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Potential of MRI with diffusion weighted imaging in characterization of BIRADS IV Breast lesions in comparison with dynamic contrast-enhanced MRI

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Abstract
Background: MRI is becoming an essential tool for the assessment of breast pathology. Diffusion-weighted images provide quantitative and qualitative information reflecting the changes in tissue cellularity and integrity of cell membranes.
Objectives: The aim of this study is to evaluate the diagnostic accuracy of DWI in the differentiation of BIRADs IV breast lesions and to assess the diagnostic performance of DWI as an adjunct to the dynamic enhanced breast MRI.
Method: MRI unit, Radiology Department, Al-Sadr Teaching Hospital, Basra, performed a randomized prospective cross-sectional research on sixty female patients from April 2022 to February 2023. All patients with suspected breast lesions (BIRAD IV) found by ultrasonography or mammography. All had diffusion-weighted and dynamic contrast MRI. All individuals were examined using a Philips (Tesla 1.5). An experienced breast imaging radiologist analyzed the images before histology.
Results: Thirty-seven malignant and twenty-three benign lesions were identified in 60 patients (mean age (of 18-64y). The mean ADC value for malignant lesions were (0.866±0.25 X 10^{-3} mm2/s) and for benign lesions were (1.40-0.11) with an observed significant difference of (P-value=0.023). The sensitivity and specificity of the Dynamic and DWI showed that DWI had a higher sensitivity (100%) compared to the Dynamic contrast study (94.6%) while regarding the specificity Dynamic had a higher specificity (100%) compared to DWI (95.7%). Conclusion: DWI is a short unenhanced scan that can be a potential adjunct to conventional breast MRI and can be used to accurately characterize breast lesions with high sensitivity and specificity.

Keywords: ADC value, breast mass, diffusion-weighted image

Introduction
Diffusion-weighted imaging (DWI) is a functional MRI technique that provides insights into the microstructural properties of tissues by measuring the movement of water molecules. This movement is quantified using the apparent diffusion coefficient (ADC), which is inversely related to tissue cellularity and membrane integrity. Malignant lesions typically show lower ADC values due to their high cellular density and reduced extracellular space, indicating restricted water diffusion. However, the variability in ADC values between benign and malignant lesions makes it challenging to establish definitive cutoffs for diagnosis [1-3]. The breast anatomy is vital for understanding imaging findings. It consists of lobes, lobules, and the terminal ductal lobular unit (TDLU), which is the primary site for many invasive cancers. The breast's vascular and lymphatic systems are complex, with arterial supply from the subclavian and axillary arteries and lymphatic drainage primarily to the axillary lymph nodes [4-6]. Breast imaging techniques like mammography, ultrasound, and MRI are crucial for early cancer detection and diagnosis. Mammography is effective for screening and detecting early-stage cancers, while ultrasound is used for evaluating palpable masses and guiding biopsies. MRI, with its high sensitivity for invasive cancer, is an excellent tool for assessing occult lesions and preoperative staging. The Breast Imaging Reporting and Data System (BIRADS) provides standardized reporting to aid in management decisions based on imaging findings [7, 8]. DWI has been particularly useful in breast imaging to differentiate between benign and malignant lesions by assessing the diffusion characteristics of tissues.

High cellular density in malignant tissues results in restricted diffusion, reflected by lower ADC values. However, other conditions like abscesses or hemorrhages can also show low ADC values, necessitating careful correlation with other MRI sequences to avoid misdiagnosis [9, 10]. In clinical practice, DWI enhances the specificity of MRI evaluations, helping to distinguish between different types of breast lesions and potentially reducing unnecessary biopsies. It requires careful attention to imaging protocols and patient positioning to ensure accurate and reliable measurements [11, 12]. The aim of study is to the study aims to assess the diagnostic accuracy of diffusion-weighted MRI (DW-MRI) and the apparent diffusion coefficient (ADC) in differentiating between benign and malignant BIRADS IV breast lesions, it seeks to establish a cutoff ADC value that effectively distinguishes between benign and malignant findings within this category, additionally, the study will evaluate the combined diagnostic performance of DWI with dynamic contrast-enhanced MRI to potentially reduce unnecessary breast biopsies.

Method

A prospective cross-sectional study was conducted from April 2022 to February 2023 at the MRI unit of Al-Sadr Teaching Hospital in Basra, enrolling 60 patients with suspicious BIRADS IV breast lesions identified via ultrasonography or mammography. The study utilized simple random sampling, and the sample size was calculated using Steven K. Thompson's formula to ensure minimized error through rigorous planning and sampling strategies. The inclusion criteria focused on patients with BIRADS IV lesions, while those with MRI contraindications, pregnancy, prior biopsies, or inability to maintain a prone position were excluded from the study. Ethical approval and verbal consent were secured from each participant, with endorsements from the Arab Board of Health Specializations and the Basra Health Directorate. MRI examinations were performed using a Philips 1.5 Tesla system, employing multiple sequences including axial T_1 and T_2 weighted images, T_2 fat suppression, DWI with multiple B-values, and dynamic contrast-enhanced T_1 post-contrast imaging. Gadolinium contrast was administered intravenously followed by a saline flush, with specific parameters set for each sequence to ensure detailed and accurate imaging. Image analysis was independently conducted by an experienced radiologist using the BI-RADS MRI vocabulary to evaluate lesion morphology, size, signal intensity, enhancement pattern, and location. ADC values were measured on the ADC map, avoiding hemorrhagic or necrotic areas of the lesions, and the dynamic curves were categorized into persistent, plateau, or washout types to aid in differentiation between benign and malignant findings. Statistical analysis was carried out using SPSS version 26, with categorical data analyzed via Chi-square and Fisher exact tests, and continuous variables compared using one-way ANOVA. Sensitivity, specificity, positive and negative predictive values were computed, and a ROC curve was used to determine the optimal ADC cutoff value for distinguishing between benign and malignant lesions. Results were considered statistically significant with a confidence interval of 95% and a P-value less than 0.05.

Results

The study involved 60 patients, divided into two groups based on lesion type: 23 with benign lesions and 37 with malignant lesions. These patients were further categorized into five age groups. There was a significant age-related difference between the two groups (p<0.001), with the majority of benign cases being younger than 30 years, while the most common age range for malignant cases was 40-49 years. Marital status also showed significant differences (P=0.001), with a higher percentage of married individuals in the malignant group (97.3%) compared to the benign group (65.2%). Additionally, body mass index (BMI) differed significantly between the groups (P=0.024), with obesity being more prevalent in the malignant group. No significant differences were found regarding geographic location of the patients, with most participants from both groups residing in central areas.

Table 1: Demographical data distribution.

Variables		Benign (No.23)	Malignant (No.37)	P value
Age	<30	12 (52.2%)	2 (5.4%)	<0.001*
	30-39	6 (26.1%)	8 (21.6%)	
	40-49	3 (13.0%)	14 (37.8%)	
	50-59	2 (8.7%)	5 (13.5%)	
	>60	0 (0.0%)	8 (21.6%)	
Address	Peripheral	10 (43.5%)	9 (24.3%)	0.121
	Central	13 (56.5%)	28 (75.7%)	
Marital status	Married	15 (65.2%)	36 (97.3%)	0.001*
	Single	8 (34.8%)	1 (2.7%)	
Body mass index (BMI)	Normal weight	7 (30.4%)	3 (8.1%)	0.024*
	Overweight	6 (26.08%)	14 (37.83%)	
	Obese	10 (43.47%)	20 (54.05%)	

* Significant at P value < 0.05

The study showed significant differences between the groups in terms of the site of the breast (P=0.006) where most of the patients with benign lesions had their mass at the lower outer quadrant of the breast followed by lower inner quadrant, upper outer quadrant, upper inner quadrant, and retro areolar (30.4%, 26.1%, 21.7%, 13.0%, 8.7%) respectively while most patients with malignant lesions had their mass at the upper outer quadrant of the breast followed by retro areolar and lower inner quadrant, or lower outer quadrant, or upper inner quadrant of the breast (64.9%, 10.8%, 8.1%) respectively. Additionally, significant differences were observed between the study groups regarding BIRAD IV subtypes (P<0.001) where most patients with benign lesions were BIRAD A followed by B, and C (60.9%, 34.8%, 4.3%) respectively while most patients with malignant lesions were BIRAD C followed by B, and A (67.6%, 24.3%, 8.1%) respectively. (Table 2).

Table 2: Breast site findings distribution.

Quadrant	Benign (%)	Malignant (%)
Lower inner quadrant	26.1%	8.1%
Upper outer quadrant	21.7%	64.9%
Lower outer quadrant	30.4%	8.1%
Retroareolar	13.0%	10.8%
Upper inner quadrant	8.7%	8.1%
BIRAD	Benign (%)	Malignant (%)
A	60.9%	8.1%
B	34.8%	24.3%
C	4.3%	67.6%

The MRI study demonstrated significant differences between benign and malignant breast lesions across various imaging characteristics: Internal Enhancement of Mass: Most patients with benign lesions displayed homogeneous

enhancement (57.16%), whereas the majority of those with malignant lesions exhibited heterogeneous enhancement (78.95%). Margin of the Mass: All benign lesions had circumscribed margins, contrasting sharply with malignant lesions, where 89.48% had un-circumscribed margins. Shape of the Mass: Benign lesions were predominantly rounded (85.71%), while malignant lesions were mostly irregular (73.68%). Enhancement Curve Type for Mass: Benign lesions commonly showed type I and II enhancement curves, whereas malignant lesions frequently had type II curves followed by type III. Internal Enhancement of Non-Mass: There was a significant variation, with benign lesions mostly showing homogeneous internal enhancement (88.88%), in contrast to the heterogeneous pattern seen predominantly in malignant lesions (55.56%). Distribution of Non-Mass: Benign lesions typically had a regional distribution, while malignant lesions often showed a segmental distribution. Enhancement Curve Type for Non-Mass: Benign lesions mostly exhibited type II enhancement curves, whereas malignant lesions were more likely to show type II curves followed by type III. As in tables 3, 4.

Table 3: MRI findings of Mass.

Variables		Benign (No.14)	Malignant (No.19)	P value
Internal enhancement of mass	Central	3 (21.42%)	0 (0.0%)	<0.001*
	Homogenous	7 (50.16%)	0 (0.0%)	
	Rim enhancement	1 (7.0%)	4 (21.05%)	
	Heterogenous	0 (0.0%)	15 (78.95%)	
	Non- septal enhancement	3 (21.42%)	0 (0.0%)	
Margin	Circumscribed	14 (100.0%)	2 (10.52%)	<0.001*
	Un Circumscribed	0 (0.0%)	17 (89.48%)	
Shape	Roud	12 (85.71%)	4 (21.05%)	<0.001*
	Irregular	0 (0.0%)	14 (73.68%)	
	Oval	2 (14.29%)	1 (5.27%)	
Enhancement curve type	I	7 (50.0%)	1 (5.27%)	<0.001
	II	7 (50.0%)	10 (52.63%)	
	III	0 (0.0%)	8 (42.10%)	

***** Significant at P value < 0.05

Table 4: MRI findings distribution of non-Mass.

Variables		Benign (No.9)	Malignant (No.18)	P value
Internal enhancement of non- mass	Clumped	0 (0.0%)	3 (16.67%)	0.024*
	Homogenous	8 (88.88%)	5 (27.77%)	
	Heterogeneous	1 (11.12%)	10 (55.56%)	
Distribution of non- mass	Focal	3 (33.33%)	4 (22.22%)	0.028*
	Linear	2 (22.23%)	2 (11.11%)	
	Regional	4 (44.44%)	2 (11.11%)	
	Segmental	0 (0.0%)	10 (55.56%)	
Enhancement curve type	I	3 (33.3%)	1 (5.56%)	<0.001*
	II	6 (66.7%)	12 (66.67%)	
	III	0 (0.0%)	5 (27.77%)	

* Significant at P value < 0.05

In terms of Histopathological findings, most patients with malignant types had ductal carcinoma followed by ductal carcinoma in situ, lobular carcinoma, lymphoma, or metastasis (45.0%, 5.0%, 6.7%, 1.7%) respectively with an ADC X 10-3 mm2/s value of (0.903±0.223, 1.112±0.418, 0.904±0.0566, 0.846, 0.115) respectively. While most benign patients had fibro adenoma followed by fibrocystic disease, ductectesia or fat necrosis, abscess, or hematoma (18.3%, 10.0%, 3.3%, 1.7%) respectively with an ADC X 10-3 mm2/s value of (1.454±0.803, 1.402±0.062, 1.365±0.014, 1.428±0.0219, 0.996, 1.423) respectively. The mean level of ADC X10-3 mm2/s was significantly higher among benign (1.40±0.111) lesion in comparison to malignant lesion (0.866±0.256) with (P- Value 0.023) (Table 5).

Table 5: Histopathological findings and thee ADC $X10^{-3}$ mm2 value.

Variables		Frequency	Percentage	ADC value
Malignant types	Ductal Carcinoma	27	(45.0%)	0.903±0.223*
	Ductal Carcinoma in situ	5	(8.3%)	1.112 ±0.418*
	Lobular carcinoma	3	(5.0%)	0.904±0.0566
	Lymphoma	1	(1.7%)	0.846
	Metastasis	1	(1.7%)	0.115
Benign types	Abscess	1	(1.7%)	0.996
	Ductectesia	2	(3.3%)	1.365±0.014
	Fibro adenoma	11	(18.3%)	1.454±0.803
	Fat necrosis	2	(3.3%)	1.428±0.0219
	Fibrocystic disease	6	(10.0%)	1.402±0.062
	Hematoma	1	(1.7%)	1.423

*P value 0.04 between the two groups

The sensitivity and specificity of the Dynamic and ADC X10^{-3} mm2 showed that ADC X10-3 mm2/s had a higher sensitivity (100%) compared to Dynamic (94.6%) while regarding the specificity Dynamic had a higher specificity (100%) compared to ADC X10-3 mm2/s (95.7%). Additionally, Dynamic had a positive predictive value of (100%) while the negative predictive value was (92%) however ADC X10-3 mm2/s had a positive predictive value of 97.4% with a negative predictive value of (100%). (Table 6).

Table 6: The sensitivity and specificity of the Dynamic and ADC X10-3 mm2/s

Variables	Sensitivity	Specificity	Positive predictive value	Negative predictive value	Accuracy rate
Dynamic	94.6%	100.0%	100.0%	92.0%	96.66%
ADC X 10-3 mm2	100.0%	95.7%	97.4%	100.0%	98.33%

* Significant at P value < 0.05

ADCX10-3mm2/s was higher among the benign lesions compared to the malignant lesions with non-significant differences between mass and non-mass in each category as recorded in the table below (Table 7).

Table 7: The histopathological findings distribution in regard to the ADC X10^{-3} mm2/s.

Variables		Frequency (No. 60)	ADC X10-3 mm2/s (Mean± SD)	P value
Benign	Mass	14 (23.3%)	1.417±0.136	0.914
	Non-mass	9 (15.0%)	1.388±0.037	
Malignant	Mass	19 (31.7%)	0.894±0.101	0.87
	Non-mass	18 (30.0%)	0.839-0.037	

Discussion

Diffusion-weighted magnetic resonance imaging (DW-MRI) is a non-invasive tool that evaluates the physiological characteristics of tissues by measuring the Brownian motion of water molecules, quantified through the apparent diffusion coefficient (ADC). Studies have shown that ADC values are generally lower in malignant tumors compared to benign ones due to higher cellular density, larger nuclei, and reduced extracellular spaces in malignant tissues. This inverse relationship between ADC values and tumor cellularity has been consistently documented across various studies, supporting the utility of DW-MRI in distinguishing between benign and malignant breast lesions [13-15]. Previous research has reported varying levels of sensitivity and specificity in using ADC values for this purpose. For instance, Al-Saadi *et al*. found a significant distinction between the ADC values of benign and malignant lesions, with a cutoff value of 1.175x10-3 mm2/sec yielding high sensitivity (95.2%) and specificity (93.8%). These findings are consistent with other studies that have also noted the diagnostic advantages of DW-MRI in breast imaging [16]. However, several factors influence the accuracy of ADC measurements, including the menstrual cycle, hormone replacement therapy, and differences in MRI protocols and field strengths. These variations can lead to discrepancies in ADC values across different studies, impacting the overall reliability of DW-MRI in clinical settings [17]. Notably, the mean ADC values for ductal carcinoma in situ (DCIS) and invasive ductal carcinoma (IDC) illustrate the variability within malignant lesions themselves. DCIS, characterized by lower cellular density and more extensive fibrous stroma, typically shows higher ADC values than IDC, which has tightly packed cells and minimal fibrous stroma. This distinction is crucial for accurate diagnosis and was observed in the study where DCIS had a mean ADC value of 1.112±0.418 x10-3 mm2/s, and IDC had 0.903±0.223 x10-3 mm2/s [18-20]. The study also explored the difference in ADC values between mass-enhancing and non-mass-enhancing (NME) lesions. Findings indicated minimal differences in ADC values between malignant mass lesions and NME lesions, which aligns with results from Partridge *et al*. and contrasts with findings by Imamura *et al*., highlighting the challenges in using DWI for NME lesions. This is partly due to NME lesions' tendency to integrate into rather than displace normal breast parenchyma, leading to higher partial volume effects and less distinct ADC measurements [15, 21]. Moreover, dynamic contrast-enhanced MRI (DCE-MRI), when used alongside DW-MRI, has demonstrated improved diagnostic performance. Kul *et al*.'s study on 84 patients underscored that combining DCE-MRI and DW-MRI enhances both sensitivity and specificity, making it a potent protocol for evaluating ambiguous breast lesions. In this combined approach, the sensitivity and specificity for DCE-MRI alone were 97.9% and 75.7% respectively, while the combined usage improved specificity to 89.2% [22]. DW-MRI serves as a critical imaging modality in breast cancer diagnostics due to its ability to characterize tissue based on the microenvironmental properties of water molecule mobility. The integration of DW-MRI with DCE-MRI promises to refine diagnostic accuracy, reduce unnecessary biopsies, and better differentiate between various types of breast lesions, enhancing the overall management of breast cancer patients [22, 23].

Conflict of Interest

Not available

Financial Support

Not available

Conclusion:

DWI is a short unenhanced scan that can be a potential adjunct to conventional breast MRI and can be used to accurately characterize breast lesions with high sensitivity and specificity.

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