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*Original Article*

# Ultrasonographic characteristics and BI-RADS-US classification of BRCA1 mutation-associated breast cancer in Guangxi, China

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**Abstract:** Objective: To retrospectively analyze and compare the ultrasonographic characteristics and BI-RADS-US classification between patients with BRCA1 mutation-associated breast cancer and those without BRCA1 gene mutation in Guangxi, China. Methods: The study was performed in 36 lesions from 34 BRCA1 mutation-associated breast cancer patients. A total of 422 lesions from 422 breast cancer patients without BRCA1 mutations served as control group. The comparison of the ultrasonographic features and BI-RADS-US classification between two the groups were reviewed. Results: More complex inner echo was disclosed in BRCA1 mutation-associated breast cancer patients ($x^2$ = 4.741, P = 0.029). The BI-RADS classification of BRCA1 mutation-associated breast cancer was lower (U = 6094.0, P = 0.022). Conclusions: BRCA1 mutation-associated breast cancer frequently displays as microlobulated margin and complex echo. It also shows more benign characteristics in morphology, and the BI-RADS classification is prone to be underestimated.

**Keywords:** Breast cancer, ultrasonography, elastography, BRCA1 gene, mutations

## Introduction

Breast cancer is the first female malignant tumor incidence in the developed countries [1-3]. As one of the important means for early diagnosis of breast cancer, ultrasound can be performed real-time, dynamic, multiple planes scanning, and can clearly display levels of mammary gland structure.

American college of radiology (ACR) presented Breast Imaging Reporting and Data System (BI-RADS) [4] to standardize and normalize the imaging features description and diagnosis classification of breast lesions. Although ACR put forward that class 4 lesions should be subdivided into 4A, 4B and 4C, but specific segmentation criterion has not been put forward [5]. Thus, it is necessary to investigate the main ultrasound signs for the diagnosis of breast cancer and improve the classification evaluation accuracy of BI-RADS-US for breast lumps.

Ultrasound Elastography (UE) was first applied in breast examination in 1991 by Ophir [6]. UE has been widely used in the differential diagnosis of benign and malignant breast tumors, and it has higher sensitivity and negative predictive value [7, 8].

Therefore, the aim of this study was to investigate the reliability of ultrasonic imaging characteristics and BI-RADS classification.

## Materials and methods

### *Subjects*

All participants were given written informed consent with details of the study. Ethical approval was granted from ethics committee of Guangxi Medical University. A total of 987 patients with breast lumps were hospitalized in the gastrointestinal and gland surgery in the first affiliated hospital of Guangxi medical university before surgery or biopsy between May 2010 and December 2012. All patients accepted bilateral breast and axillary ultrasound examination by Dr. Zhixian Li (PhD, a professional ultrasonic diagnose doctor with 30 years

**Table 1.** Ultrasonic imaging characteristics of BRCA1 mutation-associated breast cancer

| Ultrasound features | Group | | $X^2$ | *P* |
|---|---|---|---|---|
| | BRCA1 mutation* (n = 36) | Without BRCA1 mutation (n = 422) | | |
| Form | | | | |
| Oval | 6 (16.7) | 33 (7.8) | 2.294[a] | 0.130[b] |
| Irregular | 30 (83.3) | 389 (92.2) | | |
| Margin | | | | |
| Microlobulated | 18 (50.0) | 137 (32.5) | 4.671 | 0.097 |
| Burr or crab-liked | 12 (33.3) | 177 (41.9) | | |
| Others | 6 (16.7) | 108 (25.6) | | |
| Internal echo | | | | |
| Low echo-level | 28 (77.8) | 383 (90.8) | 4.741[a] | 0.029[b] |
| Mixed echo | 8 (22.2) | 39 (9.2) | | |
| The rear echo | | | | |
| Attenuation | 13 (36.1) | 203 (48.1) | 1.915 | 0.166 |
| Constant, enhance or mixed echo | 23 (63.9) | 219 (51.9) | | |
| Direction | | | | |
| Parallel to the skin | 34 (94.4) | 397 (94.1) | 0.000[a] | 1.000[b] |
| Unparallel to the skin | 2 (5.6) | 25 (5.9) | | |
| Calcification | | | | |
| Microcalcification | 18 (50.0) | 257 (60.9) | 1.643 | 0.200 |
| No calcification or big calcification | 18 (40.0) | 165 (39.1) | | |
| Mass inside blood flow | | | | |
| 0 to I | 8 (22.2) | 67 (15.9) | 0.975 | 0.323 |
| II to III | 28 (77.8) | 355 (84.1) | | |
| Elastic score | | | | |
| 1 to 3 | 4 (11.1) | 30 (7.1) | 0.300[a] | 0.584[b] |
| 4 to 5 | 32 (88.9) | 392 (92.9) | | |

Footnotes: *: 7 cases of BRCA1 gene same-sense mutation were eliminated; [a]: chi-square value correction; [b]: *P* value correction.

**Table 2.** BI-RADS classification of BRCA1 mutations related breast cancer

| BRCA1 mutation | Number | Original BI-RADS | | | | | Mann-Whitney U | P |
|---|---|---|---|---|---|---|---|---|
| | | 3 | 4A | 4B | 4C | 5 | | |
| Yes | 36 | 3 | 4 | 5 | 6 | 18 | 6094.0 | 0.022 |
| No | 422 | 3 | 11 | 65 | 70 | 273 | | |

of experiences), and they had complete clinical and pathological data and did not receive surgery or biopsy and accepted radiotherapy or chemotherapy before surgery.

After confirmation by postoperative pathological results and DNA detection, a total of 36 lesions from 34 BRCA1 mutation-associated breast cancer patients (7 cases of same-sense mutation were excluded) were included. The control group was consisted of 422 lesions from 422 breast cancer patients without BRCA1 mutations for the same period.

We retrospectively analyze and compare the differences of the ultrasonographic characteristics and BI-RADS classification between lesions in BRCA1 mutation-associated breast cancer group and group without BRCA1 mutation.

*Ultrasound*

One week preoperatively, GE LOGIQ E9 color ultrasonic diagnostic instrument and frequency 6~15 MHz probes were used to conduct examinations. All ultrasonic characteristics of the lesions and with or without axillary enlarged lymph nodes, etc, were recorded and analyzed

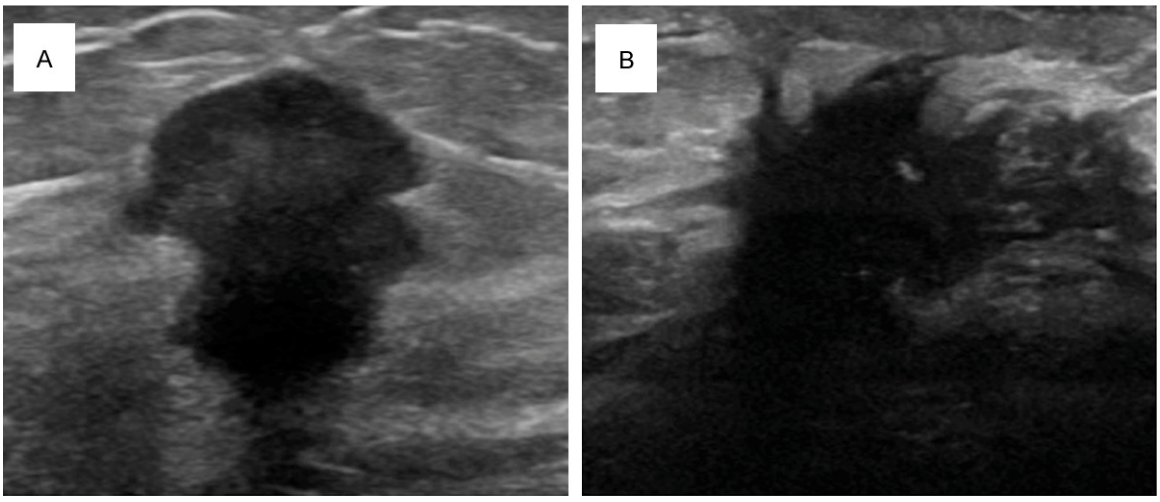


**Figure 1.** A: BRCA1 mutation-associated breast cancer tends to be benign lumps in the performance of form, the most common feature is microlobulated; B: Breast cancer without BRCA1 mutation is the more common as Burr or crab-liked.

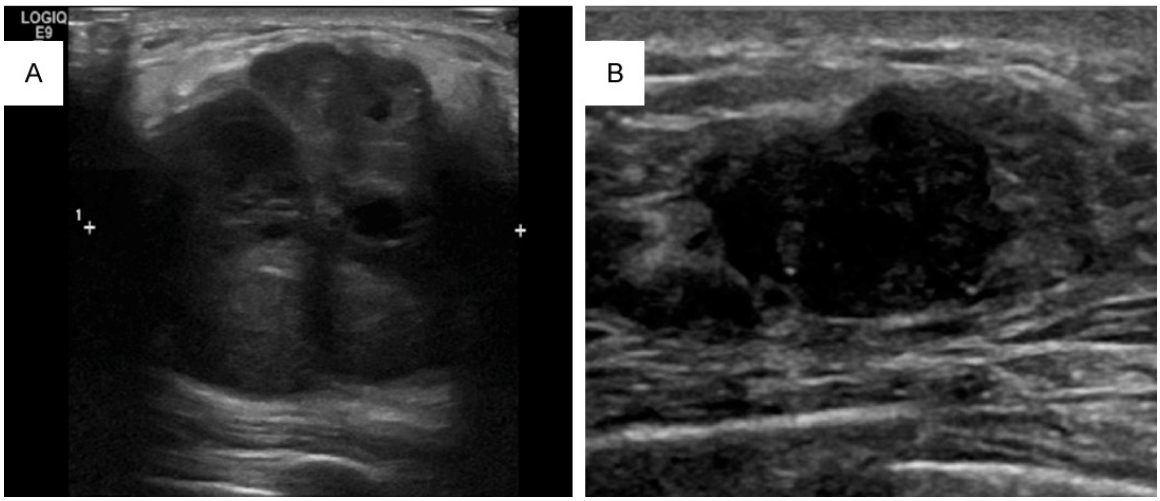


**Figure 2.** A: The inside ultrasonic performances of the BRCA1 mutation-associated lesions tend to appear with liquefaction necrosis, and preform as mixed echo; B: The inside ultrasonic performances of the breast cancer without BRCA1 mutation tend to appear with hypoechoic or no liquefaction necrosis.

according to the BI-RADS standard. Internal and peripheral blood supply of the lumps were observed by CDFI [9]. UE model was applied to detect hardness characteristics of the lumps.

*Statistical analysis*

Statistical program for social sciences (SPSS) software package version 18.0 (Chicago, IL, USA) was used to perform all the statistical analyses.

The mean ± standard deviation ($\bar{x}$ ± S) was used for representing measurement data, and in comparison between groups, two independent sample t tests were applied. Enumeration data was expressed as cases or percentage. Chi-square test was used in comparison between groups. The group comparison between ranked data was applied by Mann-Whitney U test; the difference was statistically significant was represented by $P < 0.05$.

## Results

*Ultrasonic imaging characteristics of BRCA1 gene mutation-associated breast cancer*

For 36 lesions of 34 BRCA1 mutation-associated breast cancer patients (excepted for 7 cases

of same-sense mutation), 16.7% (6/36) had forms of oval; 50.0% (18/36) had microlobulated margin; 22.2% (8/36) had liquefaction inside the tumors, and characterized by mixed echo; 36.1% (13/36) had posterior echo attenuation of the tumors; 5.6% (2/36) did not parallel to the skin; 50.0% (18/36) had microcalcification inside the tumors; 77.8% (28/36) had grade II to III blood flow inside the tumors; 88.9% (32/36) had UE scored 4 to 5 points of the tumors (**Table 1**). Compared with breast cancer without BRCA1 mutation, BRCA1 mutation-associated breast cancer appeared more of mixed echo inside the tumors ($x^2 = 4.741$, $P = 0.029$).

For the 36 cases of BRCA1 mutations related breast cancer lesions, BI-RADS 3, 4a, 4b, 4c and 5 classes were 8.3% (3/36), 11.1% (4/36), 13.9% (5/36), 16.7% (6/36), and 50.0% (18/36), respectively; for the 422 cases without BRCA1 mutation lesions BI-RADS 3, 4a, 4b, 4c and 5 classes were 0.7% (3/422), 2.6% (11/422), 15.4% (65/422), 16.6% (70/422), and 64.7% (273/422), respectively. BI-RADS classification of BRCA1 mutation-associated patients was statistically lower than those without BRCA1 mutation ($U = 6094.0$, $P = 0.022$) (**Table 2**).

## Discussion

*The imaging characteristics of BRCA1 mutations-associated breast cancer*

Shape and edge characteristics of BRCA1 mutations-associated breast cancer lumps: in 36 cases of BRCA1 mutations-associated breast lumps, 16.7% (6/36) tumors had forms for oval, while 7.8% (33/422) shaped oval in the group without BRCA1 mutation. The trend of presenting form performances as benign breast lumps in BRCA1 mutations-associated breast cancer lumps could be seen. It is worth noticing that in 36 cases of BRCA1 mutation-associated breast cancer lumps, and the most common edge was microlobulated, 50.0% (18/36) (**Figure 1**), followed by burr or crab-like, 33.3% (12/36); While the most common breast lumps edge was burr or crab-like, 41.9% (177/422), followed by microlobulated, 32.5% (137/422) in group without BRCA1 mutation. It might be associated with BRCA1 mutations in breast cancer biological characteristics. Due to some benign tumors such as fibroadenoma and lobulated edge, there were certain difficulties in differential diagnosis.

Ultrasonic characteristics inside the lesions and rear echo of BRCA1 mutation-associated breast cancer: The inside ultrasonic performances of the BRCA1 mutation-associated lesions tend to appear with liquefaction necrosis, and preform as mixed echo (**Figure 2**). At the same time, the BRCA1 mutation rate was 17.0% (8/47) in breast cancer lumps with mixed echo inside them, which was much higher than lumps with low echo-level or without liquefaction necrosis inside. The mechanism of BRCA1 mutations-associated breast lesions tending to appear with liquefaction necrosis remained to be further studied, but it also prompted us to suggest that breast cancer patients with liquefaction necrosis inside the lumps should conduct BRCA1 gene mutation detection.

The rear echo characteristics of the mass was closely related to the mass internal composition [9]. In this study, 63.9% (23/36) BRCA1 mutations breast lumps were presented with enhancement, unchanged or mixed rear echo (**Figure 3**); while in group without BRCA1 mutation cases, 51.9% (219/422) lumps were presented with enhanced, unchanged or mixed rear echo, and the former was higher than the latter, but there was no significantly statistical differences.

Internal calcification features of BRCA1 mutation-associated breast cancer: Kass et al [10] found that compared to group without BRCA1 mutation, fewer BRCA1 mutation-associated lumps appeared with internal microcalcification. 50.0% (18/36) cases appeared with internal microcalcification in the BRCA1 mutation-associated breast cancer lumps; and 60.9% (257/422) cases appeared with internal microcalcification in the group without BRCA1 mutation lumps; the former calcification detection rate was slightly lower than the latter.

The growth direction, CDFI and UE features of BRCA1 mutation-associated breast cancer lumps: the statistical difference between ultrasonographic features of the growth direction, CDFI and UE in BRCA1 mutation-associated breast cancer and those in group without BRCA1 mutation was not significant.

BI-RADS classification of BRCA1 mutations-associated breast cancer: Mesurolle et al. [11] founded that compared with BRCA1 mutation-associated breast cancer and group without BRCA1/2 mutation, the BRCA1 mutation-asso-

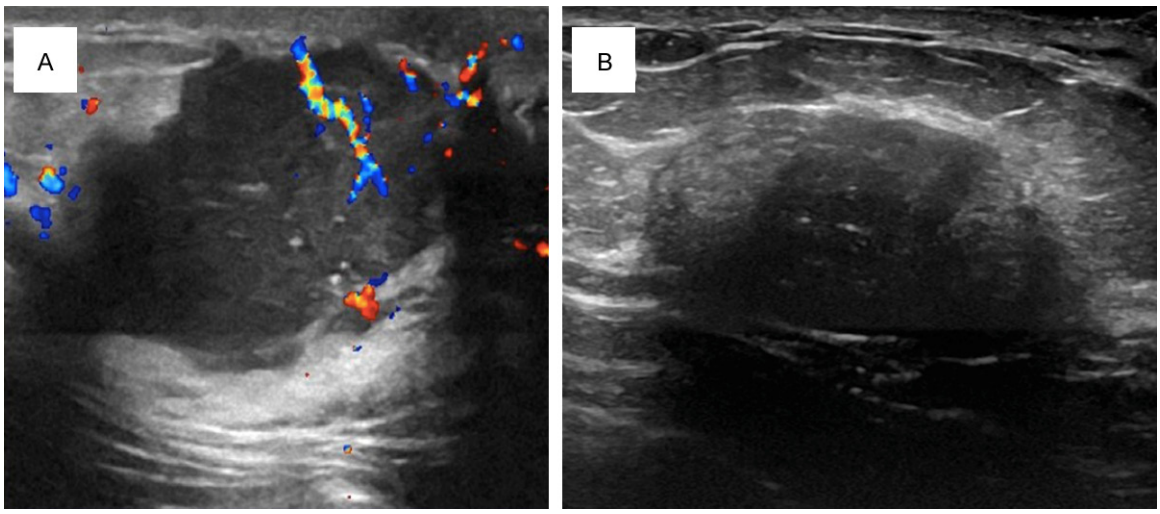


**Figure 3.** A: BRCA1 mutation-associated breast cancers are more likely to present with enhancement, unchanged or mixed rear echo; B: Breast cancer without BRCA1 mutation are more likely to present with enhanced, unchanged or mixed rear echo.

ciated breast cancer lumps appeared to have less malignant signs, and mostly diagnosed as BI-RADS class 4 lesions, but fewer BRCA1 mutation-associated breast cancer lump were diagnosed as BI-RADS class 3 lesions. In this study, the BI-RADS classification of 36 cases of BRCA1 mutation patients were obvious lower than patients without BRCA1 mutation ($U = 6094.0$, $P = 0.022$); In BRCA1 mutation patients, BI-RADS class 5 lesions were the most, accounted for 50.0% (18/36), followed by the BI-RADS class 4 lesions, 41.7% (15/36), among them class 4A, 4B, 4B were 4, 5 and 6 cases respectively; BI-RADS class 3 lesions only accounted for 8.3% (3/36).

Some researches [12] showed that the molybdenum target inspection results were not ideal for high-risk breast cancer female to take once half a year. Although breast MRI has high sensitivity and accuracy, but it was more expensive. Ultrasound is economic, simple, and beyond radioactive injury, which is more acceptable for patient, especially that UE has important application value in the early diagnosis of small breast cancer. Therefore, for BRCA1 mutation carriers, we suggest applying ultrasound examination, which can improve the detection rate of early stage of breast cancer.

In conclusion, BRCA1 mutations-associated breast cancer shows different ultrasonographic features between groups with or without BRCA1 mutations: the former usually appears to be microlobulated rather than burr or crab-like edges, and liquefaction necrosis usually appears inside the lump and performs to be mixed internal echo; and the BI-RADS classification is obvious lower than the latter group.

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## Disclosure of conflict of interest

None.

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