

Dynamic Contrast Study and Diffusion Weighted Imaging with 3T Magnetic Resonance Imaging in Differentiation of Benign from Malignant Masses of Female Breast

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Abstract

Introduction: Breast cancer is the most common cancer in females and is the 2nd leading cause of death among female after lung cancer.

Materials and Methods: Study includes 50 cases of breast masses in female came for magnetic resonance imaging (MRI) examinations between February 2015 and September 2016. MRI examination routine sequences along with dynamic contrast-enhanced (DCE) study and diffusion-weighted imaging (DWI) and the results were compared with the cytopathological examination considered as the standard diagnostic method.

Results: There were 18 benign lesions and 32 malignant lesions found in this study. DCE-MRI proved to have a sensitivity of 93.75%, and a specificity of 72.2% in diagnosing malignant pathologies. Apparent diffusion coefficient cutoff value to differentiate the benign from malignant lesions was $1.4 \times 10^{-3} \text{ mm}^2/\text{s}$ ($P < 0.001$).

Conclusion: The combined MRI protocol including DCE-MRI and DWI proved to be increasing the sensitivity and specificity of MRI in differentiating benign from malignant lesions.

Key words: Breast masses, Diffusion-weighted imaging, Dynamic contrast enhanced magnetic resonance imaging

INTRODUCTION

Breast cancer is the most common cancer in females and is the 2nd leading cause of death among female after lung cancer.¹ Survival in women with breast cancer can be increased by early diagnosis of disease.² There is a increasing clinical interest in developing noninvasive methods that can be used early in the

course of disease to assess risk and to guide subsequent treatment.³

Initial screening modality for detection and localization of breast abnormalities include conventional mammography and ultrasound sonography.⁴ Mammography has long been used for early detection of and screening for breast cancers. It is believed that mammography alone misses between 10% and 30% of all breast cancers. Possible reasons may include density of breast parenchyma and slow growing breast cancers.⁵ Ultrasound has been used as an adjunct to mammography, with particular useful in differentiating cystic from solid lesions and in facilitating guided biopsy of suspicious areas.⁵ Among the newer modalities, US elastography is used, which is based on

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tissue elasticity, three-dimensional ultrasound has also been highlighted.

Magnetic resonance imaging (MRI) is the newer non-invasive imaging modality that has been rapidly developed over the past decade and is regarded as the most potential examination modality for diagnosis of breast cancer.⁶ Dynamic contrast-enhanced MRI (DCE-MRI) is useful in local staging and breast lesion characterization.⁷ The sensitivity of DCE-MRI ranges from 85% to 100%, specificity range from 37% to 88%.^{8,9} Diffusion-weighted imaging (DWI) and apparent diffusion coefficient (ADC) values improves the differential value of MRI, amends the positive predictive value, and reduces unnecessary biopsies.¹⁰ The sensitivity of breast DWI can range from 80% to 96% and its specificity in the range of 46-91%.¹¹⁻¹⁸ Partridge *et al.*¹⁰ concluded that there is 10% improvement in the positive predictive value (PPV) when combining DWI with DCE-MRI in the differentiation of breast masses.^{19,20} 3.0 T MRI appears superior to 1.5 T, as it allows faster scanning, high signal to noise ratio, improved spatial resolution and hence allowing improved lesion characterization and anatomical detail,²¹ leading to increased accuracy in diagnosing the lesion, and predicting the malignant potential.^{21,22}

Multimodal imaging techniques provide more accurate analysis, which is confirmed by more and more evidence, but none of the imaging methods are sufficiently specific to provide a histological diagnosis. However, guided biopsies enable precise histological or cytological confirmation.

Criteria for characterization of breast masses by DCE-MRI are lesion morphology and enhancement kinetics. According to BIRAD MRI lexicon, morphological evaluation of breast lesions is done by evaluating its shape, margins, and enhancement characteristics, enhancement distribution, and internal enhancement pattern. Kinetic evaluation is done by detecting the initial and post-initial enhancement of the breast lesion.¹⁰ Here, we want to study the role of DCE-MRI study and DWI in differentiation between benign and malignant lesions.

Aims and Objectives

Aims and objectives of the study were to determine the role of DWI and DCE-MRI in the characterization of breast tumors and to determine the sensitivity and specificity of MRI study in comparison to cytopathology in differentiation between benign and malignant masses and thus reducing the unnecessary diagnostic interventional procedures.

MATERIALS AND METHODS

A prospective observational, cross-sectional, analytical study was conducted in 50 cases of female breast masses detected clinically, by ultrasound and mammography from February 2015 to September 2016 in the Department of Radiodiagnosis, Pt. Jawahar Lal Nehru Memorial Medical College, and associated Dr. B. R. A. M. Hospital, Raipur, Chhattisgarh, India. We included 20-50 years aged females having breast masses detected clinically or by ultrasonography (USG) or by mammography. All the patients underwent clinical examination, USG, mammography and then MRI scan which included DWI, and dynamic contrast study with routine sequences. Diagnosis made by MRI was compared with cytopathological diagnosis obtained after fine-needle aspiration cytology/biopsy.

We used MAGNETOM SKYRA, Siemens, Germany, 3T field strength MRI with dedicated breast coils. 70 cm open bore design. 173 cm system length. Approximately 35 m² room size. RF Tim (204 × 48) (204 × 64) (204 × 128). Gradient strength – XQ Gradients (45 mT/m at 200 T/m/s). Zero helium boil-off technology with pressure injector. The data for the study will be collected through a uniform pro forma to be filled for every patient. All patients were examined using a 3T magnetic resonance machine after taking informed consent. All patients were examined in the prone position using dedicated breast coil. MRI was done within 7-14 days of menstrual cycle in premenopausal women. Examination included image acquisition followed by image post-processing.

The conventional MRI protocol included localizing sagittal view (scout view), axial nonfat saturated T2-weighted image (T1WI) obtained by fast spin echo with the following imaging parameters: TR 5.4-6 ms, TE 2.46 ms, slice thickness 1.5 mm, field of view (FOV) 300-360 mm, FOV phase 100, distance factor 20, slice thickness 1.5 and matrix was 384 × 384, and short TI inversion recovery (STIR) with the following parameters: TR 3500-6000 ms, TE 54 ms and inversion time (TI) was 230 ms, slices 30, slice thickness was 1.5 mm, FOV 300-360 mm, FOV phase 100, and the matrix was 384 × 384. DCE-MRI was made in the axial plane with fat suppression by applying fat saturated pulse. Total duration of DCE-MRI is 7.17 min. The sequence used was 3D-T1W1 with the following parameters: TR 4.75 ms, TE 1.61 ms, flip angle 20-25, slice thickness 1.5 mm with no inter-slice gap, FOV 300-600 mm and the matrix was 288 × 320 distance factor-20 DCE-MRI was performed after injection of a bolus of gadopentetate dimeglumine, in a dose of 0.16 mmol/kg using an automated injector at a rate of 2 ml/s through a 18-20 gauge intravenous cannula inserted in an antecubital vein. Contrast injection was followed by a bolus injection of saline (total of 20 ml at 2 ml/s). Dynamic

study consists of one pre-contrast and 5 post-contrast series, each of them took about 1.08 min with a break between the pre- and post-contrast study about 20 s. Duration of contrast injection is 10 s. DWIs were obtained before dynamic images using a diffusion-weighted echo-planar imaging sequence with parallel imaging. Sensitizing diffusion gradient in three orthogonal directions with b values of 0, 800, and 1000 s/mm² were applied. The ADC maps were created automatically, and the ADC values were calculated.

Image post processing includes image subtraction which was obtained by subtracting each of pre-contrast images from each post-contrast series images, creation of time to signal intensity curves for suspicious enhancing lesions and maximum intensity projection views obtained through each orthogonal plane, producing sagittal, coronal and axial projections. STIR images were first examined to detect the presence or absence of any lesion. In DCE-MRI the type of lesion enhancement (mass or non-mass-like enhancement) was determined, and morphologic features were analyzed. For mass enhancement lesions, the shape, margins, signal intensity on STIR and T1WI were assessed as well as enhancement characteristics of the lesion. For non-mass lesions, the distribution of enhancement, and internal enhancement.

Data were expressed as a percentage and mean \pm standard deviation. Kolmogorov–Smirnov analysis was performed for checking the linearity of the data. Parameters in parametric data and Mann–Whitney *U*-test were used to check the significance of difference between two parameters in non-parametric data difference between frequency distribution of the data. Receiver operating characteristics curve was plotted to analyze to diagnostic significance of diagnostic method used. $P < 0.05$ was considered as statistically significant. Microsoft® Inc. USA was used perform the statistical analysis.

RESULTS

This study included 50 patients with age ranging from 20 to 65 years. Cytopathologic analysis of these lesions revealed 18 benign lesions (36%) and 32 malignant lesions (64%). The peak age incidence of breast mass lesion was 40-50 years. In our study, 38.9% of benign lesions and 40.6% of malignant lesions were present in retroareolar region, 22.2% of benign and 15.6% of malignant lesions were in outer and upper quadrant, 5.6% of benign lesions were in axillary tail, 5.6% of benign lesions were at multiple locations in breast, 16.7% of benign lesion and 3.1% of malignant were in outer and lower quadrant, 9.4% of malignant lesions were in upper inner and outer quadrant, 5.6% of benign and 25% of malignant lesions were in upper and inner quadrant 5.6% of benign lesion

and 6.2% of malignant lesion involved the whole breast. The association between site of the lesion and neoplasticity was not significant statistically ($P = 0.157$).

Most common benign lesions were chronic inflammation and fibroadenoma which represents 36.8% and 15.8%, respectively, while the most common malignant lesions were invasive ductal carcinoma which represents 55.6%.

Most common shape of the benign lesion was either round (61%) or oval (16.7%). Most common shape of the malignant lesion was either round (40.6%) or irregular (28%). The association between shape of the lesion and neoplasticity was not significant statistically ($P = 0.669$).

In this study, the margins of benign lesions were variable with a predominance of smooth margins (72.2%) while the margins of malignant lesions were irregular or spiculated and they represent 59.4% and 18.8%, respectively. The association between margin of the lesion and neoplasticity was statistically significant ($P = 0.002$).

In this study, the homogenous enhancement was seen in 44.4% of benign lesions and 56% of malignant lesions, heterogeneous enhancement was seen in 16.7% of benign lesions and 37.5% of malignant lesions, rim enhancement was seen in 22.2% of benign lesions and 6.2 % of malignant lesions. The association between enhancement pattern of the lesion and neoplasticity was statistically significant ($P = 0.021$).

In this study, the enhancement kinetics curve, Type I curve (Figure 1) was seen in 61.2% of benign lesions and 3.1% of malignant lesions; Type II curve (Figure 2) was seen in 27.8% of benign lesion and 71.9% of malignant; Type III curve (Figure 3) was seen in 11.1% of benign lesions and 25% of malignant lesions. The association between enhancement kinetics of the lesion and neoplasticity was statistically significant with $P = 0.0001$ (Table 1).

In all 50 lesions, we could localize and measure the ADC value of each lesion. The mean ADC of benign lesions was 1.62×10^{-3} mm²/s (range $0.74-2.2 \times 10^{-3}$), and that of malignant lesions was 1.03×10^{-3} mm²/s (range $0.60-1.7 \times 10^{-3}$). The association between DWI (ADC values) of the lesion and neoplasticity was statistically significant, with $P = 0.003$. ADC values were significantly lowered in malignant lesions compared with benign lesions. The best ADC cutoff value to differentiate between benign and malignant lesions was 1.4×10^{-3} mm²/s (Table 2).

In this study, the sensitivity and specificity of DCE-MRI examination were 93.75% and 72.2%, respectively; which was based on the combination of morphologic, diffusion (ADC values) and enhancement kinetic curve.

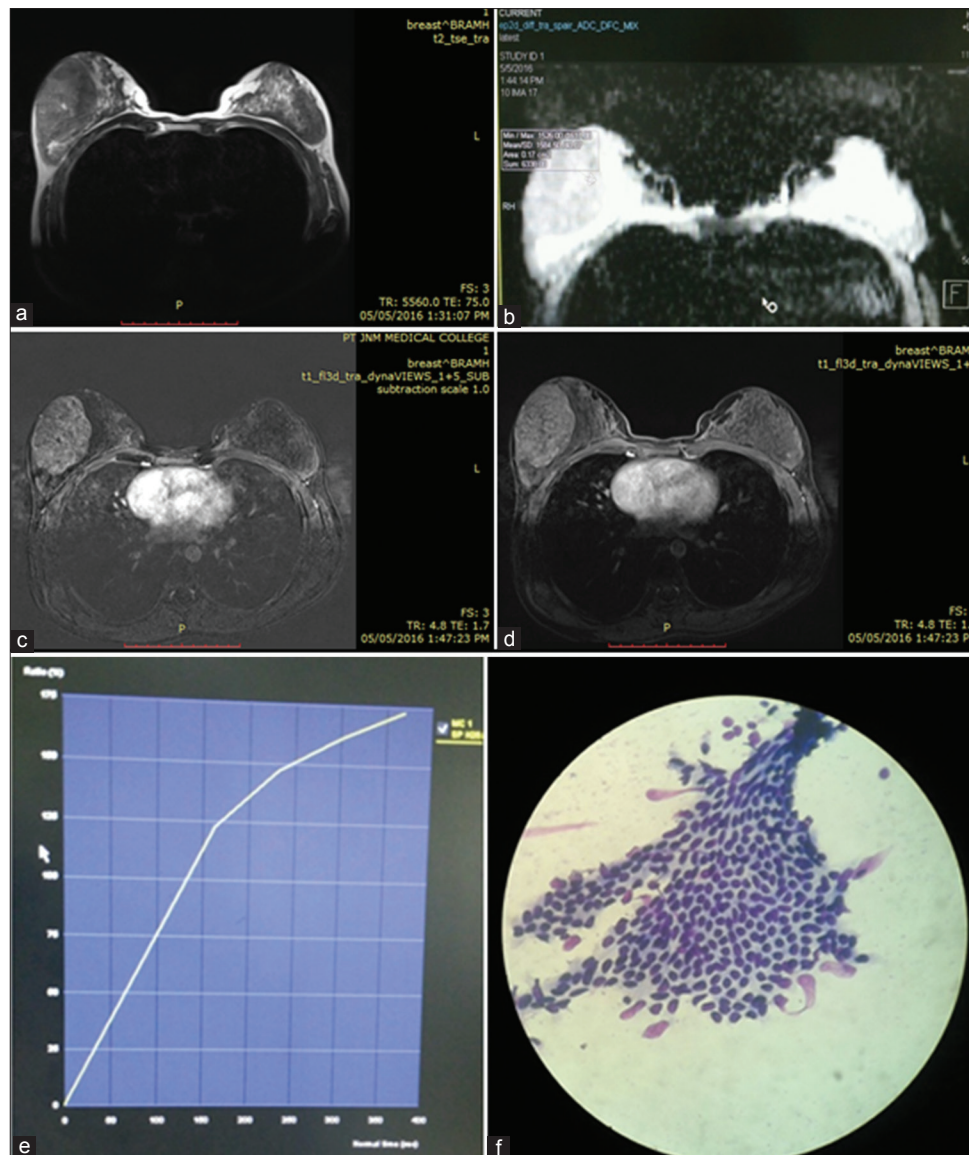


Figure 1: Right breast fibroadenoma in 20 year-old woman. (a) Axial T2 and (b) apparent diffusion coefficient (ADC) map reveals increased diffusion ($ADC = 1.5 \times 10^{-3} \text{ mm}^2/\text{s}$) within mass. (c) Dynamic contrast-enhanced and (d) subtracted image shows smooth margined, round-shaped mass with non enhancing internal septation in of right breast. (e) Time-signal intensity curve of mass shows Type I persistent curve. Mass was correctly classified as benign (BIRAD 3) according to combined imaging protocol. (f) Cytopathological image showing fibroadenoma

DISCUSSION

An analytical study of “dynamic contrast study and DWI in female breast masses using 3Tesla MRI and its comparison with cytopathological findings (benign vs. malignant)” was conducted. Cytopathologic analysis of these lesions revealed 18 benign lesions (36%) and 32 malignant lesions (64%).

This study included 50 patients ranging from 20 to 65 years age. The peak age incidence of breast mass lesion was between 40 and 50 years. The average age group of breast mass lesion was 45.94 years. The results of our study matched with the studies of Kriege *et al.*, Warner *et al.*, and Leach *et al.*²³⁻²⁵

In this study, 38.9% benign lesions and 40.6% of malignant lesions were present in retroareolar region, 22.2% of benign and 15.6% of malignant lesions were in outer and upper quadrant, 5.6% of benign lesions were in axillary tail, 5.6% of benign lesions were at multiple locations in breast, 16.7% of benign lesion and 3.1% of malignant were in outer and lower quadrant, 9.4% of malignant lesions were in upper inner and outer quadrant, 5.6% of benign and 25% of malignant lesions were in upper and inner quadrant, 5.6% of benign lesion and 6.2% of malignant lesion involved the whole breast. The association between site of the lesion and neoplasticity was statistically not significant ($P = 0.157$).

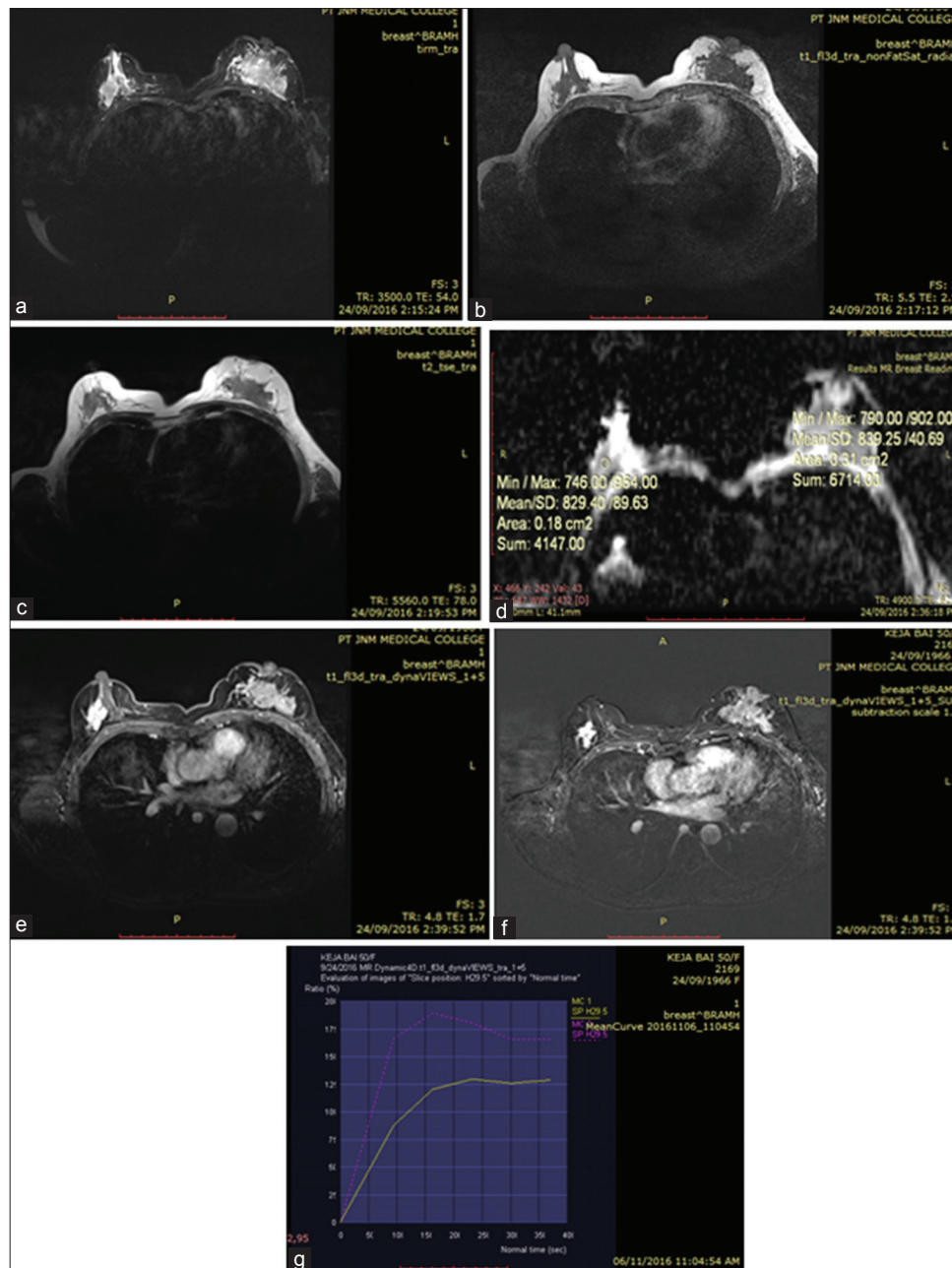


Figure 2: Bilateral infiltrating ductal carcinoma in 50-year-old woman seen at retroareolar region of left breast and upper outer quadrant of right breast. (a) Stir axial images, (b) T1 Fs axial images, (c) T2 axial, (d) diffusion axial, (e) dynamic contrast-enhanced, and (f) subtracted image shows irregular mass with irregular margins with apparent diffusion coefficient (ADC) map reveals $ADC = 0.82 \times 10^{-3} \text{ mm}^2/\text{s}$ within both the masses. (g) Time-signal intensity curve of mass shows Type II plateau curve in both the lesions. Mass was correctly classified as malignant (BIRAD 4c) according to combined imaging protocol

The results of our study differ from the previous studies conducted by Mahoney *et al.*, Darbre and El Bakry *et al.* who stated that the most common location of both benign and malignant lesions is in the upper outer quadrant.²⁶⁻²⁸ This difference may be because of small sample size in our study.

In this study, the two most common benign lesions were chronic inflammation and fibroadenoma which represents 36.8% and 15.8%, respectively, while the most common

malignant lesions were invasive ductal carcinoma which represents 55.6%. Similar finding was also observed by Li *et al.* and El Bakry *et al.*^{28,29}

In this study, most common shape of the benign lesion was either round 61% or oval 16.7%. Most common shape of the malignant lesion was either round 40.6% or irregular 28%. The association between shape of the lesion and neoplasticity was statistically not significant, $P = 0.669$.

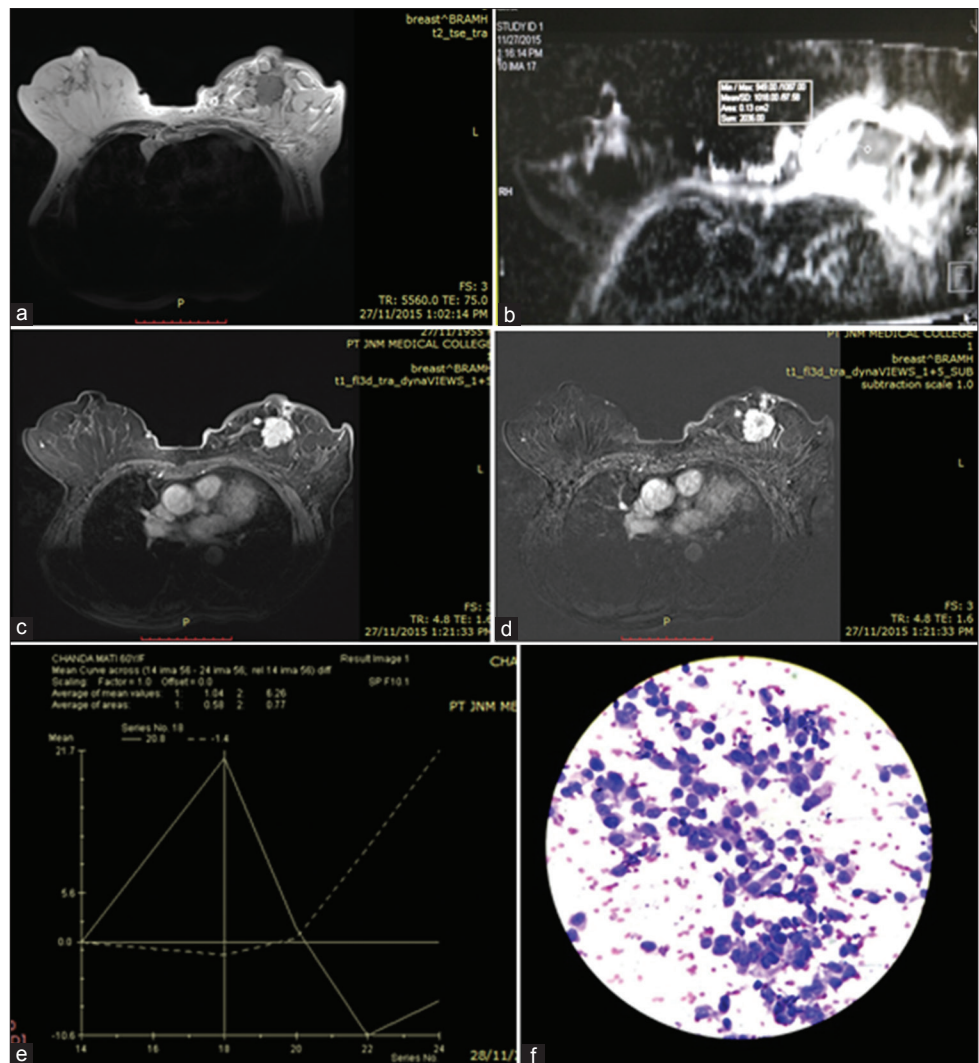


Figure 3: Infiltrating ductal carcinoma in 60-year-old woman seen at the retroareolar region of left breast (a) T2W axial, (b) diffusion weighted axial image - apparent diffusion coefficient (ADC) map reveals restricted diffusion ($\text{ADC} = 1.01 \times 10^{-3} \text{ mm}^2/\text{s}$) within mass, (c) dynamic contrast-enhanced, and (d) subtracted image shows rounded mass with irregular margins showing homogenous intense contrast enhancement. (e) Time-signal intensity curve of mass shows Type III washout curve. Mass was correctly classified as malignant (BIRAD V) according to combined imaging protocol. (f) Histopathological finding shows infiltrative ductal carcinoma

Table 1: Comparison of frequency of type of breast lesion on cytopathology in different shape of T/SI curve

Shape of T/SI curve	Final diagnosis on cytopathology		Total	P value
	Benign	Malignant		
Type I				
Count	11	1	12	<0.0001
% within final diagnosis on cytopathology	61.2	3.1	22.0	
Type II				
Count	5	23	28	
% within final diagnosis on cytopathology	27.8	71.9	56.0	
Type III				
Count	2	8	10	
% within final diagnosis on cytopathology	11.1	25.0	20.0	
Total				
Count	18	32	50	
% within final diagnosis on cytopathology	100.0	100.0	100.0	

Table 2: Comparison of frequency of type of breast lesion on cytopathology to diffusion restriction (ADC values) of lesion

Cytopathology finding	Total cases	Mean ADC value	SD	SEM	P value
Benign	18	1.6244	0.48983	0.11545	0.003
Malignant	32	1.0309	0.24453	0.04392	

SD: Standard deviation, SEM: Standard error of the mean

Our results matched with the studies of Wedegärtner *et al.*, Tozaki *et al.* and El Bakry *et al.*^{28,30,31}

In our study, the margins of benign lesions were variable with a predominance of smooth margins (72.2%) while the margins of malignant lesions were irregular or spiculated and they represent 59.4% and 18.8%, respectively. The association between margin of the lesion and neoplasticity was significant statistically ($P = 0.002$). Our results matched with studies of Mahoney *et al.* and El Bakry *et al.*^{28,32}

In this study, homogenous enhancement was seen in 44.4% of benign lesions and 56% of malignant lesions, heterogeneous enhancement was seen in 16.7% of benign lesions and 37.5% of malignant lesions, rim enhancement was seen in 22.2% of benign lesions and 6.2% of malignant lesions. The association between enhancement pattern of the lesion and neoplasticity was statistically significant ($P = 0.021$). Our results did not matched with the study of Morris *et al.* who concluded that homogeneous enhancement is suggestive of a benign process and he also concluded that the most frequent enhancement pattern among the malignant lesions was a heterogeneous enhancement (96%).³³ Our results matches with Ghazala *et al.* who stated that homogenous enhancements were found in 13.3% of benign and 86.7% of malignant. Heterogeneous enhancements were found in 9.1% of benign and 90.9% of malignant.³⁴

In this study, the enhancement kinetics curve, Type I curve was seen in 61.2% of benign lesions and 3.1% of malignant lesions; Type II curve was seen in 27.8% of benign lesion and 71.9% of malignant; Type III curve was seen in 11.1% of benign lesions and 25% of malignant lesions. The association between enhancement kinetics of the lesion and neoplasticity was statistically significant with $P = 0.0001$. Our results matched with results of Kul *et al.*³⁵ Ghazala *et al.*³⁴ El Bakry *et al.*²⁸

In all lesions, we could localize and measure the ADC value of each lesion. The mean ADC of benign lesions was $1.62 \times 10^{-3} \text{ mm}^2/\text{s}$ (range $0.74\text{--}2.2 \times 10^{-3}$) (Figure 1), and that of malignant lesions was $1.03 \times 10^{-3} \text{ mm}^2/\text{s}$ (range $0.60\text{--}1.7 \times 10^{-3}$) (Figures 2 and 3). The association between DWI (ADC values) of the lesion and neoplasticity was statistically significant with $P = 0.003$. ADC values were significantly lowered in malignant

lesions compared with benign lesions. The best ADC cutoff value to differentiate between benign and malignant lesions was $1.4 \times 10^{-3} \text{ mm}^2/\text{s}$. Our results matched with the study of Kul *et al.* who revealed the effectiveness of DWI for differentiating malignant from benign breast tumors, who stated, that, malignant lesions revealed significantly lower ADC values than benign lesions.³⁵ Our results approximately matched with El Bakry *et al.* that showed, the best ADC cutoff value to differentiate between benign and malignant lesions was $1.32 \times 10^{-3} \text{ mm}^2/\text{s}$. Malignant lesions exhibited lower mean ADC values compared with those of benign lesions.³³ Yabuuchi *et al.* who demonstrated an ADC value $<1.3 \times 10^{-3} \text{ mm}^2/\text{s}$ as the strongest indicator of malignancy.³⁶ Our results of ADC values for benign lesions did not match with Kuroki *et al.*³⁷ and Si *et al.*,³⁸ but were approximately same for malignant lesions.

In this study, the sensitivity and specificity of DCE-MRI examination were 93.75% and 72.2%, respectively; which was based on the combination of morphologic, diffusion and kinetic curve. Our results agreed with Kul *et al.* who reported higher sensitivity (97.9%) and lower specificity (75.7%) in their study.³⁵ Our results also match with the study of Ghazala *et al.* who stated that, sensitivity of MRI is 98.6%, specificity of MRI is 78.8% PPV of MRI is 90.6% negative predictive value of MRI is 95.3%, accuracy of MRI is 91.8%.³⁴ Our results match with studies of El Bakry *et al.*, in having high sensitivity, i.e., 97.2%, but does not match in having high specificity, i.e., 94.7% in the diagnosis of breast cancer.²⁸ Our results disagree with Hetta who proved low sensitivity and specificity of DCE-MRI examination, i.e., 80% and 73.33%, respectively.³⁹

CONCLUSION

MR mammography is a noninvasive, well tolerated, non-hazardous modality for detection, diagnosis, and staging of breast cancer. This study proves morphologic appearance, mean ADC value and kinetic curves help in differentiating benign from malignant lesions. ADC values are low for malignant lesions and high for benign lesions. Type I enhancement kinetic curve is more in favor of benign lesion, Type II and Type II curve are more in favor of malignant lesions. Combined DWI and DCE, MRI protocol using 3T MRI with dedicated breast coils increases the sensitivity in diagnosis of breast cancer. Thus, it can be helpful in reducing the unwanted biopsies and surgery.

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