

Meme Kitlelerinin Malign Benign Ayırımında Sonoelastografi ve ADC Değerinin Etkinliği

Effectiveness of Sonoelastography and Diffusion MRI ADC Value In Discriminating Between Malignant and Benign Lesions of the Breast

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ABSTRACT

Objective: We aimed to evaluate the diagnostic value and comparison of sonoelastography and diffusion-weighted magnetic resonance imaging in differentiation of benign and malignant breast masses.

Method: Forty-five patients who were referred to our Radiology Department for the biopsy of a known breast mass following a breast MRI were evaluated by sonoelastography using a 5-scaled Tsukuba scoring system and measurements of ADC values on diffusion weighted MRIs. Contribution of the Tsukuba scores and ADC values of the masses to the conventional methods were evaluated.

Results: Histopathological results of all masses with Tsukuba scores 1 and 2 were evaluated as benign. Histopathological results of 37.5% of patients with a Tsukuba score of 3 were found to be benign and 62.5% of the patients were found to be malignant. Histopathologically 80% of the patients with a Tsukuba score of 4 were evaluated to have malignant, while all (100 %) of the patients with a Tsukuba score of 5 were considered to have malignant disease. Statistically significant correlation was found between the histopathological results and Tsukuba scoring system ($p<0.05$). Sonoelastographic sensitivity, specificity, positive, and negative predictive values were 83.3%, 96.3%, 93.7% and 89.6%, respectively in the patients with Tsukuba scores of 4 and 5. The mean ADC values of histopathologically proven malignant, and benign masses were $0.95\pm 0.17\times 10^{-3}$ mm²/sec and $1.37\pm 0.16\times 10^{-3}$ mm²/sec, respectively. The mean ADC value of histopathologically proven malignant masses was significantly lower than histopathologically proven benign masses ($p<0.01$). At sonoelastographic evaluation, one false-positive and 5 false-negative results were found. Three out of 4 false-negative results were diagnosed correctly using ADC values. False-negativity was detected in one lesion diagnosed based on both sonoelastographic results, and ADC values.

Conclusion: We think solely sonoelastography or ADC evaluations are inadequate, however, can be used in differentiation of benign and malignant breast masses.

Keywords: breast neoplasms, sonoelastography, magnetik rezonans imajing, difüzyon

Öz

Amaç: Çalışmamızda meme kitlelerinin malign-benign ayırımında sonoelastografi ve difüzyon manyetik rezonans görüntüleme (MRG) tekniklerinin tanisal değerinin araştırılması ve karşılaştırılması amaçlanmıştır.

Yöntem: Meme kitlesi nedeniyle Hastanemiz Radyoloji Kliniği'ne histopatolojik inceleme için başvuran hastalardan MRG tetkiki yapılmış olan 45 hastaya işlem öncesi beş puanlı 'Tsukuba' skorlama yöntemi kullanılarak sonoelastografik inceleme ve difüzyon MRG incelemelerinden "apparent diffusion coefficient" (ADC) ölçümleri yapıldı. Tsukuba skorlaması ve kitle ADC değerlerinin konvansiyonel yöntemlere katkıları değerlendirildi.

Bulgular: Tsukuba skoru 1 ve 2 olan olguların tamamının histopatolojik inceleme sonucu benign değerlendirilmiştir. Tsukuba skoru 3 olan olguların %37,5'inin histopatoloji sonucu malign, %62,5'inin benign olarak saptanmıştır. Tsukuba skoru 4 olan olguların %80'inin patoloji sonucu malign iken, Tsukuba skoru 5 olan olguların %100'ü malign değerlendirilmiştir. Histopatoloji sonucu ile Tsukuba skorlaması arasında istatistiksel olarak anlamlı bir uyum bulunmaktadır ($p<0.05$). Tsukuba skor 4 ve skor 5'te duyarlılık %83,3, özgüllük %96,3, pozitif kestirim değeri %93,7 ve negatif kestirim değeri %89,6 olarak bulunmuştur. Histopatolojik olarak kanıtlanmış malign kitlelerin ortalama ADC değeri $0.95\pm 0.17\times 10^{-3}$ mm²/sn iken benign kitlelerin ADC değeri $1.37\pm 0.16\times 10^{-3}$ mm²/sn idi. Histopatolojik olarak kanıtlanmış malign kitlelerin ortalama ADC değeri, histopatolojik olarak kanıtlanmış benign kitlelerden anlamlı olarak daha düşüktü ($p<0.01$). Sonoelastografik değerlendirmede 1 yanlış pozitif ve 5 yanlış negatif sonuç saptandı. Yanlış negatif saptanan 4 lezyonun 3'üne ADC ölçümleri ile doğru tanı koyuldu. Bir lezyon hem sonoelastografik olarak, hem de ADC değerlerinde yanlış negatif saptandı.

Sonuç: Yalnızca sonoelastografi ve ADC ölçümlerinin tek başına malign-benign ayırımında yetersiz olduğunu ancak birbirlerini tamamlayıcı alternatif yöntemler olarak kullanılabileceğini düşünmekteyiz.

Anahtar kelimeler: meme kitlesi, sonoelastografi, magnetik rezonans görüntüleme, difüzyon

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INTRODUCTION

Breast cancer is the most common malignancy in women and among the leading causes of cancer-related deaths. Early diagnosis is the most important factor determining prognosis in breast cancer. Detection of the disease at an early stage increases treatment success and survival ⁽¹⁻³⁾.

Diagnostic breast USG is an inexpensive, convenient, and non-invasive method without any radiation exposure. Recently, there have been significant improvements in characterization of breast mass lesions using B-mode sonography, which can detect malignant masses with high sensitivity. However, a high false positive rate is an important problem ^(4,5).

Sonoelastography is based on the fact that softer sites in the tissues are more easily deformed to a greater extent than the harder parts when left under compression. The method semiquantitatively measures the degree of deformation in the tissue using B-mode USG devices ⁽⁶⁻⁹⁾. Important advantages of sonoelastography are similar to other USG methods, as being inexpensive, noninvasive, convenient, and commonly available, as well as allowing real-time visualization and not requiring ionizing radiation ^(9,10).

Sonoelastography is an imaging modality that measures the tissue response to compression, and thus, measures elasticity and stiffness of the tissue. Malignant lesions have higher scores than benign lesions, as malignant lesions are usually more rigid due to desmoplastic reactions ⁽¹¹⁾. Two main sonoelastography methods are being used to evaluate breast lesions. These are five-point scoring system and strain index method. The five-point scoring system shows the degree of stiffness in the lesion and its surrounding parenchyma with different color codes in real time, and the qualitative scoring can be made visually between 1 to 5 points ^(12,13). Strain index measurement determines the strain index of the lesion by proportioning the strain values of the lesion and the adjacent structures using the obtained elasticity maps. In this way, the degree of the stiffness in the lesion can be assessed quantitatively ⁽¹¹⁻¹⁴⁾. In addition, the shear wave elastography, the quantitative technique shows the elasticity of tissues in kPa. The advantage of the technique is the mini-

mal interobserver difference ⁽¹⁰⁾.

Large-scale studies evaluating contrast-enhanced MRI showed that it is highly sensitive in detecting primary or recurrent breast cancer ⁽¹⁵⁻¹⁹⁾. Many studies report rates of sensitivity over 90%, reaching 100% particularly in invasive breast cancer ⁽²⁰⁾. Breast MRI has been used for the purpose of preoperative staging in patients with breast cancer for the last two decades. Breast MRI can provide information about the morphological and dynamic properties of the lesion.

There are many studies using ADC values to discriminate malignant and benign lesions of the breast, to characterize malignant masses, and to evaluate peritumoral spread, tumoral cellularity and response to treatment ^(21,22). In terms of ADC values, there is no consensus on which maximum b value will be used to evaluate breast lesions. ADC value of benign breast lesions is generally high. ADC value is affected by tissue features that have low cellularity such as fibrosis or necrosis. Therefore ADC values decrease in fibrotic lesions, such as fibrous fibroadenomas or invasive ductal carcinoma. ADC values of cysts are higher, because of their liquid content. In general, serous content causes a low restriction in diffusion, and mucinous content causes a slightly higher diffusion restriction. Invasive ductal carcinoma shows lower ADC values than other malignant tumors, possibly due to dense tumor cells preventing the effective movements of molecules and restricting diffusion. Noninvasive ductal carcinoma shows high ADC values than ductal carcinoma due to bleeding in the necrotic center and lower cellularity ⁽¹⁵⁻¹⁷⁾.

The present study aims to investigate the contributions of five-point scoring system in sonoelastography and ADC values measured with MRI to the diagnosis and their additive value in discriminating between malignant and benign lesions of the breast that are detected with USG.

MATERIAL and METHODS

Forty-five patients who were referred to the Radiology Clinic of Umraniye Education and Research Hospital for radiological examination and had previous breast MRI scans were examined with sonoelas-

tography prior to the biopsy. MRI examinations of these patients were evaluated, and measurements were made from the ADC maps.

Cases with lesions that were larger than 3 cm -as these exceed the area of visualization in elastography- or lesions that could not be localized in the ADC map of breast MRI, cases for whom a histopathological diagnosis was not made, and cases who previously underwent surgical treatment were excluded from the study.

Ümraniye Training and Research Hospital The Clinical Research Ethics Committee of the hospital (Issue: 256) approved the study protocol, and all cases included in the study provided written informed consent.

Sonoelastography technique and evaluation of images

While the patient was lying in the normal ultrasonography position, a 12 MHz linear transducer probe was centered over the lesion and positioned perpendicular to the skin, lesion, and anterior chest wall. The examination was performed using digital USG devices (Toshiba Aplio MX and Toshiba Aplio 500) that have real-time elastography software. For each lesion, evaluation at B-mode was followed by real-time elastography mode using the same probe, and images were obtained. During real-time examination, both B-mode and elastography images of the examined area could be visualized on the monitor side by side, in two separate windows. In B-mode and elastography images, the imaging area was adjusted so that the entire mass lesion was visualized together with subcutaneous fat tissue and superficial layer of pectoral muscle. While obtaining elastography images, a slight pressure was applied perpendicular to the lesion. In our study, for every pixel of the elasticity image, color codes were determined according to the degree of strain. The color scale varied from red (the highest degree of strain (softest)) to blue (complete absence of strain (hardest)), with green showing the average strain.

Two radiologists who were experienced in breast sonography and sonoelastography and blinded to the histopathological diagnoses of the cases evaluated the B-mode sonography and sonoelastography

images that were recorded digitally during the imaging. After evaluation, an elastography score was determined for each case.

During evaluation of the sonography images, a five-point scoring system developed by Itoh et al. (13), which is known as ‘Tsukuba Elasticity Score,’ was employed (Figure 1). The scores were assigned according to the following classification:

Scores 1-3 were considered to indicate benign, and scores 4-5 malignant lesions.

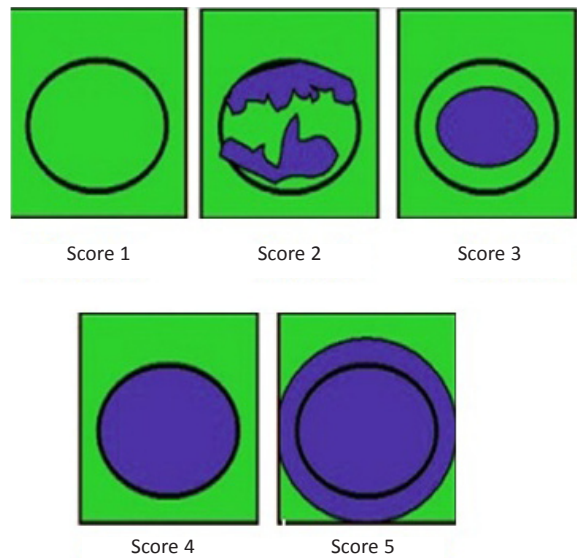


Figure 1. Schematic representation of Tsukuba scoring system.

MRI technique and evaluation of images

Breast MRI scans were performed bilaterally in each patient so as to encompass the entire breast, using 8-channel double surface breast coil, 1.5 T MRI device (Siemens Avantom). Contrast agent was administered manually as a bolus dosage of 0.1-0.2 mmol/kg. In each case, fat-suppressed T2 STIR axial images (TE:76, TR:4200, FOV=320 mm, matrix=512x512, section thickness=5 mm); turbo-spin echo T1 axial images (TE:8.7, TR:510, FOV=320 mm, matrix=512x512, section thickness=5 mm), and FLASH 3D T1A (TE:1.44, TR:4.68, FOV=320mm, matrix=512x512, section thickness=1.7 mm) non-contrast and axial dynamic images at 1st, 2nd, 3rd, 4th, and 5th minutes were obtained. Using the subtraction program that is present as standard in the Siemens MRI console, each of the non-contrast FLASH 3D images were subtracted from the dynamic images in order

to obtain the subtracted images. Before administration of the contrast agent, echo-planar diffusion and ADC images (TR=8500, TE=109, FOV=320 mm, matrix= 256x256, section thickness=5 mm) were obtained with b=1000 values. ADC measurements were made by calculating pixel values. The measurements were evaluated by manual placement of the ROI on the mass lesion and the normal fibroglandular tissue of the same breast. Measurements were repeated several times, and the lowest value was accepted.

Statistical Analysis

For evaluation of the study data, statistical analyses were made with IBM SPSS Statistics 22 program. In addition to the descriptive statistics (mean, standard deviation, frequency), comparison of quantitative data was made using one-way ANOVA for comparing more than two groups with normally distributed parameters, and the group that caused the difference was determined with Tukey HDS test. Comparison of two groups for normally distributed parameters was made with Student’s t-test. Qualitative data were compared using chi-square test, continuity (Yates) correction, and McNemar test. Sensitivity and specificity calculations were made with diagnostic screening tests. P<0.05 was accepted as statistically significant.

RESULTS

The study was conducted with a total of 45 female cases aged between 19 and 70 years. Mean age was 44.69±10.63 years. Sizes of mass lesions varied from 7 mm to 30 mm, with a mean size of 16.41±6.37 mm.

For histopathological examination, fine needle aspiration biopsy (FNAB) was performed in 19 (42.2%), and Tru-Cut biopsy in 26 (57.8%) cases.

Detected benign lesions included fibroadenomas (n=9), fibroadenomatoid changes (n=3), fibrocystic changes (n=12), and papillomas (n=3). Detected malignant lesions, included invasive ductal carcinomas (n=17), and invasive lobular carcinoma (n=1).

Tsukuba scores of 1 (n=4; 8.9%), 2 (n=17: 37.8%), 3 (n=8: 17.8%), 4 (n=5: 11.1%), and 5 (n=11: 24.4%) were detected in respective number of cases. Based on the Tsukuba scores, 16 lesions (35.6%) were diag-

nosed as malignant, while 29 lesions (64.4%) as benign.

Pathological examination results were benign in all cases with Tsukuba scores 1 and 2. Among cases with Tsukuba score 3, 37.5% were malignant and 62.5% were benign. Eighty percent of the cases with Tsukuba score 4 were malignant, while all (100%) of the cases with score 5 had malignant pathology.

Table 1. Distribution of pathology results according to Tsukuba scores.

Tsukuba	Pathology	
	Malignant n	Benign %
1	0 (0%)	4 (100%)
2	0 (0%)	17 (100%)
3	3 (37.5%)	5 (62.5%)
4	4 (80%)	1 (20%)
5	11 (100%)	0 (0%)

There was a statistically significant concordance between pathology results and Tsukuba scores (p<0.05). The rate of accurate diagnosis of malignancy was 40% based on the pathology results, and 35.6% based on Tsukuba scores. Compared to pathology results, Tsukuba scores had diagnostic sensitivity of 83.3%, specificity of 96.3%, positive predictive value of 93.75% and negative predictive value of 89.66%.

Table 2. Concordance between Tsukuba score and pathology result.

Tsukuba	Pathology			p
	Malignant n (%)	Benign n (%)	Total n (%)	
Malignant	15 (33.3%)	1 (2.2%)	16 (35.6%)	0.001**
Benign	3 (6.7%)	26 (57.8%)	29 (64.4%)	
Total	18 (40%)	27 (60%)	45 (100%)	

McNemar Test ** p<0.01

ADC values of the mass lesions of cases varied between 0.74x10⁻³ mm²/sec and 1.8x10⁻³ mm²/sec, with a mean lesion ADC value of 1.2x10⁻³ mm²/sec. ADC values of the normal breast tissue varied between 1.02x10⁻³ mm²/sec and 2.91x10⁻³ mm²/sec, with a mean ADC value of 1.6x10⁻³ mm²/sec.

After categorizing the lesions as benign and malig-

nant, the mean ADC value of the malignant lesions was $0.95 \pm 0.17 \times 10^{-3} \text{ mm}^2/\text{sec}$, while the mean ADC value of the benign lesions was $1.37 \pm 0.16 \times 10^{-3} \text{ mm}^2/\text{sec}$. Mean ADC value of the lesions was significantly lower in cases with malignant pathology results compared to the cases with benign pathology results ($p < 0.01$).

Table 3. Concordance of mass lesion ADC and normal breast ADC values with the pathology results.

	Pathology		p
	Malignant Mean±SS (Min-Max) $\times 10^{-3}$	Benign Mean±SS (Min-Max) $\times 10^{-3}$	
Mass ADC	0.95 ± 0.17 (0.74-1.51)	1.37 ± 0.16 (1.1-1.8)	0.001**
Breast ADC	1.58 ± 0.45 (1.02-2.91)	1.61 ± 0.30 (1.17-2.25)	0.771

Student t Test, ** $p < 0.01$

Mean normal breast tissue ADC values did not show a statistically significant difference according to the pathology results of the cases ($p > 0.05$).

Table 4. Evaluation of lesion ADC values according to Tsukuba score.

Tsukuba	n	Mass ADC $\times 10^{-3}$		p
		Min-Max	Mean±SD	
1	4	1.39-1.49	1.45 ± 0.04	¹ 0.001**
2	17	1.11-1.8	1.34 ± 0.16	
3	8	0.85-1.66	1.23 ± 0.32	
4	5	0.75-1.33	0.96 ± 0.22	
5	11	0.74-1.51	0.99 ± 0.21	
Malignant	16	0.74-1.51	0.99 ± 0.21	² 0.001**
Benign	29	0.85-1.8	1.33 ± 0.21	

¹ One-way ANOVA test, ² Student t test, ** $p < 0.01$

In comparison of Tsukuba scores of the lesions and ADC values, mean ADC values of lesions showed a statistically significant difference according to Tsukuba scores ($p < 0.01$). Mean ADC value of the cases with Tsukuba score 1 was significantly higher than mean lesion ADC value of cases with Tsukuba scores of 4 ($p = 0.011$) or 5 ($p = 0.006$). Mean ADC value of the cases with Tsukuba score of 2 was significantly higher than mean ADC value of the cases with Tsukuba scores of 4 ($p = 0.008$) or 5 ($p = 0.001$). There was no statistically significant difference in comparison of other Tsukuba scores regarding mean ADC values of the lesions ($p > 0.05$).

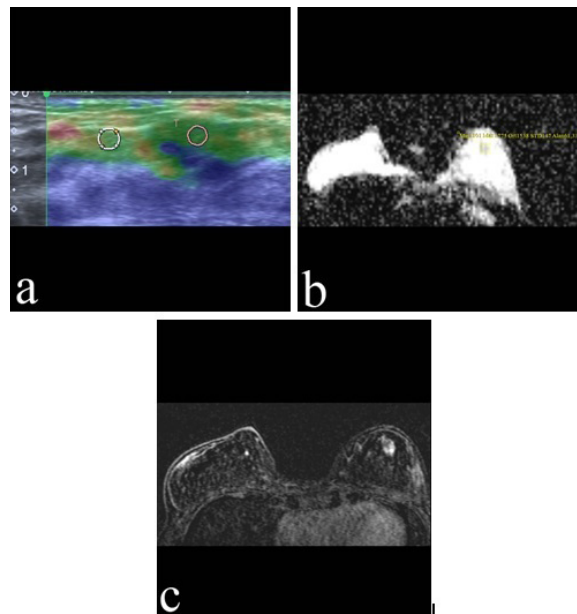


Figure 2. A 25 year-old female case. (a) In sonoelastographic examination, the lesion is coded predominantly as green, showing equal elasticity with the surrounding breast parenchyma, and was evaluated as Tsukuba elasticity score 1. (b) Post-contrast administration axial T1A FLASH 3D subtraction image. (c) ADC value in DWI was calculated as $1.538 \times 10^{-3} \text{ mm}^2/\text{sec}$. Histopathological diagnosis of the case was fibrocystic changes.

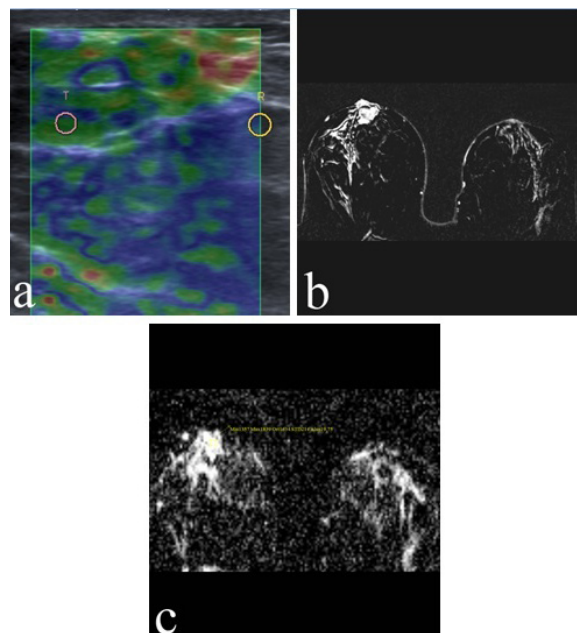


Figure 3. A 29 year-old female case. (a) In sonoelastographic examination, the lesion included blue and green areas, showing inhomogeneous elasticity, and was evaluated as Tsukuba elasticity score 2. (b) Post-contrast administration axial T1A FLASH 3D subtraction image. (c) ADC value in DWI was calculated as $1.634 \times 10^{-3} \text{ mm}^2/\text{sec}$. Histopathological diagnosis of the case was fibroadenomatoid changes.

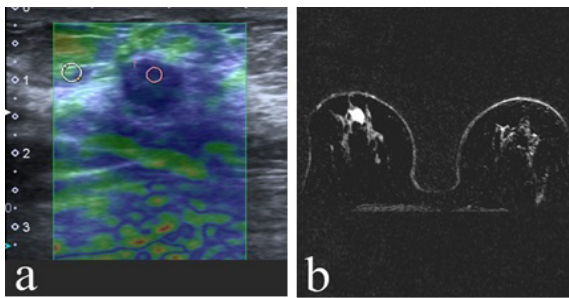


Figure 4. A 57 year-old female case. (a) In sonoelastographic examination, the surrounding tissue observed has not lost its elasticity, and the lesion coded as blue was evaluated as Tsukuba elasticity score 4. (b) Post-contrast axial T1A FLASH 3D subtraction image. (c) ADC value in DWI was calculated as $0.898 \times 10^{-3} \text{ mm}^2/\text{sec}$. Histopathological diagnosis of the case was intraductal carcinoma.

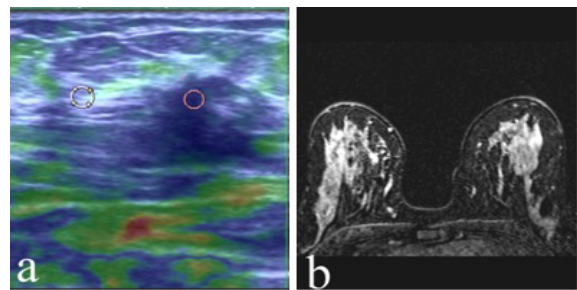


Figure 6. A 42 year-old female case. The malignant lesion was evaluated as false negative based on ADC measurement, while Tsukuba score identified it correctly. (a) In sonoelastographic examination, the lesion was evaluated as Tsukuba elasticity score 5. (b) Post-contrast axial T1A FLASH 3D subtraction image. (c) ADC value in DWI was calculated as $1.414 \times 10^{-3} \text{ mm}^2/\text{sec}$. Histopathological diagnosis of the case was invasive lobular carcinoma..

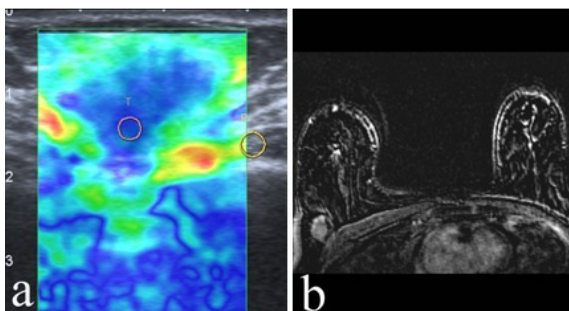


Figure 5. A 55 year-old female case. (a) In sonoelastographic examination, the surrounding tissue was observed to have lost its elasticity, and the lesion coded as blue was evaluated as Tsukuba elasticity score 5. (b) Post-contrast axial T1A FLASH 3D subtraction image. (c) ADC value in DWI was calculated as $0.74 \times 10^{-3} \text{ mm}^2/\text{sec}$. Histopathological diagnosis of the case was invasive breast carcinoma.

Malignant lesions detected based on Tsukuba scores had significantly lower mean ADC values compared to benign lesions ($p < 0.01$).

DISCUSSION

Sonoelastography may show the degree of tissue stiffness in real time with color codes, and a qualitative elasticity score between 1 to 5 points can be assigned. The five-point scoring system developed by Itoh et al. (13,14), known as “Tsukuba elasticity score,” is commonly used in sonoelastographic evaluation of breast lesions. In this scoring system, the color pattern of the lesion and the surrounding breast tissue are evaluated and assigned a score on a scale of five points. We used this Tsukuba elasticity score in our study. In comparison to histopathological examination results, Tsukuba elasticity score was found to have a sensitivity of 83.3%, specificity of 96.3%, positive predictive value of 93.75%, and negative predictive value of 89.66%. Itoh et al. (13) evaluated 111 lesions and found the sensitivity and specificity of this five-point scoring method as 86.5% and 89.8%, respectively. Zhu et al. (23) evaluated 139

lesions and they found its sensitivity and specificity as 85.5% and 86.6%, respectively. Yıldız et al. evaluated 80 patients and they found sensitivity and specificity as 85.71% and 86.44%, respectively⁽¹⁰⁾. Our results are consistent with the results of previous studies using scoring methods. These findings support the utilization of this scoring system as a complementary diagnostic method to increase specificity.

In our study, we used 1.5 T magnet power device with EPI-DWI sequence and a b value of 1000 to generate ADC values. Mean ADC values of 18 malignant ($0.95 \pm 0.17 \times 10^{-3}$ mm²/sec), 27 benign lesions ($1.37 \pm 0.16 \times 10^{-3}$ mm²/sec), and normal tissue (1.6×10^{-3} mm²/sec) were as stated. Mean ADC value of lesions that were histopathologically reported as malignant was significantly lower compared to mean ADC value of lesions that were histopathologically benign ($p < 0.01$).

In their study, Guo et al.⁽²³⁾ used EPI sequences and took b values as 0 and 1000 mm²/sec, and they found mean ADC values of 31 malignant (0.97×10^{-3} mm²/sec), and 24 benign lesions (1.57×10^{-3} mm²/sec) as indicated. Using similar sequence (EPI), we obtained similar results to those of Guo et al.

Woodhams et al. used b value as 0 and 700 mm²/sec to calculate ADC values in 191 mass lesions. They found mean ADC values for malignant ($1.22 \pm 0.31 \times 10^{-3}$ mm²/sec), and benign lesions ($1.67 \pm 0.54 \times 10^{-3}$ mm²/sec), and normal tissue ($2.09 \pm 0.27 \times 10^{-3}$ mm²/sec) as indicated⁽²⁴⁾. Yılmaz et al. used two different b values ($b = 400, 800$ s mm²) and found highly significant differences between the mean ADC values for normal parenchyma and malignancy ($p < 0.001$)⁽²⁵⁾.

Our mean ADC value for malignant lesions was slightly lower than that found by Woodhams et al. The reason for this is that 17 of the 18 malignant lesions in our study were invasive ductal carcinomas. Woodhams et al. showed that invasive ductal carcinoma had lower ADC values compared to noninvasive ductal carcinoma. They found mean ADC values in invasive ductal, and noninvasive ductal carcinomas as 1.20×10^{-3} mm²/sec, and 1.35×10^{-3} mm²/sec, respectively Park et al. reported mean ADC value in invasive ductal carcinoma as 0.89×10^{-3} mm²/sec, and their result was consistent with ours⁽²⁴⁾.

There are limited number of studies investigating sonoelastography and diffusion ADC value in discriminating breast lesions. Satake et al.⁽²⁶⁾ investigated ultrasound elastography and MRI diffusion ADC values in 115 patients with only BI-RADS Category 4 and 5 lesions and they found mean elasticity score for malignant masses (4.1 ± 0.8) was significantly higher than that for benign masses (2.7 ± 1.1) and also mean ADC value for malignant masses ($0.89 \times 10^{-3} \pm 0.28 \times 10^{-3}$ mm²/s) was significantly lower than that of benign masses ($1.1 \times 10^{-3} \pm 0.34 \times 10^{-3}$ mm²/s). For BI-RADS category 4 masses, in the univariate analysis, the elasticity score ($p = 0.002$) was a statistically significant predictor for malignancy, whereas the ADC value ($p = 0.054$) was not significant. Using multivariate analysis, the elasticity score was also statistically significant ($p = 0.005$) for BIRADS category 4 masses. In the univariate analysis, neither the elasticity score ($p = 0.993$) nor the ADC value ($p = 0.998$) was a statistically significant predictor of malignancy in BI-RADS category 5 masses. BI-RADS category 1-3 masses were not included in their study. In our study, in comparison of Tsukuba scores of the lesions and ADC values, mean ADC values of the lesions showed a statistically significant difference according to Tsukuba scores ($p < 0.01$). Mean ADC values of the lesions in cases with Tsukuba score 1 and 2 were significantly higher than mean ADC values of the lesions in cases with Tsukuba score 4 or 5. Malignant lesions diagnosed based on Tsukuba scores had significantly lower mean ADC values compared to benign lesions. In addition in our study, 3 of the 4 lesions that had false negative results according to five-point scoring system were correctly identified as malignant with ADC measurements, while 1 lesion had false negative result with both sonoelastography and ADC. Two lesions that were evaluated as benign based on ADC values were diagnosed as malignant in histopathological examination; while both lesions were identified accurately with sonoelastography.

There are some limitations of this study. The sample size was relatively low. Sonoelastographic evaluation was performed using color-coded maps overlaying B-mode sonographic images and therefore, could not be performed independent of the B-mode sonographic examination which created a potential for bias. Furthermore, elastographic images were assigned a score on a scale of 5, but this process involved

the observer's interpretation and was not completely objective. Regarding ADC measurement, currently there is no standard b value in diffusion MRI, and different b values yield different results. Also, small cystic, necrotic components within the lesion can lead to overestimation of ADC.

CONCLUSION

Sonoelastography opens a new dimension in imaging by providing information regarding the mechanical properties of the examined tissue, and therefore it is a valuable imaging method. Rather than being used alone in discriminating between benign and malignant breast lesions, the sonoelastographic five-point Tsukuba scoring system can be used as an ancillary method in order to increase diagnostic specificity and prevent unnecessary biopsies and interventions.

Diffusion-weighted MRI is a rapid, sensitive, alternative imaging modality for characterization of breast lesions through calculation of ADC values. Additionally, since DWI is a noninvasive diagnostic method, it can prevent unnecessary biopsies.

Sonoelastography and ADC may be insufficient on their own to make a discrimination between benign and malignant breast lesions. However, these two can be used as complementary alternative methods to increase diagnostic sensitivity and specificity.

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REFERENCES

- Denise RA, Caroline C, Bruce JH, et al. Imaging and cancer: Research strategy of the American College of Radiology Imaging Network. *Radiology*. 2005;235(3):741-51. <https://doi.org/10.1148/radiol.2353041760>
- Leung JWT. Screening mammography reduced morbidity of breast cancer treatment. *AJR Am J Roentgenol*. 2005;184(5):1508-9. <https://doi.org/10.2214/ajr.184.5.01841508>
- Mahesh M. Digital mammography: An overview. *Radiographics*. 2004;24(6):1747-60. <https://doi.org/10.1148/rg.246045102>
- Zhi H, Xiao XY, Yang HY, et al. Semi-quantitating stiffness of breast solid lesions in ultrasonic elastography. *Acad Radiol*. 2008;15(11):1347-53. <https://doi.org/10.1016/j.acra.2008.08.003>
- Thomas A, Degenhardt F, Farrokh A, Wojcinski S, Slowinski T, Fischer T. Significant differentiation of focal breast lesions: calculation of strain ratio in breast sonoelastography. *Acad Radiol*. 2010;17(5):558-63. <https://doi.org/10.1016/j.acra.2009.12.006>
- Lyshchik A, Higashi T, Asato R, Tanaka S, Ito J, Mai JJ, et al. Thyroid gland tumor diagnosis at US elastography. *Radiology*. 2005;237(1):202-11. <https://doi.org/10.1148/radiol.2363041248>
- Vorländer C, Wolff J, Saalabian S, Lienenlücke RH, Wahl RA. Real-time ultrasound elastography-a noninvasive diagnostic procedure for evaluating dominant thyroid nodules. *Langenbecks Arch Surg*. 2010;395(7):865-71. <https://doi.org/10.1007/s00423-010-0685-3>
- Ning CP, Jiang SQ, Zhang T, Sun LT, Liu YJ, Tian JW. The value of strain ratio in differential diagnosis of solid nodules. *Eur J Radiol*. 2012;81(2):286-91. <https://doi.org/10.1016/j.ejrad.2010.12.010>
- Rago T, Santini F, Scutari M, Pinchera A, Vitti P. Elastography: New developments in ultrasound for predicting malignancy in thyroid nodules. *J Clin Endocrinol Metab*. 2007;92(8):2917-22. <https://doi.org/10.1210/jc.2007-0641>
- Yildiz MS, Goya C, Adin ME. Contribution of sonoelastography to diagnosis in distinguishing benign and malignant breast masses. *J Ultrasound Med*. 2020;39(7):1395-403. <https://doi.org/10.1002/jum.15236>
- Cochlin DL, Ganatra RH, Griffiths DF. Elastography in the detection of prostatic cancer. *Clin Radiol*. 2002;57(11):1014-20. <https://doi.org/10.1053/crad.2002.0989>
- Yerli H, Yilmaz T, Ural B, Gülay H. Solid meme kitlelerinin sonoelastografi ile değerlendirilmesinin tanılal önemi. *Ulus Cerrahi Derg*. 2013;29(2):67-71. <https://doi.org/10.5152/UCD.2013.40>
- Itoh A, Ueno E, Tohno E, et al. Breast disease: clinical application of US elastography for diagnosis. *Radiology*. 2006;239(2):341-50. <https://doi.org/10.1148/radiol.2391041676>
- Tardivon A, El Khoury C, Thibault F, et al. Elastography of the breast: a prospective study of 122 lesions [in French]. *J Radiol*. 2007;88(5 Pt 1):657-62. [https://doi.org/10.1016/S0221-0363\(07\)89872-6](https://doi.org/10.1016/S0221-0363(07)89872-6)
- Tan SLL, Rahmat K, Rozalli FI, et al. Differentiation between benign and malignant breast lesions using quantitative diffusion-weighted sequence on 3 T MRI. *Clin Radiol*. 2014;69(1):63-71. <https://doi.org/10.1016/j.crad.2013.08.007>
- Chen X, Li WL, Zhang YL, Wu Q, Guo YM, Bai ZL. Meta-analysis of quantitative diffusion-weighted MR imaging in the differential diagnosis of breast lesions. *BMC Cancer*. 2010;10:693. <https://doi.org/10.1186/1471-2407-10-693>
- Pereira FPA, Martins G, Oliveira RVC. Diffusion magnetic resonance imaging of the breast. *Magn Reson Imaging Clin N Am*. 2011;19(1):95-110. <https://doi.org/10.1016/j.mric.2010.09.001>
- Kolb TM, Lichy J, Newhouse JH. Comparison of the performance of screening mammography, physical examination and breast US and evaluation of factors that influences them: an analysis of 27,825 patient evaluations. *Radiology*. 2002;225(1):165-75. <https://doi.org/10.1148/radiol.2251011667>
- Kaiser WA. Dynamic spiral MR mammography. *Radiology*. 2000;215(3):919-20. <https://doi.org/10.1148/radiology.215.3.r00ap45919>

20. Esen G. Meme MRG, gövde manyetik rezonans. Manyetik Rezonans Derneği Yayınları; 2005.
21. Sinha S, Lucas-Quesada FA, Sinha U, DeBruhl N, Bassett LW. In vivo diffusion-weighted MRI of the breast: potential for lesion characterization. *J Magn Reson Imaging*. 2002;15(6):693-704. <https://doi.org/10.1002/jmri.10116>
22. Abdel Razek AAK, Gaballa G, Denewer A, et al. Diffusion weighted MR imaging of the breast. *Acad Radiol*. 2010; 17(3):382-6. <https://doi.org/10.1016/j.acra.2009.10.014>
23. Zhu QL, Jiang YX, Liu JB, et al. Real-time ultrasound elastography: its potential role in assessment of breast lesions. *Ultrasound Med Biol*. 2008;34(8):1232-8. <https://doi.org/10.1016/j.ultrasmedbio.2008.01.004>
24. Woodhams R, Matsunaga K, Kan S, Hata H, Ozaki M, Iwabuchi K, et al. ADC mapping of benign and malignant breast tumors. *Magn Reson Med Sci*. 2005;4(1):35-42. <https://doi.org/10.2463/mrms.4.35>
25. Yılmaz R, Bayramoglu Z, Kartal MG, Çalışkan E, Salmaslıoğlu A, Dursun M, et al. Stromal fibrosis: imaging features with diagnostic contribution of diffusion-weighted MRI. *Br J Radiol*. 2018;91(1085):20170706. <https://doi.org/10.1259/bjr.20170706>
26. Satake H, Nishio A, Ikeda M, Ishigaki S, Shimamoto K, Hirano M, et al. Predictive value for malignancy of suspicious breast masses of BI-RADS categories 4 and 5 using ultrasound elastography and MR diffusion-weighted imaging. *AJR Am J Roentgenol*. 2011;196(1):202-9. <https://doi.org/10.2214/AJR.09.4108>