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Comparison of Strain Elastography Findings of Breast Lesions with Histopathological Results- Breast Elastrography

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Abstract: Objectives: Elastography is an adjunctive method used in the evaluation of breast lesions combined with ultrasonography. The goal of this study is to analyse the efficiency of strain elastography and its concordance with pathological results on patients who have sonographically demarcated breast lesions. **Materials and methods:** 39 female patients with breast lesion were included in this study. Strain elastography technique was applied and lesions were categorized into 5 groups by Tsukuba scoring system, and each lesion was scored. Strain ratio value was measured for each lesion. The collected data was compared with the histopathological results which were taken as gold standard. **Results:** The mean age of the patients was calculated as 46±12. 26 of 39 lesions were determined as benign, 13 lesions as malignant. The mean SR of the benign lesions was calculated as 2,02±1,73 and the mean SR of the malignant lesions is calculated as 5,7±4,2 ($p < 0,002$). The threshold value of strain ratio is calculated as 2,36 according to ROC curve. While 20 of the benign lesions' SR values were below the threshold value, 6 were above. On the other hand, 11 of the malignant lesions' SR values were above threshold value whereas 2 were under. All benign lesions had an elasticity score representing benignancy. 11 of the malignant lesions had an elasticity score representing malignancy; however, elasticity scores of 2 lesions indicated benignancy. **Conclusion:** Strain elastography technique of benign and malignant breast lesions may reduce the necessity of biopsy and lower the costs.

Keywords: Elastography; Breast lesions; Strain ratio; Elasticity score

Introduction

Breast cancer is the most common cancer in women. The first imaging modality in the screen and the diagnosis of breast cancer is mammography (MG). Ultrasonography (US) is an imaging modality as a first choice under the age of 35 but not in cancer screening. However, developing of high resolution US probes, doppler US which allows

detection of vascularisation of lesion in addition to standart B-mode, and determine the stiffness of lesion with US device compatible with sonoelastography made US an irreplaceable method of breast imaging. Determination of stiffness of lesion via elastography is thought to be useful for differantiation of benign and malignant lesions and each passing day further researchs are added to literature to specify the contribution of elastography to true diagnosis. Strain elastography and shear-wave elastography are generally preferred techniques to utilize breast lesions.

1. Materials and Methods

The study was conducted prospectively. Between March and April 2016, 39 female patients aged 19-70 years diagnosed with a breast mass underwent tru-cut biopsy at the Radiology Clinic of the Health Sciences University Doctor Lutfi Kırdar Training and Research Hospital. Informed consent forms were obtained from all patients and ethics committee approval was obtained.

Patients under the age of 18 were excluded.

All patients were assessed in the supine position utilizing a 14 Mhz linear probe. At least five successive compressions and decompressions were done in line with the strain elastography method. Strain values were determined for the lesion and referenced tissue at the same depth using the maximum compression time graph. While measuring the strain value inside the lesion, the region of interest (ROI) of the reference tissue was adjusted to the same size as the investigation area's ROI (**Figure 1**). As long as the cursor stays inside the lesion, the ROI size does not affect the elastography data [1]. The strain ratio (SR) was obtained as the ratio of the strain value of the reference tissue around the lesion to the strain value of the lesion. At least three elastogram pictures were collected. The SR with the most significant value obtained throughout the investigation was chosen.

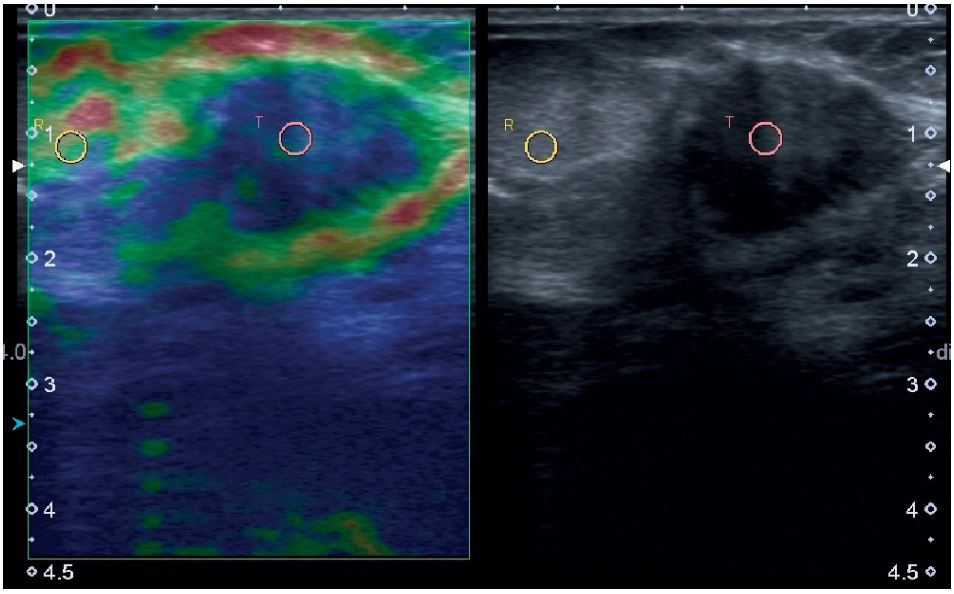


Fig 1. The diameter of the ROI within the lesion and the reference tissue is same.

The Tsukuba scoring system, developed by Itoh and Ueno, was used to determine the elasticity of the lesion. According to the Tsukuba scoring method, the lesions were divided into five categories. Our research calibrated the gadget to display hard tissues in blue, soft tissues in red, and medium-hard tissues in green. As a result, the lesion is mainly coded green and receives a score of 1, if its tone is comparable to that of the surrounding breast parenchyma; if it is primarily green yet has blue-coded parts, it receives a score of 2; if the central area is coded blue and the peripheral is coded green, the score is 3; if it is blue coded, it receives a score of 4; finally, the score was evaluated as 5, if it was coded completely blue and if the surrounding tissue also had blue color coding and caused stiffness in an area larger than the actual size of the lesion measured by B-mode. Scores 1, 2, and 3 were evaluated as benign, whereas scores 4 and

5 were evaluated as malignant. Cystic lesions have a characteristic look with three layers of color coding, and they are excluded from the Tsukuba scoring system [2].

The BI-RADS classification determined based on the patients' breast USG or MG results were used. The BI-RADS classification with the highest value indicating malignancy was used. The elastographically classified benign and malignant lesions were compared to the BI-RADS classification and histopathology results, and statistical measurements were performed.

2. Statistical Analysis

The International Business Machines-Statistical Package for the Social Sciences (IBM SPSS) 22.0 package program was used to conduct statistical analysis in this study.

Frequency, percentage, mean, standard deviation (SD), and median, minimum (min), and maximum (max) values are included in descriptive statistics. The Shapiro-Wilk test was used to verify the assumption of normality in analyzing the difference between the two groups' measurement values, and the Mann-Whitney U test was utilized to assume a normal distribution in the data. The Receiver Operating Characteristic (ROC) analysis was used to classify patients as benign or malignant based on their SR values and establish the cut-off threshold. The findings of the ROC analysis are presented in the form of the Area Under the Curve (AUC), cut-off points, sensitivity, selectivity, PPV (Positive Predictive Value), NEV (Negative Predictive Value), and 95% Confidence Intervals (CI) for each measure. Statistical significance was defined as P values less than 0.05.

3. Results

The mean age of the patients was determined to be 46±12 years. 26 of the 39 lesions examined histopathologically were benign. In contrast, 13 were malignant. 13 benign lesions were reported as fibroadenoma and fibroadenomatoid changes (% 50), seven as fibrocystic changes (% 27), two as granulomatous mastitis (% 7,5), two as fat necrosis (% 7,5), one as sclerosing adenosis (% 4) and one as galactocele (%4). Of the lesions found to be malignant, 11 were reported as invasive ductal carcinoma (85%), one as mucinous carcinoma (7.5%), and one as invasive micropapillary carcinoma (7.5%) (**Figure 2**).

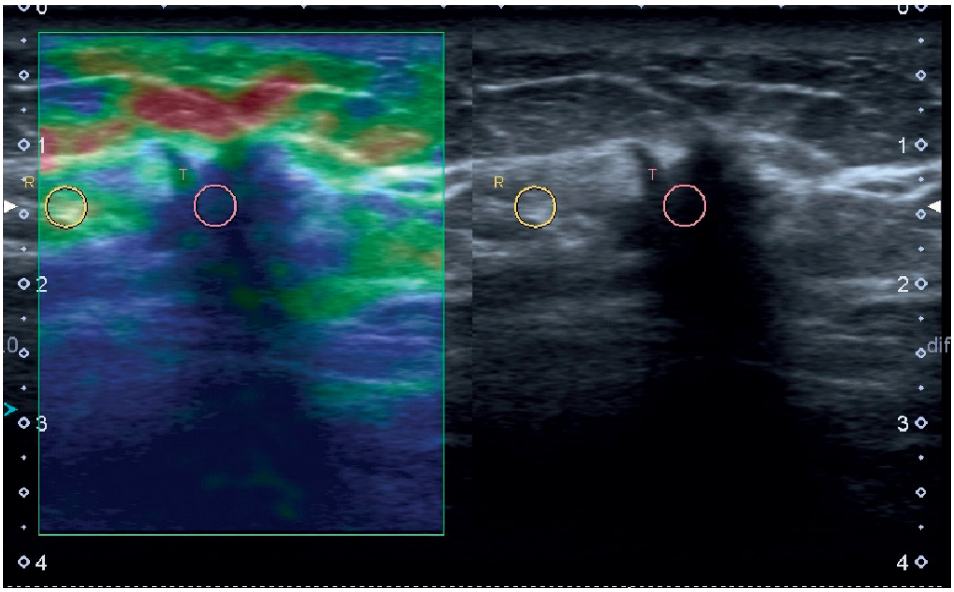


Fig 2. In a 64-year-old patient, BI-RADS 5, a hypoechoic solid lesion with spiculated contour and prominent posterior shadow, is completely blue-coded in the elastogram image and creates blue-coded areas in the surrounding tissue. Tsukuba score is 5. The strain ratio was measured as 5.67. Pathologic diagnosis: Invasive ductal carcinoma

According to the ROC curve, the strain ratio (SR) threshold value was calculated to be 2.36. The mean SR value of malignant lesions was 5.7, whereas benign lesions had a mean SR value of 2.02. As a result, malignant lesions had significantly higher SR values than benign lesions (p = 0.002). The SR values of

malignant patients are significantly greater than those of benign patients (p = 0.002). The comparison revealed that patients with BI-RADS 5 had substantially greater SR values than patients with BI-RADS 4 (p = 0.001).

When the Tsukuba score distributions were examined concerning the patients' pathology findings, it was discovered that there was just one patient with a score of 1 who was diagnosed as benign. 12 patients with a score of 2 were reported as benign, while two were classified as malignant. None of the patients with a 3-point score were diagnosed with cancer. All 7 patients with a 4-point score and 4 patients with a 5-point score were reported as malignant. Only 2 of 28 patients with Tsukuba scores of 1,2 and 3 were reported as malignant. Each of the 11 patients having a Tsukuba score of 4 or 5 was reported as malignant. According to pathology results, which are considered the gold standard, 84.6 % diagnosed as malignant were classified as malignant by the Tsukuba score, whereas 100% of patients diagnosed as benign were classified as benign by the Tsukuba score. The Tsukuba score indicates that 100% of patients suspected of being malignant are indeed malignant, whereas 92.8 % classed as benign are genuinely benign (**Table 1 and 2**).

Table 1: Values according to Tsukuba score

TP*	TN**	FP***	FN****
11	26	0	2

**True Positive (TP), **True Negative (TN), ***False Positive (FP), and ****False Negative (FN)*

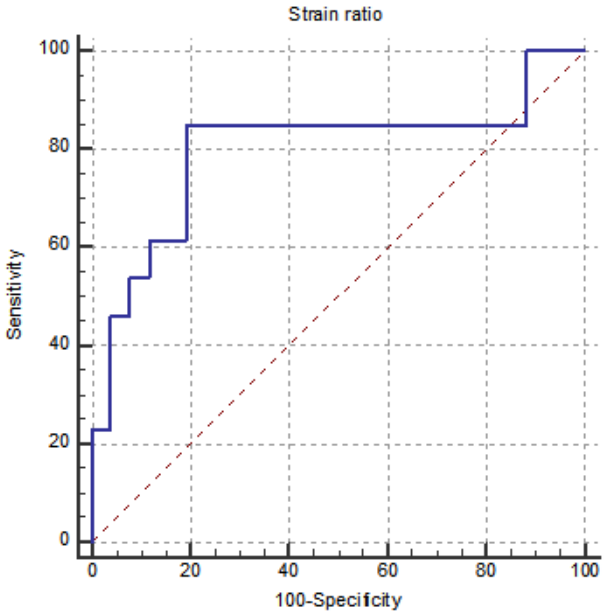
Table 2: Diagnostic test criteria in the differentiation of benign and malignant according to Tsukuba Score

Sensitivity(%95 CI*)	Specifity(%95 CI*)	PPV**(%95 CI*)	NPV*** (%95 CI*)
84,6(55–98)	100(84-100)	100(68-100)	92,8(75-99)

**CI = Confidence Intervals, **PPV = Positive Predictive Value, ***NPV = Negative Predictive Value*

The area under the curve was found to be 79.6% (95% CI: 0.64-0.91) in ROC graph drawn for SR values in the differentiation of benign-malignant, and it was statistically significant (p = 0.001). The ROC curve indicated that the sensitivity (95 % confidence interval [CI]: 54.6-98.1) was 84.6 %, the specificity (CI: 60.6-93.4) was 80.8 %, and the cut-off value was 2.36 (**Table 3**).

Tablo 3: ROC curve



SR values were less than the threshold value (2,36) in all patients in the BI-RADS 2 and 3 groups. 5 of the 22 lesions evaluated in the BI-RADS 4 group were over the threshold, whereas seventeen were below it. 2 of these patients were diagnosed as malignant, while the other 20 were classified as benign. In the BI-RADS 5 group, 12 of the 15 lesions were measured over the threshold, while 3 were measured below. 11 of these patients were diagnosed with cancer, while 4 were diagnosed with benign disease (**Table 4 and 5**).

Table 4: Values according to the strain ratio threshold value

TP*	TN**	FP***	FN****
11	20	6	2

**True Positive (TP), **True Negative (TN), ***False Positive (FP), and ****False Negative (FN)*

Table 5: Diagnostic test criteria in the differentiation of benign and malignant according to the strain ratio threshold value

Sensitivity (%95 CI*)	Specifity (%95 CI*)	PPV** (%95 CI*)	NPV*** (%95 CI*)
84,62(55-98)	76,92(56-91)	64,7(38-86)	90,9(71-99)

**CI = Confidence Intervals, **PPV = Positive Predictive Value, ***NPV = Negative Predictive Value*

4. Discussion

Breast cancer is responsible for 30% of all cancers and 18% of cancer-related deaths in women [3]. MG is employed as the gold standard screening approach in the diagnosis of breast cancer and women over the age of 40. Although the inclusion of US or MRI to MG-based breast imaging boosted the detection rate of lesions, the necessary specificity rates for cancer detection have not yet been performed [4]. To do this, efforts are being undertaken to create novel imaging techniques that will enhance the sensitivity and specificity of current imaging methods [5]. Elastographic examinations may be conducted using semi-static or dynamic techniques. Strain elastography is the most frequently utilized kind of elastography nowadays. It provides very trustworthy information for localized lesions such as those found in the breast. Besides that, shear-wave elastography is more advantageous in the diagnosis of diffuse organ disorders [6].

Stiffness is mainly induced by the broad desmoplastic response generated by malignant lesions [7]. In the literature, there is no absolute SR value or scoring method for malignant lesions. However, SR greater than 3 are considered worrisome for cancer. However, elastography's reliability declines with lesions more than 4 cm in depth [8]. The Tsukuba scoring method is the most often used technique for scoring lesion stiffness, with score of 4 and 5 suggesting malignancy [2].

While most BI-RADS 3 and 4 lesions are benign, tissue diagnosis is used, and unneeded biopsies may be performed when malignancy cannot be applied out.

Numerous significant studies have been published in the literature on the strain elastography approach, which is thought to minimize the difficulties associated with diagnosing breast lesions using traditional techniques. Chang et al. discovered that shear-wave elastography has a higher sensitivity (95.8%), whereas strain elastography has a higher specificity (84.8%) [9]. According to Mutala et al., strain elastography has an 86% sensitivity and a 96% specificity [10].

Carlsen et al. evaluated the eight most complete studies combining B-mode USG and strain elastography data and found that when B-mode and SE data were combined, sensitivity declined dramatically, but specificity rise significantly [11]. Elkharbotly et al. found that when US, Doppler US, and SE were combined, the maximum sensitivity and specificity of 88.9% and 88.4%, respectively, were obtained [12].

Although no exact SR threshold value could be determined to discriminate malignant from benign lesions due to these investigations, it can be concluded that SE is a more effective tool for identifying benign lesions [13].

Malignant lesions had a higher SR than benign lesions. In a study by Zhi et al. [14] and Mousa et al. [15], a statistically significant difference in the SR values of benign and malignant lesions was found.

Our study discovered that the SR measurement has a greater than 90% accuracy rate, particularly when it comes to eliminating the diagnosis of malignancy or determining if the lesion is benign. According to Gheonea et al., the SR value had a sensitivity of 93.3% and a specificity of 92.9% for discriminating benign from malignant lesions [16]. Although the SR value had comparable sensitivity to our study in discriminating benign and malignant lesions, its specificity was relatively high. We believe that this is because the SR threshold value of 3.67 is higher than the value used in our study.

In our study, only two patients were diagnosed as pathologically malignant, even though their SR value was less than 2.36. Although one of these patients was reported with invasive ductal carcinoma (NST: Non-specific type), necrotic regions inside the lesion were reported histopathologically. The elastographic inaccuracy is thought to be caused by the presence of necrosis, which often occurs inside the tumor as a consequence of a nutritional deficiency in fast-developing tumors. The second lesion, which has a low SR value but is malignant, gets a histological diagnosis of mucinous carcinoma. As is well known,

mucinous carcinoma histological examination shows tumor cells suspended in mucin [17]. It is believed that this mucin content provides the tumor with flexibility and results in low SR values. Due to the causes above, the elastography score of both lesions was evaluated as Tsukuba 2, and both the SR value and the elastography score of the lesions were regarded as benign.

Six of the seventeen patients with an SR of 2.36 or above had benign histopathology. Three patients had fibrocystic alterations, two patients had fibroadenoma, and one patient had fat necrosis. Elasticity scores of Tsukuba 2 and 3 were evaluated in all six lesions indicative of malignancy based on the SR threshold value calculated in our study. As a result, we believe that the elasticity score of elastography contributes significantly to the diagnosis of benign and malignant lesions and that the elasticity score of the lesion should always be evaluated in lesions with high SR values. The Tsukuba scoring system seems to predict malignant lesions accurately and differentiates benign lesions from malignant lesions.

Apart from the necrosis areas and mucin content of malignant lesions and the intense fibrosis component of benign lesions, which we found in our study and which may cause errors in elastography results, other factors such as calcification, bleeding areas, the presence of cystic component, the excess stromal cell content of the lesion, surgical scar tissue, and breast tissue edema may also affect elasticity scores and SR values, resulting in false-positive and false-negative results.

Using strain elastography, lesions that are difficult to diagnose with B-mode USG, such as granulomatous mastitis, may be readily identified as benign. Karakaya et al. discovered that granulomatous mastitis patients' elasticity score and SR values favored benignity [18]. Even if malignancy is ruled out with elastography in these patients, tissue diagnosis may be necessary to rule out underlying infectious causes such as tuberculosis or other granulomatous disorders such as sarcoidosis.

As is well known, fat necrosis's morphological characteristics and radiological results vary according to its stage [19]. The fibrotic component and calcification of fat necrosis in the late stage are thought to have contributed to the elevated SR value in our case.

According to the American College of Radiology's (ACR) BI-RADS classification, BI-RADS 5 lesions have a greater than 95% likelihood of malignancy and are generally straightforward to infer owing to radiological features that strongly suggest malignancy. However, BI-RADS 3 and BI-RADS 4 encompass lesions with a broad range of malignancy risks, ranging from 2-95 percent, and are sometimes difficult to discriminate between malignant and benign lesions radiographically, necessitating needless biopsy. Elastography examinations are critical for elucidating this group of lesions. Sickles et al. found that all tumors that grew in size during the follow-up of lesions deemed perhaps benign but diagnosed as malignant by biopsy were early stage, with no recurrence noted in any of them throughout the 5-year follow-up. This study advocate avoiding biopsy and developing a follow-up procedure for lesions thought to be most likely benign [20]. The probability of malignancy in BI-RADS 4 lesions ranges between 2 and 95%. Pathological diagnosis of BI-RADS 4B and 4C lesions is now a widely recognized technique. In a study conducted by Wiratkapun et al., the malignancy rate for BI-RADS 4A, 4B, and 4C lesions was 9%, 21%, and 57%, respectively [21]. Given that most BI-RADS 4 lesions are benign, it is reasonable to assume that the use of elastography, particularly in this group of patients, will reduce the number of needless biopsies and associated costs. In our study, the elasticity score and SR value favored benignity in 80% of lesions classified as BI-RADS 4 and pathologically diagnosed as benign. However, it should be borne in mind that fibrocystic alterations and fibroadenomas with a high fibrotic component, like malignant lesions, may develop stiffness and become less elastic. These characteristics may contribute to the erroneous interpretation of elastography data in favor of malignancy. Even though the lesions are benign, a biopsy is always necessary for these situations because of the worrisome sonographic and elastographic results. Moukhtar et al. found that when combined with the BI-RADS classification, elastography raised the specificity and PPV in lesion differentiation by 89.5% and 86.8%, respectively, while maintaining the BI-RADS classification at 95% and 94.7%, respectively. Sensitivity and NPV were shown to be increased [22]. Duma et al. discovered that although the BI-RADS classification and elastography findings were consistent, the BI-RADS classification's sensitivity, specificity, and PPV were somewhat higher, but the NPV was much higher than elastography.

The explanation for this is that BI-RADS 2 lesions with characteristic mammographic features such as calcified fibroadenoma and fat necrosis are recognized as complicated and have a high elastography score on elastography [23].

The technique of strain elastography is a promising and widely utilized technique. Although combining the elasticity score and SR values yields more successful results, due to a variety of factors, including the lesion itself, the characteristics of the adjacent breast tissue, and the knowledge and skill of the radiologist performing the elastography technique, it is not possible to distinguish malignant and benign lesions with absolute accuracy using only the elastography technique. We believe that further comprehensive research is necessary to address this.

There are certain limitations to our study's execution. The study's limitations may be described as the study's limited sample size, poor histopathological diagnosis variety, single-center execution, and reliance on the user due to the strain elastography technique.

Conclusion

Strain elastography is a simple, practical, low-cost, and reliable technique. The broad adoption of alternative approaches to aid in the distinguishing of malignant and benign breast lesions will help reduce the necessity for and expense of biopsy. However, larger-scale research with a more significant number of patients is required.

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