

# The Correlation between Conventional Two-Dimensional Ultrasound Combined with Elastography and Histopathological Grading of Ductal Carcinoma in Situ

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**Abstract:** Objective To investigate the correlation between conventional two-dimensional ultrasonographic features of ductal carcinoma in situ (DCIS) of the breast and its combined elastic (UE) and clinical development. Methods From April 2016 to April 2019, 138 patients with DCIS confirmed by operation and pathology were enrolled in this study. All patients underwent routine two-dimensional ultrasound examination. The ultrasound traditional practices of DCIS (including the presentation or observation of masses, certification and ultrasound traditional typing), elastic hardness score and its relationship with pathological grading were analyzed. Results Among 138 patients, 78 were mass type, 60 were non-mass type, 97 were calcified type and 41 were non-calcified type. UE score showed that none of 138 DCIS patients had 1 and 2 scores. The elastic hardness scores of lump with calcification type, lump without calcification type, non-lump with calcification type, non-lump with calcification type and non-lump with calcification type were 3.04%, 36.73%, 61.22% and 10.34%, 55.17%, 34.48% per cent and 4.17%, 39.58%, and 25.00%, 56.25 per cent and 33.33%, 41.67 per cent respectively. The differences in elastic hardness scores of the four ultrasound types were statistically significant ( $P < 0.05$ ). The low, medium and high levels of tumor group and non-tumor group were 34.52%, 32.05%, 33.33%, 6.67%, 40.00 and 53.33%, and 53.33%, respectively, with statistically significant differences ( $P < 0.05$ ). The low, medium and high levels of calcification group and non-calcification group were 14.43%, 39.18%, 46.39%, 41.46%, 26.83% and 31.71%, respectively. The differences between the two groups were statistically significant ( $P < 0.05$ ). There were 14.29%, 36.73%, and 34.48%, 48.98 per cent 44.83%, and 16.67%, 20.69 per cent 33.33%, 50.00 and 50.00%, 16.67% and 33.33% of low, medium and high grades of mass with calcification, mass without calcification, non-mass with calcification and non-mass with calcification, respectively ( $P < 0.05$ ). The elastic hardness scores of low, middle and high grades were 55.56%, 11.11%, 33.33 and 34.48%, 33.33 39.66%, and 8.45%, 25.86 per cent 35.21% and 56.34%, respectively, with significant differences ( $P < 0.05$ ). Conclusion DCIS conventional two-dimensional ultrasonography and elastography are significantly correlated with clinicopathological grading.

## 1. Introduction

Mammary duct carcinoma in situ (ductal carcinoma in situ, DCIS) is a malignant, proliferative, clonal lesion. It is reported that the proportion of DCIS in invasive breast cancer cases in Europe and the United States has increased from less than 5% to 20%~30%, while the detection rate of domestic DCIS is only 7.80% and 18.80%<sup>[1]</sup> According to previous reports, the lesions of epithelial cells in the mammary duct DCIS, often do not break through the basement membrane and invade the interstitial tissue, and do not have the ability to infiltrate and invade the local vasculature to induce metastasis. Some studies have shown that DCIS is a precursor lesion of invasive breast cancer, and the risk of developing invasive breast cancer is 8~11 times that of normal people. DCIS current standard therapies include radiation therapy, local breast conserving surgery, total breast resection and/or endocrine therapy, and epidemiological findings DCIS surgical outcomes are affected by the nuclear level, so accurate judgment of DCIS histopathological grade is a key

indicator of their choice of treatment, and because it is related to the risk of invasive carcinoma, it is particularly important for patients to choose the best treatment option<sup>[2]</sup>. Ultrasound is considered to be a repeatable, non-invasive screening method, has been widely used for breast examination and is easily accepted by patients, but there have been few reports of DCIS, especially in combination with ultrasound elastography (ultrasonic elastography, UE). Therefore, this paper aims to explore the correlation between DCIS ultrasound findings and application UE diagnosis and pathological grading in order to guide the diagnosis and treatment of early breast cancer.

## **2. Information and Methodology**

### **2.1 General Information**

From April 2016 to April 2019, 138 DCIS patients confirmed by surgery and pathology were admitted to our hospital, Retrospective analysis, Approved by the Medical Ethics Committee of our hospital. Inclusion criteria :1 were confirmed by pathology after surgical resection; 2 Women; No serious cardiovascular and cerebrovascular diseases and major organ dysfunction; 4 Informed consent; 5 Clinical data are complete. Exclusion criteria :(1) Biopsy or pathological results confirmed that the lesion was invasive carcinoma; 2 pathological examination showed DCIS with microinvasive or invasive carcinoma invasion; History of chest radiotherapy; 4 before entering the group received endocrine therapy, chemotherapy, radiotherapy and other anticancer treatment; 5 Complicated with metaplastic carcinoma, mucinous adenocarcinoma and other malignant lesions. 138 patients aged 28~80, Average ( $52.40 \pm 10.84$ ) years; Maximum mass diameter 0.60~5.70 cm, Mean ( $2.50 \pm 1.23$ ) cm; Location :70 cases of left breast, 68 cases of right breast; Mass site :58 cases in the upper quadrant, 41 cases in the upper quadrant, 19 cases in the lower quadrant, In 14 cases, 6 cases by areola.

### **2.2 Method**

Ultrasonic examination using Hitachi HI VISION Preirus ultrasonic diagnostic instrument, equipped with elastic imaging software, bilateral mammary gland and bilateral axillary examination, high frequency linear array probe, probe frequency 9~14 MHz. Supine position, natural abduction of both arms, head-shaped, bilateral breast and armpit full exposure. Based on the conventional two-dimensional ultrasound mode, the nipple was taken as the center, and the quadrant area and bilateral armpit of the breast were continuously radiated to observe the location, size, shape, aspect ratio, boundary, internal echo, calcification and other basic conditions. The gain, depth and focus were adjusted according to the location of the lesion, so that the image display could achieve the best effect. Then switch to UE mode, ask the patient to breathe quietly, put the probe vertically on the skin, apply mild vibration, vibration stroke should not exceed 1 mm, probe gently touch the skin, use fine vibration and rapid circulation. select areas of interest, including areas from the subcutaneously to the pectoralis major (not covering ribs, lungs), were selected. Pay attention to select the wide display area of interest, ensure that the lesion does not exceed 1/4 of the area of interest, observe the two-dimensional ultrasound and the corresponding elastic imaging, refer to Japanese breast and Thyroid gland Ultrasound Society (JABTS) in 2003 In the published ultrasound guidelines Proposal submitted Of course JABTS classification system<sup>[3]</sup> According to the features of shape and margin distribution, there are four types: mass with calcification, mass without calcification, non-mass with calcification, non-mass without calcification.

The 1.2.2 elastic hardness score was assessed by two high-year-old ultrasound doctors by blind method, and the elastic score (Tsukuba score) advocated by the Japanese Tsukuba was 5 points<sup>[4]</sup> to score the benign and malignant elastic images of the lesions, 1~5 showed that the elastic coefficient of lesion tissue relative to normal breast tissue was from small to large, Among them ,1~3 are relatively soft tissue, It is benign; 4~5 divided into relatively hard tissue, It is malignant. According to the UE color image line color pattern diagnosis, And combined with the evaluation score line qualitative judgment, Describe the distribution of 1~5 colors, 1~5 points indicating soft to hard tissue, The colors are red → yellow → green → blue; Among them, (1) The whole or most of

the lesions were green; It shows green around the lesion, The center is blue; The results showed that the proportion of blue and green in the lesion area was similar; Four points showed a small amount of green in the lesion, Mostly blue; Five points showed that the lesions were basically blue, The interior is not accompanied or accompanied by green.

After 1.2.3 pathological examination, the specimens were removed and fixed by formalin. After embedding, slicing, hematoxylin and eosin staining, two experienced pathologists used double-blind method to read and diagnose the lesions. DCIS Pathology Classification<sup>[5]</sup>The DCIS were divided into three categories according to the degree of nuclear heterogeneity, necrosis, mitosis and calcification in the lumen :(1) low level: uniform nuclear size, uniform chromatin, non-significant nucleolus, rare mitotic image ;(2) middle level: similar to low-grade DCIS cell composition, but not shaped, necrotic in the lumen, some middle-grade nuclei, occasionally nucleolus, coarse chromatin; sometimes accompanied by small calcification of high-grade or low-grade DCIS ;(3) high level: highly typical change to powdery necrosis.

### 2.3 Observation Indicators

DCIS sonographic findings (including presence or absence of mass, calcification and ultrasound typing), elastic hardness scores and their relationship with pathological grading were observed.

### 2.4 Statistical Methods

Using SPSS19.0 software to process the above data, the counting data is represented by percentage (%), and the  $\chi^2$  between groups is obtained 2 Test ;( $\pm$ s) to represent the measurement data, between groups t value test.  $P < 0.05$  was statistically significant.

## 3. Fruit

### 3.1 Dcis Ultrasound Findings

All patients successfully completed DCIS tests, According to the presence or absence of a mass, In the mass group ,78 cases, In 56 cases (71.79%), 22 cases (28.21%), Parallel growth (aspect ratio  $<1$  or  $=1$ )63(80.77%), 15 cases (19.23%) of nonparallel growth (aspect ratio  $>1$ ); Non-mass group ,60 cases, Catheter dilatation in 2 cases (3.33%), 43 cases (71.67%), Structural distortion in 15 cases (25.00%). There were 97 calcified cases and 41 calcified cases, Mass with calcification in calcified group (all showed microcalcification), Catheter dilatation with calcification in 1 case (1.03%), Structural distortion with calcification in 14 cases (14.43%), Low echo area with calcification in 30 cases (30.93%), There were 3 cases with dot strong echo (3.09%).

### 3.2 Dcis Analysis of Elastic Hardness Score of Four Ultrasound Manifests

Ultrasound classification showed that 138 DCIS patients had mass with calcification type 49 cases, mass without calcification type 29 cases, non-mass with calcification type 48 cases, non-mass without calcification type 12 cases. UE score showed that there were no 1 and 2 points in 138 DCIS patients.3,4,5 2.04%,36.73%,61.22% and 10.34%,55.17%,34.48% and 4.17%,39.58%,56.25% and 25.00%,41.67%,33.33%, Four types of ultrasonic elastic hardness scores were statistically significant ( $P < 0.05$ ), See table 1.

Table 1 Dcis Relationship Between Ultrasonic Typing and Elastic Hardness Score [n (%)]1

Ultrasonic typing	3 minutes	4 minutes	5 minutes	$\chi^2$	$P$
Mass with calcified type (n =49)	1(2.04)	18(36.73)	30(61.22)	13.950	0.030
Mass without calcification (n =29)	3(10.34)	16(55.17)	10(34.48) <sup>①</sup>		
Non-mass with calcified type (n =48)	2(4.17)	19(39.58)	27(56.25)		
Non-mass without calcification (n =12)	3(25.00)	5(41.67)	4(33.33)		

Note: Compared with mass with calcification type, ① $P < 0.05$

### 3.3 Dcis Relationship between Ultrasound Findings, Elastic Hardness Score and Pathological Grade

Among 138 DCIS patients, Pathology was classified as low grade 31, Middle level 49 cases, High level 58 cases. The low, middle and high grade of mass group and non-mass group were 34.52%,32.05%,33.33% and 6.67%,40.00%,53.33%, difference between the two groups was statistically significant ( $P < 0.05$ ). The lower, middle and higher grades of calcified group and non-calcified group were 14.43%,39.18%,46.39% and 41.46%,26.83%,31.71%, difference between the two groups was statistically significant ( $P < 0.05$ ). The low, middle and high grades of mass with calcification, mass without calcification, non-mass with calcification, non-mass without calcification were 14.29%,36.73%,48.98% and 34.48%,44.83%,20.69% and 16.67%,33.33%,50.00% and 50.00%,16.67%,33.33%, Four types of ultrasound were statistically significant ( $P < 0.05$ ).The elastic hardness scores were 55.56%,11.11%,33.33% and 34.48%,39.66%,25.86% and 8.45%,35.21%,56.34%, difference was statistically significant ( $P < 0.05$ ). See table 2.

Table 2 Dcis Relationship Between Ultrasonic Findings, Elastic Hardness Score and Pathological Grade [n (%)]].1

Ultrasound findings	Low Level	Middle level	High level	$\chi^2$	P
No mass				15.624	0.000
Mass	27(34.52)	25(32.05)	26(33.33)		
Non-mass	4(6.67)	24(40.00)	32(53.33)		
Calcification				12.089	0.002
Calculated	14(14.43)	38(39.18)	45(46.39)		
No calcification	17(41.46)	11(26.83)	13(31.71)		
Ultrasonic typing				14.733	0.022
Mass with calcified type	7(14.29)	18(36.73)	24(48.98)		
The mass is not calcified	10(34.48)	13(44.83)	6(20.69)		
Non-mass with calcified type	8(16.67)	16(33.33)	24(50.00)		
Non-mass without calcification	6(50.00)	2(16.67)	4(33.33)		
Elastic Hardness Score				23.343	0.000
3 minutes	5(55.56)	1(11.11)	3(33.33)		
4 minutes	20(34.48)	23(39.66)	15(25.86)		
5 minutes	6(8.45)	25(35.21)	40(56.34)		

#### 4. Discussion

DCIS is a tumor lesion in the mammary duct. It is a proliferative lesion originating from the lobular unit of the terminal duct of the mammary gland. Compared with invasive ductal carcinoma, many biological behavior characteristics are similar, but the former cancer cells have not broken through the basement membrane. According to reports, in a wide range of breast cancer screening countries, the DCIS detection rate of imaging examination methods accounted for more than 85%, about 10% of patients due to clinical symptoms and less than 5% of patients due to other breast diseases surgery, was found in the removal of pathological specimens. Ultrasound is widely used in breast disease examination because of its advantages of no trauma, real time, convenient operation, repeated examination and interventional diagnosis and treatment, especially DCIS, its diagnosis rate is about 75%. At present, it has been proved that it is of great significance to understand the characteristics of DCIS ultrasound sonogram in time, to accurately judge the location of the lesion, to analyze the pathological classification and to evaluate the prognosis.

DCIS ultrasound is complex and diverse, the most common manifestations are mass type and non-mass type. According to Liu Huimin and other reports ,82 patients with simple DCIS showed that the mass type was 60.98%, mainly hypoechoic mass, and a few had cystic solid mixed mass, while the non-mass type was 39.02%, with lamellar hypoechoic area, structural disorder and mild dilatation of catheter. Yu Rong<sup>[6]</sup>also found DCIS common ultrasound features were hypoechoic masses, ductal dilatation, etc. According to the results of this study, the mass group accounted for 56.52% and the non-mass group 43.48%, in which the ultrasound DCIS the mass group showed blurred margin, irregular hypoechoic nodules, or low echo nodules with smooth edges and regular morphology, similar to benign breast lesions. Some reports have shown that the sensitivity and specificity of UE hardness score in the diagnosis of breast malignant lesions are 82.6 and 84.3,

suggesting that UE hardness score has important reference value in differentiating benign and malignant breast masses<sup>[7]</sup> There are also reports that ultrasound findings combined with UE exploration in the diagnosis of mass DCIS sensitivity of more than 80 percent<sup>[8]</sup> In this study, A total of 74 cases of ultrasound showed substantial mass (with or without calcification) with DCIS elastic hardness of more than 4 points, The detection rate was 94.87%, Similar to these studies, The results suggest that ultrasound combined with UE detection, increased hardness of cancerous tissue can improve DCIS diagnosis rate, Reduce the rate of missed diagnosis. Besides, Among the 60 non-mass type DCIS ultrasound findings in this study, 95.65% in this article, It has certain diagnostic specificity.

microcalcification is DCIS characteristic ultrasound, Most of the previous reports used molybdenum target examination as the main auxiliary imaging examination, The sensitivity and specificity of microcalcification were higher, As high as 60%~75%, Most of the microcalcifications on molybdenum target showed branching, fine, segmental or diffuse distribution. Ultrasound is difficult to detect breast adipose tissue and small microcalcification hidden at the edge of the tumor, There is a phenomenon of missed diagnosis. However, the use of high frequency ultrasonic probe has a high display rate of microcalcification, Zhao Min et al confirmed that the detection rate of small calcifications in malignant tumors was 68.5% by high frequency ultrasound, sensitivity of the diagnostic DCIS is as high as 86.8%. In this study, The calcification group accounted for 70.29%, Similar to domestic research results; However, 35.51% of the DCIS with microcalcification showed mass type, Non-mass type 34.78%, The pathological types were mostly middle-high level, In the non-mass group, the hyperechoic appearance was distended duct structure distortion, Dilated catheter lumen with multiple small punctate strong echo, Or just multiple tiny punctate strong echoes, Pathological findings showed moderate to high grade acne necrosis, Because of the characteristic necrosis in the lumen, So it's characteristic, Combined UE exploration calcification group elastic score above 4 points accounted for 96.91%, suggesting that conventional two-dimensional ultrasound combined with UE analysis can improve the diagnosis rate of non-mass DCIS.

Studies have shown that DCIS progression is different, high-level DCIS may develop into poorly differentiated myeloid carcinoma or invasive ductal carcinoma, with a higher risk of local recurrence and distant metastasis, while low-level DCIS may develop into invasive ductal carcinoma with better differentiation. in this study, most of the high-grade DCIS ultrasound showed boundary blurred hypoechoic mass with microcalcification, while the middle and low-grade DCIS mostly showed hypoechoic mass with clear boundary, or cystic solid mixed mass, and the higher grade of microcalcification was less DCIS, indicating that microcalcification DCIS was more malignant and more invasive than non-calcified type. low grade DCIS relatively low invasiveness, slow growth progression and relatively “lazy” biological behavior, so ultrasound image specificity is low.

## 5. Conclusion

To sum up, DCIS pathological classification has some correlation with ultrasonic manifestation, elastic hardness score, some DCIS with no malignant manifestation or with microcalcification DCIS elastic hardness is larger, combined with DCIS ultrasonic manifestation, UE and clinicopathological classification, it plays an important role in improving the diagnosis rate.

## References

- [1] Moriya T, Silverberg SG. Intraductal carcinoma (due carcinoma in situ) of the last. A comparison of pure noninvasiveness factors with those including differential procedures of imported carcinoma. *Cancer*, Vol.74, No.11, pp.2972-2978, 2015.
- [2] Liu Yuqiong, Huang Huifan, Zhang Min, et al. Clinical and pathological analysis of metastatic breast cancer with carcinoma in situ. *pattern Chinese Journal of Pathology*, Vol.47, No.10,

pp.784-785, 2018.

[3] Watanabe T, Yamaguchi T, Tsunoda H, et al. Ultrasound Image Classification of Ductal Carcinoma in Situ (DCIS) of the Breast: Analysis of 705 DCIS Sessions. *Ultrasound in Medicine & Biology*, Vol.43, No.5, pp.918, 2017.

[4] Itoh A, Ueno E, Tohno E, et al. Breast disease: clinical application of US elastography for diagnosis. *Radiology*, Vol.239, No.2, pp.341-350, 2006.

[5] Adler DD, Carson PL, Rubin JM, et al. Doppler ultrasound color flow imaging in the study of breast cancer: Preliminary findings. *Ultrasound Med Biol*, Vol.16, No.6, pp.553-559, 1990.

[6] Yu Rong, Li Shengli, Chen Jian, et al. Differential analysis of ultrasound and histopathological features of calcified and calcified breast ductal carcinoma in situ. *Chinese Journal of Ultrasonic Imaging*, Vol.25, No.6, pp.506-509, 2016.

[7] Liang Xingfen, Li Tianming, Wu Shimei. Diagnostic Value of Ultrasound Elastic Imaging Hardness Score and Area Ratio in Preoperative. of Breast benign and Malignant Mass Laboratory Medicine and Clinic, Vol.13, No.2, pp.89-91, 2016.

[8] Szynglarewicz B, Kasprzak P, Halon A, et al. Preoperatively diagnosed ductal cancers in situ of the breast presenting as even small masses are of high risk for the invasive cancer foci in postoperative specimen. *World J Surg Oncol*, Vol.13, No.1, pp.218-221, 2015.