

The Role of Multiparametric MRI in Distinguishing Fibroepithelial Breast Lesions from Malignant Neoplasms: A Critical Analysis

✉ Tanju Kisbet¹, ✉ Mehmet Ali Nazlı², ✉ Melis Baykara Ulsan³, ✉ Özgür Kılıçkesmez²

¹Department of Radiology, University of Health Sciences, Prof. Dr. Cemil Taşçıoğlu City Hospital, İstanbul, Türkiye

²Department of Radiology, University of Health Sciences, Başakşehir Çam and Sakura City Hospital, İstanbul, Türkiye

³Department of Radiology, University of Health Sciences, İstanbul Training and Research Hospital, İstanbul, Türkiye

ABSTRACT

Objective: In this study, we aimed to investigate the contribution of magnetic resonance imaging (MRI) parameters to the differentiation of fibroepithelial lesions of the breast from malignant breast masses.

Materials and Methods: We enrolled 200 patients, 100 with fibroepithelial lesions and 100 with breast cancer, from the Radiology Clinic Breast Polyclinic at İstanbul Training and Research Hospital between 2016 and 2017. Thirty patients from each group were excluded for various reasons. MRIs were conducted using a 1.5 Tesla MRI device (GE Healthcare Signa HDi 1.5T), with dynamic contrast-enhanced breast MRI performed in the prone position with a breast coil. Axial T1-weighted, axial T2-weighted, sagittal T2-weighted, diffusion-weighted imaging (DWI), and dynamic contrast-enhanced images were obtained for all patients, with DWI images acquired using b values of 0 and 850. Following non-contrast imaging, 0.1 mmol/kg of contrast agent (gadolinium preparation) was injected at a rate of 3 mL/s, and six consecutive phased series images were obtained for the same region.

Results: In our study, study groups were formed with 70 patients in each group. We found that fibroepithelial lesions in our study were significantly younger in age, smaller in size, with oval smooth contours, higher apparent diffusion coefficient values, reaching the peak contrast enhancement later, and demonstrating a Type 1 curve pattern compared to the malignant group.

Conclusion: In conclusion, dynamic breast MRI contributes to the differentiation between malignant masses with suspicion of malignancy and benign fibroepithelial lesions.

Keywords: Breast cancer, fibroepithelial lesions, multiparametrik MRG

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INTRODUCTION

Breast cancer is one of the significant health issues for women worldwide and in Türkiye. It is the second most frequently diagnosed cancer type in women after lung cancer and ranks first in cancer-related deaths among women in our country. The 5-year survival rate for breast cancer patients varies by stage, reported as 73% in developed countries and 53% in developing countries. This notable difference can be attributed to early detection through screening mammog-

raphy (MG) and better treatment opportunities in developed countries. The fatality rate of breast cancer is 30% in developed countries (190,000 deaths out of 636,000 cases) and 43% in less developed countries. Globally, around one million new cases of breast cancer are diagnosed each year, with an estimated ten thousand cases in Türkiye. Breast cancer has gained particular importance among public health concerns in recent years due to advancements in diagnostic capabilities and improved treatment success rates.^[1,2]



Address for Correspondence: Tanju Kisbet, Department of Radiology, University of Health Sciences, Prof. Dr. Cemil Taşçıoğlu City Hospital, İstanbul, Türkiye
E-mail: tanjukisbet10@gmail.com **ORCID ID:** 0000-0002-9485-0959

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There are two objectives in breast imaging: one is screening asymptomatic women, and the other is evaluating symptomatic cases. The purpose of screening is to detect breast cancer at an early stage because early diagnosis is the most crucial factor affecting prognosis. Therefore, screening methods have become increasingly important.^[1,3]

The primary method for diagnosing breast cancer is MG. However, in cases where MG is insufficient for diagnosis, diagnostic ultrasound (USG) and magnetic resonance imaging (MRI) contribute to the diagnostic process.^[1] Therefore, in this study, we aimed to investigate the contribution of MRI parameters to the differentiation of fibroepithelial lesions of the breast from malignant breast tumors.

MATERIALS and METHODS

Our study included a total of 200 patients divided into two groups: 100 patients diagnosed and monitored for fibroepithelial lesions, and 100 patients diagnosed with breast cancer, who presented to the MG clinic of a training and research hospital between the years 2016 and 2017. This research has been approved by the The University of Health Sciences, Istanbul Training and Research Hospital Clinical Research Ethics Committee (Decision No: 9; Decision Date: January 14, 2022). This study has been conducted in accordance with the Helsinki Declaration. All participants provided informed consent to participate in this study. Subsequently, two study groups were formed, each consisting of 70 patients from both groups.

A dynamic contrast-enhanced breast MRI examination in the prone position was performed using a 1.5 Tesla MRI machine (GE Healthcare Signa HDi 1.5T) available at our clinic. All examinations included axial T1-weighted, axial T2-weighted, sagittal T2-weighted, diffusion-weighted, and dynamic contrast-enhanced images. Diffusion-weighted images (DWI) were obtained using $b=0$ and $b=850$ values. For dynamic imaging, following the acquisition of pre-contrast images, a contrast agent (gadolinium-based) at a dose of 0.1 mmol/kg was injected intravenously at a rate of 3 mL/s. Six consecutive sets of phase series images were acquired for the same region. The total examination duration averaged 30 minutes.

The obtained dynamic images were processed using the subtraction program standard in the MRI console. Subtraction series, assisting in revealing the contrast enhancement profile, were generated by subtracting post-contrast images from the corresponding pre-contrast images on a pixel-by-pixel basis. Subsequent image analysis was performed on the GE Advantage Workstation console. Our study assessed lesion localization, size, morphology, con-

tour characteristics, T2 signal, MRI contrast kinetics, contrast-enhanced peak phase, DWI and apparent diffusion coefficient (ADC) maps, and values of ADC and E-ADC (exponential apparent diffusion coefficient).

The T2 signal intensity was measured using a region of interest (ROI) of 20–50 mm² from the brightest area on sagittal fat-suppressed images. Subsequently, the acquired DWIs were processed on the workstation (GE Advantage Workstation) using specialized software to generate ADC maps. Within the ADC map, ADC values were measured using a 20–50 mm² ROI from different regions of the lesion, excluding cystic, necrotic, and hemorrhagic areas. The lowest ADC value among these measurements was selected.

In the analysis, the Statistical Package for Social Sciences (SPSS Inc., Chicago, IL, USA) 22.0 software by IBM was utilized. Descriptive statistics such as mean, standard deviation, median, minimum, maximum, frequency, and ratio values were employed to describe the data. The distribution of variables was assessed using the Kolmogorov-Smirnov test. The Mann-Whitney U test was used for analyzing quantitative independent variables, while the chi-square test was applied for analyzing qualitative independent variables. The significance level and cutoff value were investigated using a receiver operating characteristic curve. The significance level was explored through univariate and multivariate logistic regression for both quantitative and qualitative independent variables.

RESULTS

We initiated our study with a cohort of 100 cases diagnosed and monitored for fibroepithelial lesions and 100 cases diagnosed with breast cancer at our hospital. Subsequently, study groups were formed with 70 patients each from both groups. Thirty patients from the fibroepithelial lesion group were excluded from the study due to the lack of a histopathological diagnosis and non-contrast enhancement on MR imaging. In the malignant group, 30 patients were excluded due to the absence of a clearly demarcated mass morphology.

The age distribution of patients ranged from 18 to 80 years, with a mean of 44.1 ± 15.7 . The mean age in the benign group was 35.7 ± 12.3 , whereas in the malignant group, it was 52.6 ± 14.2 . Statistical analysis indicated that patients in the malignant group were significantly older compared to those in the benign group ($p < 0.05$). The measured sizes of the largest masses in patients ranged from 3 mm to 70 mm, with a mean of 23.4 ± 13.2 . The mean sizes were calculated as 19.7 ± 11.4 in the benign group and 27.2 ± 13.9 in the malignant group. It was determined that the size in the

Table 1. Comparison results of the groups according to age and mass size

Variables	Benign group (n=70)		Malignant group (n=70)		p*
	Mean±SD	Median	Mean±SD	Median	
Age	35.7±12.3	39	52.6±14.2	51.5	<0.001
Mass size	19.7±11.4	16.5	27.2±13.9	25	<0.001

*: Mann-Whitney U Test. SD: Standard deviation

malignant group was significantly larger compared to the benign group ($p<0.05$) (Table 1).

The most common morphology in the benign group was oval shape at 57.1%, while in the malignant group, irregular shape was observed most frequently at 88.6%. The proportion of irregular morphology in the malignant group was significantly higher compared to the benign group ($p<0.001$) (Table 2).

The T2 signal intensity (SI) measurements in the cases showed a mean of 328.7 ± 151.1 in the benign group and 314.3 ± 147.7 in the malignant group. The T2 SI values did not show a significant difference between the malignant and benign groups ($p>0.05$). Regarding the evaluation of the distribution of ADC values in mass lesions on MRI, the mean ADC values were measured as $(1592.1\pm442.6)\times10^{-6}$ mm²/s in the benign group and $(993.1\pm294.1)\times10^{-6}$ mm²/s in the malignant group. The ADC value in the malignant group was found to be significantly lower compared to the benign group ($p<0.05$). When E-ADC values were compared, the E-ADC values in the malignant group were significantly higher than those in the benign group ($p<0.05$) (Table 3) (Appendix 1).

When assessing the contrast enhancement patterns of masses on MRI, the predominant pattern in the benign group was type I, observed in 80% of cases, while in the malignant group, the type II pattern predominated at 38.6%. Type II and type III contrast enhancement patterns were significantly more prevalent in the malignant group compared to the

Table 2. Comparison results of mass morphology percentages of the groups

Morphology	Benign group (n=70)		Malignant group (n=70)		p*
	n	%	n	%	
Spherical	29	41.4	4	5.7	<0.001
Oval	40	57.1	4	5.7	
Irregular	1	1.4	62	88.6	

*: Mann-Whitney U Test

benign group ($p<0.05$). When comparing the contrast enhancement morphology of the masses, heterogeneous enhancement was most commonly noted in both groups. It was determined to be 50% in the benign group and 54.3% in the malignant group. The peripheral contrast morphology ratio in the malignant group was significantly higher compared to the benign group ($p<0.05$), while homogeneous contrast uptake was significantly lower in malignant cases compared to benign cases ($p<0.05$) (Table 4).

The ADC value demonstrated significant [area under the curve 0.873 (0.808–0.938)] effectiveness in distinguishing between malignant and benign patients. The ADC 1100 cut-off value exhibited significant [area under the curve 0.850 (0.781–0.919)] effectiveness in discriminating between malignant and benign patients. Sensitivity was 87.1%, positive predictive value was 83.6%, specificity was 82.9%, and negative predictive value was 86.6% (Table 5, Fig. 1). The E-ADC value showed significant [area under the curve 0.871 (0.805–0.937)] effectiveness in discriminating between malignant and benign patients. The E-ADC 380 cut-off value demonstrated significant [area under the curve 0.857 (0.790–0.924)] effectiveness in distinguishing between malignant and benign patients. Sensitivity was 85.7%, positive predictive value was 85.7%, specificity was 85.7%, and negative predictive value was 85.7% (Table 5, Fig. 2).

Table 3. Comparative results of T2 SI, ADC, and E-ADC mean values

Variables	Benign group (n=70)		Malignant group (n=70)		p*
	Mean±SD	Median	Mean±SD	Median	
T2SI	328.7±151.1	286.4	314.3±147.7	270.2	0.502
ADC ($\times10^{-6}$)	1592.1±442.6	1590	993.1±294.1	981.5	<0.001
E-ADC ($\times10^{-3}$)	284.8±108.3	268	456.2±109.7	443	<0.001

*: Mann-Whitney U Test. T2 SI: T2 Signal intensity; ADC: Apparent diffusion coefficient; E-ADC: Exponential diffusion coefficient; SD: Standard deviation

Table 4. Comparison results of contrast enhancement curve patterns and morphologies of masses between groups

Variables	Benign group (n=70)		Malignant group (n=70)		p*
	n	%	n	%	
MRI contrast curve pattern					
Type I	56	80	17	24.3	<0.001
Type II	12	17.1	27	38.6	
Type III	2	2.9	26	37.1	
Contrast morphology					
Homogeneous	26	37.1	5	7.1	<0.001
Peripheral	9	12.9	27	38.6	
Heterogeneous	35	50	38	54.3	

*: Chi-square Test. MRI: Magnetic resonance imaging

DISCUSSION

Breast cancer is one of the significant health issues for women globally and in Türkiye. The 5-year survival rate for breast cancer patients varies by stage, reported at 73% in developed countries and 53% in developing nations. This notable difference can be attributed to early detection through screening MG and improved treatment options in developed countries.

Early detection is the most effective method for reducing mortality in breast cancer. The gold standard radiological imaging method to evaluate the breast in women with symptoms and signs is MG. The sensitivity of MG in detecting breast cancer can reach 90%. It has been observed that early diagnosis through mammographic screenings can reduce breast cancer mortality by 30–60%.^[1,2,4]

There are two aims in breast imaging: screening asymptomatic women and evaluating symptomatic cases. Early diagnosis is the most crucial factor influencing prognosis. Therefore, screening methods have gained importance. The purpose of screening is to detect breast cancer at an early stage.^[1,3]

ACR has developed a common terminology worldwide based on the BI-RADS system for MG and USG. In mass lesions, the presence of irregular margins and spiculated extensions, as well as linear and segmental distribution in microcalcifications, indicate a high likelihood of malignancy. In USG, spiculation, irregular margins, marked hypoechoic characteristics, and posterior acoustic shadowing are important criteria for diagnosing malignancy.^[5]

Table 5. ROC curve analysis of ADC and E-ADC values

Variable	AUC	95% CI	p
ADC	0.873	0.808–0.938	<0.001
Cut-off 1100×10 ⁻⁶	0.850	0.781–0.919	<0.001
Sensitivity			87.1%
Positive prediction			83.6%
Sppecificity			82.9%
Negative prediction			86.6%
E-ADC	0.871	0.805–0.937	<0.001
Cut-off 380	0.857	0.790–0.924	<0.001
Sensitivity			85.7%
Positive prediction			85.7%
Specificity			85.7%
Negative prediction			85.7%

ROC: Receiver operating characteristic; ADC: Apparent diffusion coefficient; E-ADC: Exponential diffusion coefficient; AUC: Area under the curve; CI: Confidence interval

MRI is a valuable method used in breast imaging, albeit an expensive and less specific imaging modality as a screening tool. Among radiological modalities, MRI offers the highest soft tissue contrast resolution. Breast MRI is helpful in evaluating multicentricity and multifocality, assessing the true size and extent of lesions, distinguishing residual lesions and granulation tissue post-surgery, and aiding in the detection of occult carcinomas. Additionally, it is employed for evaluating indeterminate lesions identified mammographically and sonographically, assessing implants, analyzing the mammographic appearance seen in a single projection, and investigating cases of spontaneous nipple discharge. The advantages of MRI include no ionizing radiation, high soft tissue resolution, and the ability to perform dynamic contrast-enhanced examinations. Studies have reported sensitivities ranging from 90% to 95% and specificities between 37% and 97% in various investigations.^[6–10]

When evaluating lesions in breast MRI, morphological features, alongside contrast enhancement morphological characteristics and kinetic parameters related to contrast uptake, are assessed. The shape, margins, and distribution of the lesion are the most critical factors determining the lesion's morphology. A round or oval shape is highly suggestive of benignity, whereas some carcinomas have been reported to exhibit smooth, round, and oval shapes. Morphologically, the most important criteria supporting malignancy in breast MRI include irregular shape and irregular and/or spiculated margins. Contrast-enhanced MRI complements MG and USG by demonstrating increased vascularity compared to normal breast tissue in carcinomas,

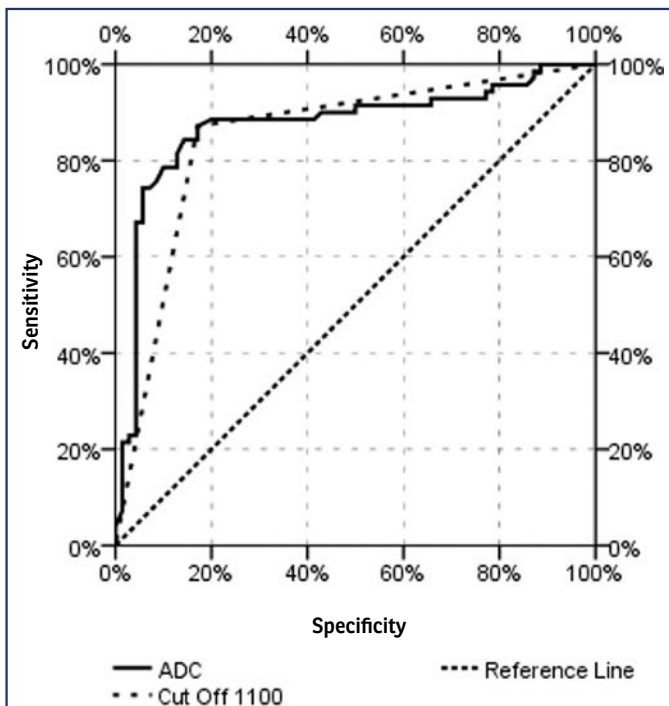


Figure 1. ROC curve of ADC values

ROC: Receiver operating characteristic; ADC: Apparent diffusion coefficient

high permeability in tumor capillaries, and broad extracellular compartments within the tumor tissue.^[11,12]

In the study conducted by Goto et al.,^[13] involving 144 malignant and 60 benign lesions, irregular shape was found in 89% of malignant lesions and 10% of benign lesions. Furthermore, in the same study, 83% of benign lesions had smooth margins, while only 3% of malignant lesions had regular margins, with irregular or spiculated margins detected in 97% of malignant lesions. Our study comprised 140 cases, with 70 being malignant and 70 benign. The most common morphology in the benign group was oval in 57.1% of cases, whereas in the malignant group, irregular morphology was observed in 88.6% of cases. The rate of irregular morphology in the malignant group was significantly higher compared to the benign group.

In a study by Tozaki et al.,^[14] only 7% of benign lesions exhibited irregular margins, and none of the benign lesions showed spiculated margins. In malignant lesions, 47% had irregular margins, and 43% had spiculated margins. Evaluating the lesion contours in our study, in the benign group, regular contours were most commonly observed at 65.7%, while in the malignant group, spiculated contours were observed most frequently at 88.6%. The rate of spiculated contours in the malignant group was significantly higher compared to the benign group.

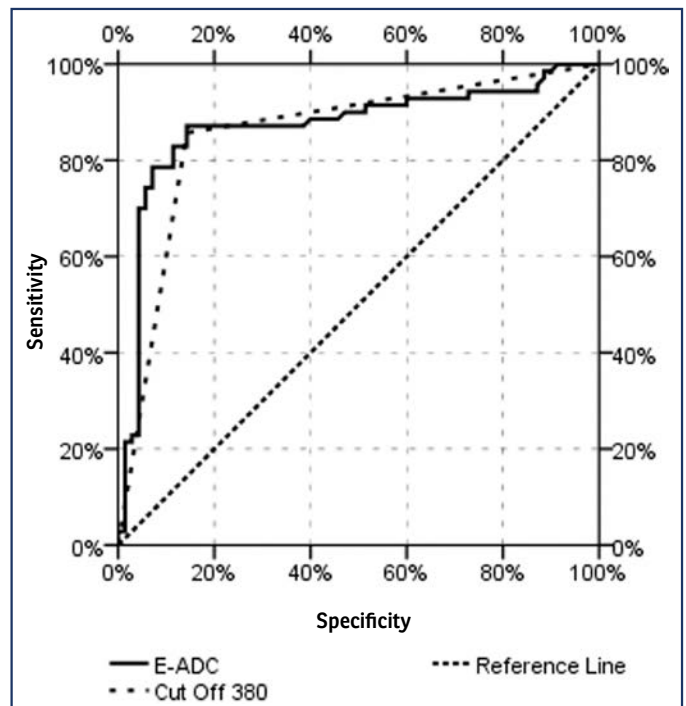


Figure 2. ROC curve of E-ADC values

E-ADC: Exponential diffusion coefficient

Heterogeneous enhancement of signal is one of the most important findings supporting malignancy. Conversely, homogeneous signal enhancement suggests benignity. In a recent study by Igarashi et al.,^[15] involving 27 mucinous cancers and 22 fibroadenomas, heterogeneous and rim-enhancing contrast uptake was more commonly observed in mucinous cancers. The study concluded that the most important feature in characterizing lesions was the heterogeneous delayed enhancement pattern.

In a study by Kuhl et al.,^[16] they compared the contrast uptake curve pattern of a total of 266 lesions with the pathology of the lesions. They reported that among 165 lesions diagnosed as benign, 83% exhibited type 1, 11.5% exhibited type 2, and 5.5% exhibited type 3 curve patterns. Malignant lesions showed that 57.4% exhibited type 3, 33.6% exhibited type 2, and 8.9% exhibited type 1 curve patterns. In another study by Bluemke et al.,^[17] they found that the type 1 curve pattern was obtained in 83% of benign lesions and 9% of malignant lesions. In terms of contrast enhancement curve, in our study, benign lesions predominantly exhibited type 1 contrast kinetics, while malignant lesions showed more type 2 and type 3 enhancement patterns. Type 1 curve pattern was most commonly observed in the benign group at 80%, whereas in the malignant group, the type 2 curve pattern was more prevalent at 38.6%. Significantly higher rates of

type 2 and type 3 MR contrast curve patterns were found in the malignant group compared to the benign group.

In the literature, it has been reported that malignant breast masses have lower ADC values compared to benign masses. In a recent study by Varshitha et al.,^[18] multiparametric MRI was used to evaluate the correlation between breast masses and pathology results. Twenty-nine out of thirty-four malignant lesions demonstrated correlation between histopathology results and multiparametric MR. Chen et al.^[19] conducted a meta-analysis including 13 studies and reported that the mean ADC values of malignant breast masses ranged from 0.87 to 1.36×10^{-3} mm²/s, while the mean ADC values of benign breast lesions varied between 1.00 to 1.82×10^{-3} mm²/s. In our study, we observed significant efficacy of ADC values in distinguishing between malignant and benign patients. However, we noted that the reliability of these values decreases when the lesion sizes are small.

CONCLUSION

In conclusion, dynamic breast MRI contributes to the diagnosis of masses with suspected malignancy, distinguishing them from benign fibroepithelial lesions. The morphology, contour, contrast enhancement pattern, contrast uptake curve of the mass, and ADC values are useful in distinguishing between benign and malignant masses. We consider that MRI has become an alternative method with diagnostic effectiveness and problem-solving capability in selected cases.

Disclosures

Online Appendix Files: [https://jag.journalagent.com/cm/abs_files/CM-83007/CM-83007_\(3\)_supp.pdf](https://jag.journalagent.com/cm/abs_files/CM-83007/CM-83007_(3)_supp.pdf)

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Informed Consent: Informed consent was obtained from all participants.

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