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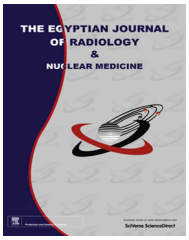

ORIGINAL ARTICLE

Assessment of breast mass: Utility of diffusion-weighted MR and MR spectroscopy imaging

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Abstract *Background:* Using diffusion-weighted imaging (DWI) combined to MRI is helpful to distinguish malignant versus benign breast lesions. Proton magnetic resonance spectroscopy provides biochemical information about the tissue under investigation.
Patient and methods: The study included 30 patients with suspicious breast lesions detected by clinical examination, mammography and/or breast ultrasound. All patients included in this study were subjected to Mammographic examination, ultrasound examination, and MRI examination including diffusion-weighted imaging and proton MR spectroscopy.
Results: In this study the sensitivity of MRS was 90%, its specificity was 78.6%, accuracy was 85%, PPV was 85.7% and NPV was 84.6%. Regarding the sensitivity of diffusion and apparent diffusion coefficient (ADC), it was 90%, while its specificity was 92.8% and 91.1%, 94.7%, 86.6% for the accuracy, PPV and NPV respectively.
Conclusion: The combination of MRS and DWI with magnetic resonance imaging should provide complementary information not available by either modality alone.
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1. Introduction

Breast cancer is now a significant cause of worldwide morbidity and mortality. Further, the increasing rate of breast cancer continues to be a major area of concern for both clinicians and researchers. Increased awareness in the affected population leads to more frequent physical examinations and diagnostic imaging procedures which results in earlier diagnosis and hence improved prognosis (1).

The majority of the lesions that occur in the breast are benign. It is important to recognize benign lesions and distinguish them from breast cancer (2).

Breast MRI may be used to distinguish between benign and malignant areas, reducing the number of breast biopsies done to evaluate a suspicious breast mass. Although MRI can detect tumors in dense breast tissue, it cannot detect tiny specks of calcium (known as microcalcifications), which account for half of the cancers detected by mammography (3).

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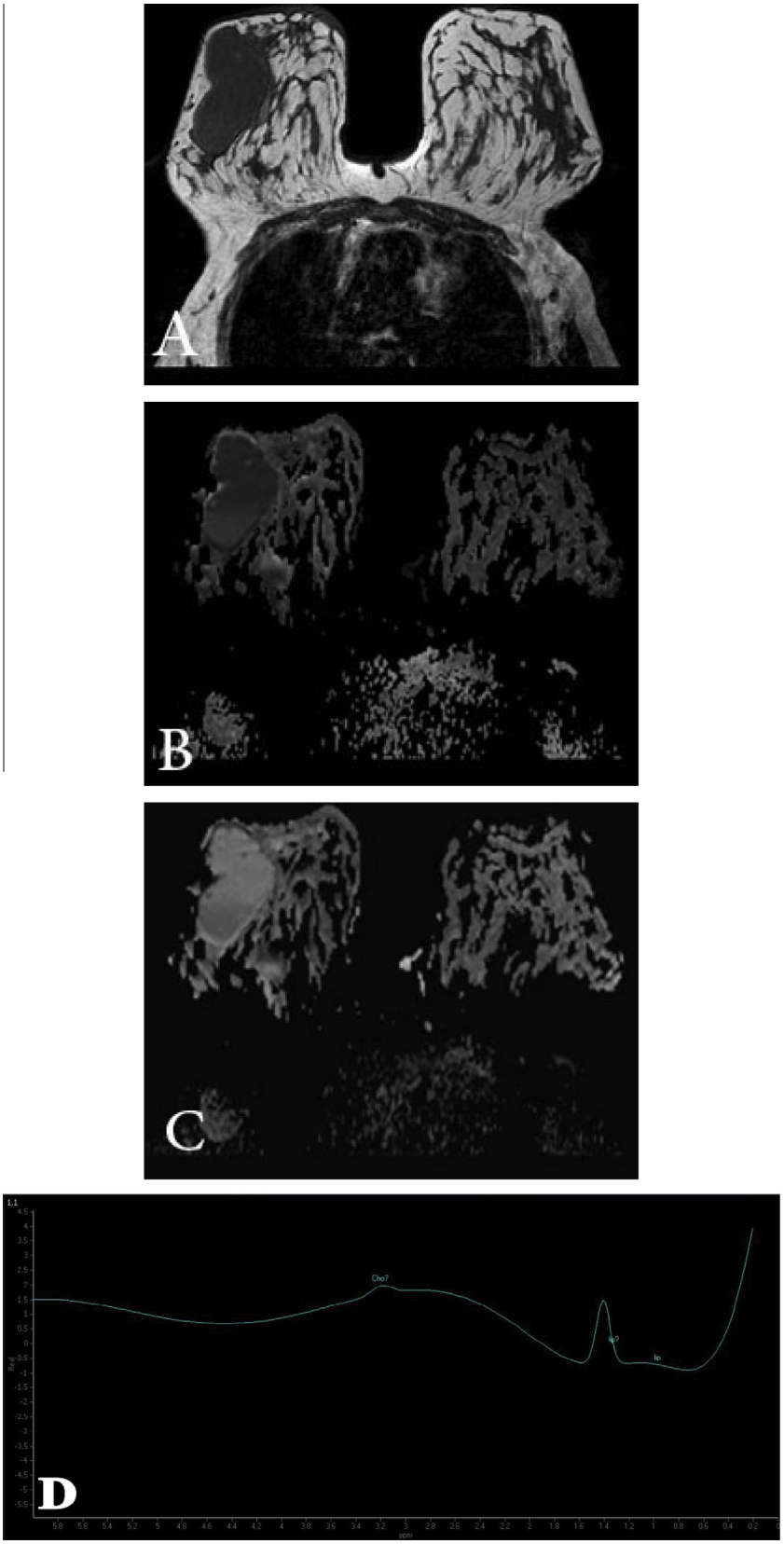

Fig. 1 A 29 year old female patient: (A) Axial T1WI shows a large well-defined hypointense cystic lesion seen at right upper outer quadrant with smooth margin. (B) DWI at $b = 1000$ shows low signal mass denoting facilitated diffusion. (C) Apparent ADC map reveals hyperintense mass (the mean ADC value of the cystic lesion $= 1.82 \times 10^{-3}$ mm^2/s). (D) MRS of the lesion reveals broad choline peak. The lesion histopathologically proved as infected cystic lesion.

And hence using diffusion-weighted imaging (DWI) combined to MRI enhances such differentiation between malignant and benign breast lesions (4).

Magnetic resonance (MR) spectroscopy is providing biochemical information about the tissue under investigation (5). Several studies over the past decade documented that Cho is specific to malignancy and can be used to differentiate cancerous from benign tissues (6).

The aims of this work were to assess the role of diffusion-weighted imaging and proton magnetic resonance spectroscopy in evaluation of breast masses and comparing the results with histopathology.

2. Patient and methods

The current study is cross sectional study included 30 patients with suspicious breast lesions detected by clinical examination, mammography and/or breast ultrasound; their mean age was 42 years (±10.4) (age range, 19–65 years). They were referred to Radiology Department, Zagazig University Hospitals from General Surgery and Oncology Departments.

All patients were subjected to the following:

(1): Full clinical history:

- Personal history, including the age, occupation and residency.
- Past history, including history of breast pain, lump, breast surgery as well as history of any procedure which might interfere with the MRI examination (e.g. cardiac pacemaker placement or cerebral aneurysm surgery).

(2): Physical examination:
Breast examination focused on palpable lumps, skin thickening, nipple retraction and examination of the axilla for any palpable enlarged nodes.

(3): Mammographic examination
Digital mammography was reviewed (mediolateral oblique and craniocaudal views). Mammographic images were evaluated as regards the presence or absence of suspicious lesion.

(4): Ultrasound examination:
Ultrasound was reviewed for the presence or absence of breast masses.

(5): MRI examination:
MRI was done in Zagazig University Hospital using Philips Achieva 1.5T scanner with a dedicated breast coil.

Before the examination, the patient's consents were taken and patients were informed about the duration of the examination and the importance of remaining still during image acquisition. The patient lies prone on the examination couch with her breasts in the dedicated breast coil; the patient's arms are positioned beside her head. Her head is supported with a head holder and a pillow is placed under her legs to make her tolerate the prone position.

2.1. Sequences

The study starts with a three plane localizer then with axial T1WI [TR, msec 450 and TE, msec 1], T2WI [TR, msec 4000 and TE 120, msec 10) and fat saturated T2WI or T1WI which were obtained with slice thickness of 3 mm and 1 mm interslice gap. FOV was set at 360 mm. The following parameters were used.

2.2. MRI interpretation

MRI images were reviewed and evaluated for Lesional number and site of lesions, shape (round, oval, lobulated, irregular), margins (smooth, spiculated, irregular), and signal intensity in T1WI and T2WI. Nature of the lesion (cystic or solid), and presence of signal voids or internal septations. Skin thickening, nipple retraction, pectoralis major invasion and presence of enlarged axillary lymph nodes.

2.3. Diffusion-weighted imaging

DWI was performed using Philips Achieva 1.5T scanner; reduction factor 2, 7000/71.5 number of excitations 2; matrix 240 × 240 field of view, 34 cm; slice thickness, 3 mm, 0, *b* factor = (0 and 1000 s/mm^2), and the scanning time was 4 min. Respiratory triggering was used for better resolution. The ADC value is a quantitative measurement of diffusion that is calculated on the basis of the attenuation in signal intensity between at least two diffusion-weighted images according to the following equation:

$$\text{ADC value} = -\text{In}(S_{DW}/S_{SE})/b,$$

where S_{DW} is the attenuated spin-echo signal and is the full spin-echo signal without diffusion attenuation and b value (expressed in seconds per square millimeter) represents the strength of diffusion weighting

The apparent diffusion coefficient (ADC) values were automatically calculated by placing the ROI well within the confines of the lesion. Fatty glandular parenchyma, which shows homogeneous signal intensity on the ADC map, was used as a reference. The scanner software provides the mean value within the ROI, which equals the ADC value (multiplied by 10^{-3}). Diffusion weighted images and ADC maps are then examined regarding the signal intensity and the mean ADC of each lesion.

2.4. Proton MR spectroscopy

Before MR spectroscopy, local homogeneity of the field is verified by shimming. Also effectiveness of fat and water suppression is checked. PRESS sequence is then performed (TR/TE 1500/136 ms; bandwidth 1 kHz; 512 excitations); single Voxel is placed upon the suspicious area. The sequence includes three successive selective pulses positioned in the three orthogonal planes and intersecting in the Voxel we want to study. The acquisition time was about 10 min. Postprocessing of the acquired data is then performed and includes different signal filters, frequency correction, phase correction, baseline correction and curve fitting to optimize the spectral profile. Choline peak is at 3.2 ppm.

MRS was analyzed according to the presence or absence of choline peak in the spectrum, and whether the peak – if present – is tall or broad.

- Tall peak was interpreted as malignant.
- Broad peak was interpreted as benign.
- No peak was interpreted as benign.

(6): Histopathological correlation:
From the 34 evaluated lesions 20 lesions were resected surgically whereas patients with the other lesions underwent ultrasound guided biopsy, 9 with FNAB and 5 with core biopsy. The histopathological diagnosis was obtained in all lesions and was the standard of reference.

(7): Data analysis:
Data were statistically described in terms of frequencies (number of cases) and percentages when appropriate. Accuracy was represented using the terms sensitivity, specificity, positive predictive value, negative predictive value, and overall accuracy.

3. Result

This study included 30 female patients with 34 breast lesions, their ages ranged from 19 to 65 years with a mean of 42.24 ± 10.6 years. As regards the age distribution of the patients the most common age is 50–60 years. The age of patients is younger in cases with benign lesions, and 10 patients had previous breast surgery. Conventional MRI, diffusion-weighted images and MRI spectroscopy were performed to all patients after taking their consent. Previous ultrasound and mammography were reviewed if present. Histopathological diagnosis was performed in all patients (surgical specimen in 20 lesions, FNAB in 9 lesions and core biopsy in 5 lesions).

As regards the patient complaint, 58.8% of patients complain of painless lump, 20.5% complain of painful lump, 32.3% show skin thickening and nipple retraction, 8.8% complain of pain and 29.4% came for follow-up. Ten cases (33.3%) had positive family history while twenty cases (66.7%) had negative family history (see Figs. 1–4 and Tables 1–8).

4. Discussion

Screening for breast cancer has been shown to decrease mortality, and mammography is the main screening tool; ultrasound and magnetic resonance imaging have been used as adjunctive tools, mainly for women who may be at increased risk for the development of breast cancer (7,8).

In our study histopathological diagnosis of benign lesions (14 cases) included 50% fibroadenomas, 14.3% papillomas, 14.3% infected cystic lesions, 14.3% fibrocystic and 7.1% radial scars (9), reported that fibroadenoma is the most common benign breast mass comprising about 88% of benign masses.

On the other hand, the histopathologic diagnosis of malignant lesions (20 cases) in this study included 60% invasive ductal carcinomas, 25% invasive lobular carcinomas, 5% medullary carcinomas , 5% inflammatory carcinoma and 5% mucinous carcinomas. Our results coincide with (10) which reported invasive ductal carcinoma is the most common malignant breast mass comprising about 73% of malignant masses.

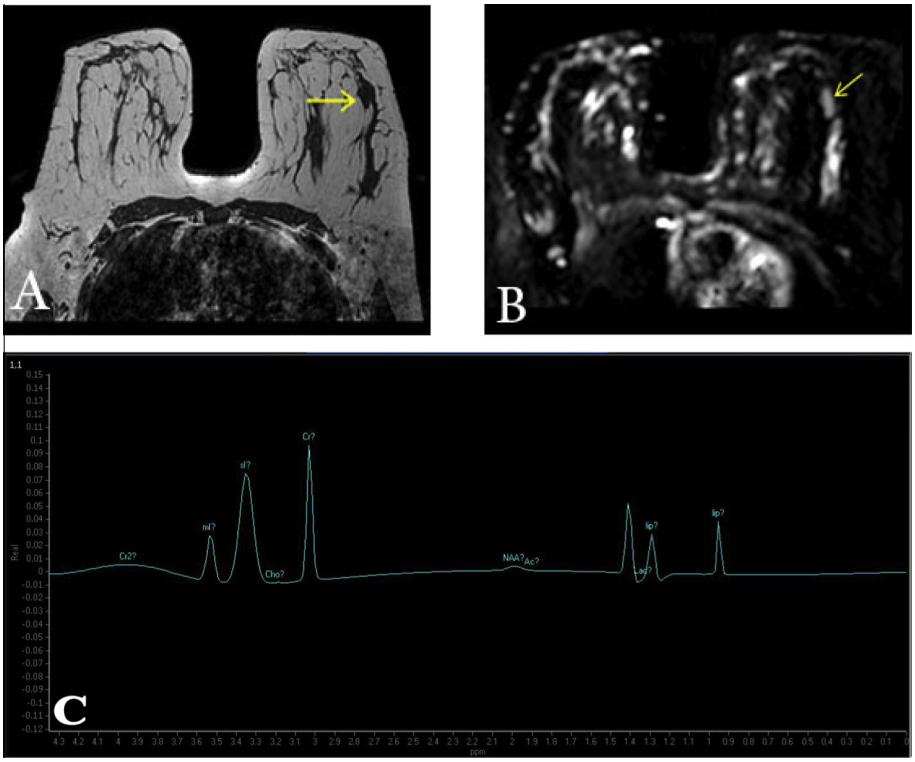

Fig. 2 A 33 year old female patient: (A) Axial T1WI shows small fairly defined hypointense breast mass (yellow arrow) at left upper outer quadrant with well-defined margins. (B) Apparent ADC map reveals hyperintense mass (yellow arrow) with facilitated diffusion (the mean ADC value of the cystic lesion = 1.42×10^{-3} mm^2/s). (C) MRS of the lesion reveals absent choline peak. The lesion histopathologically proved as fibroadenoma.

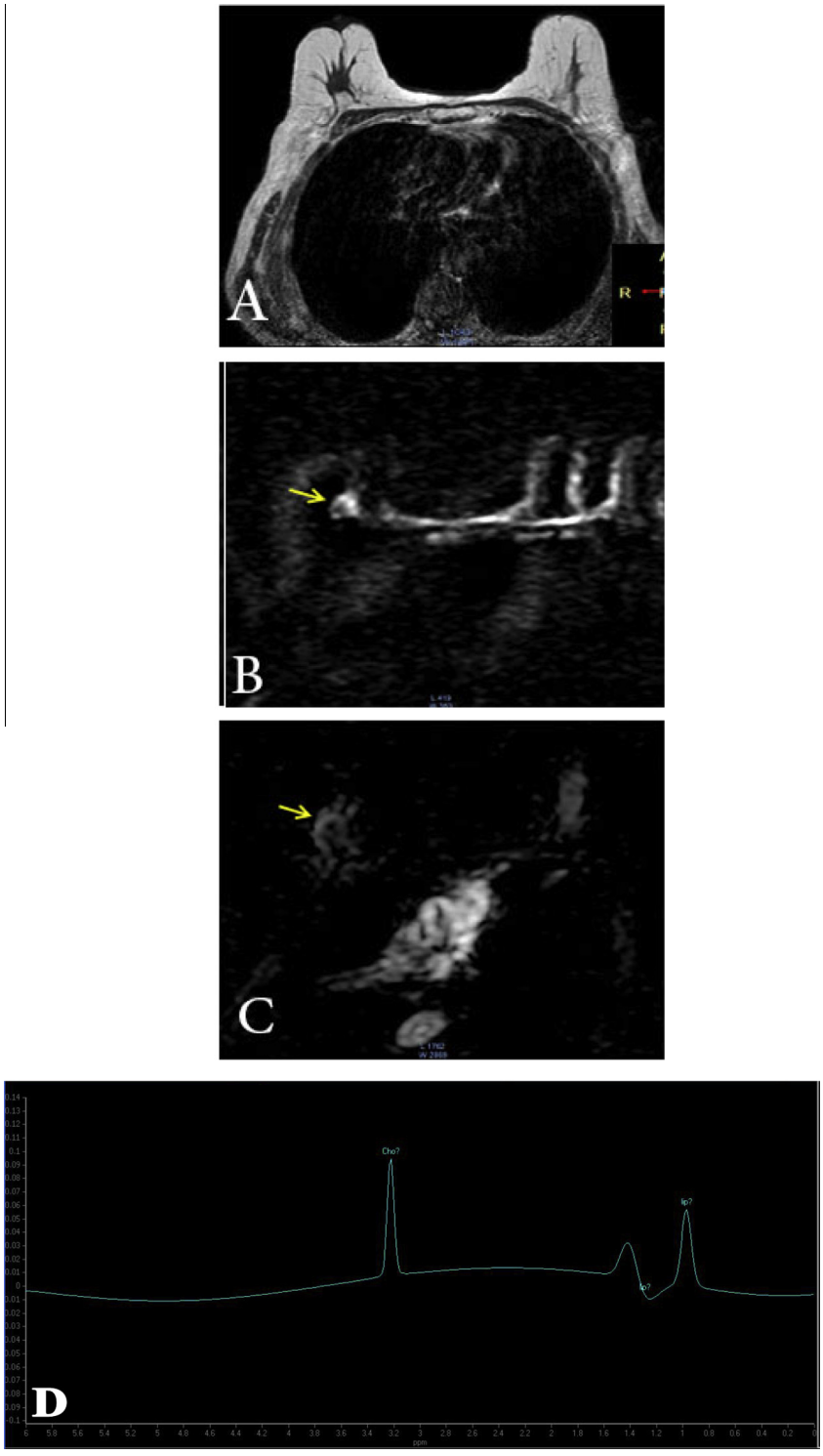

Fig. 3 A 63 year old female patient: (A) Axial T1WI shows right upper central ill-defined hypointense breast mass with speculated margins. (B) DWI at $b = 1000$ shows bright signal of the mass (yellow arrow) denoting restriction. (C) Apparent ADC map reveals hypointense mass (yellow arrow) (the mean ADC value of the cystic lesion = 0.79×10^{-3} mm^2/s). (D) MRS of the lesion reveals tall choline peak. The lesion histopathologically proved as invasive lobular carcinoma.

The most frequent finding in benign lesions was smooth margin or smooth shape/margin (80–82%) while the features with highest positive predictive value for carcinoma were speculated margin in 100% and irregular shape in 97% (11). Also (12), reported that 14% of malignant lesions are round, oval or lobulated and 86% are irregular in shape.

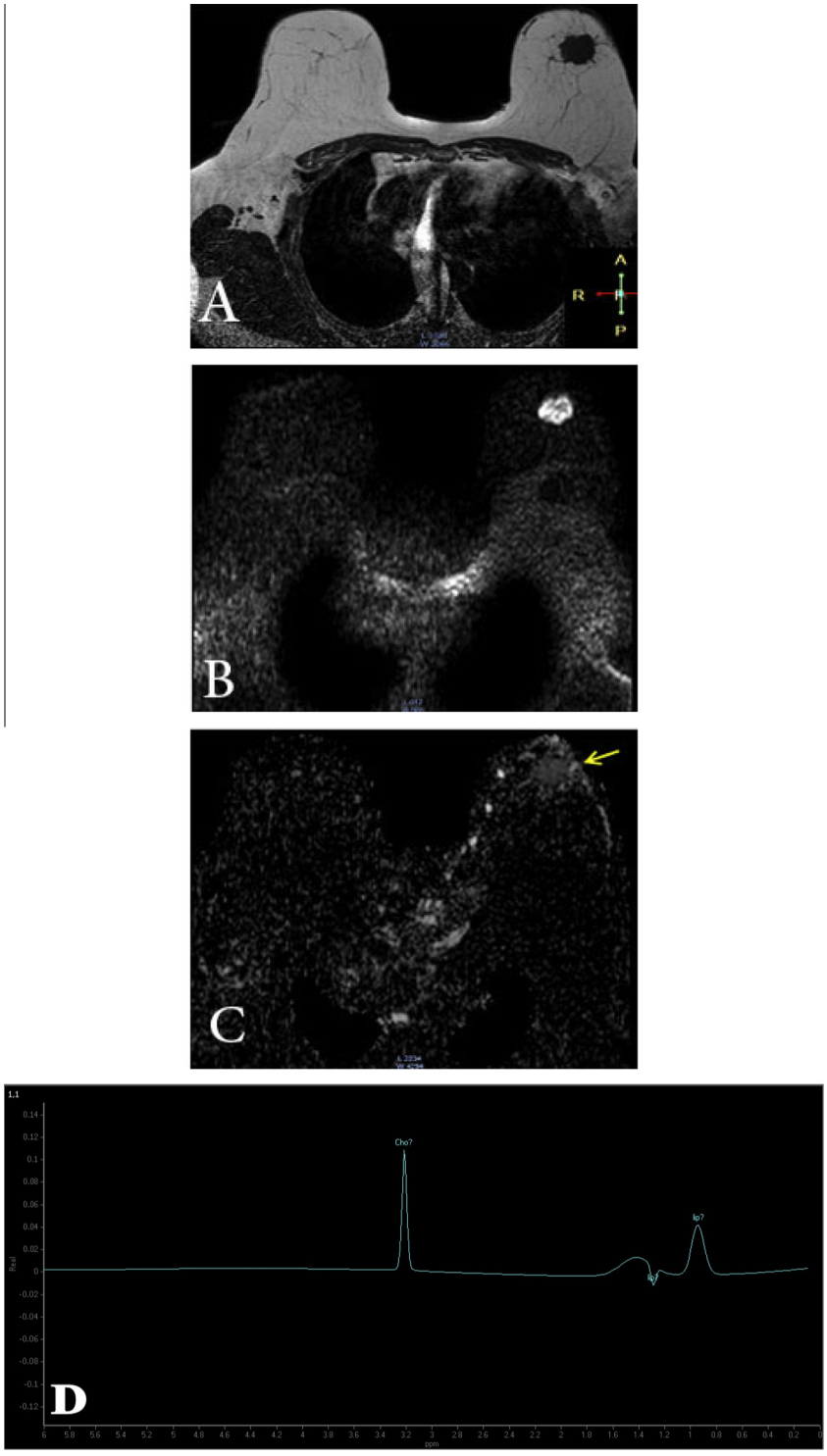

Fig. 4 A 47 year old female patient: (A) Axial T1WI shows left upper outer quadrant breast ill-defined hypointense mass with irregular margin. (B) DWI at $b = 1000$ shows bright signal of the mass denoting restriction. (C) Apparent ADC map reveals hypointense mass (yellow arrow) (the mean ADC value of the cystic lesion $= 0.90 \times 10^{-3}$ mm^2/s). (D) MRS of the lesion reveals tall choline peak. The lesion histopathologically proved as invasive ductal carcinoma.

Our study reported that all 34 breast lesions were iso to hypointense in T1WI while in T2WI, 64.3% of benign lesions are iso to hypointense and 35.7% are hyperintense, 90% of malignant lesions are iso to hypointense and 10% are hyperintense in T2WI. Low T2 internal septations are detected in 2 (15.4%) benign lesions and none of malignant lesions. This is in agreement with (13) who stated that T2 signal intensity was not a significant predictor of malignancy and

all masses in their study with internal septa were fibroadenomas. However (14) stated that internal septations, a description usually associated with fibroadenomas, are a sign that is no longer exclusive to benign lesions. In their study which included 55 lesions, one lesion with internal septa proved to be well differentiated invasive ductal carcinoma.

Complementary MR techniques have emerged as MRI investigates anatomic changes associated with neoplastic disease, while 1H MRS is able to examine the biochemistry of tissue and to detect spatial deviations from normal biochemistry in neoplastic tissues (7).

The goal of obtaining non-invasive biopsy information through the use of such methodology has pushed the development of several optimized localized MRS procedures as a unique means to probe the biochemistry of living systems with diagnostic importance by its ability to measure endogenous metabolites non-invasively as well as changes in tissue metabolism (15).

Unlike for the brain and prostate, breast spectra typically exhibit only a single metabolite peak located at approximately 3.2 ppm, which is elevated in cancer in comparison with normal breast tissues (16). 1H MRS is not a method for detecting breast lesions but rather a method for their characterization. As choline containing compounds are believed to be precursors of the phospholipids that compose cell membranes, increases in Cho signals are thought to reflect increased membrane cellular synthesis associated with malignancy (9).

MRS of the breast, has shown that choline-containing compounds can be detected in most breast cancers (17), whereas choline is generally not detectable in normal breast tissues. Thus MR spectroscopy can be helpful in diagnosis of indeterminate lesions based on the well-established principle that malignant tissues show elevated concentrations of choline, a product of membrane synthesis, so elevated choline is considered as marker for cancer (18).

In our study, 78.6% of benign lesions showed no or broad choline peak whereas tall choline peak was detected in 21.4% of lesions. On the other hand, 90% of malignant lesions showed tall choline peak and 10% had no or broad choline peak.

Based upon absence of choline, 11 benign lesions were diagnosed correctly; yet, choline peak was observed in 3 benign lesions (3 were false positive, 2 were fibroadenomas and the third was intraductal papilloma). As regards malignant lesions, 18 were correctly diagnosed on the basis of choline peak and 2 showed absent choline (2 false negative intraductal carcinomas). Sensitivity of MRS was 90.8%, its specificity was 78.6%, and accuracy was 85%. PPV was 85.7% and NPV was 84.6%.

Our results were in agreement with (19), who reported the overall combined sensitivity and specificity of MRS as 83% and 85%, respectively and also with (18), who reported that the sensitivity and specificity were 93.6% (88/94) and 77.9% (152/195), respectively; however (17) reported sensitivity of 100%, and specificity of 88%. The major limiting factor that affects sensitivity was the small size of the tumor and this agrees with this feature which was noted by (18), who found decreasing diagnostic sensitivity of choline detection with smaller lesion sizes. (19), who included small lesions in their diagnostic study, reported a diagnostic sensitivity of 82% in lesions larger than 15 mm in maximum length, but only 42% when considering all lesions.

In our study false positive choline peak was detected in 3 benign lesions. This finding was in agreement with (18), who reported that seven false positive cases were encountered. The histologic diagnoses in the seven false-positive mass lesions by MRS included were fibroadenomas and three of these were found in lactating females. In these cases the peak of choline was characteristically short and bifid and also (20), reported that most studies have reported some false positives with no specific benign pathology implicated.

In our study, false negative results were observed in 2 malignant lesions (2 false negative intraductal carcinomas) in agreement with (18) and explained by the lesional necrosis.

Table 1 Anatomical distribution of lesions, and distribution of the detected breast lesions in correlation with histopathological results.

Quadrant	Count	%	Benign (no. = 14)	Malignant (no. = 20)
UOQ	15	44.1	5	10
LOQ	6	17.6	3	3
LIQ	5	14.7	3	2
UIO	4	11.8	2	2
Retro-areolar	2	5.9	0	2
More > one quadrant	2	5.9	1	1

Regarding 14 benign lesions, 7 (50%) were fibroadenomas, 2 (14.2%) papillomas, 2 (14%) abscess, 2 (14.2%) fibrocystic diseases and 1 (7.1%) radial scar, whereas regarding 20 malignant lesions 12 (60%) were invasive ductal carcinomas and 5 (25%) were invasive lobular carcinomas, 1 (5%) medullary carcinoma, 1 (5%) inflammatory carcinoma and 1 (5%) radial scar.

Table 2 Evaluation by non-contrast MR imaging of the patients.

Noncontrast MR criteria	Benign (no. = 14)		Malignant (no. = 20)	
	No.	%	No.	%
Shape				
Rounded	5	35.7	2	10
Oval	4	28.5	2	10
Irregular	2	14.2	10	50
Lobulated	3	21.4	6	30
Border				
Well defined	11	78.6	2	10
Speculated	–	–	10	50
Ill-defined	3	21.4	8	40
T1 signal				
Iso to low	14	100	20	100
High	–	–	–	–
T2 signal				
Iso to low	9	64.3	18	90
High	5	35.7	2	10
Low T2 internal septations				
Present	2	15.4	–	–
Absent	12	85.7	20	100

Table 3 Signs associated with benign and malignant lesions.

Associated signs	Benign		Malignant	
Skin thickening				
Present	1	7.1%	15	75%
Absent	13	92.9%	5	25%
Nipple retraction				
Present	–	–	15	75%
Absent	14	100%	5	25%
Axillary lymphadenopathy				
Present	4	28.6%	12	60%
Absent	10	71.4%	8	40%

N.B: One patient had more than one finding.

MRS evaluation: Regarding choline peak in our study, 8 cases (23.5%) had no choline peak, 5 (14.7%) had broad peak while 21 (61.8%) had tall peak. The tall peak only is considered a marker for malignancy. No and broad choline peaks are considered benign.

Table 4 Presence of choline peak in the detected lesions.

Choline peak	Benign		Malignant	
	No.	%	No.	%
Present (tall peak)	3	21.4	18	90
Absent (broad or no peak)	11	78.6	2	10

The diffusion criteria were assessed for breast lesions as restricted or facilitated. 92.9% of benign lesions showed facilitated diffusion while 7.1% of benign lesions showed restricted diffusion while 90% of malignant lesions showed restricted diffusion and 10% of malignant lesions showed facilitated diffusion.

Table 5 The characters of lesions on DW images in relation to the histopathology.

Diffusion	Benign	Malignant
Restricted	1 (7.1%)	18 (90%)
Facilitated	13 (92.9%)	2 (10%)
Total	14	20

Table 6 The minimum, maximum and mean of the ADC values ($\times 10^{-3}$ mm^2/s) in benign and malignant mass lesions.

Pathology	Minimum	Maximum	Mean
Benign	0.9	2.12	1.54
Malignant	0.56	1.4	0.86

Table 7 Comparison between MRI findings, diffusion and MRS.

		Correct diagnosis	False +ve	False −ve	Total
MRI findings	Benign	9	5	–	14
	Malignant	16	–	4	20
MRS	Benign	11	3	–	14
	Malignant	18	–	2	20
Diffusion and ADC	Benign	13	1	–	14
	Malignant	18	–	2	20

MRI findings, MRS and DWI correct diagnosis, false positive and false negative finding reported in Table 7.

Table 8 Sensitivity, specificity, accuracy, positive predictive value (PPV) and negative predictive value (NPV) of MRI diagnosis, diffusion and MRS.

	Sensitivity (%)	Specificity (%)	Accuracy (%)	PPV (%)	NPV (%)
MRI diagnosis	80	64.3	73.5	76.2	69.2
MRS	90	78.6	85	85.7	84.6
Diffusion and ADC	90	92.8	91.1	94.7	86.6

In the breast, some reports have shown a diagnostic potential of DWI to differentiate between benign and malignant breast masses, excellent detection, and location of the breast cancer is supposed to be possible without the use of a contrast agent, in spite of the significant geometrical distortion on DWI (21,22).

Hence, DWI is a promising tool in screening for breast cancer without using contrast medium. Investigations on DWI of the breast so far mainly focused on ADC measurements in order to differentiate between benign and malignant lesions. SMD analysis of reported mean ADC values indicates major diffusivity differences between benign and malignant lesions. This fact is reflected in the reported high sensitivity and specificity values (23,24).

In our study 92.9% of benign lesions showed facilitated diffusion while 7.1% of benign lesions showed restricted diffusion, 90% of malignant lesions showed restricted diffusion and 10% of malignant lesions showed facilitated diffusion sensitivity of diffusion; ADC was 90%, its specificity was 92.8%, accuracy was 91.1%, PPV was 94.7% and NPV was 86.6%. Our DWI results show lower ADC value of the malignant lesions. This was in agreement with (25) who reported that low value is due to increased cellularity of the densely packed randomly organized tumor cells, with (26) who reported the sensitivity and specificity as high as 92% and 96%, respectively and with (27), who reported that ADC values for the detection of malignant lesions showed a sensitivity of 97.22% and a specificity of 100%; however (28) reported a specificity of 67% (43/64) and a sensitivity of 97% (61/63) for mass and focal lesions, regardless of lesion size.

The single false positive case found in this study was diagnosed as malignant according to its morphologic and plain MRI picture and the two false negative cases were diagnosed as benign and found to be mucinous and medullary carcinoma. This agrees with (29) who suggest it is due to lower cell density and higher extracellular water content and the high cellularity in cases such as the papilloma seen in our study, and resulted in misleading ADC values.

5. Conclusion

Both DWI and MRS are useful diagnostic modalities for characterization and differentiation between benign and malignant breast lumps. Our preliminary results showed that combination of DWI and calculated ADC values and metabolite spectrum acquired by MRS add more information to MRI and should be considered as an additional and complementary tool to conventional MRI for differentiating benign from malignant masses.

Conflict of interest

The authors declare that there are no conflict of interests.

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