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Role of magnetic resonance imaging in the evaluation of non-palpable breast masses

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Abstract

Background: Dynamic contrast-enhanced magnetic resonance imaging (DCE-MRI) provides anatomical and functional information with high sensitivity and variable specificity, making it a useful tool in the detection of breast cancer. The noninvasive functional imaging method known as diffusion-weighted imaging (DWI), sensitive to tissue microstructure and cellularity. The aim of this work was to assess the role of DCE-MRI and DWI in the evaluation of non-palpable breast masses.

Methods: Fifty female cases participated in a prospective research who were suspected to have non-palpable breast masses accidentally discovered or suspected by ultrasound and referred to MR units. All cases were subjected to complete personal and medical history, full clinical examination, laboratory investigations, mammogram and breast ultrasound and breast MRI.

Results: DCE-MRI could predict non-palpable malignant lumps with 89.66% sensitivity, 95.24% specificity, 96.30% (PPV), 86.96% (NPV) and 92% accuracy. MRI could predict non-palpable benign lumps with 90.48% sensitivity, 96.55% specificity, 95% (PPV), 93.33% (NPV) and 94% accuracy. DWI could predict malignant masses with 93.10% sensitivity, 71.43% specificity, 81.82% (PPV), 88.24% (NPV) and accuracy 84%.

Conclusions: DCE-MRI outperformed DWI-MRI in diagnostic performance; however, DWI-MRI still demonstrated good diagnostic performance with a 93.1% sensitivity and specificity of 71.4%. Both are excellent non-invasive techniques that are very useful in assessing non-palpable breast masses.

Keywords: Magnetic resonance imaging, non-palpable breast masses, diffusion-weighted imaging, dynamic contrast-enhanced

Introduction

Breast cancer has a higher incidence in industrialized countries than in less-developed ones. As a leading killer of women, early detection of cancer is crucial to lowering mortality rates [1].

Masses in the breast that cannot be detected during a regular clinical exam but are detectable on a mammogram are known as non-palpable breast lumps [2].

Breast cancer screening and diagnostic procedures have progressed to the point that non-palpable breast masses are increasingly being found. These approaches include mammography, breast ultrasonography, magnetic resonance imaging, fine-needle aspiration cytology, core biopsy, and vacuum-assisted core biopsy [3].

Not all of these lumps are cancerous. Twenty percent to thirty percent of these small growths are cancerous [4].

Magnetic resonance imaging (MRI) of the breast has been shown to be a sensitive imaging technique for the detection and characterisation of breast masses [5, 6]. High levels of sensitivity in detecting breast cancer, with varying degrees of specificity [5] are offered by dynamic contrast-enhanced (DCE)-MRI, which provides morphological and functional lesion information. Anxiety in cases awaiting biopsy findings that show benignity may emerge from a diagnosis with only moderate specificity, which may lead to unnecessary follow-up case work-up and biopsies [5, 6].

Over the past few decades, methods have been incorporated into the routine clinical interpretation of breast MRI exams that look at other MRI sequences alongside DCE-MRI images to avoid this limitation and assess more functional data [6, 7].

Because of its sensitivity to tissue microstructure and cellularity, diffusion-weighted imaging (DWI) is a crucial component of noninvasive functional imaging. A quantitative measure of diffusion, the apparent diffusion coefficient (ADC) is increasingly being utilized to describe and differentiate lumps^[8].

The b-value quantifies the degree to which diffusion is weighted. Only entities with both a strong water signal and severe diffusion limitation, like most malignant breast tumors, should be discernible on very high b value images^[9].

The purpose of this research was to assess the role of dynamic DCE-MRI and DWI in the evaluation of non-palpable breast masses.

Patients and Methods

Fifty female cases aged between 35 to 62 years participated in a prospective research, with mean age 51 years \pm 6.5 who were suspected to have non-palpable breast masses accidentally discovered or suspected by ultrasound and referred to MR units of Radio diagnosis Department at Tanta University Hospital from August 2020 to August 2022.

The research was done after approval from the Ethical Committee Tanta University Hospitals (approval code: 33017/03/19). An informed written consent was obtained from each case.

Exclusion criteria were un-cooperative cases with mental or behavioral disorders, presence of cardiac pacemakers, and ferromagnetic intracranial aneurysm clips, claustrophobia, and history of allergy from intravenous contrast media (Gadolinium).

A thorough medical and personal history was taken from each patient, including any known incidences of breast cancer in the patient's family and if treated by surgery, chemotherapy and radiotherapy, presence of breast mass, axillary lumps, breast pain or nipple discharge, full clinical examination as general and local of the breast and axilla to detect masses, nipple retraction, and axillary lymph nodes, and laboratory investigations. Mammogram and breast ultrasound and breast magnetic resonance imaging (MRI) were performed for all cases.

After reassuring the case by explaining the procedure and the length of the examination, the machinery sounds that are typically heard during the assessment, and the value of remaining motionless, cases were asked to change into hospital gowns and remove all metallic objects, including hairpins, coins, and earrings.

Case positioning

The case was immobilized between scans by having an intravenous line put into the dorsum of their hand. The case was put in a prone posture on an MR imaging platform designed to support a dependent breast position during the MRI breast procedure. For the breasts, a special coil was employed. To reduce the likelihood of a false positive MRI due to enhancing lumps caused by the highest hormone levels, MRI was done between days 5 and 15 of the menstrual cycle or after the case had stopped taking

hormone replacement treatment for 4 to 6 weeks. When cancer recurrence was feared, an MRI was done 6 months after surgery and 9 months (or more ideally 12 months) after radiation therapy.

Pulse sequences and scanning planes

The Radio-diagnosis and Imaging Department at Tanta University Hospital used an MRI apparatus with intensity field 1.5 Tesla, with bilateral breast coils, to conduct the MR scans to both breasts in one setting.

The following sequences were collected from localization scans performed in the transverse, sagittal, and coronal planes: Images were acquired using the following parameters and parameters for each plane: fast spin echo (FSE) T1WI (TR=8.6 ms, TE 4.7 ms) in the transverse plane, T2WI with fat suppression (TIRM), (TR=5600 ms, TE=59 ms) in the transverse plane; slice thickness: 4 mm; spacing: 1mm; image matrix: 320x314, STIR (TR=3000 ms, TE The entire breast was imaged seven times before and immediately after the intravenous injection of 0.1 mg of Gd-DTPA/Kg using a 2D fast spoiled gradient-recalled echo sequence with fat suppression in T1WI (TR=4.3 ms, TE=1.3 ms, flip angle 80o axial scan, FOV 34x34 cm, image matrix 448x322).

In the reporting; Lesion features such as size, location, distribution, and associated discoveries, as well as kinetic enhancement characteristics, should be described. In the end, the lesion was classified into one of the American College of Radiology's (ACR) Breast Imaging-Reporting and Data System (BI-RADS) classifications.

Statistical analysis

IBM SPSS Statistics v.26 (Chicago, Illinois, USA) was used for the statistical analysis. The unpaired Student t- test was used to compare the two groups' means and standard deviations (SDs) for the quantitative variables. When applicable, the Chi-square test or Fisher's exact test was used to analyze qualitative variables presented as frequencies and percentages. In this research, statistical significance was defined as a two-tailed P value below 0.05.

Results

The age of research participants ranged from 35 and 62 years with a mean age of 51 years. Around half of the participants were between 50 and 60 years old, while 34% were between 40 and 50 years old, 12% were younger than 40, and 6% were older than 60 years. The mean BMI was 25.5 ± 2.6 kg/m². 54% of the participants were from rural areas while 46% were from urban residencies. 29 cases (58%) had malignant breast lumps while 21 cases (42%) had benign lumps as per histopathological findings. ductal carcinoma (DC) was the most frequent malignant pathology (59%), followed by lobular carcinoma (LC) (31%), and DC in 10% of the malignant lumps. For the benign lumps, seroma and fibroadenoma represented 38% and 19% of the benign lumps, respectively, followed by lipoma, fibrocystic changes, and fat necrosis (9.5%, each). 52% had lumps in their right breast compared to 46% in the left. Only one case (2%) had bilateral breast lumps. Table 1.

Table 1: Case demographics, histopathological findings and mass site distribution (n = 50)

		(n=50)	
Age (years)	Mean ± SD	51.4 ± 6.82	
	35 – 40 years	6 (12%)	
	40 – 50 years	17 (34%)	
	50 – 60 years	24 (48%)	
	60 – 70 years	3 (6%)	
BMI (kg/m ²)		25.55 ± 2.64	
Residence			
Rural		27 (54%)	
Urban		23 (46%)	
Histopathological findings	Malignant lumps (n=29)	DC in situ	3 (6%)
		LC	9 (18%)
		DC	17 (34%)
	Benign lumps (n=21)	Hamartoma	1 (2%)
		Fibroadenosis	1 (2%)
		Abscess	1 (2%)
		Lipoma	2 (4%)
		Fat necrosis	2 (4%)
		Fibrocystic changes	2 (4%)
		Fibroadenoma	4 (8%)
		Seroma	8 (16%)
Mass site or Side of lesion			
Right breast		26 (52%)	
Left breast		23 (46%)	
Bilateral breasts		1 (2%)	

Data are presented as mean ± SD or frequency (%). BMI: Body mass index. LC: lobular carcinoma. DC: ductal carcinoma.

Regarding the Dynamic MRI evaluation of the breast masses 54% of cases had lumps demonstrated ill-defined border, followed by 38% demonstrated well-defined border, and partially defined border in 8%. And regarding to pattern of enhancement 42% of cases demonstrated homogenous enhancement, followed by heterogeneous enhancement were found in 48% and (6, 4%) of cases demonstrated central and peripheral enhancement respectively. Regarding the BI-RADs scores, BI-RADS (V) lumps were 54%, followed by BIRADS (II) were 28%, BIRADS (III) and BIRADS (IV) were 12% and 6% respectively. Table 2.

Table 2: Dynamic MRI evaluation and MRI BI-RADS evaluation among the studied cases

	Count (%)	
Border	Ill-defined	27 (54%)
	Well-defined	19 (38%)
	Partially defined	4 (8%)
Pattern of enhancement	homogenous	21 (42%)
	Peripheral	2 (4%)
	Central	3 (6%)
	heterogeneous	24 (48%)
BI-RADS Score	0	0 (0%)
	I	0 (0%)
	II	14 (28%)
	III	6 (12%)
	IV	3 (6%)
	V	27 (54%)
	VI	0 (0%)

Data are presented as frequency (%). BI-RADS: Breast Imaging Reporting and Database System, MRI: Magnetic resonance imaging

Washout curves (Type III) were seen in 54%, followed by

rising curves (Type I) in 40%. Plateau curves (Type II) were seen in 6% of the cases. Table 3.

Table 3: Dynamic curves types among the studied cases

Impression	Post initial of the curve	(n=50)
Benign lumps	Rising	20 (40%)
Suspicious lumps	Plateau	3 (6%)
Malignant lumps	Washout	27 (54%)

Data are presented as frequency (%).

For benign lumps, the type I curve was seen in 90.5% of the lumps followed by type II and III curves in only one lesion (4.8% for each). For malignant lumps, the type III curve was seen in 89.7% of the lumps followed by type II in 6.9% and type I in 3.4%. Table 4.

Table 4: Association between histopathological findings and DCE-MRI curve types among the studied cases

MRI curve types	Benign (n=21)	Malignant (n=29)
Type I	19 (90.5%)	1 (3.4%)
Type II	1 (4.8%)	2 (6.9%)
Type III	1 (4.8%)	26 (89.7%)

Data are presented as frequency (%). MRI: Magnetic resonance imaging

DCE-MRI correctly identified 26 of the 29 malignant lumps and correctly identified 20 of the 21 non-malignant cases. DCE-MRI correctly identified 19 of the 21 benign lumps and correctly identified 28 of the 29 non-benign lumps. Diffusion-weighted imaging (DWI) MRI correctly identified 27 of the 29 malignant lumps, while correctly identified 15 of the 21 benign lumps. Table 5.

Table 5: Association of DCE-MRI and DWI with histopathology in the evaluation of non-palpable breast masses

		Histopathology		P
		Malignant lesion (n=29)	Benign lesion (n=21)	
DCE-MRI	Malignant	26 (89.7%)	1 (4.8%)	<0.001*
	Non-malignant	3 (10.3%)	20 (95.2%)	
	Benign	1 (3.4%)	19 (90.5%)	<0.001*
	Non- benign	28 (96.6%)	2 (9.5%)	
DWI	Malignant	27 (93.1%)	6 (28.6%)	<0.001*
	Benign	2 (6.9%)	15 (71.4%)	

Data are presented as frequency (%), * significant as P value ≤ 0.05. MRI: Magnetic resonance imaging, DWI: Diffusion-weighted imaging

DCE-MRI could predict non-palpable malignant lumps with 89.66% sensitivity, 95.24% specificity, 96.30% (PPV), 86.96% (NPV) and accuracy 92%. MRI could predict non-palpable benign lumps with 90.48% sensitivity, 96.55%

specificity, 95% (PPV), 93.33% (NPV) and accuracy 94%. DWI could predict malignant masses with sensitivity of 93.10%, specificity of 71.43%, PPV 81.82%, NPV 88.24% and accuracy 84%. Table 6.

Table 6: Diagnostic value of DCE-MRI in the evaluation of non-palpable breast masses and DWI in malignant masses' detection

		Statistic	Sensitivity	Specificity	PPV	NPV	Accuracy
DCE-MRI	Malignant lumps	Value	89.66%	95.24%	96.30%	86.96%	92%
		95% CI	72.63% to 97.82%	76.17% to 99.88%	81.03% to 99.91%	66.42% to 97.22%	80.77% to 97.78%
	Benign lumps	Value	90.48%	96.55%	95%	93.33%	94%
		95% CI	69.63% to 98.83%	82.22% to 99.91%	75.13% to 99.87%	77.92% to 99.18%	83.45% to 98.75%
DWI	Value	93.10%	71.43%	81.82%	88.24%	84%	
	95% CI	77.23% - 99.15%	47.82% - 88.72%	69.44% - 89.91%	65.71% - 96.71%	70.89% - 92.83%	

DCE-MRI: Dynamic Contrast Enhanced Magnetic resonance imaging, DWI: Diffusion-weighted imaging, CI: Confidence interval, PPV: Positive predictive value, NPV: Negative predictive value.

Case 1: A female case aged 40 years old, presented with nipple discharge from the left breast. The case underwent

modified radical mastectomy and the histopathological diagnosis was confirmed with DC. Figure 1.

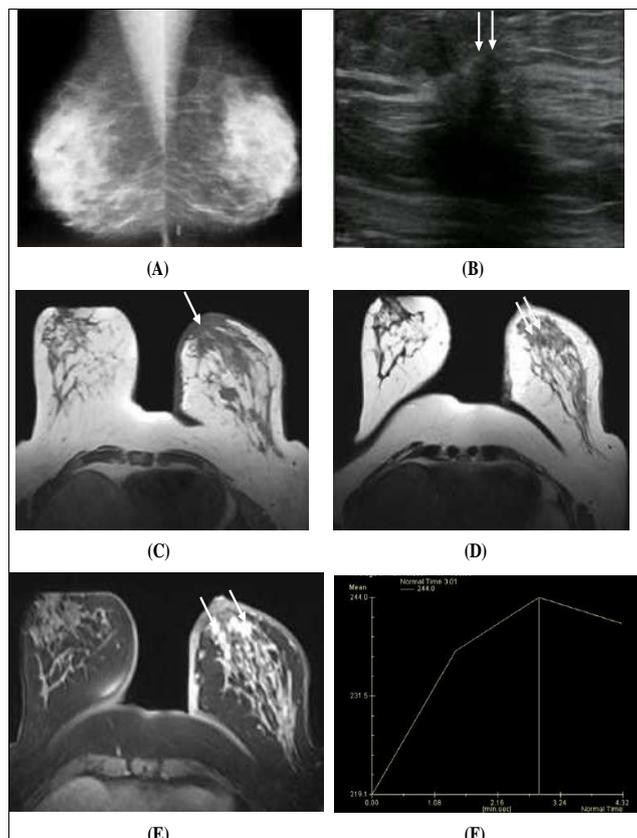


Fig 1: Overall, the MRI findings corroborate the malignant character of the lumps, and the MRI was used to determine a ranking (BIRADS V). A) Left breast mammography ML view: dense breast parenchyma's (ACR-C), B) left B mode ultrasonography: dense breast shows irregular spiculated outline mass of acoustically opaque soft tissue detected retroareolarly in the left breast, C) Axial T1WI pre-contrast: multiple irregular small hypo intense lumps mainly at retro areolar of the left breast, D) Axial T2 WI: slightly hyperintense enhancement of lumps, E) Gadolinium enhancement axial T1: moderate homogenous enhancement of lumps, F) Enhancement Kinetic curve: (type III) washout curve pattern.

Case 2: A female case aged 39 years old, had cancer in right breast 8 months ago treated with conservative surgery and

received chemotherapy and radiotherapy. Figure 2.

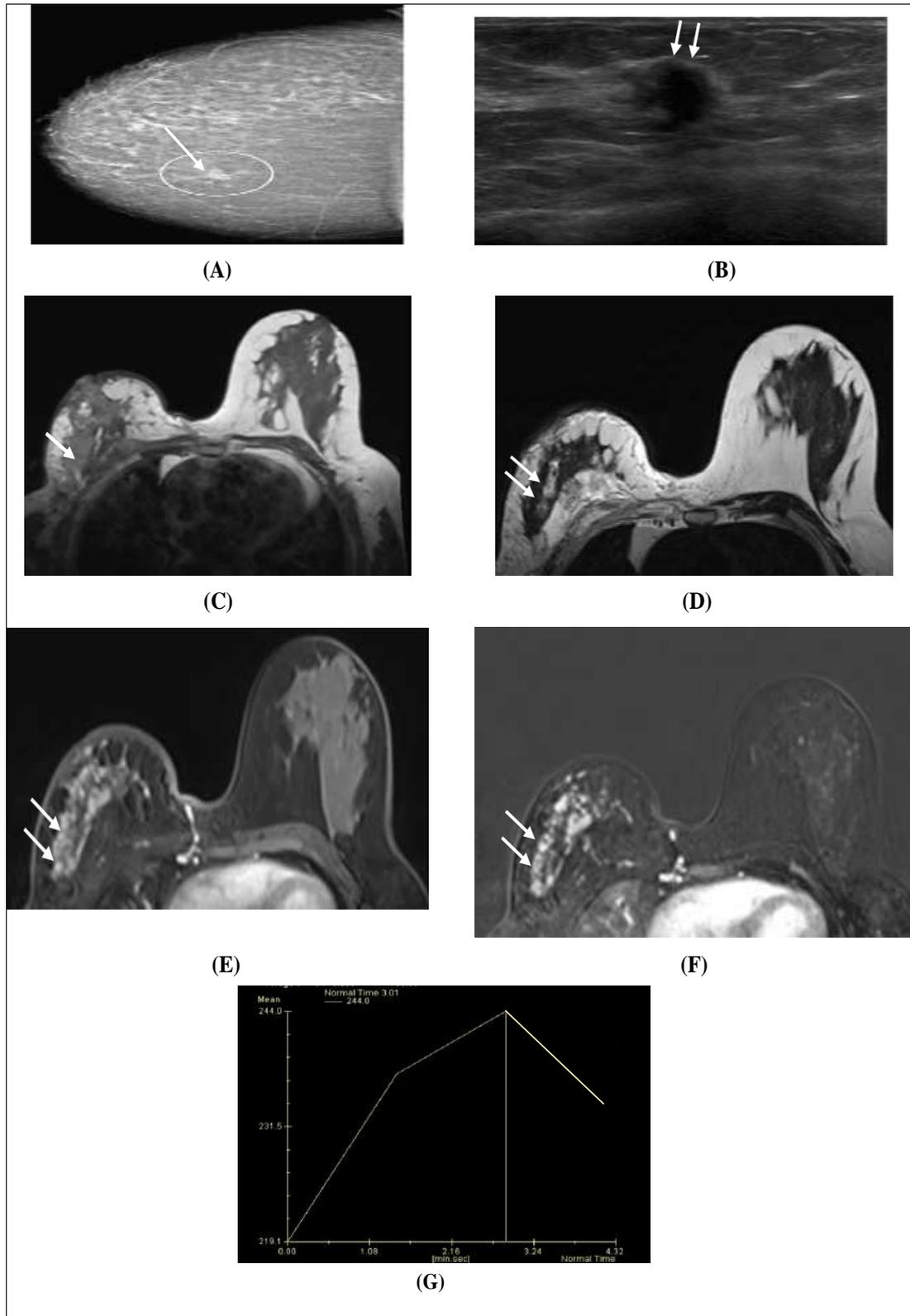


Fig 2: Overall MRI features revealed malignant nature of lumps (BIRADS V) & Histopathology was done & proved invasive lobular carcinoma. A) Right breast mammography ML view: ill-defined opacity seen at lower quadrant with no calcification, B) Right breast B-mode ultrasonography: irregular spiculated outline hypoechoic soft tissue lesion with posterior acoustic shadowing seen at right breast outer quadrant 8 o'clock, C) Axial T1WI pre-contrast: deformed contour of the right breast with several small hypoacoustic lumps at the outer quadrant, D) Axial T2WI: the lumps appear slightly hyperintense, E) Gadolinium-enhanced axial T1: heterogeneous regional non mass lesion enhancement, F) The hyperintense lump in the lower outer quarter of the right breast is more clearly seen in an axial subtraction post-contrast image, G) Enhancement Kinetic curve: type (III) curve washout pattern.

Case 3: A female case aged 50 y, had cancer in left breast 2 years ago, with conservative surgery followed by radio and chemotherapy. Figure 3.

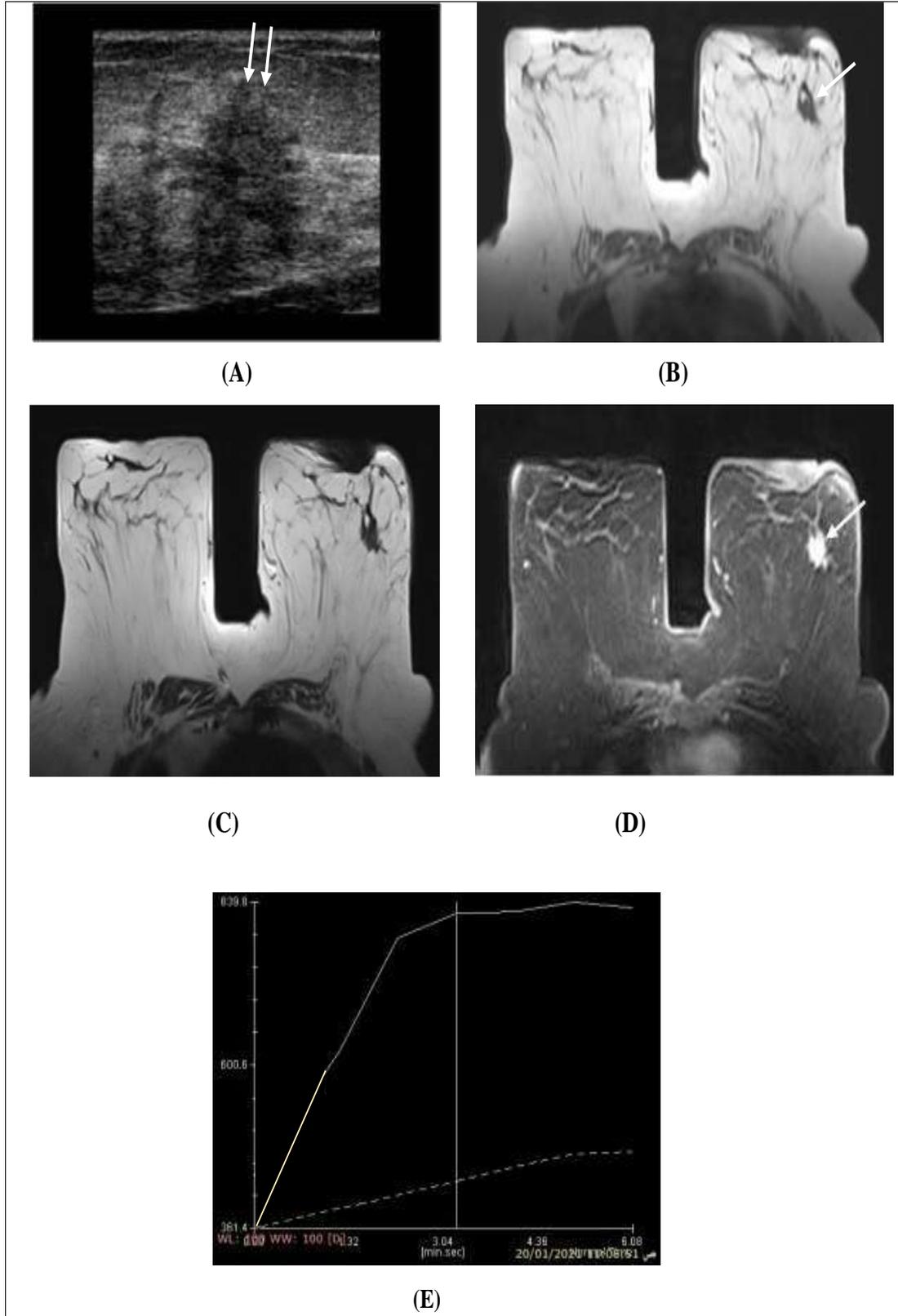


Fig 3: Overall MRI features consistent with the possibility of fat necrosis and recurrent malignancy, (BIRADS IV) histopathology done and proven with fat necrosis. A) An irregularly shaped, spiculated, hypoechoic soft tissue lump with posterior acoustic shading was detected on B-mode ultrasonography of the left breast at 10 o'clock., B) Axial T1 WI pre-contrast: decreased size of the left breast with deformed contour with a well-defined irregular outline hypo intense mass lesion is seen at the upper outer quadrant, C) Axial T2 WI: the mass appears hypo intense, D) Gadolinium Enhanced axial T1 WI Fat-SAT: homogenous hyperintense enhancement of mass with interstitial edema & thickened skin, E) Enhancement Kinetic curve: type (II) It shows early uptake & continuous in late phases followed by a plateau

Discussion

Currently, breast contrast-enhanced MRI (CE-MRI) is the most sensitive detection method available for the diagnosis of breast cancer. Breast cancer and benign diseases can be distinguished with the help of noninvasive imaging techniques like dynamic contrast-enhanced magnetic resonance imaging (DCE-MRI) and diffusion-weighted imaging (DWI-MRI). Characterizing the lesion using morphological analysis and enhancing patterns with kinetic curves^[10].

The age of research participants ranged from 35 and 62 years with a mean age of 51 years. This is comparable with the research by Merckel *et al.*^[11], which had a mean participant's age of 55 years.

In the research by Yadav *et al.*^[12], participants' age ranged between 20 and 68 years with a mean age of 42 years which is inconsistent with the findings of our research. This discrepancy in age distribution could be attributed to the fact that our research included only cases with non-palpable breast lumps while the research by Yadav *et al.*, included only palpable breast masses. Another probable factor is the presence of different baseline population characteristics between both studies such that the research by Yadav *et al.*^[12], had a higher risk group which manifests at younger ages.

In our research, most participants (82%) were aged between 40 and 60 years, fewer cases (12%) were younger than 40 with no cases under 35 years, while only 6% were older than 60 years. This was consistent with the latest recommendations by the American Cancer Society^[13], which recommends the start of annual mammogram screening for women 40 years or older. Despite that the starting age for breast cancer screening is debatable, cases who are at high risk of breast cancer are encouraged to start image screening including mammograms or MRIs typically at age 30.

Of the 50 cases included in our research, 29 cases (58%) had malignant breast lumps while 21 cases (42%) lumps had benign lumps, as per histopathological findings. This was consistent with the findings of the research by Yadav *et al.*^[12], in which 37 out of the 68 (54%) of the palpable breast lumps detected turned out to be malignant by histopathology.

This was inconsistent with the findings of the research by Merckel *et al.*^[11], which reported breast malignancy in only 78 out of 207 cases (38%). This lower rate could be explained by the fact that it included cases from a breast cancer screening program, while our cases were symptomatic cases who hold a higher risk of malignancy^[14]. Our research demonstrated that the most common malignant pathological finding was DC (59%), followed by LC (31%). DC in situ was the least common malignant pathological finding representing only 10% of malignant lumps. This was consistent with the research by Yadav *et al.*^[12], in which DC and LC were the most common malignant pathologies (46, and 30%, respectively), followed by DC in situ in 16%. Invasive ductal and lobular carcinoma was the most seen malignancy (58%) in the research by Merckel *et al.*^[11]. However, ductal carcinoma in situ was diagnosed in 42% of cases which was relatively higher than our research.

Regarding the benign lumps, seroma and fibroadenoma represented 38% and 19% of the benign pathological findings, respectively, followed by lipoma, fibrocystic changes, and fat necrosis (9.5%, each). The research by

Yadav *et al.*^[12] demonstrated that fibroadenoma was the most common benign finding (45%), followed by benign cysts, mastitis, and fat necrosis (23, 16, 6%, respectively). Regarding the MRI findings in our research, 48% of the findings were enhancing masses, followed by non-mass enhancement in 32% of the lumps, and enhancing foci in 20%. In the research by Giess *et al.*^[15], it was reported that mass enhancement was the most common MRI finding (73%), while non-mass enhancement occurred in 27% person of the lumps. The discrepancy between this research and our research could be attributed to the fact that this research might have considered the enhancing foci as mass-enhancing lumps. Other findings such as suspicious lymphadenopathy, fibrocystic disease, and cystic lumps were found in 14, 12%, and 8% of the findings, respectively^[15].

We used BI-RADs MRI lexicon to classify the MRI findings of our cases^[16].

Regarding the BI-RADs scores, BI-RADS II lumps were 28%, III were 12%, IV were 6%, and V were 54%. Our research demonstrated that lumps that required diagnostic follow-up constituted more than half of the lumps (BI-RADS IV and V).

This was consistent with the findings of the research by Merckel *et al.*^[11], which reported that about 56% of the findings in cases with non-palpable breast lumps, were evaluated by an expert radiologist as BI-RADS IV and V and required diagnostic follow-up.

Our research demonstrated that contrast-enhanced breast MRI demonstrated high sensitivity 89.6% for malignant lumps and 90.5% for benign lumps, which indicates that this MRI technique has a great potential in ruling out breast cancer and minimizing false negative results which was a characteristic of a good screening test.

These findings were consistent with the findings of Merckel *et al.*^[11], which reported the sensitivity of DCE-MRI of an expert reader to be 95%.

Our research demonstrated that DCE-MRI of the breast had higher sensitivity when compared to the sensitivity of mammographic imaging reported in other studies as in the research by Yabuuchi *et al.*^[17], which was as low as 40%.

The same research reported a CE-MRI sensitivity of 86% which was slightly smaller than our research.

On the other hand, the specificity of CE-MRI in our research was 95.24% for malignant lumps and 96.55% for benign lumps which was considered comparable to the findings in the research by Yabuuchi *et al.*^[17], which reported a specificity of 100% for contrast-enhanced magnetic resonance imaging.

The positive and negative predictive values of CE-MRI for malignant lumps were 96.3% and 86.96% respectively, and for benign lumps were 95% and 93.33% respectively which was comparable with the research by Yabuuchi *et al.*^[17] which reported values of 100%, and 78%, respectively.

A research by Bluemke *et al.*^[18] demonstrated that DCE-MRI had a PPV 72.4%, and a negative predictive value of 85.4%.

These findings demonstrated that the sensitivity of DCE-MRI was in the range reported in many studies, while the specificity ranged greatly among the literatures. This could be attributed to different baseline characteristics and malignancy risks among included participants^[1, 19, 20].

Our research demonstrated that sensitivity, specificity, PPV, and NPV the DW-MRI for malignant lumps were 93.10%

and 71.43%, 81.82%, and 88.24% respectively which were lower than those of the DCE- MRI. This illustrated that CE-MRI outperformed the DWI.

The research by Yabuuchi *et al.* [17] reported that DW-MRI had sensitivity, specificity, PPV, and NPV 50%, 95%, 95%, and 49%, respectively.

This was inconsistent with the findings of our research. However, different baseline risks in included cases together with different expertise in reading the MRI could alter the findings.

Regarding the dynamic curves, the most common observed curve type was type III (54%) followed by type I (40%) and type II (6%). Type I curve was the most exclusive to benign lumps and it had a 90% sensitivity for benign lumps. Also, the type III curve was most exclusive to malignant lumps with a 90% sensitivity.

Type II curve was underrepresented in our sample, but it was distributed equally in both benign and malignant lumps. The research by Yadav *et al.* [12] demonstrated that the type III curve had a sensitivity of a 92% which was consistent with the findings in our research.

Limitations: Our research was didn't assess the malignancy risk for the included cases which could affect the findings rates in our research. Our research didn't assess the background breast enhancement of each breast which might limit the accuracy the underlying lesion detection.

A systematic review and meta-analysis by Thompson *et al.* [21] demonstrated that higher levels of background enhancement are associated with a higher risk of malignancy in women with a high-risk malignancy. These different characteristics show different malignancy probabilities. We did not research the correlation between BI-RADS score and risk of malignancy. However, it was well established by the ACR that BI-RADS IV lumps have a malignancy likelihood that ranged from 2 to 95%, while BIRADS V lumps had a likelihood greater than 95% [16].

Conclusions

DCE-MRI had an excellent diagnostic performance in diagnosing malignant masses with a sensitivity of 89.6% and a specificity of 95.2%, which indicated the great potential in ruling out breast cancer. DCE-MRI outperformed DWI-MRI in diagnostic performance; however, DWI-MRI still demonstrated good diagnostic performance with a 93.1% sensitivity and specificity of 71.4%. DCE-MRI and DWI-MRI are excellent non-invasive techniques that are very useful in assessing non-palpable breast masses.

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Conflict of Interest: Nil

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