woman (BI-RADS 4, subtlety 4, pathology benign).

Fig.3 Irregular or lobulated masses from malignant and benign lesions

mammograms ($P<0.000\ 1$). However, the oval or round masses with spiculated margins were only found in malignant mammograms. Additionally, the circumscribed margin was found as the predominant margin feature of benign oval or round mass, and the rate was higher in benign mammograms than that in malignant mammograms ($P=0.001$). For other margin features, no statistically significant difference was found between benign and malignant mammograms (Tab.4).

3.4 Architectural feature comparison

Architectural distortion (Fig.5) rate was higher in malignant mammograms than that in benign mammograms (5.2% and 1.7% in malignant and benign mammograms, respectively, $P=0.042$). The

Tab.3 Distribution of margin category for irregular or lobulated mass

Category	Malignant	Benign	*P* value
Spiculated margin	83 (58.9%)	2 (3.7%)	<0.000 1
Obscured or ill-defined margin	41 (29.0%)	24 (44.4%)	0.042 0
Circumscribed margin	10 (7.1%)	27 (50.0%)	<0.000 1
Mircrolobulated margin	7 (5.0%)	1 (1.9%)	0.564 0
Total	141 (100.0%)	54 (100.0%)	

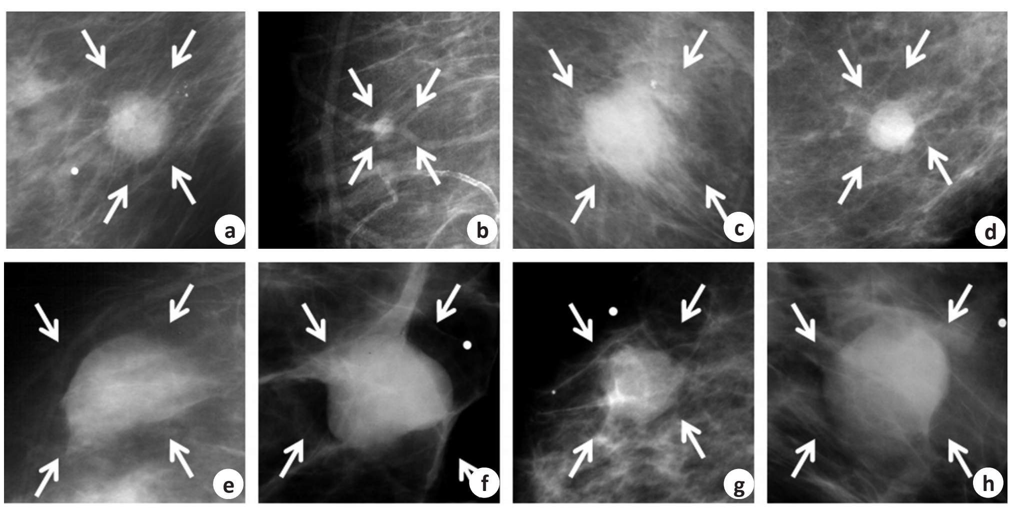
Tab.4 Distribution of margin category for oval or round mass

Category	Malignant	Benign	*P* value
Spiculated margin	6 (33.3%)	0 (0.0%)	<0.000 1
Obscured or ill-defined margin	8 (44.4%)	29 (34.1%)	0.407 0
Circumscribed margin	3 (16.7%)	52 (61.2%)	0.001 0
Mircrolobulated margin	1 (5.6%)	3 (3.5%)	1.000 0
N/A margin	0 (0.0%)	1 (1.2%)	1.000 0
Total	18 (100.0%)	85 (100.0%)	

asymmetric breast tissue and focal asymmetric density (Fig.5) were also found in malignant mammography group (Tab.1).

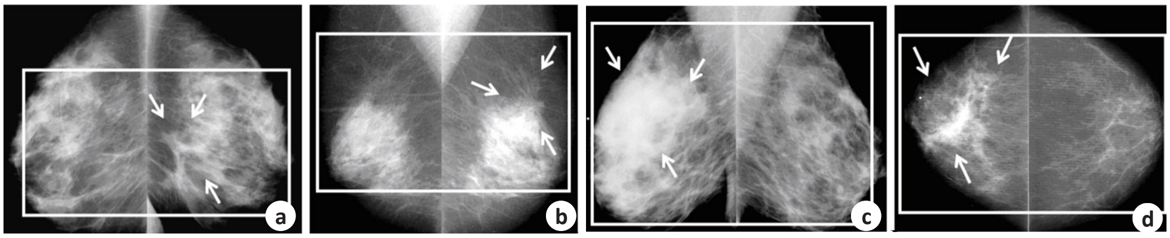
4 Discussion

The clustered calcifications are relevant to the detection of breast malignant lesions, and the percentages of malignancies detected on the basis of clustered calcifications at digital screening reported by Skaane, et al[24], Del Turco, et al[25], Stefanie, et al[26], and Jonathan, et al[27] were respectively 32%, 37%, 32%, and 25%. The percentage reported by Jonathan, et al[27] is similar to the 24% in the study. However, sometimes the clustered calcifications are also the sole suspicious feature of the benign lesions in mammogram. The averaged number of calcification in an area of 1 cm × 1 cm in mammogram is less than 10, while the malignant calcification number was more than 21, which is consistent with previous study, in which they suggested that a region containing 21 or more calcifications in an area of 1 cm × 1 cm could be



Suspicious area in Fig.4a detected on the basis of round mass with spiculated margins (arrows) was from an 82-year-old woman (BI-RADS 5, subtlety 5, patho-logy malignant). Suspicious area in Fig.4b detected on the basis of oval mass with circumscribed margins (arrows) was from a 75-year-old woman (BI-RADS 4, subtlety 3, pathology malignant). Suspicious area in Fig.4c detected on the basis of oval mass with microlobulated margins (arrows) was from a 59-year-old woman (BI-RADS 5, subtlety 5, pathology mali-gnant). Suspicious area Fig.4d detected on the basis of round mass with obscured margins (arrows) was from a 60-year-old woman (BI-RADS 3, subtlety 5, pathology malignant). Suspicious area in Fig.4e detected on the basis of oval mass with ill-defined margins (arrows) was from a 34-year-old woman (BI-RADS 4, subtlety 4, pathology benign). Suspicious area in Fig.4f detected on the basis of oval mass with circumscribed margins (arrows) was from a 39-year-old woman (BI-RADS 4, subtlety 4, pathology benign). Suspicious area in Fig.4g detected on the basis of round mass with microlobulated margins (arrows) was from a 59-year-old woman (BI-RADS 4, subtlety 5, pathology benign). Suspicious area Fig.4h detected on the basis of round mass with obscured margins (arrows) was from a 48-year-old woman (BI-RADS 4, subtlety 5, pathology benign).

Fig.4 Oval or round masses from malignant and benign lesions



Suspicious area in Fig.5a detected on the basis of architectural distortion with ill-defined margins (arrows) was from a 61-year-old woman (BI-RADS 5, subtlety 5, pathology malignant). Suspicious area in Fig.5b detected on the basis of architectural distortion with ill-defined spiculated margins (arrows) was form a 64-year-old woman (BI-RADS 4, subtlety 3, patho-logy benign). Suspicious area in Fig.5c detected on the basis of focal asymmetric density with N/A margins (arrows) was from a 33-year-old woman (BI-RADS 5, subtlety 3, pathology malignant). Suspicious area in Fig.5d detected on the basis of asymmetric breast tissue with ill-defined margins (arrows) was from a 60-year-old woman (BI-RADS 5, subtlety 5, pathology malignant).

Fig.5 Architectural distortion and asymmetric breast tissue

diagnosed as the malignant lesion[28]. In addition, the lucent-center calcifications are frequently benign.

Malignant mass features include irregular shape, spiculated or irregular margins, or high density in mammograms. Masses have benign features if round, oval, or lobular in shape with circumscribed margins are found[29]. In the study, irregular or lobulated masses rate was 60.5% (141 of 233) for the malignant lesions, and 58.9% (83 of 141) of these lesions was manifested as spiculated margins. The oval or round masses rate was 36.5% (85 of 233) for the benign lesions, and 61.2% (52 of 85) of these lesions was manifested as circumscribed margins. The results suggest that the irregular or lobulated masses with spiculated margins are dominant malignant feature in mammogram, which mainly due to breast cancer which does not respect normal breast structures but grows through them instead creating abnormal lines. These straight lines created by breast cancer represent early spiculation around a mass. The oval or round masses with circumscribed margins are dominant benign features in mammogram, which mainly due to the tumor growth that differs markedly between benignancy and malignancy. Benign lesions form the so-called pseudocapsule that prevents the tumor growth from invading the surrounding normal tissues. In this condition, benign tumors have well-defined contours with round, oval and smoother shapes and margins. In contrast, malignant tumors (without the pseudocapsule) tend to invade the surrounding tissues, resulting in tumors with irregular or lobulated shape and spiculated margins[30]. For masses with microlobulated margins, and oval or round masses with obscured or ill-defined margins, no statistically significant difference was found between benign and malignant mammograms. In this condition, ultrasonography can be used to differentiate benign from malignant solid lesions[31].

Architectural distortion has a higher probability of malignancy, which due to invasive lobular carcinoma spreading in single-layer sheets of tumor cells similar to a spider web. The increase of breast density and the less compliance of breast tissue may result in architectural distortion[29].

A focal asymmetry has benign features when no outward convex margin or associated straightening of Cooper ligaments is found. However, early breast cancer may be manifested as a focal asymmetry in mammogram[29]. For asymmetry breast tissue feature, no statistically significant difference was found between benign and malignant mammograms.

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（编辑：谭斯允）

乳腺良恶性病变的影像学特征

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【摘 要】为了比较乳腺恶性和良性病变在数字化乳腺X线图像中的影像学特征,在美国南佛罗里达大学的数字化乳腺X线图像数据库中随机选取466名病人的数字化乳房X线图像。在乳腺成像领域有着5年以上经验的放射学专家对乳腺恶性和良性病变的影像学特征进行比较。两样本*t*检验表明恶性乳腺病变在1 cm×1 cm区域内的钙化数量明显高于良性乳腺病变(P<0.001)。同时,恶性乳腺病变中的不规则或有毛刺状边缘的分叶状肿块的比例明显高于良性乳腺病变(P<0.000 1)。而不规则或边缘局限的分叶状肿块的比较结果却截然相反。此外,良性乳腺病变中边缘局限的椭圆或圆形肿块的比例明显高于恶性乳腺病变(P=0.001)。然而,当前研究数据表明只有恶性乳腺病变表现出边缘局限的椭圆或圆形肿块。恶性乳腺病变的结构扭曲率(5.2%)略高于良性乳腺病变(1.7%)(P=0.042)。其他的影像学特征并没有明显差异。本研究表明恶性乳腺病变的主要影像学特征为有毛刺状边缘或者结构扭曲的肿块、钙化集中(在1 cm×1 cm区域内的钙化数量超过21个),而良性乳腺病变的主要影像学特征为边缘局限的肿块。

【关键词】乳腺;病变;数字化乳腺X线图像;钙化;乳腺良性病变X线图像;乳腺恶性病变X线图像
【中图分类号】R814 **【文献标志码】**A **【文章编号】**1005-202X(2016)10-0973-09

【收稿日期】2016-03-12
【基金项目】山东省自然科学基金(ZR2015HL095);泰安市科技发展计划(2015NS2159);泰山医学院博士启动基金(20072009)
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