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Original article

Role of Multiparametric Magnetic Resonant Imaging (Mpmri) in Assessment of Post Operative Recurrent Breast Masses

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Abstract:

Background: Detection of breast recurrence malignancies -in cases previously treated for breast cancer with either breast conserving surgery or with radical mastectomy - is much more difficult than diagnosis of the primary tumor. Multiparametric magnetic resonant imaging of the breast aims to simultaneously quantify and visualize multiple functional processes at the cellular and molecular levels.
Purpose: To assess the diagnostic value of multiparametric magnetic resonant imaging in assessment of post-operative breast masses and differentiating recurrent malignancy from other post-operative lesions. **Patient and methods:** This prospective study carried on thirty female patients who underwent breast conserving surgery or radical mastectomy. Patients were examined by sono-mammography that aroused suspicious of breast lesions followed by DCE-MRI & DWI-MRI with or without MRS to exclude recurrence. Multiparametric MRI with 2 (DCE MRI and DWI) or 3 (DCE MRI, DWI, and MRS) parameters was done at 1.5- T MR Machine. Histopathology or short-term imaging follow up was used as the gold standard. **Results:** MP MRI showed no false negatives and there was a significant reduction in false-positive lesions (only two) compared with DCE MRI with 100% sensitivity, 88.9%specificity, 85.7 % PPV, 100 % NPV and 93.3 % accuracy. MP MRI allows an increase in both sensitivity and particularly specificity, resulting in a significantly improved diagnostic accuracy. **Conclusion:** Multiparametric Magnetic Resonance Imaging (MP MRI) has a great diagnostic accuracy for post-operative detection of recurrent breast cancer.

Key words: Multiparametric breast MRI; post-operative breast masses; breast cancer.

Abbreviations:

BCT: Breast Conservative Therapy, MRI: Magnetic Resonance Imaging, DCE: Dynamic Contrast Enhancement, DWI : Diffusion Weighted Images, BIRADS : Breast Imaging-Reporting and Data System, S.I. : Signal Intensity, ROI : Region of Interest, ADC : Apparent Diffusion Coefficient, SD : Standard Deviation, ROC : Receiver Operating Characteristic.

Introduction:

Women who have been treated for breast cancer - with either breast conserving surgery or with radical mastectomy- still have chance in developing a second breast cancer including loco-regional recurrences and contralateral breast cancers (1). In such cases, diagnosis can be much more difficult than diagnosis of the primary tumor as in those cases; presence of post-operative scar tissue which might be extensive can produce architectural distortion, increases density on mammography and in some cases can mimic malignancy or obscure locally recurrent breast cancer leading to equivocal results by mammography and ultrasonography (2, 3).

Multi-parametric Magnetic Resonance Imaging (MPMRI) of the breast comprises different established MRI parameters (DCE-MRI, DWI and MRSI) (4). DCE-MRI can help differentiation malignant lesions from benign postoperative changes by the morphological criteria regarding the site, size, margins, and different types of enhancement according to the time–intensity curves (5,6).

MRI breast specificity can be improved by addition of diffusion-weighted imaging (DWI) with dynamic contrast-enhancedsequences and thus, could improve MRI diagnostic accuracy (7).

MRSI reflects the chemical composition of a given tissue by demonstrating spatially localized signal spectra, which provide information about the varying levels of detectable metabolites. In breast imaging, the additional value of MRSI is largely based on the detection of choline (Cho), a biomarker of increased cellular turnover, which is typically increased in malignant tumors and thus aids in the characterization of breast tumors (4).

Purpose:

To assess the diagnostic value of multiparametric magnetic resonant imaging in assessment of post-operative breast masses and differentiating recurrent malignancy from other post-operative lesions.

Patients and methods:

This prospective cross section study carried on thirty female patients from December 2019 to May 2021 at General Organization of Teaching Hospitals and Institutes (GOTHI) hospitals, with the following inclusion and exclusion criteria:

Inclusion:

Patients underwent surgical treatment of previous breast cancer either with conservative breast surgery (CBS) or radical mastectomy showing suspicious breast lesion at mammography, ultrasound and/or clinical examination during routine follow-up either at the operative bed or in the contralateral side.

Exclusion

Contraindications to gadolinium-based contrast media: Pregnant women, chronic renal impairment (serum creatinine > 1.5 mg/dl), previous allergy to the contrast media. Inability to lie prone, marked obesity, extremely large breasts, implantable devices that are not MRI compatible e.g., patients with metallic valves, pacemakers and cochlear implants.

The study's protocol was approved by institutional ethical committee. The patients were aware of examination; informed consent was obtained from patients.

Examination Technique:

MRI studies were done for 30 patients using a closed MRI machine with magnets of intensity field 1.5 T.

The patients were examined by:

A- ***Fast spin echo T1WI, T2WI*** with fat suppression.

B- ***DWI*** of the whole breast in transverse plane with a single excitation echo planar imaging sequence, b-values were 50, 400 and 800s/mm^2. ADC value measurement: ROI was drawn in the center of the lesion at b-800 DWI. A small ROI was used at area close to tumor edge to obtain the greatest accuracy.

C- ***DCE- MRI*** was done by 2-dimensional fast spoiled gradient-recalled echo with fat suppression at T1WI, FOV 34 X 34cm, slice thickness 1mm.

Prior to the imaging, a 12G venous lodging cannula was inserted. T1 -weighted images were done in transverse plane prior to, and just after a bolus injection of 0.2mmol gadopentetate dimeglumine/kilogram of body weight at a rate of 3ml/s, followed by a 10-ml saline flush using automatic injector. 5-phase dynamic images were obtained at 1, 2, 3, 4 and 5 minutes respectively.

Dynamic analysis with generation of enhancement percentage versus time curves done by positioning of Region of Interest (ROI) at center of identified enhancing lesions that had a diameter >5mm. Then, time to Signal Intensity (S.I.) curve for any suspicious enhancing lesions was obtained.

D- ***MRSI***: After completing the DCE-MRI, the acquisition of MR spectrum was performed using the localized single-voxel technique with the point-resolved spectroscopic sequence (PRESS). The spectroscopic voxel was placed on the post injection subtraction images. It was carefully positioned to cover the enhanced lesion on the subtraction images and avoid contaminations with the surrounding tissues.

Data Analysis

DCE-MRI of the Breast: contrast-enhancing lesions descriptors according to the American College of Radiology, BI-RADS lexicon was used (8). Lesions were classified as masses or non-mass like enhancing lesions (NMLEs). The mass lesions described regarding shape (regular, irregular), margin (smooth, irregular, speculated), enhancement pattern (homogenous, heterogeneous, rim enhancement). NMLE described regarding the distribution (focal, regional, segmental, ductal, linear, and diffuse), the pattern of enhancement (homogenous, heterogeneous, and clumped).

Lesion enhancement kinetics was used to assess functional information. The initial enhancement phase was either slow, medium or rapid. The delayed phase was either persistent, plateau, or washout patterns of enhancement. The most suspicious lesions were that which displayed rapid initial enhancement followed by washout pattern on delayed phase. Lesions with MRI BI-RADS ≥4 considered positive for malignancy and lesions with BI-RADS ≤3 considered negative for malignancy (8).

Diffusion-Weighted Imaging

According to DWI, lesions were diagnosed positive showed restricted pattern of diffusion which means high signal on DWI and low signal on the ADC map. Lesions were diagnosed negative showed either absence of high signal on DWI or showed high signal on DWI that remains high on the corresponding ADC maps; a phenomenon called the T2 shine through effect.

MRSI in our study, the assessment of MR spectroscopy based on the qualitative analysis with detection of the tCho peak resonant at 3.2 ppm. Regarding MRS, the lesion considered as positive lesion in the presence of the tCho peak, and in absence of the tCho peak the lesion diagnosed as negative lesion. In our study, MRSI was done to 15 out of 30 cases, as there were many technical challenges of breast MRS.

MP MRI considered positive if two or three MRI parameters were indicative of malignancy.

Statistical analysis:

Data were collected, revised, coded and entered to the Statistical Package for Social Science (IBM SPSS) version 23. The quantitative data were presented as mean, standard deviations and ranges when parametric. Also, qualitative variables were presented as number and percentages. The comparison between groups with qualitative data was done by using Chi-square test. The comparison between two groups with quantitative data and parametric distribution were done by using independent t-test. Receiver operating characteristic curve (ROC) was used to determine sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), Area under curve (AUC) of the studied parameters to predict malignancy of the studied patients.

The confidence interval was set to 95% and the margin of error accepted was set to 5%. So, the p-value was considered significant as the following:

P > 0.05: Nonsignificant

P < 0.05: Significant

P < 0.01: Highly significant.

Results:

This prospective study was carried out on 30 female patients with age range between 40-54Ys with a mean± SD of 48.50 ± 4.58. All patients underwent breast surgeries, 26 patients (86.7%) underwent CBS, and 4 patients (13.3%) underwent MRM. Pathology was done for 17 from 30 patients (56.7%) and 13 patients (43.3%) underwent short interval imaging follow up. Twelve patients out of 17 were proven for presence of malignancies, while malignancy was excluded in the remaining 5 cases (2 cases of fat necrosis and fibrosis, 2cases of cicatricial fibrosis and 1 case of lymphoid hyperplasia). The 13 patients underwent follow up (3 cases of fibroadenoms, 7 cases post-operative scar, , 2 cases of fat necrosis, 1 case intra-mammary lymph node) were diagnosed as negative cases showing no time interval changes or newly developed lesions on follow up imaging. According to the pathology and imaging follow up, 12 cases (40%) were pathologically proven to have malignant lesions (IDC n =10, 83.3%, ILB n =2, 16.6%) and 18 cases (60%) were proven to have benign lesions either pathologically or by imaging follow up (Table 1).

On post contrast breast MRI, we detected 23 mass enhanced lesions (76.7%) and 7 non mass enhanced lesions (23.3%). Out of 23 enhanced mass lesions, ;10 (43.5%) lesions showed regular margins, 10 (43.5%) lesions with irregular margins and 3 (13%) lesions with speculated margins. According to the pattern of enhancement, 13 (43.3%) lesions showed homogenous enhancement, 13 (43.3%) lesions showed heterogeneous enhancement, 2 (6.7%) lesions of clumped enhancement, and 2 (6.7%) lesions of rim enhancement (Table 2).

Table 1: lesions subtypes proved pathologically or with short term imaging follow up within the studied cases.

Pathology - imaging follow up		**No.**	**%**
Benign		18	60.0%
Malignant		12	40.0%
Benign **(no.=18)**	Small fibroadenoma	3	16.7%
	Fat necrosis and fibrosis	2	11.1%
	Postoperative scar	7	38.9%
	Intramammary LN	2	11.1%
	Lymphoid hyperplasis	1	5.6%
	Sicatricial fibrosis	1	5.6%
	Fat necrosis	1	5.6%
	Cicatricial fibrosis	1	5.6%
Malignant **(no.= 12)**	IDC*	10	83.3%
	ILC**	2	16.7%

*IDC: invasive ductal carcinom ** ILC: invasive lobular carcinoma

Type I curve seen in 13 lesions (43.3 %) denoting benign nature, all of them were proven to be benign. Type II curve seen in 11 lesions (36.7%) elicited plateau curve; denoting suspicious nature, 5 out of 11 lesions proved to be benign however 6 lesions proved to be malignant. Type III curve seen in 6 lesions (20%) had washout curve, denoting malignant nature, all proved to be malignant (Table 3).

Table 2: DCE-MRI different morphology and pattern of enhancement in the studied cases.

		No.	**%**
Morphology	Non-mass	7	23.3%
	Mass	23	76.7%
Morphology	Irregular mass	10	43.5%
	Regular mass	10	43.5%
	Speculated mass	3	13.0%
Contrast enhancement	Homogeneous	13	43.3%
	Heterogeneous	13	43.3%
	Clumped	2	6.7%
	RIM enhanced	2	6.7%
Type of curve	Type 1	13	43.3%

Type 2	11	36.7%
Type 3	6	20.0%

According to BI-RADS classification depending on MRI study (including combined morphological, contrast enhancement pattern and dynamic enhancement curve), our cases were divided into two groups:

- Group I include (BI-RADS 2, 3) denoting DCE-MRI non-suspicious breast lesions considered as negative cases n= 14 (46.7%), 13 were proven benign however 1 case was proved to be malignant.
- Group II include (BI-RADS 4, 5) denoting DCE-MRI suspicious breast lesions considered as positive cases n = 16 (53.3%), 11 were proven malignant; however, 5 lesions were proved to be benign with pathology or imaging follow up (Table 4).

In our study DCE-MRI showed 91.7% sensitivity, 72.2% specificity, 68.8% positive predictive value, 92.9% negative predictive value and 80% accuracy in evaluation of post-operative breast cancer patients.

On visual analysis of S.I. at diffusion sequence, 13 cases (43.3%) showed diffusion restriction with ADC range of (0.6-1.2 X 10^{-3} mm^2 /s), while 17 cases (56.7%) showed facilitated diffusion with ADC range of (1.3-2.3 X 10^{-3} mm^2 /s).

According to the ADC values, 12 lesions (26.7%) were proven to be malignancies showed mean ADC values of 0.99 ± 0.21X 10^{-3} mm^2/s and ADC range of (0.6 – 1.3X 10^{-3} mm^2/s), however 18 lesions proved to be benign showed mean ADC value of 1.95 ± 0.36X 10^{-3} mm^2/s and ADC range of (1.1 – 2.3X 10^{-3} mm^2/s).

Table 3: Correlation between Types of dynamic curves and local recurrence & other post-operative changes in studied cases.

		Pathology - imaging follow up				Test value*	P-value	Sig.
		Benign, n =18		Malignant, n = 12				
		No.	%	No.	%			
Type of curve	Type 1, n = 13	13	72.2%	0	0.0%	13.392	0.001	HS
	Type 2, n = 11	5	27.8%	6	50.0%			
	Type 3, n = 6	0	0.0%	6	50.0%			

P-value >0.05: Nonsignificant (NS); P-value <0.05: Significant (S); P-value< 0.01: highly significant (HS)

*: Chi-square test

Table 4: Correlation between the DCE-MRI finding and local recurrence & other post-operative changes in studied cases.

		Pathology - imaging follow up				**Test value***	**P-value**	**Sig.**
		Benign, n = 18		**Malignant, n =12**				
		No.	**%**	**No.**	**%**			
Dynamic diagnosis	Negative, n = 14	13	72.2%	1	8.3%	11.808	0.001	HS
	Positive, n= 16	5	27.8%	11	91.7%			

P-value >0.05: Nonsignificant (NS); P-value <0.05: Significant (S); P-value< 0.01: highly significant (HS)
*: Chi-square test; •: Independent t-test

The ROC curve (**Figure** 1) Indicated a good statistical performance of the ADC values to predict the presence of malignant lesions (area under the curve=0.975).
Regarding DWI, out of 13 lesions with evidence of restricted diffusion; 11 lesions were proved to be malignant (**Figure** 2), and 2 lesions were proven benign. However out of 17 lesions with facilitated diffusion; 16 were proved to be benign and only one 1 lesion proved to be malignant (Table 5).

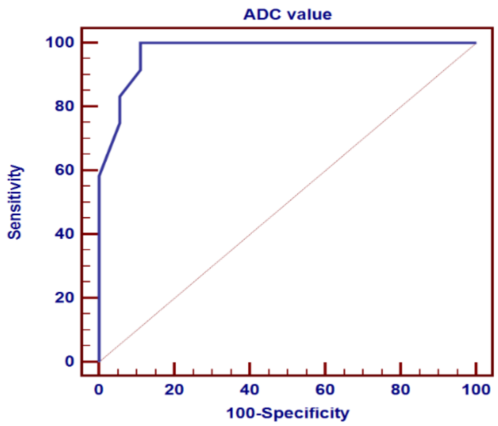

Figure (1): Receiver Operating Characteristic (ROC) curve of ADC value in the studied group.

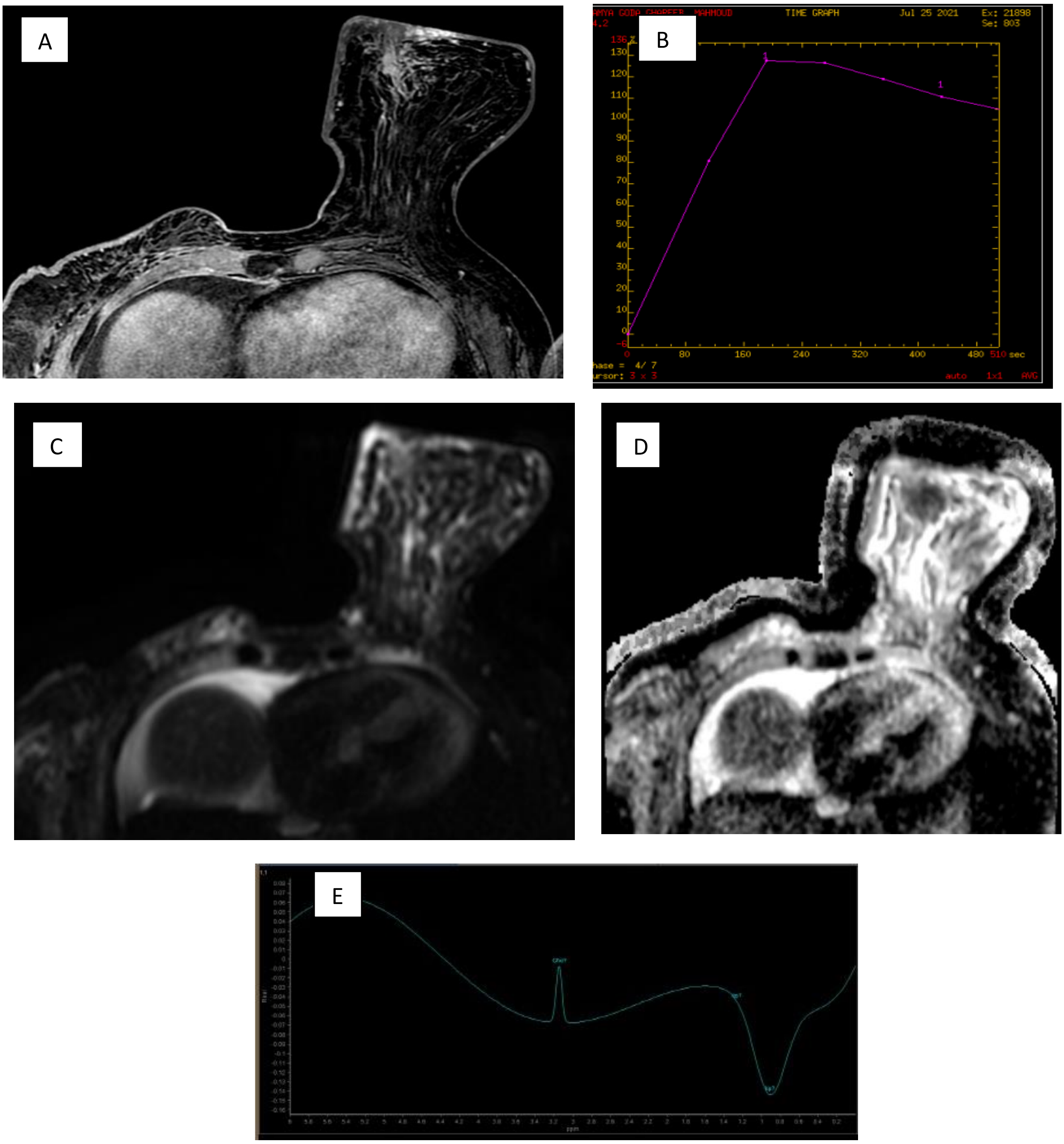

Figure (2): A 52-year-old female with history of right breast cancer managed by mastectomy on follow-up. (A) Post contrast T1 axial images showed left breast skin thickening with retro areolar ill-defined suspicious lesion measuring 16x11mm. (B) Type III intensity curve, and (C) DWI showed hyper intense signal denoting restricted diffusion (D) ADC map showed hypo intense lesion with ADC value 1.2 x10^{-3} mm^2/s. (E) MRS curve showing choline peak. MRI diagnosis was neoplastic recurrence. Histopathology revealed recurrent IDC

In our study, DWI showed 91.7% sensitivity, 88.9% specificity, 84.6% positive predictive value, 94.1% negative predictive value and 94.1% accuracy in evaluation of post-operative breast cancer patients.

In the current study, we depend on the qualitative analysis of MR spectroscopy as we considered the lesions showed tCho peak resonant at 3.2 ppm as a positive lesion, however in the absence of the choline peak the lesion diagnosed as a negative lesion. Due to many technical challenges MRS was done to 15 out of 30 cases included in our study. Six cases (40%) showed tCho peak at MRS curve and 9 cases (60%) showed no tCho peak.

According to MPMRI diagnosis - either with two (DC-MRI and DWI) or three (DCE-MRI, DWI and MRS) MRI parameters- in our study the lesion was considered positive if two or more parameters were indicative of malignancy, otherwise we considered it as a negative lesion. Regarding to MPMRI, 14 lesions were diagnosed as positive lesions; 12 were proved to be malignant and 2 proved to be benign. However, 14 lesions were diagnosed as negative cases; all proved to be benign (Table 6).

In our study, MPMRI diagnosis showed 100% sensitivity, 88.9% specificity, 85.7% positive predictive value, 100% negative predictive value and 93.3% accuracy in evaluation of post-operative breast cancer patients.

Table 5: Correlation between the DWI finding and local recurrence & other post-operative changes in studied cases.

		Pathology - imaging follow up		Test value	P-value	Sig.
		Benign No. = 18	**Malignant No. = 12**			
Diffuse restriction	Facilitated, n = 17	16 (88.9%)	1 (8.3%)	19.027 *	< 0.001	HS
	Restricted, n = 13	2 (11.1%)	11 (91.7%)			

P-value >0.05: Nonsignificant (NS); P-value <0.05: Significant (S); P-value< 0.01: highly significant (HS)
*: Chi-square test; •: Independent t-test

Table 6: Correlation between MPMRI diagnosis and local recurrence & other post-operative changes in studied cases.

		Pathology - imaging follow up				Test value*	P-value	Sig.
		Benign, n = 18		**Malignant, n = 12**				
		No.	**%**	**No.**	**%**			
MpMRI diagnosis	Negative, n = 16	16	88.9%	0	0.0%	22.857	< 0.001	HS
	Positive, n = 14	2	11.1%	12	100.0%			

P-value >0.05: Nonsignificant (NS); P-value <0.05: Significant (S); P-value< 0.01: highly significant (HS)
*: Chi-square test; •: Independent t-test

Discussion:

This study was carried on 30 female patients with age range between 40-54Ys with a mean± SD of 48.50 ± 4.58. In the comparison of malignant and benign lesions, there were no statistically significant differences in patient age (9).

Our results agreed with other studies (10) which noted that the association of speculated and irregular border of focal mass with malignancy and regular, smooth masses had a negative predictive value for malignancy.

However, there was no statistical significance regarding the mass as opposed to non-mass MRI features, in prediction of malignancies (9).

In our study regarding to MRI kinetic analysis curves: 6 (50%) cases out of 12 recurrent malignant lesions showed type III washout curve (Figure 3), however 6 lesions showed type II plateau curve (11).

Regarding to type II curve, 5 lesions were proved to be benign (2 cases of fat necrosis and 3 post-operative scars); this is in agreement with that fat necrosis and post-operative scar are a common and challenging pitfall in interpretation of post-BCT on MR imaging (8).

In our study, DWI with proposed cut off ADC value 1.25 x 10^{-3} mm^2 /s based upon published results in the literature, there was one false negative case of ADC value 1.3 x 10^{-3} mm^2 /s, pathologically proved to be IDC. However, there were two false positive lesions proved to be fat necrosis and cicatricial fibrosis, and this in agreement with previous study reported that fat necrosis and scar tissue can show lower ADC values (12, 13)

Mean ADC values were significantly different in malignant vs. benign lesions (Figure 4, 5). ($0.99 \pm 0.21 \times 10^{-3}$ cm^2/sec vs. $1.9 \pm 0.36 \times 10^{-3}$ cm^2/sec for the malignant and benign lesions, respectively, $p<0.001$). A cut-off value of 1.30×10^{-3} mm^2/sec for ADC detected with receiver operating characteristic analysis yielded 100% sensitivity and 88.89% specificity for the differentiation between benign and malignant lesions (14).

MRSI applied for 15 (50%) cases out of 30 cases included in our study that was due to many technical drawbacks; the relatively long time required (including pre-acquisition adjustment), the difficulty to detect weak choline signal from a small lesion. The single-voxel technique, which is the most commonly used technique, allows only one lesion to be examined at a time. In addition, the lesion must be around 1 cm^3 in size for the data to be meaningful. Prior contrast material–enhanced MR imaging is required for lesion localization and MR spectroscopic voxel placement, The accumulation of contrast agent in the lesion can affect 1H MR spectroscopic quality due to T2* broadening effect. It is difficult to achieve sufficient simultaneous suppression of water and lipid resonances, making it difficult to quantify choline concentration. Thus, the majority of 1H MR spectroscopic studies are none or semi-quantitative (15).

In our study, DCE MRI revealed one false negative lesion proved by pathology to be IDC and 5 false positive cases with 91.7% sensitivity, 72.2% specificity, 68.8 % PPV, 92.9 % NPV and 80 % accuracy. However, MP MRI showed no false negatives and there was a significant reduction in false-positive lesions (only two) compared with DCE MRI with 100% sensitivity, 88.9%specificity, 85.7 % PPV, 100 % NPV and 93.3 % accuracy. This was matched with other studies (16) revealed that MP MRI allows an increase in both sensitivity and particularly specificity, resulting in a significantly improved diagnostic accuracy.

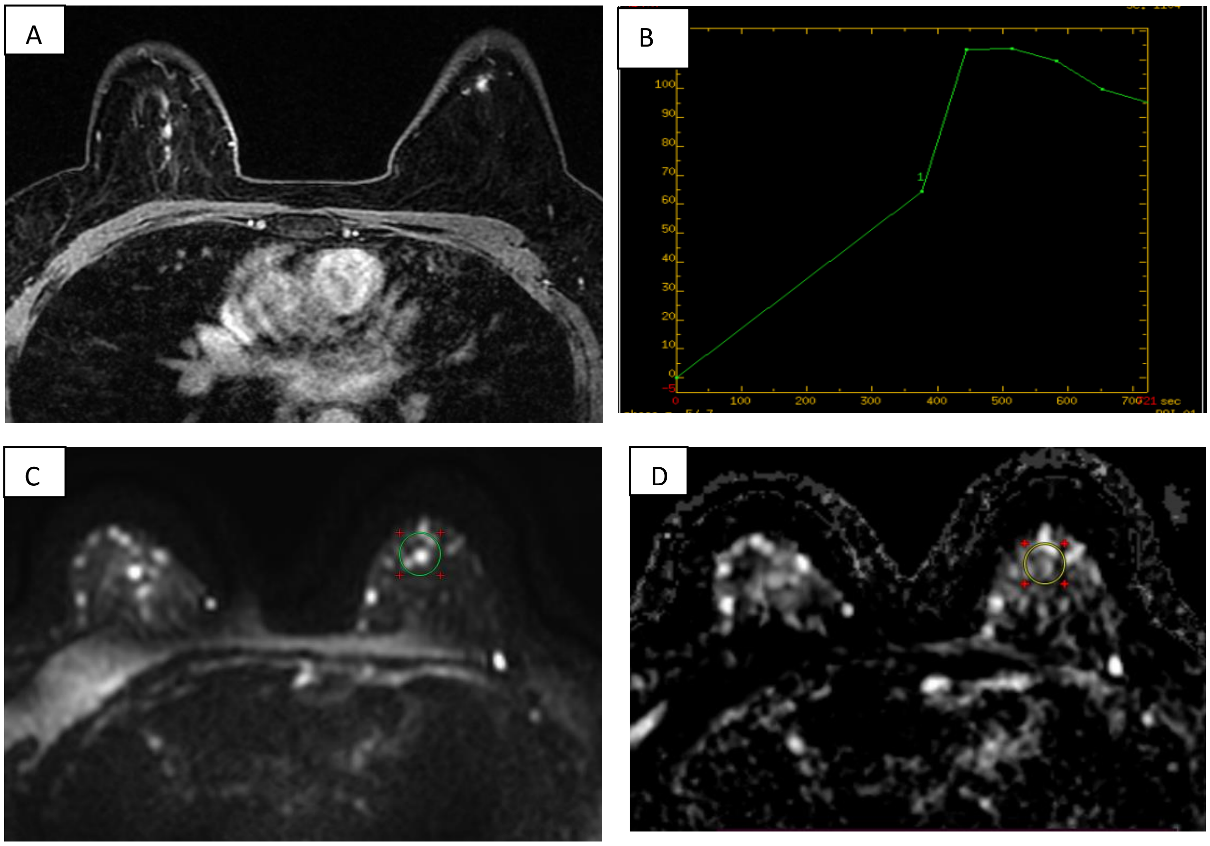

Figure (3): A 47-year-old female with history of right breast cancer managed by conservative breast surgery on follow-up. (a) Post contrast T1 axial images showed left breast small soft tissue nodule measuring about 5mm. (b) Type III time intensity curve, and (C) DWI showed hyper intense signal denoting restricted diffusion (d) ADC map showed hypo intense lesion with ADC value 0.9 $x10^{-3}$ mm^2/s. MRI diagnosis was neoplastic recurrence. Histopathology revealed recurrent ID

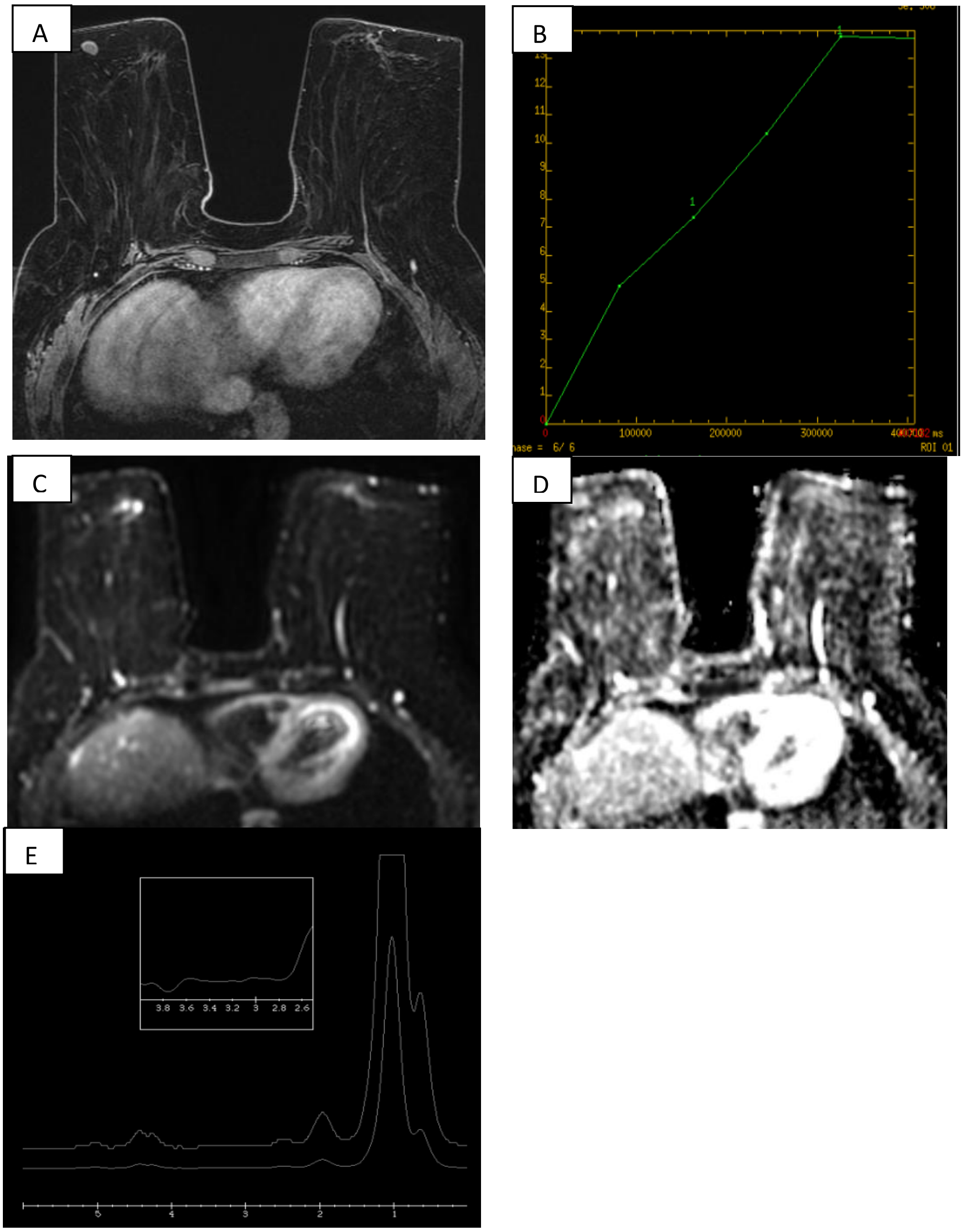

Figure (4): 43-year-old female with history of right breast cancer managed by lumpectomy on follow-up ultrasound, showing right breast lesion with suspicious features. (a) Post contrast T1 axial images showed right breast small oval shaped homogenously enhanced soft tissue lesion. (b) Type I-time intensity curve, and (C) DWI showed hyper intense signal denoting restricted diffusion (d) ADC map showed hypo intense lesion with ADC value 2.1 $x10^{-3}mm^2/s$. (d) MRS curve shows no choline peak. MRI diagnosis was benign lesion likely fibroadenoma, confirmed later by imaging follow up.

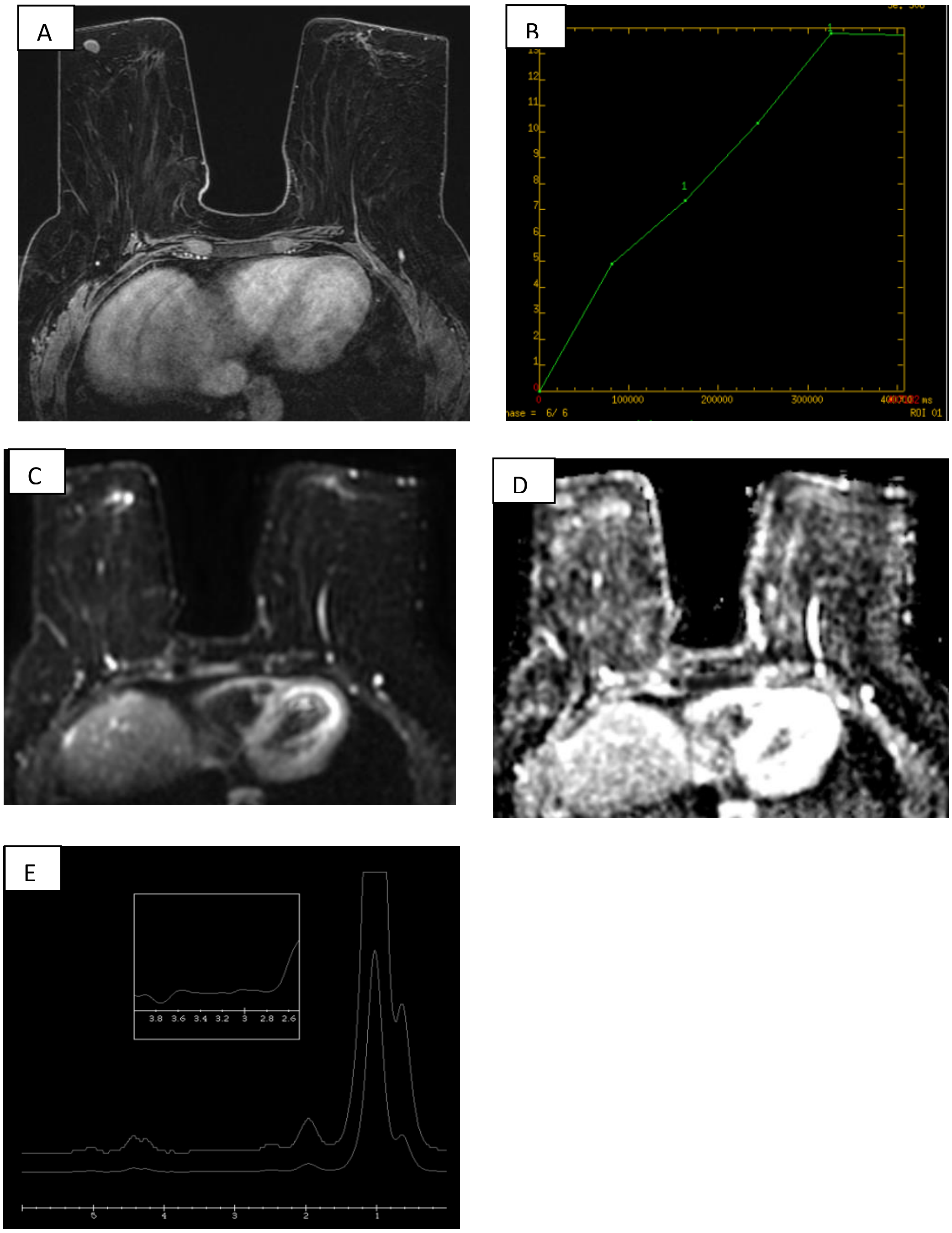

Figure (5): A 54-year-old female with history of right breast cancer managed by lumpectomy on follow-up (A) Post contrast T1 axial images showing right breast operative bed non mass like lesion measuring 2.8x0.5 cm, (B)showing type II curve of dynamic enhancement. DWI showed hyper intense signal denoting restricted diffusion (d) ADC map showed hypo intense lesion with ADC value 2.2x10−3 mm2/s. (d) MRS curve no choline peak. MRI diagnosis was Likely post-operative/radiation sequel which was confirmed later by imaging follow up.

Conclusion:

Combination between multiple MRI parameters (DCE-MRI, DWI, and MRSI) will be of great value in differentiating local recurrence from other post-operative sequels in patients with recurrent breast cancer. In conclusion, MP MRI has a great diagnostic accuracy for post-operative detection of recurrent breast cancer.

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