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Original Article

Effect of Breast Fibroglandular Tissue Density in Tumor Visualization and Characterization on Diffusion MRI

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Abstract

Objective: This study aimed to investigate the effect of breast fibroglandular tissue density on tumor visibility and characterization efficacy in diffusion-weighted magnetic resonance imaging (DWI-MRI).

Methods: After ethics committee approval from Karadeniz Technical University (No: 2025/16, Date: 25.03.2025), 2 independent readers retrospectively evaluated the images of 216 consecutive patients (age range, 16-85 years; mean, 45.5 years) who underwent breast MRI for suspicious clinical-radiological findings and later received a definite diagnosis. Only diffusion-weighted images were used at all stages of evaluation. Evaluation parameters were tumor visibility (4-point scale), malignancy probability (7-point scale), and tumor apparent diffusion coefficient (ADC) value. The most suspicious single index lesion was evaluated for each patient. The malignancy scores were determined by considering the morphologic features and the signal of tumors on the ADC map. The ADC values were measured manually on an MRI workstation. Later on, breast densities determined jointly by the readers using T1-weighted images according to the Breast Imaging Reporting and Data System (BI-RADS) classification. Student's *t*-test, Chi-square test, and receiver operating characteristic analysis were used to statistically compare tumor visibility and diagnostic efficacies in different breast density groups (A, B = non-dense, C, D = dense).

Results: Of the 216 patients, 116 (54%) had dense while 100 (46%) had non-dense breast tissue. Around 131 (61%) of the lesions were malignant and 85 (39%) were benign. In 80%-90% of cases with either dense or non-dense breasts, high-moderate tumor visibility was obtained. There was no significant difference between the dense and non-dense breasts in terms of tumor visibility ($P \geq .216$) (Table 1). The mean ADC value in malignant tumors was lower than in benign tumors ($P < .001$). The agreement between the malignancy scores of the readers was moderate (kappa = 0.597, $P < .001$). Diagnostic accuracy values in dense breasts were generally higher than in non-dense breasts (Tables 2 and 3). However, for neither of the evaluation methods nor readers, the result was statistically significant ($P \geq .154$).

Conclusion: In dense breasts, the risk of cancer is higher and the diagnostic efficacy of mammography is low. Therefore, additional methods are needed to increase the diagnostic efficacy in malignant tumors. Diffusion MRI is a very popular, highly efficient, easy-to-apply non-contrast-enhanced MR-based molecular imaging method. It has become a standard in routine clinical applications as an adjunct to breast dynamic contrast-enhanced MRI but it is also suitable for standalone use.

In conclusion, malignant tumors are highly visible on diffusion MRI and differentiation of malignant from benign tumors can be made with 80%-90% accuracy regardless of breast density. It provides both qualitative and quantitative data. Qualitative data might also be used to grade malignancy probability like in the BI-RADS system. As a result, especially in dense breasts, diffusion MRI might be used in addition to mammography to improve the cancer detection ability.

Keywords: Breast, Diffusion-weighted MRI, DWI-MRI, Fibroglandular tissue density

INTRODUCTION

Breast cancer is a relatively common and potentially life-threatening serious disease that affects millions of women globally.[1] The diagnosis of breast cancer on mammography is limited in dense breast. While the detection rate is close to 100% in American College of Radiology (ACR) type 1 fibroglandular breast density, this rate decreases to 50% in ACR type 4 dense breast patterns.[2]

Breast density, a significant patient-specific variable, is one of the most critical determinants of diagnostic accuracy in mammography. The presence of dense fibroglandular tissue not only indicates an increased risk of cancer (4-6 fold) but also diminishes diagnostic efficacy in mammography.[3] Consequently, patients with dense breast patterns require additional modalities to enhance diagnostic accuracy.[4]

Magnetic resonance imaging (MRI) is a valuable complementary imaging modality to mammography and ultrasound for the assessment of suspicious breast lesions.[5] Despite its high diagnostic accuracy, its limited accessibility, high cost, time-consuming nature, and requirement for contrast agents restrict its widespread use. Consequently, while its utility in improving cancer detection in dense breasts is well-established, it has not been universally adopted for screening purposes.

Research is ongoing to enhance the diagnostic specificity of breast MRI through the development of novel imaging sequences and post-processing algorithms. In this context, diffusion-weighted imaging has emerged as a valuable tool for breast lesion characterization, being increasingly incorporated into routine MRI protocols in recent years.[6]

Diffusion-weighted magnetic resonance imaging (DWI-MRI) is a non-invasive imaging modality that provides both qualitative and quantitative data without the need for contrast agents.

Diffusion-weighted imaging is a non-invasive molecular imaging modality that quantifies the random Brownian motion of water molecules within tissues. This technique characterizes tissue microstructure, with the diffusion of water molecules being primarily influenced by tissue cell density. The apparent diffusion coefficient (ADC) is a quantitative parameter used to assess the degree of diffusion.[7]

The DWI-MRI is an advanced radiological imaging technique that has demonstrated high efficacy in characterizing breast tumors.[8] Key parameters assessed in DWI include the ADC value, DWI signal intensity, and tumor morphology. By evaluating ADC values and tumor morphology, DWI can differentiate between benign and malignant tumors with an accuracy of 80%-90%.

To assess the potential utility of DWI-MRI as an alternative diagnostic modality in patients with dense breast tissue, it is crucial to evaluate the efficacy of DWI in visualizing and characterizing breast tumors.

This study aimed to evaluate the effect of breast fibroglandular tissue density on tumor visualization and characterization in DWI-MRI.

MATERIAL AND METHODS

Subjects

This retrospective study received approval from the Karadeniz Technical University Ethics Committee (Approval no: 2025/16 Date: March 25, 2025). Written informed consent forms were obtained from all patients participating in the study.

After ethical community approval, 2 independent readers (R1 and R2) retrospectively evaluated DWI MR images of 216 consecutive patients (age range, 16-85 years; mean, 45.5 years) who underwent breast MRI due to suspicious clinical-radiological findings and received a definitive diagnosis.

Of the total cases, 189 received a definitive diagnosis based on histopathological examination of surgically excised or needle-biopsied specimens, while 27 cases were diagnosed based on stable lesion characteristics observed for over 2 years.

Lesions characterized as focus and non-mass enhancement, cysts, and patients who had undergone neoadjuvant chemotherapy were excluded from the study.

MAIN POINTS

- This study reveals diffusion-weighted magnetic resonance imaging (DWI-MRI) demonstrates high diagnostic efficacy in both dense and non-dense breasts, offering a promising tool for breast cancer detection.
- Despite higher tumor visibility in non-dense breasts, the diagnostic accuracy was not significantly affected by breast density.
- The DWI-MRI can be a valuable adjunct to mammography, especially in challenging cases such as dense breasts.

Table 1. Tumor Visibility at Different Breast Densities

	Average Visibility Score	
Breast Density	**R1**	**R2**
Non-dense (type a, b)	2.60	2.62
Dense (type c,d)	2.32	2.34
P	.032	.022

Table 2. Diagnostic Efficiency of Diffusion MRI According to BI-RADS Scoring in Different Breast Densities BI-RADS Score

	R1			R2		
	Sensitivity	**Specifity**	**AUC**	**Sensitivity**	**Specifity**	**AUC**
Non-dense	86%	45%	0.820	94%	56%	0.827
Dense	93%	54%	0.893	92%	65%	0.901
P	.395	.590	.184	.886	.575	.167

Table 3. Diagnostic Efficiency of Diffusion MRI Calculated from ADC Value at Different Breast Densities ADC

	R1			R2		
	Sensitivity	**Specifity**	**AUC**	**Sensitivity**	**Specifity**	**AUC**
Non-dense	79%	65%	0.704	88%	59%	0.782
Dense	89%	72%	0.805	97%	70%	0.835
P	.228	.645	.154	.135	.420	.401

Magnetic Resonance Imaging Protocol

Imaging was performed on 1.5T MRI systems (Siemens Magnetom Symphony and Aera; Siemens Healthcare, Erlangen, Germany) using dedicated phased-array breast coils.

The imaging protocol included T2-weighted (TR/TE, 4000/70 ms; FOV read 350; 3 mm thickness; number of slices 20), dynamic contrast-enhanced T1-weighted (TR/TE, 700/12 ms; FOV read 350; thickness 2 mm; number of slices 30), and diffusion-weighted sequences (DWI technical parameters; 4-channel coil, axial plan, Diffusion MRI sequence–2B SE-EPI; TR/TE 5400/94; Slice thickness 3 mm; In-plane reszolüsyon (mm); 1.7 × 1.7; Matrix 192 × 192; Fat Supression; Bandwidth (BW) 1370; b value 50, 400, 1000; Acquisition time (min) 2.38).

For dynamic contrast enhancement, 0.1 mmol/kg body weight of gadolinium-based contrast agent was administered intravenously at a rate of 2 mL/s, followed by a 20-mL saline flush. Diffusion-weighted imaging was acquired prior to dynamic contrast-enhanced imaging. Apparent diffusion coefficient maps were automatically generated.

Qualitative Analysis of Magnetic Resonance Imaging

Image interpretation was performed independently by 2 experienced radiologists (Radiologist H.A.A.K. with 20 years and Radiologist S.K. with 25 years of breast MRI experience) on a Leonardo workstation (Siemens Healthcare).

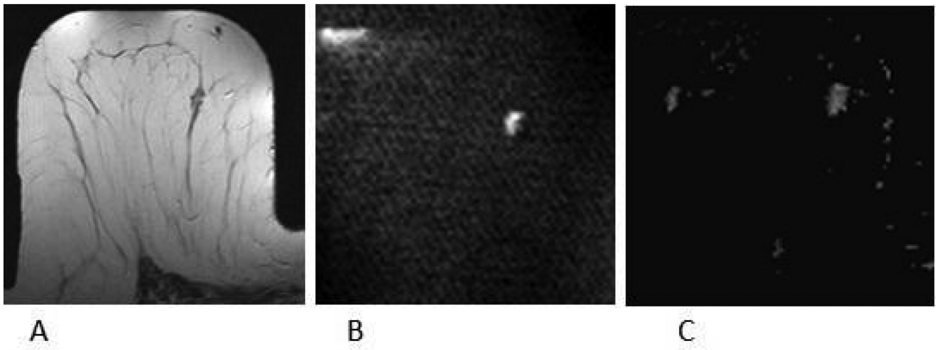

Figure 1. Invasive ductal carcinoma of 11 mm. An irregularly shaped mass is visible on the T2-weighted image (A). The mass is highly visible and has high DWI signal as seen on the high b value image. Malignancy score was 5-6 on qualitative assessment (B). The ADC value of the mass was measured as 0.95-1.02 × 10^{-3} mm^2/s on ADC map (C).

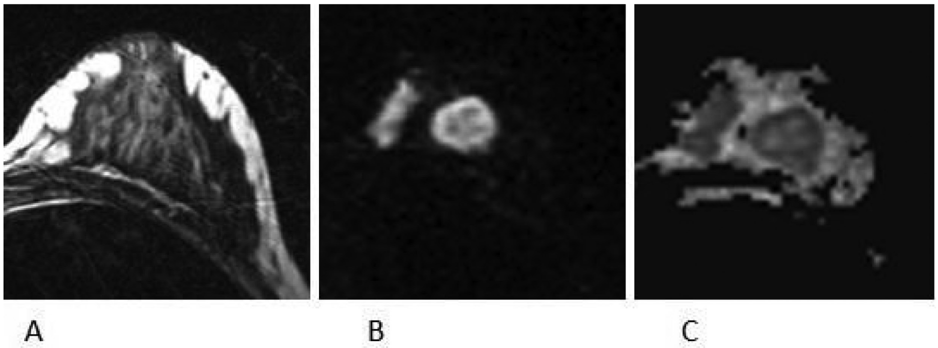

Figure 2. Invasive ductal carcinoma of 21 mm. Due to dense breast pattern tumor is not visible on the T2-weighted image (A). The mass is highly visible and has high DWI signal on the high b value image. Malignancy score was 7 (B). The ADC value was 0.56-0.72 × 10^{-3} mm^2/s, measured on the ADC map (C).

Evaluations for DWI were conducted in separate sessions separated by a 3-week interval. Throughout the interpretation process, the radiologists remained blinded to clinical information and final diagnostic outcomes.

Evaluation parameters included tumor visibility (scored on a 4-point scale: 0 not seen, 1=poor, 2=moderate, 3=high), Breast Imaging Reporting and Data System (BI-RADS) score, and tumor ADC value. Each case was evaluated based on a single, index lesion that was considered to be the most suspicious.

The BI-RADS score (7-point scale) (citation BI-RADS 2013) was determined considering the morphological features of the tumor on diffusion-weighted images and the signal intensity on the ADC map. Tumor ADC values were measured from the ADC maps. The effectiveness of tumor visibility and characterization in different breast densities (a, b=non-dense; c, d=dense) was compared using Student's *t*-test, chi-square test, and receiver operating characteristic (ROC) analysis.

Quantitative Analysis of Magnetic Resonance Imaging

Tumor size and ADC values were assessed by a single radiologist (X) following the completion of morphologic evaluations. This assessment constituted the final stage of the independent reading sessions conducted by this radiologist. Tumor size was determined on the axial slice demonstrating the largest tumor dimension. The ADC values were measured on ADC maps utilizing circular regions of interest encompassing at least 3 pixels. Measurements were acquired from the region within the tumor exhibiting the most pronounced diffusion restriction. A minimum of 3 measurements were performed, and the lowest value was utilized for subsequent analysis.

Statistical Analysis

Statistical analyses were conducted using SPSS Statistics version 23.0 (IBM SPSS Corp.; Armonk, NY, USA).

Inter-method and inter-reader agreement was assessed using Cohen's kappa statistics. Kappa values were calculated 0.597, $P < .001$. The discriminative ability of DWI parameters was evaluated using ROC curve analysis. Sensitivity, specificity, and area under the curve (AUC) values were calculated for each MRI system to assess the diagnostic performance.

Statistical significance was defined as a *P*-value less than .05.

RESULTS

A total of 86 benign and 130 malignant cases were included in the study. One hundred and sixteen cases had dense breast parenchyma, while 100 had non-dense parenchyma. The mean tumor visibility score on DWI-MRI was significantly higher in non-dense breasts compared to dense breasts ($P < .03$) (Table 1). The diagnostic performance of DWI for

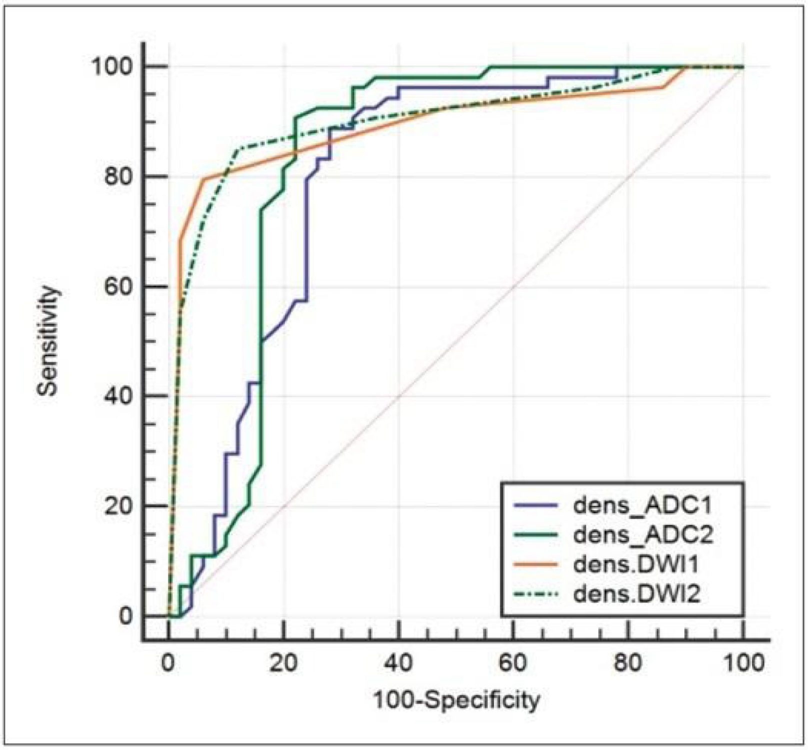

Figure 3. Sensitivity, specificity, and diagnostic accuracies (AUC value) were calculated from the BI-RADS score and ADC value of dense breast densities. No difference was found in the sensitivity, specificity, and AUC value calculated from the BI-RADS score and ADC value in different breast densities (P > .05).

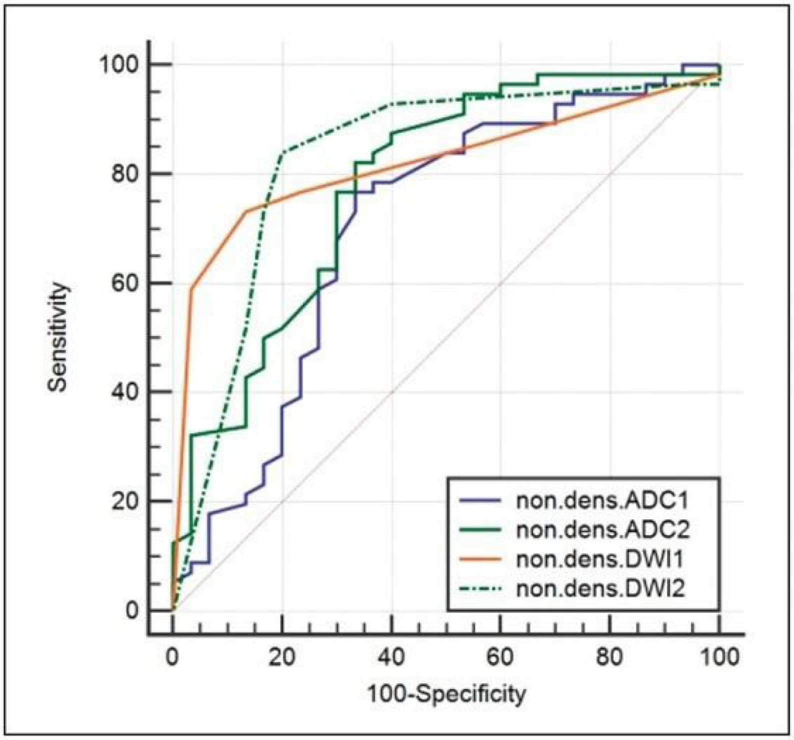

Figure 4. Sensitivity, specificity, and AUC value calculated from the BI-RADS score and ADC value of non-dense breast densities. No difference was found in the sensitivity, specificity, and AUC value calculated from the BI-RADS score and ADC value in different breast densities (P > .05).

cancer detection was calculated 89%-97% in dense breasts and 79%-94% in non-dense breasts (Figures 1 and 2). However, there were no significant differences in sensitivity, specificity, and diagnostic accuracy (AUC value) based on BI-RADS score (Table 2) and ADC value (Table 3) across different breast densities ($P > .05$) (Figures 3 and 4).

The mean ADC value was significantly lower in malignant tumors compared to benign tumors ($P < .001$).

There was a moderate level of inter-observer agreement in BI-RADS assessment (kappa = 0.597, $P < .001$).

DISCUSSION

The results indicate that DWI-MRI can effectively visualize and characterize breast lesions without being influenced by breast fibroglandular tissue density. This conclusion is supported by the observation of significantly lower mean ADC values in malignant lesions compared to benign lesions.

These findings corroborate the observations of previous research which demonstrated diminished ADC values in malignant breast neoplasms.[1] This reduction is attributed to the increased cellular density and restricted water movement within these tumors.

The DWI-MRI is an advanced radiological imaging technique with high efficacy in characterizing breast tumors even in dense breasts. By evaluating the ADC value and tumor morphological features, benign and malignant tumors can be differentiated with 80%-90% accuracy. However, the diagnostic accuracy of DWI-MRI is influenced by various technical and patient-related factors.

Breast fibroglandular tissue density, a significant patient-related variable, is a major determinant of diagnostic efficacy in mammography. Effective fat suppression in DWI-MRI is indispensable for enhancing tumor visibility and reducing artifacts. While it might be expected that DWI-MRI would have reduced diagnostic efficacy in breasts with excessive fatty tissue due to suppression issues and artifacts, this study demonstrated that the diagnostic efficacy of DWI-MRI is not affected by breast density and tumor visibility is higher in fatty breasts.

In a retrospective study performed by Wielema et al[9] in 400 consecutive patients with no history of breast surgery or breast implants, dense breasts were found to have excellent fat suppression and significantly higher DWI image quality than non-dense breasts. The findings provide further evidence in support of the conclusions drawn in this study with quantitative ADC calculations.

According to this study results, DWI-MRI demonstrates a high sensitivity for the detection of malignant breast tumors, independent of breast fibroglandular tissue density.

Tumor visibility and the diagnostic accuracy of DWI are not influenced by fibroglandular tissue density.

This retrospective study has several limitations. The distribution of benign and malignant tumors may not be representative of the general population, and histopathological correlation was lacking in 27 cases. Additionally, the study's focus was limited to index tumors. Larger-scale studies are required to fully document the efficacy of DWI in all its applications.

Diffusion-weighted MRI can serve as a valuable adjunct to conventional mammography in improving the detection of breast cancer, particularly in women with dense breasts.
The diagnostic efficacy of DWI-MRI is unaffected by breast fibroglandular tissue density. Diffusion-weighted imaging demonstrates a high detection rate of cancer in dense breasts, making it a potential alternative to mammography in clinical settings where mammography is less effective.

Data Availability Statement: The data that support the findings of this study are available on request from the corresponding author.

Ethics Committee Approval: This study was approved by the ethics committee of Karadeniz Technical University (Approval No: 2025/16 Date: 25.03.2025).

Informed Consent: Written informed consent was obtained from from the patients who agreed to take part in the study.

Peer-review: Externally peer-reviewed.

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