# A Preliminary Comparative Study of Young's Modulus Versus Shear Modulus in the Diagnosis of Breast Cancer

*Huaiyu Wu, MD,* Weiyu Liang, MD,* Yang Jiao, MD,* Hong Song, MD,* Quanzhou Peng, MD,† Hui Luo, MD,* Yuanji Zhang, MD,* Jinfeng Xu, MD,* † and Fajin Dong, MD* †*

**Purpose:** The purpose of this study was to compare the diagnostic value of Young's modulus ($E$) and shear modulus ($G$) in the differential diagnosis of benign and malignant breast masses using sound touch elastography (STE) and to explore the relationship between $G$ and $E$ in breast lesions.

**Methods:** A total of 96 consecutive women with 110 pathologically confirmed breast masses were included. All masses were detected by conventional and STE ultrasound. $E_{mean}$, $E_{max}$, $E_{min}$, $E_{SD}$, $G_{mean}$, $G_{max}$, $G_{min}$, and $G_{SD}$ were determined and evaluated for evidence of significant differences between benign and malignant breast masses. Receiver operator characteristics were used to compare the diagnostic efficacy of $E$ and $G$ and to determine the $G$ cutoff value that would aid in the differential diagnosis of breast cancer.

**Results:** $E_{mean}$, $E_{max}$, $E_{SD}$, $G_{mean}$, $G_{max}$, and $G_{SD}$ in cases of malignant breast masses were significantly higher than those in cases of benign masses ($P < 0.05$). There was no significant difference between $E_{min}$ and $G_{min}$ ($P = 0.565$). In applying the $E_{mean}$, $E_{max}$, $E_{SD}$, $G_{mean}$, $G_{max}$, and $G_{SD}$ to the receiver operator characteristics: (1) the area under the curve (AUC) of $G_{mean}$ and $G_{max}$ is greater than the AUC of $E_{mean}$ and $E_{max}$, and the AUC of $E_{SD}$ is equal to the AUC of $G_{SD}$. (2) The sensitivity and specificity were highest when the $G_{mean}$ was 10.14 kPa. They were 84.1% and 80.3% respectively. (3) The sensitivity and specificity were highest when the $G_{max}$ was 52.20 kPa. They were 88.6% and 87.9% respectively.

**Conclusions:** These preliminary results of STE evaluation of breast masses suggest that the diagnostic value of $G$ is greater than $E$. Furthermore, STE is a valuable tool in the differential diagnosis of breast lesions.

**Key Words:** elastic imaging technique, shear modulus, Young's modulus, breast cancer, differential diagnosis

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*Department of Ultrasound, Shenzhen Medical Ultrasound Engineering Center, and †Department of Pathology, Shenzhen People's Hospital, the Second Clinical Medical College of Jinan University, Shenzhen, China.

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Huaiyu Wu and Weiyu Liang shared the first authorship.

Address correspondence to: Fajin Dong, MD; Jinfeng Xu, MD, Department of Ultrasound, Shenzhen Medical Ultrasound Engineering Center, Shenzhen People's Hospital, the Second Clinical Medical College of Jinan University, No 1017, Dongmen North Rd, Shenzhen 518020, China (e-mail: dongfajin@szhospital.com; xujinfeng@szhospital.com).



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Breast cancer is the main cause of cancer-related deaths among women worldwide.[1] Studies[2] have shown that when breast cancer patients undergo early diagnosis and effective treatment, the survival rate can be greatly improved. Unfortunately, inaccurate breast examinations have contributed to a persistently high breast cancer mortality.[3]

Ultrasound (US) has a good specificity and sensitivity in the detection of breast lesions.[4,5] Ultrasound can clearly show the hierarchical structure of breast tissue, can accurately position masses, and offers a dynamic evaluation of its echotexture characteristics and blood flow. Furthermore, compared with the mammography, US is not affected by tissue density, is not radioactive, and is suitable for all age groups, especially young women and pregnant women.[6] Therefore, in clinical work, US has become one of the important techniques for breast examinations.

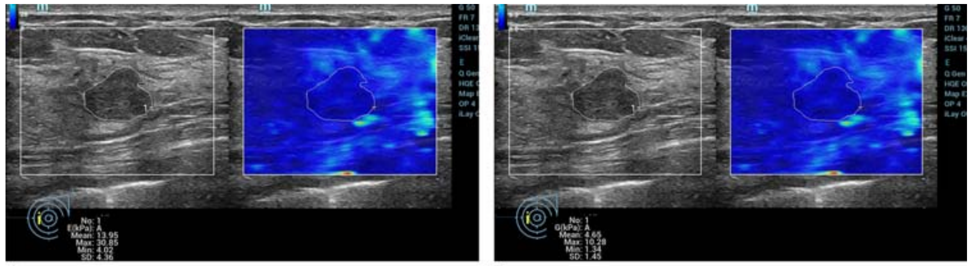
Elastography is a quantitative method for imaging tissue elasticity.[7,8] Young's modulus ($E$) and shear modulus ($G$) are both physical constants derived from this method that are used to assess tissue elasticity. The former is widely used in evaluating the elasticity of isotropic tissue, and the latter reflects the ability of anisotropic tissue to resist shear strain and thus measures the elasticity of anisotropic tissue.

Sound touch elastography (STE) uses the ultrawide beam tracing technique to receive the shear wave data in the whole box of interest at 1 time so as to achieve real-time 2-dimensional shear wave elastic imaging.[9] Sound touch elastography can obtain the quantitative elasticity parameters $E$ and $G$ of the mass and noninvasively assess the stiffness of reactive tissue. In this study, we compared the diagnostic value of $E$ and $G$ and investigated the clinical value of $G$ in the differential diagnosis of benign and malignant breast masses.

## MATERIALS AND METHODS

### Inclusion Criteria

We included solid masses that were found by conventional ultrasound scan and that the maximum mass diameter was less than 25 mm (because of the region of interest maximum 30 mm × 25 mm). No masses were exposed to radiotherapy and chemotherapy, radiofrequency, or biopsy intervention measures before STE examination. Pathology results were available for all specimens.



A B

**FIGURE 1.** Breast fibroadenoma of the left breast in a 32-year-old woman. A, The *E* value of the mass was measured by STE. B, The *G* value of the mass was measured by STE.

## Patients

This retrospective study was approved by the ethics committee, and all patients provided verbal informed consent for the analysis of their imaging data. Based on the inclusion criteria, a total of 96 consecutive patients (110 masses) were included from August 2016 to October 2016 (age range, 14–73; mean ± SD, 38 ± 11 years). All patients underwent conventional and elastographic US.

## Instruments and Research Methods

A Mindray Resona 7 (China) ultrasonic diagnostic apparatus and an 11-3 M linear array probe (frequency range, 3–11 MHz) were used for the research protocol. All US examinations were completed by the same physician who had more than 5 years of experience and was previously trained in the application of elastographic US.

For each patient, the STE and conventional ultrasounds were performed on the same day. Conventional US was performed, and the following characteristics of the mass were recorded: the location, size, shape, border, echotexture, presence or absence of calcifications, rear echotexture, and blood flow. Then, the STE was performed, ensuring that the maximum section of the mass was located in the center of the region of interest. The masses were measured 5 times to obtain the shear wave elastic images, and the data were stored in the instrument. Stored images underwent tracing the mass's margin to automatically determine the mean, max, min, and SD of the *E* and *G*, respectively. The research results were compared with the pathologic findings.

## Statistical Analysis

The data were analyzed using SPSS20.0 software, and the receiver operator characteristic (ROC) analysis was performed by GraphPad Prism 6. Measurement data were analyzed by *t* test (expressed as ± s). $P < 0.05$ was considered statistically significant.

The area under the curve (AUC) was determined by the ROC curve to determine the Young's modulus ($E_{mean}$, $E_{max}$, $E_{min}$, and $E_{SD}$) and shear modulus ($G_{mean}$, $G_{max}$, $G_{min}$, and $G_{SD}$) in benign and malignant breast masses. The AUC of the ROC reflects the accuracy of the diagnostic test.[10] The diagnostic accuracy was judged by comparing the different elasticity parameters and AUC size. The most effective cutoff value was obtained when the sensitivity and specificity were optimal after the comparison.

# RESULTS

## Pathological Results

A total of 110 masses from 96 patients were examined. There were 66 benign breast masses, accounting for 60.0% (66/110) that included 28 cases of aberrations of normal development and involution without fibroadenoma, accounting for 42.4% (28/66), and 36 cases of fibroadenoma, accounting for 54.5% (36/66). The remaining 2 are intraductal papilloma, accounting for 3.1% (2/66). There were 44 malignant masses, which accounted for 40.0% (44/110), 42 of which were infiltrating nonspecific type of carcinoma, accounting for 95.5% (42/44), and 2 breast ductal carcinoma in situ left, accounting for 4.5% (2/44).

## Conventional US Results

Conventional US diagnosed 58 benign breast masses, accounting for 52.7% (58/110), and 52 malignant masses, accounting for 47.3% (52/110).

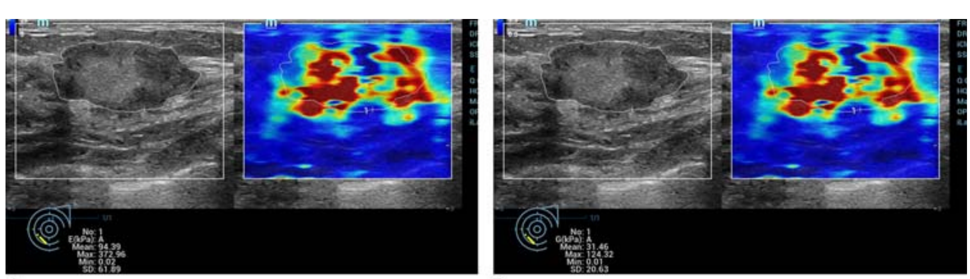


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**FIGURE 2.** Infiltrating nonspecific type of carcinoma in a 41-year-old woman. A, The *E* value of the mass was measured by STE. B, The *G* value of the mass was measured by STE.

**TABLE 1.** Parameters of *E* and *G* in Benign and Malignant Breast Masses

| STE Quantitatively Elastic Parameters | Pathological Result | | |
|---|---|---|---|
| | Benign | Malignant | *P* |
| $E_{mean}$, kPa | 26.01 ± 16.39 | 52.62 ± 25.52 | <0.05 |
| $E_{max}$, kPa | 82.53 ± 66.69 | 257.19 ± 106.62 | <0.05 |
| $E_{min}$, kPa | 7.13 ± 4.92 | 4.33 ± 4.45 | 0.565 |
| $E_{SD}$, kPa | 12.09 ± 8.49 | 35.05 ± 15.63 | <0.05 |
| $G_{mean}$, kPa | 8.68 ± 5.46 | 17.62 ± 8.45 | <0.05 |
| $G_{max}$, kPa | 27.51 ± 22.23 | 88.04 ± 32.91 | <0.05 |
| $G_{min}$, kPa | 2.38 ± 1.64 | 1.44 ± 1.48 | 0.565 |
| $G_{SD}$, kPa | 4.04 ± 2.86 | 11.68 ± 5.21 | <0.05 |

## STE Results

Figure 1 and Figure 2 present the STE results: the $E_{mean}$, $E_{max}$, $E_{min}$, $E_{SD}$, $G_{mean}$, $G_{max}$, $G_{min}$, and $G_{SD}$ values obtained from the benign and malignant masses. The $E_{mean}$, $E_{max}$, $E_{SD}$, $G_{mean}$, $G_{max}$, and $G_{SD}$ values associated with malignant masses were significantly higher than those obtained from the benign masses ($P < 0.05$). However, there was no significant difference in the $E_{min}$ and $G_{min}$ between benign and malignant masses ($P = 0.565$) (see Table 1 for details).

Figure 3 shows the ROC of *E* and *G* diagnosed breast masses. (1) The AUCs of the $E_{mean}$, $E_{max}$, and $E_{SD}$ were 0.862, 0.912, and 0.907, respectively, and the AUCs of the $G_{mean}$, $G_{max}$, and $G_{SD}$ were 0.864, 0.914, and 0.911, respectively. The results demonstrate that the diagnostic accuracy of $G_{mean}$ and $G_{max}$ are higher than that of $E_{mean}$ and $E_{max}$, but $E_{SD}$ is the same as $G_{SD}$. A follow-up study was performed using *G* to determine. (2) When the $G_{mean}$ was 10.14 kPa, the specificity and sensitivity were highest. The sensitivity, specificity, positive predictive value, negative predictive value, positive likelihood ratio, and negative likelihood ratio were 84.1% (37/44), 80.3% (53/66), 74.0% (37/50), 88.3% (53/60), 4.25, and 0.20, respectively. (3) The specificity and sensitivity were highest when the $G_{max}$ was 52.20 kPa. The sensitivity, specificity, positive predictive value, negative predictive value, positive likelihood ratio, and negative likelihood ratio were 88.6% (39/44), 87.9% (58/66), 83.0% (39/47), 92.1% (58/66), 7.33, and 0.13, respectively. Table 2 and Table 3 present the details of the STE and pathology results.

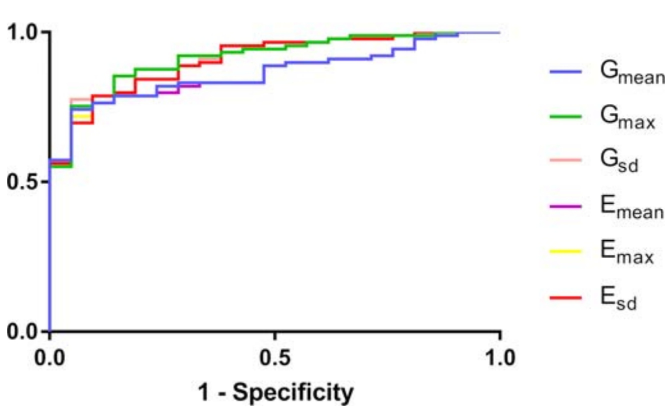


**FIGURE 3.** The ROC curve shows *E* and *G* in the differential diagnosis of breast cancer.

**TABLE 2.** STE $G_{mean}$ Results Compared With Pathological Results

| $G_{mean}$ | Pathology | | |
|---|---|---|---|
| | Benign | Malignant | Total |
| Benign | 53 | 7 | 60 |
| Malignant | 13 | 37 | 50 |
| Total | 66 | 44 | 110 |

## DISCUSSIONS

In 2018, the Chinese National Cancer Center released the latest data[11] revealing that there were approximately 46,600 new cases of breast cancer and 1.13 million breast cancer-related deaths. In 2013, breast cancer was ranked as the number 1 in Chinese women with malignant tumors. Therefore, the early diagnosis of breast cancer and the implementation of effective treatment are even more important.

At present, surgery is the main treatment modality for breast cancer. Breast-conserving surgery is one of the most common types of surgery.[12] Compared with the traditional surgical approach, breast-conserving surgery uses a smaller operative incision and has less of a negative impact on patients' limb function. Existing research[13] shows that, after axillary lymph node dissection, there are 20% arm lymphedema and 24% restricted range of motion in shoulder flexion in the radical modified mastectomy group versus 8% and 7% in the breast-conserving surgery group. Furthermore, because the breast is not removed, the quality of life for patients is improved from both a psychological and physiological perspective.[14]

At present, various studies[15–17] have demonstrated that US is an effective imaging tool for diagnosing breast disease. Sound touch elastography can obtain information about tissue stiffness using the ultrawide beam tracing technique, which can be expressed by 3 kinds of elastic quantitative parameters: Young's modulus (*E*), shear wave velocity (Cs), and shear modulus (*G*). Previously, numerous studies[18–21] showed that *E* and Cs were very effective in differentiating benign from malignant breast lesions. At present, *G* has been applied to evaluate the musculoskeletal system, which has obvious anisotropy on US.[22] In this case, a larger *G* correlates with greater stiffness. However, applying *G* to differentiate benign from malignant breast masses has not been reported.

First, Young's modulus ($E_{mean}$, $E_{max}$, $E_{min}$, and $E_{SD}$) and shear modulus ($G_{mean}$, $G_{max}$, $G_{min}$, and $G_{SD}$) were determined using STE so as to quantitatively study the stiffness of the breast

**TABLE 3.** STE $G_{max}$ Results Compared With Pathological Results

| $G_{max}$ | Pathology | | |
|---|---|---|---|
| | Benign | Malignant | Total |
| Benign | 58 | 5 | 63 |
| Malignant | 8 | 39 | 47 |
| Total | 66 | 44 | 110 |

masses. The results showed that $E_{mean}$, $E_{max}$, $E_{SD}$, $G_{mean}$, $G_{max}$, and $G_{SD}$ values were significantly higher for the malignant than the benign masses ($P < 0.05$). This result is closely correlated with the histopathological components of the masses. Wang et al[23] have shown that fibrous collagen content in malignant breast tumors is significantly higher than that in benign tumors. Jodele et al[24] found that, during tumor progression, tumor matrix collagen expression markedly increases with the gradual deposition and structural changes of collagen. Levental et al[25] showed that, as the process unfolds from normal tissue to precancer masses to tumor formation, cross-linking of collagen in the extracellular matrix occurs in breast cancer. During this process, the breast tumor gradually hardens. Thus, malignant masses are more solid than benign masses. In addition, the pathological components of breast cancer are complicated by the simultaneous development of areas of necrosis within an otherwise solid tumor. This combination of solid and soft areas within the tumor results in a wider range of measurements of stiffness ($E$, 4.33 ± 4.45 to 257.19 ± 106.62; $G$, 1.44 ± 1.48 to 88.04 ± 32.91). Consequently, the SD increases. There were no significant differences in the $E_{min}$ and $G_{min}$ values between the benign and malignant masses. This finding may potentially be explained by tumor characteristics. For example, a tumor that is small or in the early stages of development may have a high degree of differentiation or an atypical collagen formation with masses that are less lower stiff limit overall.[18] The development of local necrosis can lead to a reduction in stiffness that approximates that seen in benign masses. In summary, the degree of elasticity measured in benign and malignant breast masses in this study was consistent with the pathologic findings.

We also compared the diagnostic efficacy of $E_{mean}$, $E_{max}$, $E_{SD}$, $G_{mean}$, $G_{max}$, and $G_{SD}$ values and found that $G_{mean}$ and $G_{max}$ were superior to $E_{mean}$ and $E_{max}$, confirming that $G$ is more suitable than $E$ for evaluating mammary gland masses with anisotropy. $E$ determines the amount of stiffness based on the assumption that human tissue is isotropic. However, human tissue, including breast tumors, shows to be anisotropic.[26,27] Therefore, because $G$ may more accurately reflect the quality of stiffness in breast masses, promoting this approach may lead to a more rigorous assessment of this characteristic in breast lesions.

In this study, 44 malignant masses were identified by the pathology. $G_{mean}$ suggested the presence of malignancy in 37 cases, and $G_{max}$ in 39 cases. Pathological examination identified benign masses in 66 cases; whereas $G_{mean}$ pointed to benign masses in 53 cases, $G_{max}$ suggested 58 cases of benign tumors. Misdiagnoses may have resulted from the presence of necrosis in a malignant tumor causing $G_{mean}$ and $G_{max}$ to fall below the critical value such that STE would suggest a benign mass.

Substantial domestic and international research has supported the diagnostic value of shear wave elastic imaging technology. However, more in-depth study is needed to improve the diagnostic accuracy of US elastography before it can be widely adopted for clinical application and thereby contribute significantly to patient care.

It is important to note that the results of this study are preliminary and that the sample contained few cases of malignancy. The results must therefore be confirmed with future studies that include a larger sample size. To our knowledge, there have been no publications to date evaluating the application of $G$ to measure stiffness in breast masses.

In summary, STE that provides $G$ not only allows ultrasound physicians to obtain quantitative data regarding the degree of stiffness in breast masses but potentially provides more accurate and rigorous elastic quantitative parameters when compared with $E$. Although the application of $G$ in the diagnosis of breast cancer has a high sensitivity and specificity, it cannot be used as the only criterion for making a diagnosis that must rely on a comprehensive assessment of clinical manifestations, conventional US results and other imaging studies. Sound touch elastography is an effective complement to conventional US and can also provide additional information that may aid physicians in their differential diagnosis of breast cancer.

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