The Value of Virtual Touch Quantification Combined with Ultrasound BI-RADS Classification in The Differential Diagnosis of Benign and Malignant Breast Tumors

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Abstract  
Purpose: To explore the differential diagnosis value of combined virtual touch quantification (VTQ) and ultrasound BI-RADS classification in benign and malignant breast tumors. Method: VTQ examination were performed in 138 patients with 142 BI-RADS classified as grade 3 and 4 breast masses by ordinary ultrasonography. The acoustic palpation shear wave velocity (SWV), that was VTQ value, was also measured and compared with postoperative pathology, then the differences between the benign and malignant mammary glands were analyzed. Result: The ROC curve area of VTQ in diagnosing malignant breast masses was 0.91 (95%CI: 0.86–0.96). The sensitivity, specificity, accuracy and positive predictive value of the diagnosis of breast malignant tumors with SWV=3.4m/s as the VTQ diagnostic boundary were 82.7%, 78.1%, 82.4% and 85.9%, respectively. The sensitivity, specificity, accuracy and positive predictive value of the diagnosis of breast malignant tumors by ultrasound BI-RADS classification were 85.2%, 78.7%, 82.4%, and 84.1%, respectively. The sensitivity, specificity, accuracy and positive predictive value of parallel diagnosis of breast malignant tumors by VTQ (with diagnosis limit of 3.4m/s) and ultrasound BI-RADS classification were 96.3%, 63.9%, 82.4%, and 78.0%, respectively. Conclusion: VTQ technology and ultrasound BI-RADS classification are helpful for differential diagnosis of benign and malignant breast masses, and their combined application can improve the detection rate of malignant breast tumors.

Key words: BI-RADS Ultrasound Examination; Breast Disease; Virtual Touch Quantification; BI-RADS.

El Valor de la Cuantificación del Tacto Virtual Combinada con la Clasificación de Ultrasonido BI-RADS en el Diagnóstico Diferencial de Los Tumores Mamarios Benignos y Malignos

Resumen  
Objetivo: explorar el diagnóstico diferencial valor combinado de cuantificación (vtq toque virtual clasificación bi - RADS) y ultrasonido en tumores de mama benignos y malignos.Método: vtq examen fueron realizadas en 138 pacientes con 142 bi - RADS clasificado como grado 3 y 4 masas mamarias por ultrasonografía ordinaria. La acustica palpación de velocidad de onda cortante (SWV), que fue vtq valor, también fue medido y comparado con la patología, entonces las diferencias entre las glándulas mamarias benignas y malignas fueron analizados.Resultado: la curva ROC zona de vtq en diagnosticar masas malignas de mama fue de 0,91 (IC del 95%: 0,86 – 0,96).La sensibilidad, la especificidad, precisión y valor predictivo positivo de el diagnóstico de tumores malignos de mama con SWV = 3.8m / s como el diagnóstico se vtq fronteras 82.7%, el 78.1%, el 82.4% y el 85.9%, respectivamente.La sensibilidad, la especificidad, precisión y valor predictivo positivo del diagnostico de ultrasonido de mama tumores malignos por clasificación bi - RADS se 85.2%, el 78.7%, el 82.4% y 84.1%, respectivamente.La sensibilidad, la especificidad, precisión y valor predictivo positivo paralelas de diagnostico de tumores malignos de mama vtq con diagnóstico limite de 3.4m / S) y ultrasonido clasificación bi - RADS se 96.3%, el 63.9%, el 82.4% y 78%, respectivamente.Conclusión: la tecnología de ultrasonido vtq clasificación bi - RADS y son utiles para el diagnostico diferencial de las masas benignas y malignas de mama y su aplicación combinada puede mejorar la tasa de detección de tumores malignos de mama.

Palabras clave: Examen de Ultrasonido Bi-RADS; Enfermedad de Mama; Virtual Toque bi-RADS Cuantificación
1. Introduction

In recent years, studies have shown that the hardness of breast tumors is closely related to the degree of malignancy, and ultrasound elastography has high application value for the differential diagnosis of breast tumor because it can detect the hardness information of the tissue [1]. In previous studies [2,3], the virtual touch quantification (VTQ) value of benign and malignant breast tumors was discussed and studied, and the reports were different at home and abroad. The purpose of this study was to explore the VTQ boundary value of benign and malignant breast tumors and the clinical application value of the hierarchical combined diagnosis with ultrasound BI-RADS classification in order to improve the detection rate of BI-RADS grade 3 and grade 4 malignant tumors which are difficult to distinguish between benign and malignant in ultrasonic BI-RADS classification.

2. Materials and Methods

2.1. Research object

A total of 139 patients aged from 18 to 82 years old, with an average age of (54.6 ± 12.4) years old (54.6 ± 12.4 years), were included in the hospitalized breast surgery at our hospital from October 2013 to June 2015. The nodule size was 0.7 to 4.2 cm and the average size was (1.7 ± 0.3) cm. Among them, there were 138 females and 1 male, all of whom were found to have breast tumors for the first time. The lesions were mainly solid, and the ultrasonic BI-RADS grade of the breast lesions was 3 or 4. Excluding patients undergoing any treatment, if the breast mass less than the size of the sample frame (6mm*5mm) was measured by SWV, the peripheral gland tissue will be included in the sampling frame, and the SWV value was deviate from the actual SWV value of the tumor, so it is excluded. Surgical pathology results were used as the gold standard, and breast malignant lesions confirmed by operation and pathology were case group and benign lesion as control group. All lesions were examined with VTQ. The diagnostic value of conventional ultrasound and VTQ in the diagnosis of breast lesions was evaluated respectively. And the diagnostic value of the combined application of ultrasound BI-RADS classification and VTQ in the diagnosis of breast lesions was evaluated by parallel diagnostic test.

2.2. Instruments and methods

Using a Siemens Acuson S2000 color doppler ultrasound diagnostic device, the linear array probe is 9L4, frequency from 4.0 to 9.0MHz. Two-dimensional ultrasonography of the breast was performed firstly to observe the characteristics of gray-scale ultrasound (morphology, size, margin, boundary, internal echo, posterior echo, etc.) and color Doppler flow characteristics. According to the above ultrasound findings, BI-RADS classification of breast masses was evaluated and recorded. Then switch to the elastography mode, instructed the patient to hold the breath, put the elastic sampling frame in the mass, tried to avoid the coarse calcification and the liquefied necrotic area as far as possible, and carried out VTQ measurements at least 5 different positions, measured 3~5 times in the same position, and calculated the average value. The shear wave speed (shear wave velocity, SWV) was read and recorded, and the examination data and images were preserved. The examination process was performed independently by a chief physician and a chief physician, and the breast lumps were evaluated strictly in accordance with the BI-RADS classification standard [4]. During the operation, the operation error is eliminated. When the shear wave velocity is “X.XX m/s”, it is determined that its velocity exceeds the upper limit of the instrument's detectable velocity of 8.4 m/s, and the velocity value is recorded as 8.4 m/s.

2.3. Statistical analysis

Using SPSS19.0 statistical software, the count data is expressed as mean ± standard deviation, and the measurement data is expressed by rate. The postoperative pathological findings were used as the gold standard to evaluate the diagnostic value (sensitivity, specificity, accuracy, and positive predictive value) of conventional ultrasound for malignant breast masses. Receiver operating characteristic curve (ROC) was used to evaluate the diagnostic value of VTQ for malignant breast lumps and determine the diagnostic boundary, and to evaluate the value of VTQ value after the demarcation point for the diagnosis of malignant breast masses. To further evaluate the diagnostic value of BI-RADS classification and VTQ value in parallel diagnosis of malignant breast masses.

3. Results
3.1. Pathological results

One patient in the enrolled group was excluded because he had undergone breast augmentation surgery and could not judge whether the compression of the prosthesis on the tumor affected the test results. Finally, 142 lesions diagnosed by pathological diagnosis were selected, including 60 benign lesions, 49 fibroadenoma, 8 breast adenopathy, 2 intraductal papilloma (size of lesion 0.6-0.7 cm), 1 lobulated tumor, 82 malignant lesions, 68 infiltrating ductal carcinomas, 9 ductal carcinomas in situ (the lesion size was 0.7-0.9 cm), 2 mucinous carcinomas, 2 medullary carcinomas, and 1 infiltrating lobular carcinoma.

3.2. The diagnostic value of VTQ

The area under the ROC curve for the diagnostic value of VTQ for malignant breast mass was 0.91 (95% CI: 0.86-0.96). The point at the top left corner of the ROC curve was selected as the diagnostic threshold, and the corresponding SWV was 3.4 m/s. 3.4m/s was used as the diagnosis threshold, <3.4m/s was considered benign, and ≥3.4m/s was considered as malignant. Among the 142 tumors, VTQ diagnosed 78 malignant tumors and 64 benign ones. The sensitivity, specificity, accuracy and positive predictive value of VTQ in the diagnosis of breast cancer with SWV=3.4m/s as the diagnostic boundary were 82.7%, 78.1%, 82.4% and 85.9%, respectively. (Figures 1, 2, table 1)

![Figure 1. ROC curve of diagnostic value of VTQ technique for malignant breast masses (VTQ: virtual touch quantification)](image)

**Table 1.** The value of VTQ technique in the diagnosis of malignant breast mass

<table>
<thead>
<tr>
<th>SWV(m/s)</th>
<th>Pathological diagnosis</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Malignant</td>
<td>Benign</td>
</tr>
<tr>
<td>Malignant (≥3.4)</td>
<td>67</td>
<td>11</td>
</tr>
<tr>
<td>Benign (&lt;3.4)</td>
<td>14</td>
<td>50</td>
</tr>
<tr>
<td>Total</td>
<td>81</td>
<td>61</td>
</tr>
</tbody>
</table>

Note: SWV: shear wave velocity

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Figure 2. VTQ images of benign and malignant breast tumors. A: VTQ images of BI-RADS grade 3 mass with SWV of 2.7 m/s; B: Figure A’s pathological findings of mammary fibroma (HE staining, X10); C: VTQ images of BI-RADS grade 4 mass with SWV of 6.54 m/s; D: The pathological findings of Figure C are invasive ductal carcinoma (HE staining, X20).

3.3. Diagnostic value of ultrasound BI-RADS classification

Of the 142 tumors, 82 were diagnosed by ultrasound at BI-RADS level 4 and 60 at BI-RADS level 3. The sensitivity, specificity, accuracy and positive predictive value of ultrasound BI-RADS classification in the diagnosis of malignant breast masses were 85.2%, 78.7%, 82.4% and 84.1% respectively. (Table 2)

<table>
<thead>
<tr>
<th>Ultrasound BI-RADS</th>
<th>Pathological diagnosis</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Malignant</td>
<td>Benign</td>
</tr>
<tr>
<td>level 4</td>
<td>69</td>
<td>13</td>
</tr>
<tr>
<td>level 3</td>
<td>12</td>
<td>48</td>
</tr>
<tr>
<td>Total</td>
<td>81</td>
<td>61</td>
</tr>
</tbody>
</table>

3.4. Diagnostic Value of Ultrasound BI-RADS Combined with VTQ Technique for Malignant Breast Masses

A breast cancer ultrasound BI-RADS classification and VTQ (with a diagnostic threshold of 3.4 m/s) were used as a parallel test for diagnostic tests. In the parallel test, there were 100 malignant masses and 42 benign masses in 142 masses. The sensitivity, specificity, accuracy and positive predictive value of BI-RADS classification and VTQ (3.4m/s as diagnostic value) in parallel diagnosis of breast malignancy were 96.3%, 63.9%, 82.4% and 78%, respectively. (Table 3, Figure 3)
Table 3. Diagnostic Value of Combined VTQ Technique and Ultrasound BI-RADS in Diagnosis of Malignant Breast Masses

<table>
<thead>
<tr>
<th>Parallel test</th>
<th>Pathological diagnosis</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Malignant</td>
<td>Benign</td>
</tr>
<tr>
<td>Malignant</td>
<td>78</td>
<td>22</td>
</tr>
<tr>
<td>Benign</td>
<td>3</td>
<td>39</td>
</tr>
<tr>
<td>Total</td>
<td>81</td>
<td>61</td>
</tr>
</tbody>
</table>

4. Discussion

In recent years, ultrasound elastography and VTQ technology have begun to be used to observe breast lesions [5-7], the quantitative techniques for quantifying the tissue hardness can be quantified by shear wave velocity. Ultrasound elastography is based on the relationship between the elasticity (or hardness) of biological tissue and the biological characteristics of lesions, providing a new way of thinking for the differential diagnosis of breast lesions. The principle of VTQ technology is to produce shear waves with transverse motion after the action of impulse waves, sequence detection of pulse waves collects these subtle changes, the system will account its speed, which is equal to or represents the elasticity of the organization [8]. In addition, VTQ examination is not affected by factors such as tumor depth, and quantitative analysis can also be carried out for breast tumors that are difficult to be detected by palpation [9].

In this study, 3.4m/s was used as the cut-off value for differential diagnosis of benign and malignant breast tumors. The difference of VTQ velocity between benign and malignant tumors was statistically significant (P <0.05). The sensitivity, specificity, accuracy and positive predictive value of the diagnosis of breast cancer were 82.7%, 78.1%, 82.4% and 85.9%, respectively. It is shown that the VTQ technique alone can provide the elasticity information of the lesion and can make a preliminary judgment on the nature of the breast mass. The hardness of the tissue was closely related to the composition. Liquefaction, necrosis and hemorrhage in the malignant tumor will cause the hardness to decrease. The degree of internal fibrosis in the benign tumor or the calcification will increase the hardness. The above situation will lead to missed diagnosis and misdiagnosis of malignant tumor to some extent. For example, the tumor cells in the medullary carcinoma of the breast had a follicular arrangement with less fiber components, so the texture was softer [10]. The SWV of two cases of medullary carcinoma of the breast in this group were 2.50m/s and 1.94m/s, respectively.

In this study, the sensitivity, specificity, accuracy and positive predictive value of ultrasound BI-RADS classification in diagnosing breast malignant tumors were 85.2%, 78.7%, 82.4% and 84.1% respectively. It indicates that this classification method can be used for preliminary diagnosis and differential diagnosis of benign and malignant breast lesions, and it also has certain guiding significance for clinical diagnosis and treatment. However, because of the specificity of the shape, running, and echo characteristics of some benign and malignant lesions in BI-RADS level 3 and 4, for example, inflammatory lesions are also characterized by unclear borders and abundant blood flow, while some malignant lesions are characterized by morphological rules and parallel to the chest wall. Therefore, it is easy to make misdiagnosis of malignant lesions by using conventional ultrasound alone to diagnose benign and malignant breast masses.

The BI-RADS classification standard considers the malignant possibility of BI-RADS grade 3 lesions to be less than 2%. Uematsu et al. [11] reported that 7% of the pathological changes of BI-RADS level 3 were confirmed as malignant, Shi Jian et al. [12] found that 24.14% of the BI-RADS level 3 lesions were malignant. In contrast to histopathology, 12 of the 60 BI-RADS level 3 lesions were malignant lesions, accounting for 20%. Studies [13] have shown that high-grade malignant breast cancers, such as triple-negative breast cancer (TNBC) and familial breast cancer, tend to show the morphological characteristics of benign tumors. In this study, malignant lesions in BI-RADS level 3 included TNBC in 5 cases, which may be the reason for the high proportion of malignant lesions in BI-RADS level 3 lesions in this study. It is suggested that clinicians should be vigilant for the BI-RADS 3 level ultrasound, follow up or take more active diagnosis and treatment. Of the 82 BI-RADS level 4 lesions, 69 were malignant (84%), which was consistent with the proportion of malignant lesions in grade 4 lesions in the BI-RADS grading standard (2% to 95%).

The early detection and correct treatment of breast malignant tumors can effectively improve the survival rate of patients and have a positive effect on improving the prognosis. Therefore, the judgment of the nature of breast tumors is even more important. As an important means of breast examination, ultrasound can find the tumor early, and the ultrasound BI-RADS classification and VTQ technique can also be used to judge the benign and malignant lesions of the breast. However, there are some inadequacies in the judgment of the benign and malignant breast tumor because of the overlapping of the two ultrasonic features and the tissue hardness information, which may cause the misdiagnosis of the malignant lesions. After the combined application of ultrasound BI-RADS and VTQ technology, the sensitivity of ultrasonic examination of breast malignant tumor...
can be improved significantly. It can make up for the shortcomings of low sensitivity and high misdiagnosis rate of single examination, which can effectively improve the detection rate of ultrasound examination of breast malignant tumor, which suggests that the clinician should take a more appropriate treatment for breast masses to avoid the delay of treatment.

References


