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RESEARCH COMMUNICATION

Diagnostic Potential of Strain Ratio Measurement and a 5 Point Scoring Method for Detection of Breast Cancer: Chinese Experience

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Abstract

Aim: To evaluate the differential diagnostic potential of lesion stiffness assessed by the sonoelastographic strain index ratio (SR) and elastographic color scoring system (UE) for breast lesions. Materials and Methods: Three hundred and forty two breast masses (158 benign and 184 malignant) from 325 consecutive patients (mean age 44.2 years; range 16-81)who had been scheduled for a sonographically guided core biopsy were examined with grey scale sonography,doppler sonography and sonoelastography. Each lesion was classified with ACR's BI-RADS assessment category (2, 3 and 4A=Benign and; 4B, 4C, 5=Malignant) and the 5-point scoring system proposed by Itoh et al, with scoring 1-3=benign and 4-5=malignant. Strain and area ratios of each lesion were calculated within the same machine. Histological diagnosis was used as the reference standard. The area under the curve (AUC) and cut-off point were obtained by receiver operating curve and the cross table Fischer Test was carried out for assessing diagnostic value. Sensitivity, specificity, PPV, NPV, accuracy and false-discovery rates were compared. Results: The mean strain ratios for benign and malignant lesions were 1.87 and 7.9 respectively. (P<0.0001). When a cutoff point of 3.54 was used, SR had a sensitivity of 94.6%, a specificity 94.3%, a PPV of 95.1%, an NPV of 93.7% and an accuracy of 94.4%. The AUC values were 0.90 for the 5 point scoring system (UE) and 0.96 for the strain index ratio. The overall diagnostic performance was SR method was better (P<0.05). Conclusions: Strain ratio measurement could be another effective predictor in elastography imaging besides 5 the point scoring system for differential diagnosis of breast lesions.

Keywords: Elastography - strain ratio - breast cancer - differential diagnosis

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Introduction

Breast cancer is the top cancer in women both in the developed and the developing world. One in eight women will be diagnosed with breast cancer in a lifetime in the United States. Despite being the most common cancer, 5-year relative survival rate of breast carcinoma is still over 80% when they are detected in early phase (Brenner et al., 2007). The incidence of breast cancer varies greatly around the world, being comparatively lower in less-developed countries then in the more-developed countries. Though the incidence of breast cancer in china is comparatively lower than the Western countries. But, researches have revealed that the incidence of breast cancer in China has been increasing annually (Tian et al., 2005). Larger cities like Shanghai, Beijing, Tianjing, Wuhan, Guangzhou etc, have higher mortality and morbidity rate then small cities and even higher then to rural areas. In recent years significant increases in the incidence has been reported. The rate of incidence from 1978 (17/100,000 to 52/100,000) to 2009 has been tripled. In China, breast cancer is the second most common cancer but the first most common cancer in the female populations living in the city areas. According to the Ministry of Health, PRC, Shanghai and Beijing are the two larger cities having incidence of 52/100,000 and 45/100,000 respectively. The increasing incidence rate was due to the change of risk, change of life style and change of society rather than the change of population structure and size (Yang et al., 2005). The estimated breast cancer mortality rate has been increased between 1991 and 2005. The increase was sharper in the younger age group than in the older age group (Yang et al., 2004). Similarly, in another study, the analysis of Center for Health Information and Statistics (CHIS) dataset showed that the increasing mortality rate of breast cancer was confined to the younger age group (Yang et al 2003). Both increased risk and change of population structure/size contributed to the increase of mortality rates (Yang et al, .2004). The incidence of breast cancer is increasing in the developing world due to increase life expectancy, increase urbanization and adoption of western lifestyles. Although some risk reduction might be achieved with prevention, these strategies cannot eliminate the majority of breast cancers that develop in low- and middle-income countries where breast cancer is diagnosed in very late stages. Therefore, early detection in order to

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improve breast cancer outcome and survival remains the cornerstone of breast cancer control. Current detection methods include mammography, ultrasound, and magnetic resonance imaging. Each method offers its own benefits but also suffers from limitations. Ultrasound elastography has gained considerable interest as a possible alternative for breast cancer detection in recent years.

The basic principle of elastography is that tissue compression produces displacement within the tissue and that the displacement is smaller in harder tissue than in softer tissue. The displacement produced in real time is superimposed to the B-mode image represented by different color. Till date RTE is not yet used in routine clinical practice, however it has shown to be useful is the differential diagnosis of breast cancer (Zhi et al., 2007; Parajuly et al., 2010), thyroid cancer (Rago et al., 2007) and prostate cancer (Kamoi et al., 2008). In this study we diagnose the breast lesion by 5 point scoring method with color mapping of strain images; benign 1-3 and malignant 4-5. After then, we investigated whether strain ratio measurement method can be applied as another effective predictor in characterizing lesions more precisely.

Materials and Methods

Patients

From February 2010 to August 2011, 325 patients with 342 lesions in the breast were included in the study. Examination was carried out in the tertiary centre of West China i.e. (Huaxi Hospital of West China Medical School), which is also a largest hospital in China. Patients mean age was 44.17years, with a range of 16 to 81 years. All patients were first examined with sonography and those patients with mass were further analyzed with UE. Informed consent for diagnostic procedures was obtained from each patient. All the examinations were performed before any biopsy, fine needle aspirations or surgeries.

Study Design

In each patient, bilateral whole breast sonography was performed in the transverse and longitudinal planes using a Hitachi HA-700 (Hitachi Medical, Tokyo, Japan) US scanner equipped with 7.5-13.0MHz liner- array transducer. Using B-Mode ultrasound, sonographic features of breast lesions (size, shape, margin, internal echogenicity, presence/absence of calcification, posterior acoustic phenomena, anterior posterior-width ratio, and presence/absence of lymph node enlargement, presence/ absence of intra-tumoral blood flow) were prospectively recorded in a computer database system. With these features they were classified to BI-RADS lexicon by single observer (XY), who had 25 years of experience on breast sonography.

Ultrasound elastography was performed simultaneously as the scanner was equipped with sonoelastography unit; hence the stiffness of lesion could be measured using different colors. On B-mode, we displayed the target lesion and moved the ROI (region of interest) around the lesion, making sure that the target tissue occupied no more than one third of the total area of the ROI. To obtain the strain index, a rectangular region of interest (ROI) box was first set to include the area from the subcutaneous fat layer to the superficial portion of the pectoralis muscle layer and to focus on the target mass. Next, the target mass was vertically compressed with very light pressure by the transducer to depict the subcutaneous fat layer as mixed red and green and the muscle layer as blue. The sonoelastographic images were displayed with 256 color mapping from red (softest component) to green (intermediate stiffness) to blue (hardest component) according to the level of strain. On a representative static image, relative strain values of the mass and surrounding normal mammary tissue /subcutaneous fat were measured. The first ROI (A) for the mass strain was manually drawn and placed in the inner margin of a hypoechoic mass. The second ROI (B) for the strain was placed in the normal mammary tissue adjacent to the lesions at a depth similar or to the subcutaneous fat tissue. The strain index, defined as the fat/normal mammary tissue to mass strain ratio, was calculated automatically by an embedded software program in the ultrasound unit. Screen capture images including the measured strain index and areas of the ROI were saved to a picture archiving and communications system for later analysis. Acquisition of the strain index took approximately 2 minutes per case. Those images which did not achieve these criteria were excluded from the study. Importantly to obtain images that were appropriate for analysis, we applied more coupling gel on the skin surface, above the target lesions, so that no any manual pressure interfere with the vibrations (pressure) induced by the sonoelastographic unit. The probe was held lightly and perpendicular to the ROI during the elastography. The elastographic unit was equipped with pressure bar in the lower left of the image. The pressure was kept constant with a range of 3-4 during the acquisition of images.

Image analysis

The final assessment of the lesions as seen on conventional US were classified according to the American College of Radiology Breast Imaging Reporting and Data System (Levy et al., 2007). Findings were classified as following category 2: benign finding; category 3: probably benign finding; category 4: suspicious abnormality (4A: Probability for being benign is high, 4B: less probability for being benign, 4C: high probability for being malignancy). 5: highly suggestive of malignancy.

The elasticity images were evaluated by using the score system described by Itoh et al. (2006), which includes a five point scale: Score 1: even strain over the whole hypoechoic area. The entire lesion is evenly shaded in green, as in the breast tissue. Score 2: strain over most of the hypoechoic area with some areas spared. The hypoechoic area is a mosaic pattern of green and blue. Score 3: strain at the periphery with sparing of the centre lesion. The central part of the lesion is blue, the peripheral part is green. Score 4: no strain over the entire hypoechoic lesion. The entire area is blue. Score 5: no strain over the entire hypoechoic lesion or in the surrounding area .Both the lesion and its surrounding area are blue.

Green indicates medium tissue stiffness, red indicating soft tissue and blue indicating area for hard tissue.

Elasticity images were evaluated according to the score pattern above. Elasticity Score of 1, 2 and 3 was considered as "Benign" and the Score 4, 5 was considered as "Malignant".

After image obtained for 5 score classification system, we used the strain ratio measurement method, which the US machine was equipped with. The strain ratio of the target lesion and the same depth of breast tissue/subcutaneous fat as the reference were measured, which reflected the stiffness of the lesion. Thereafter, we contoured the target lesion as A, and then selected the same depth level of normal breast tissue/subcutaneous fat as B. Then obtained the strain ratio of the lesion B/A, which reflected the lesion stiffness. Similarly, the area of lesion as seen on grey scale sonography represented by A1 was compared to the area of lesion as seen on elastography, represented by A2. Thus area ratio of the lesion A1/A2 is obtained, which reflects that the malignant lesions have increased area in elastogram than for benign lesions (Zhu et al., 2008).

Statistical Analysis

The software package SPSS 16 for Windows software (SPSS Inc, Chicago, IL) was used for statistical data analysis. Interpretation of the various diagnostic procedures was compared with the histological findings with regard to sensitivity, specificity, accuracy, false discovery rate, positive and negative predictive values.

Thus ,we first compared the diagnostic performances of grey scale sonography using the BI-RADS classification and the performances of 5 point scoring system using cross table Fischer`s test. The diagnostic sensitivity, specificity, accuracy, positive and negative predictive value and false discovery rate were calculated. Secondly ,we compared the mean strain ratio of malignant and benign lesions with t-test and compared the strain ratios of different histological types (two-tailed, assuming equal variance). We calculated the diagnostic potentiality of strain ratio index in differentiation of malignant and benign lesions by Receiver Operating Curve (ROC) and was compared it to the 5-Score classification system. The strain index was divided into 5 groups according to range: range 1. 0.0-1.0; range 2, 1.1 to 2.0; range 3, 2.1 to3.0; range 4, 3.1 to 4.0; and range 5, 4.1 and greater. The best cut off point in characterizing the lesion was calculated by Youden Index (Sensitivity +Specificity-1). Two-sided p<0.05 was considered statistically significant.

Results

Pathological Diagnosis

All 342 lesions of 325 patients underwent breast biopsy. The patient mean age was 44.17 years range (16-81). Histological analysis revealed that out of 342, 184 (53.80%) were malignant and 158 (46.20%) were benign. The result showed that fibroadenoma (53.16%) and invasive ductal carcinoma (82.06%) was the commonest benign and malignant lesions respectively. Lesion size ranged from 4 mm to 10.0 cm in maximum diameter. Size for benign lesion range from 4 mm to 10.0 cm and for malignant 8 mm to 9.5 cm

Table 1. Comparative Study of Conventional Sonography (USG), UE and SR (when cut-off point was set to 3.54) in the Differentiation of Mmalignant from Benign Lesions.

Modality	Conventional USG	UE	SR
Sensitivity	91.84(169/184)	77.71(143/184)	94.56(174/184)
Specificity	84.81(134/158)	96.20(152/158)	94.30(149/158)
PPV	87.56(169/193)	95.97(143/149)	95.08(174/183)
NPV	89.93(134/149)	78.75(152/193)	93.71(149/159)
Accuracy	88.59(303/342)	86.25(295/342)	94.44(323/342)
False discovery rate	8.15 (15/184)	22.28 (41/184)	5.43 (10/184)

With regard to sensitivity, conventional sonography was better than the 5 score UE classification system (Table 1). However, sensitivity for characterizing the breast lesions for SR was higher than both the methods; (conventional USG or UE). The specificity of UE was significantly higher than those of conventional sonography, however no significant differences noted in SR and UE (Table 1). The accuracy rate for SR was significantly higher than that of conventional sonography and UE (P<0.005; Table 1). The accuracy rate for conventional sonography was slightly higher than that of UE. The positive predictive value of UE was highest among the SR and sonography. SR method has higher negative predictive value than rest of the methods. Of the total lesions, UE has highest false discovery rate (Table 1). Out of 184 malignant lesions, only 10 lesions (5.43%) were mistakenly diagnosed as benign on SR method.

Strain Ratio of Breast Lesions

Comparing the same depth of breast tissue/subcutaneous fat tissue, the mean strain ratio for malignant lesion was 9.08, ranging from (0.7-37.7) and for the benign lesions mean strain ratio was 1.7, ranging from (0.3-11.15). There were statistically significant differences between the strain ratios of benign and malignant lesions (P<0.0001). The major common histotype lesions were invasive ductal carcinoma (IDC), fibroadenoma and fibrocystic mastopathy. The mean strain ratios for them were 8.9, 1.69 and and 1.67 respectively. There were significant differences of strain ratio between the IDC and fibroadenoma or fibrocystic mastopathy (P<0.00001). But no significant differences between the strain ratios of fibroadenoma and fibro cystic mastopathy noted.

The following below curve (Figure 1) demonstrates the receiver operating curve (ROC) for strain ratio measurement method in characterizing the nature of breast lesion; malignant or benign. The area under the curve (AUC) was 0.962 with 95% CI level ranging from 0.940-0.985. The maximal Youden Index was 0.89 while calculating the best cut-off point. The best cutoff point was 3.54. With this best cutoff point the sensitivity, specificity and accuracy for SR index method was 94.56%, 94.30% and 94.44% respectively.

Comparing of diagnostic performance between the SR measurement method and 5 points scoring system

The Area under the Curve (AUC) of strain ratio measurement method was 0.96 and for the 5 point scoring

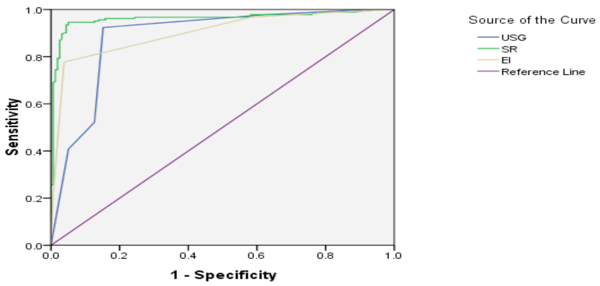

Figure 1. Comparing the ROCs for Strain Ratio Measurement Method, 5 Point Scoring System as Classified by Itoh et al (2006) and Conventional US Modality in Characterizing the Nature of Breast Lesions; Malignant and Benign

method (EI) was 0.90. The difference of their diagnostic performance was statistically significant (P<0.00001). Figure shows the comparison of the ROC of these two diagnostic methods.

With regard to specificity and positive predictive value, no significant difference between the two methods was found. When calculating the highest value of sensitivity and specificity for characterizing the lesions, cut off point of 3.54 was obtained. With the sensitivity of strain ratio measurement method was significantly higher than that of 5-scoring system (P<0.05). The negative predictive value for SR method was highly improved by 15% than that of 5-point scoring system.

Of the total 158 lesions, 48.1% of benign lesions have strain ratio in the range of 1.1-2.0.When taking the cutoff point of 3.54, nine breast lesions have strain ratio greater than 3.54. Most of the malignant lesions with the majority of invasive ductal carcinoma in histotype had strain ratio greater than 4.1 in the range. It clearly shows that there is a difference between the strain ratio for the benign and malignant lesions (P<0.00005).

Diagnostic performance between the SR measurement method 5 points scoring system and conventional US

As shown in the Table 1, different diagnostic performance of three methods in detecting the malignant from the benign lesions is compared by studying through the Receiver Operating Curve (ROC). AUC for SR, UE and USG were 0.96, 0.90 and 0.88 respectively. According to the results obtained, conventional USG showed higher sensitivity (91.8%) than UE (77.7%); 5 -Point Scoring System). Among the three methods, SR was highly sensitive in detecting the cancer. The Specificity of UE was significantly higher than that of conventional USG (P<0.001). However no significant changes of specificity seen among SR method and UE method. Following the same old trained 5-Point scoring method, UE has highest false discovery rate among the three. Out of 184 malignant lesions, SR method missed only 10 malignant cancers.

Regarding distributions of BI-RADS scores for benign and malignant lesions 84.8 %(134/158) of benign lesions were scored (1-3). Benign lesions that were suspected to be malignant on sonography were 24. Among 24, 12 were scored 4B, 8 scored 4C and the remaining 4 were scored 5. Similarly, of the total 184 cancers, except 15, rest of the 169 lesions were scored 4B, 4C and 5. Hence, when we make the cut-off point of 4B as a malignant, the sensitivity of sonography to rule out the benign and malignant lesions according to BIRADS lexicons.

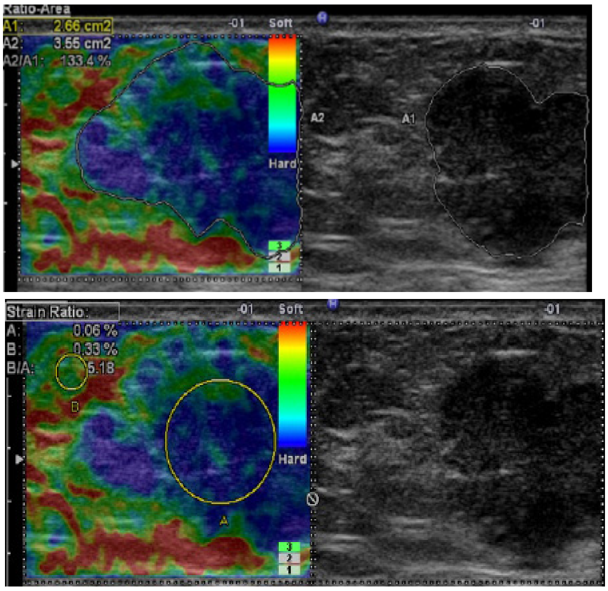

Figure 2 An Invasive Ductal Carcinoma in a 55-year-old Woman. a) Compared to area seen on grey scale (A1) image, UE image revealed a mass with larger area (A2) b) the strain ratio index was 5.18 characterizingmalignancy, but only 3 on 5-point scoring system

Similarly, when we considered the UE score of 1, 2 and 3 as a benign, and 4, 5 as a malignant. The sensitivity and specificity to rule out malignant and benign for UE were 77.71 %(143/184), and 96.20 %(152/158) respectively. The sensitivity of UE is not improved and we found that it is even lower than the sensitivity of conventional US. However the specificity is significantly higher than the conventional US. A total of 41 malignant lesions were missed by 5-point scoring classification. Among them, 24 malignant lesions scored 3 and 16 scored 2. Most of the malignant lesions that were missed on UE were large on size with degenerative changes.

Breast tumor size assessment with conventional US and real time tissue elastography

In our study, of the 342 lesions (184 malignant; 158 benign), size ranges from 0.4 cm to 10.0 cm. The distribution of the lesion size were categorized in the Table. The mean size for benign lesion was 1.9 cm and for malignant 3.16 cm. Of the 158 benign lesions, majority of the lesions 50.6% (80/158) were in the range of 1.0-2.0 cm. Similarly, Of the 184 malignant lesions, 127 lesions (69.02%) were above 2.0 cm.

While comparing the size and area of the total breast lesions in conventional US and real time elastogram, previous report has shown that for malignant lesions with speculated and angular margins malignant features, the size/area on RTE is greater than the size on conventional sonography (Zhu et al., 2008). In our study, of the 185 malignant lesions, 155 (83.73%) malignant lesions showed increase in size/area in real time elastography than in conventional sonography (Table 2, Figure 2a, 2b). Twenty malignant lesions did not showed change in area and nine had decreased area in RTE. As we know that

Table 2. Comparison of Breast Lesion Sizes (n=342) Between Conventional USG and RTE

UE Measurement	Malignant	Benign	Total
Increased (Area)	155	10	165
No change (Area)	20	18	38
Decreased (Area)	9	130	139
Total	184	158	342

benign masses did not produce desmoplastic reactions and also most of them have regular margins and border, the size of these lesions on elastogram do not changes or decreases (Zhu et al., 2008). In our study of the 158 benign lesions, 82.3% of the breast benign lesions (130/158) showed decreased area on RTE. Only 10 of the lesions, showed increased size on RTE (Table 2). Hence, taking size ratio or area ratio as a factor in characterizing the nature of breast lesions i.e. malignant or benign. The sensitivity for detecting breast cancer is 84.23% (155/184). For benign lesions, assuming that the area do not changes or decreased on elastogram, specificity increases up to 93.7%(148/158).

Discussion

In our study, we studied the different approach of Elastographic Imaging for diagnostic potential of breast lesions. In our previous preclinical study, we found the different measurement of stiffness produced in the benign and malignant lesions which were mapped with color (Parajuly et al., 2010). In this study, we found that strain ratio were different in benign and malignant lesions. The study showed that the major histotype lesions like; Fibroadenoma, Fibrocystic Mastopathy and Invasive Ductal carcinoma have different strain ratios. Benign lesions like fibroadenoma and fibrocystic mastopathy do not have significance differences in strain ratio; while IDC and FA or FC showed significance differences in the study, which was similar to the study conducted by Zhi et al. (2010) and Nariya et al. (2010).

The elastic properties within the normal tissue, fibroadenoma and cancer are different (Sarvazyan et al., 1995; Walz et al., 1995) assessing that the neo-plastic tumors are significantly harder than the fibroadenomas. However, we should recognize some development features of fibroadenoma and cancer, when they are in various stages of growth. If we consider the FN (false negative) result, when both UE and sonography were used, should be aware that the sonographic and elastographic features of medullary carcinoma which resembled like benign, with round shape and circumscribed margin. Most of them also lack desmoplastic reaction (Sewell et al., 1995). The lesion was missed in by all three methods. Similarly, poor stroma and lack of sonographic conspicuousness and the very early stage of cancerous features may misguide the results. Hence, nine carcinomas in situ and one medullary carcionoma were missed by SR index method. They all have the SR less than 3.54.

Similarly taking account the diagnostic potential of UE, twenty four and sixteen breast cancers which were categorized as Score 3 and 2 respectively were missed by UE when following the 5 point scoring classification. Around 70% of the malignant lesions recruited in the study were larger than 2 cm. Research has shown that for large lesions SR index method has high performances than 5-point Scoring system (Zhi et al., 2008). It is because that the lesion had more chances of having necrosis, degeneration, hemorrhage etc. These all process may affect the stiffness strain produced inside the lesions. Sometime it is difficult to provide the correct score number, mostly for the lesion with score 2 and 4.

Similarly score 3 lesions have different strain images. In Itoh et al.'s (2006) classification, score 3 has the central part of the lesion, blue and the peripheral part is green. He did not discuss about the how much percentage of the central part should be classified as score 3 or how much peripheral part with green should be scored 3. The discussion still is on the way and lots of researches on this topic are still in the progress. In Shen et al.'s (2008) study proposed 7 point elastographic scoring system, and achieved the sensitivity of 81.6% and specificity of 99.14%.

When talking about false positive, there were 24 breast lesions which were missed on conventional US, 6 on UE methods and 9 on SR index method. The interpretation difficulties arouse when the lesions with sonographic conspicuousness is not clear. Especially in the chronic inflammation, hyperplasia, giant lobulated fibroadenoma, giant phyllodes tumor, sclerosing papilloma and atypical hyperplasia leading to upgrading and worsening in classification both at sonography, UE and SR index method. Presence of calcification even worsens the diagnosis on US, UE and SR method. Research has shown that there is an overlap of elasticity between the benign and malignant lesions of the breast which could interfere with UE diagnosis and limit the usage of UE (Bodian et al., 1993). In this study we found 3.54 was the best cutoff point to characterize the nature of breast lesions with the sensitivity of 94.56%, specificity 94.30% and accuracy of 94.44%. With SR measurement method, we significantly improved the diagnostic performances than UE method. In this study of the 158 benign lesions we had nine benign lesions with strain ratio higher than 3.54. Of the nine lesions, most of them had calcification.

Similarly, talking about the changes in size of the lesions when examined on sonography and elastography, we found 84.23 % of the malignant lesions with poorly defined border and speculated margins had increased area on elastogram. No changes in size or decrease in size for benign lesion was seen on 82.77%. The study was similar to the study conducted by Zhu et al. (2008).

Finally, SR was superior to conventional sonography and 5-point scoring method both in sensitivity (94.56% vs. 91.84% and 94.56% vs. 77.71%) and accuracy (94.44% vs. 88.59% and 94.44% vs. 86.25%). Though there was no significance differences in specificity between UE and SR ,but specificity was highly improved in UE imaging than in conventional USG (96.20% vs. 84.81%). Our results were similar to those reported by (Garra et al., 1997; Itoh et al., 2006; Zhi et al., 2008; Parajuly et al., 2010; Zhi et al., 2010). We have fewer reports on the precise cut-off point reported on the literature. Nariya et al. (2010) reported that cut off point of 2.24 describe the best diagnostic performances among the non-palpable breast masses.

Similarly in a study of Zhi et al. (2010), 3.05 was the best cut-off point with highest sensitivity and specificity and accuracy than 5-point scoring method for differential diagnosis of breast lesions. However, the above both study could not be clinically applicable because of their own limitation. The above described cut-off point of 2.24 was just for non-palpable masses. Similarly, study conducted by Zhi et al. (2010) has also several limitations. In his study breast masses more than 4 cm was not included. The strain ratio of the lesion was compared with the normal mammary tissue of the same depth. He excluded the fat to lesion ratio for the stain measurement. However, in our study we included the breast size mass up to 10.0cm and strain ratio was compared with both the fat to lesion and/ or normal mammary tissue of same depth as the lesion.

The study has several limitations. UE requires training and practice to learn the appropriate technique. In our experience, most of the images which were excluded from the study belonged to the initial period of the learning curve. Perpendicularly firmly held US probe on the breast surface overlying the lesion is mandatory to obtain correct elasticity images. When the operator is well trained, the UE can be performed straight forwardly after the US conventional study and it needs only a short extra time of 5 mins on average.

Besides, we did not evaluate intraobserver and interobserver variability for acquisition of the strain index and UE images. Similarly, we recruit all the cases that came for biopsy. Size should be taken into consider because large lesions with deformed swelled breast would not give correct information about the strain and the stiffness. The maximum diameter that we recruit for the study was 10.0 cm. During our experience, we realize that size more than 5cm should not be recruited in the study. Because, we cannot compare the strain index of large mass (ROI) and the surrounding normal tissue or fat at the same time correctly (our experience). As it is the preclinical study performed in a single hospital. More and more researches should be carried out in multi hospital for its standard values.

In conclusion, ultrasound elastography (UE) is a simple, non-invasive diagnostic examination that provides information about the stiffness of a mass. Thus, utilizing the newly emerged technology along with conventional sonography will be of great clinical value in detecting the malignant lesions. Strain ratio measurement method could also be used as an important factor in characterizing the stiffness of the lesion. It could be an effective predictor than the 5 point scoring method in detecting the malignancy of the lesions. However combined use of UE and SR can effectively decline the rate of unnecessary biopsies and can be an important tool for relieving the burden to the patients, family, society, and finally to the country.

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