Role of Diffusion Weighted Magnetic Resonance Imaging in Evaluation of Suspicious Breast Lesions

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Abstract

Introduction: Diffusion weighted Imaging "DWI" is a specific modality to produce images of tissues weighted with the local microstructural characteristics of water diffusion. DWI can give information as regards cellularity of breast lesions and it can be used for distinguishing between benign and malignant breast lesions, differentiating surgical scar from recurrence and monitoring therapies in locally advanced breast cancer

Aim of the work: To assess the diagnostic value of diffusion weighted imaging as an adjuvant to breast magnetic resonance imaging for detection and differentiation of suspicious breast lesions and correlation with histopathologic findings, available clinical data or follow up.

Methods: The studied group included 50 female patients referred for MRI breast for workup of a suspicious clinical, mammographic, or sonographic abnormality. Diffusion weighted imaging (DWI) was added to the routine study. Results of the contrast enhanced bilateral breast MRI and DWI of the 50 patients were all reported and compared with the histo-pathological results of surgery or biopsy and with the results of follow up of lesions that were not surgically removed or biopsied.

Results: there was a highly significant relation between DWI and histopathological/ Follow Up results with p value = 0.000. The sensitivity, specificity, positive and negative predictive values of DWI for characterization of suspicious breast lesions in patients included in the study, were 89.5%, 100%, 100%, and 93.94% respectively.

Conclusion: DWI is a short unenhanced scan that can be inserted easily into standard clinical breast MRI protocols as a potential adjunct that can be added routinely to conventional breast MRI, and can accurately differentiate benign from malignant breast lesions with high sensitivity and specificity.

Key words: Magnetic Resonance Imaging, Suspicious Breast Lesions.

INTRODUCTION

Compared with mammography and breast ultrasonography, contrast material–enhanced MRI is a breast imaging technique that offers not only information on lesion cross-sectional morphology but also on functional lesion features such as tissue perfusion and enhancement kinetics[1].

Although, breast MRI demonstrated excellent sensitivity, its low specificity continues to represent a limit, particularly in patients referred for further clarification of an inconclusive conventional breast imaging finding[2].

To increase breast MRI specificity, DWI, that has shown great promise in the detection of most tumor types throughout the entire body and showed superior lesion to background contrast, could represent an important resource[3].

Diffusion Weighted Imaging is a specific modality to produce images of tissues weighted with the local microstructural characteristics of water diffusion[4]. Diffusion Weighted Imaging reflects the random thermal motion of molecules (Brownian motion) [4]. The Brownian motion of protons in bulk water produces the signal in DWI. So, DWI can

provide important biological information about the composition of tissues, their physical properties, their microstructure, and their architectural organization. This information is available noninvasively and without contrast administration[5]. So, DWI can give information as regards cellularity of breast lesions and it can be used for distinguishing between benign and malignant breast lesions, differentiating surgical scar from recurrence and monitoring therapies in locally advanced breast cancer[6].

We aimed at this study to assess the diagnostic value of diffusion weighted imaging as an adjuvant to breast magnetic resonance imaging for detection and differentiation of suspicious breast lesions and correlation with histopathologic findings, available clinical data or follow up.

PATIENTS & METHODS

During the period between October 2010 and February 2013, 50 female patients, ranging in age from 22-59 years, were included in the study who were referred to perform Contrast-enhanced bilateral breast MRI at Ain Shams University Hospitals and Misr Radiology Center for workup of a suspicious clinical, mammographic, or sonographic abnormality, were included in the study. Diffusion study was added to the routine study. We excluded patients with bad general conditions or those having contraindication for MRI.

The protocol of our study was approved by The Research Ethics Committee at the Faculty of Medicine, Ain Shams University. Informed consent, including potential risks and benefits of the procedure, was obtained from all patients.

MRI was performed using a 1.5Tesla superconductive Philips scanner. Following the patients' informed consent and exclusion of contraindications, patients were placed in prone position and examined using bilateral breast surface coils.

MRI protocol was: both axial T1W & T2W images, axial/ sagittal STIR "short tau inversion recovery and axial/ sagittal T1W post-contrast fat sat.

For DWI, it was performed prior to contrast administration not only to negate any possible effects of the presence of contrast agent may have on water diffusion within the tumor tissue but also to nullify any T2 shortening resulting from the contrast agent. Echo-planar imaging "EPI" DW imaging was performed in the transverse plane with tri-directional diffusion gradients by using b values: 0, 400& 800 sec/mm^2 to increase sensitivity to cellular packing. The other parameters were as follows: Time of Repetition (TR) $\geq$10036 ms, Time to Echo (TE) = 80 ms, Number of excitations (NEX)= 2, matrix 256x256 with Field of view (FOV): 421, ST= 3mm, slice gap 0mm.

Lesions detected by MRI in both breasts were evaluated. Morphologic assessment, kinetic (contrast enhancement) and diffusion analysis were performed on each lesion using dedicated post-processing and display software.

The analysis of enhancement kinetics is done by measuring the signal intensity in region of interest (ROI), and tracking its course over the dynamic series (time–signal intensity curve). ROIs were placed into the area that exhibits strongest enhancement on the first postcontrast image.

We first examined the diffusion map and looked for corresponding increased signal on DWI, then we looked for corresponding ADC map to first qualitatively assess corresponding signal whether low signal corresponding to low ADC values with true diffusion restriction or increased signal with high ADC values that go more with low cellular lesions. The mean ADC of each lesion detected is measured by drawing ROI over the lesion. If the lesion was less than 3 cm, ADC was measured twice and the two measurements were averaged. To ensure that the same areas

were measured, ROIs were copied and pasted from DW images to ADC maps.

Analysis of data was done by using SPSS (Statistical Program for Social Science version 15) as follows: **Description** of quantitative variables as mean, SD and range, **Description** of qualitative variables as number and percentage, **Chi-square** test was used to compare qualitative variables "**P value** <0.05 significant and **P value** <0.01 highly significant" and finally we calculated: Sensitivity, Specificity, PPV (positive predictive value) and NPV (negative predictive value).

RESULTS

This study included 50 female patients. The mean age of included women was 41.58 ± 9.42 years (range 22 - 59 years). Among the studied cases the most common clinical presentation was

breast lump and previous history of surgery for breast carcinoma to differentiate recurrence from post surgical scarring.

Among the 50 studied patients, 21 patients were followed up for having lesions which are thought to be probably benign and the follow up of these lesions didn't show growth

over time and confirmed the benign nature of such lesions and 29 patients among the studied group had been subjected for biopsy and 18 patients were discovered to have malignant lesions and 11 patients were classified as benign lesions "figure 1".
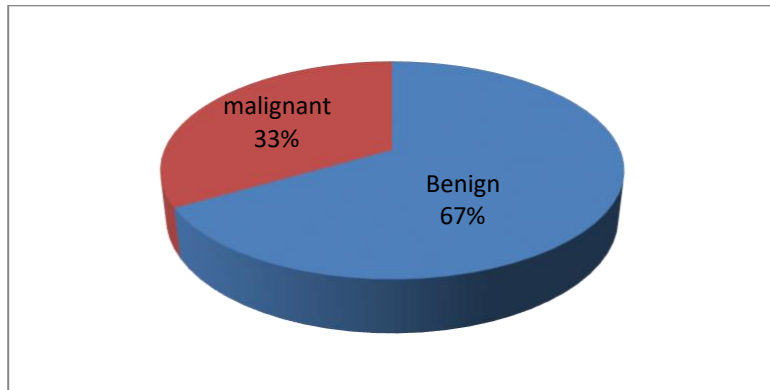

Figure 1: pie chart showing histopathalogical and follow up results among the studied group.

Table 3: Distribution of the studied group as regards histopathology findings and Follow up:

	Number	%
- Fibroadenoma	15	30%
- Benign post-operative scarring	10	20%
- Intraductal papilloma	3	6%
- Phylloids	1	2%
- Abcess	1	2%
- Sclerosing adenosis	1	2%
- Mastitis	1	2%
- Invasive Ductal Carcinoma "IDC"	15	30%
- Invasive Lobular Carcinoma "ILC"	1	2%
- Undifferentiated Carcinoma	1	2%
- IDC/ DCIS	1	2%

Table 4: The correlation between the MR lesion type and pathology/ Follow Up results:

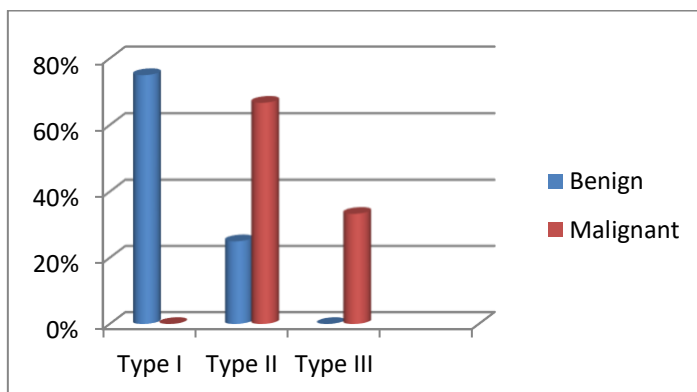|		Pathology/ Follow Up results		Total
		Benign	Malignant	
MR shape	Mass	23	8	31
	Non Mass	9	10	19
Total		32	18	50

Figure 2: A column chart showing the correlation between type of dynamic curve and pathology/ Follow up results.
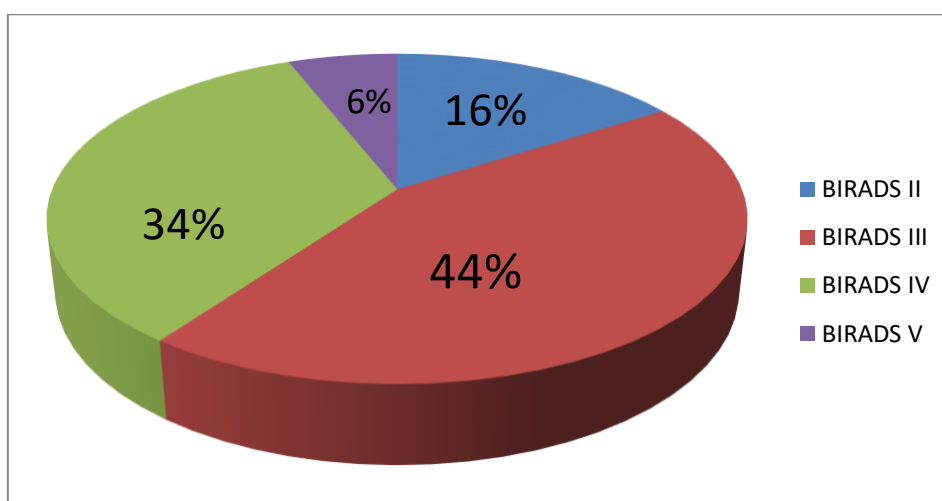

Figure 3: A pie chart showing different MRI findings among the studied group.

In this study and based on previous experience and results of prior studies done on this issue by **Tozaki and Maruyama** [3],**Yilli et al.**[7] and **Palle and Reddy** [5], we considered an ADC value of 1.1 x 10^{-3} mm^2 is a cut off value for differentiating benign from malignant lesions with values below were considered malignant and those above considered benign.

The diffusion study was not able to demonstrate one lesion among the studied group and it was reported as negative. The diffusion study was able to accurately detect 17 lesions as malignant and among the 32 lesions reported as benign, one of them turned out to be malignant "Table 5" and "figure 4".

Table (5) Showing the correlation between the DWI outcome and pathology/ follow up "FUP" results:

		Pathology/FUP		Total	P
		Benign	Malignant		
DWI	Negative	1	0	1	
	Benign pattern	31	1	32	
	Malignant pattern	0	17	17	0.000*
Total		32	18	50	

P* ≤0.001 = highly significant.

We found also highly significant relation between our results by DWI and histo-pathological/ Follow Up results with p value = 0.000.
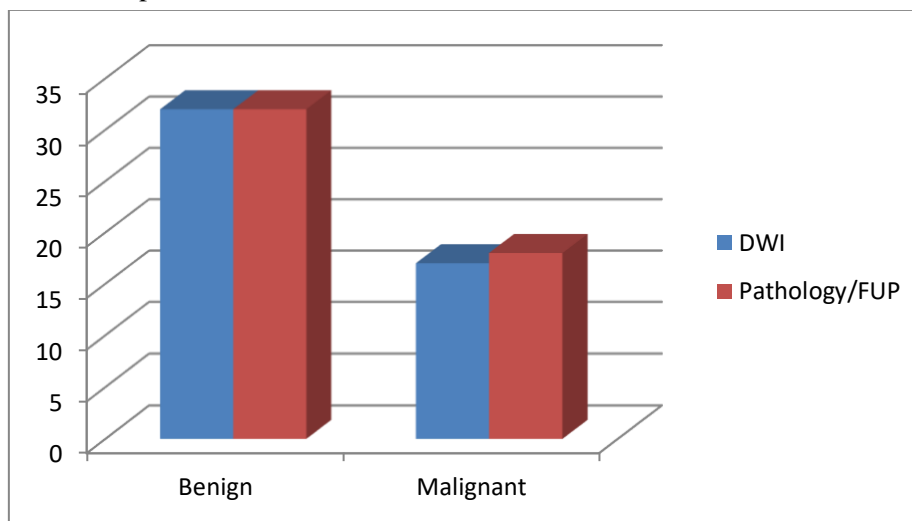

Figure 4: a column chart for comparison between DWI versus pathology and follow up results.

The mean ADC values (with the SD "standard deviation") as well as the minimum and maximum values for malignant, benign and all cases were calculated and were as in table 6.

Table (6) Showing the distribution of the ADC values among the studied cases:

	Malignant	Benign	Total
Mean ADC value:	0.897×10^{-3}	1.83×10^{-3}	1.4873×10^{-3}
SD:	0.18397	0.462	0.59313
Minimum value:	0.60×10^{-3}	1.14×10^{-3}	0.60×10^{-3}
Maximum value:	1.3×10^{-3}	2.7×10^{-3}	2.7×10^{-3}

Figure 4 shows the mean ADC value for the benign lesion was higher than the cut value used while figure 5 shows that malignancy has lower mean ADC value.

The sensitivity of the DWI in characterization of different breast lesions was: 89.5%, specificity: 100%, PPV: 100% and NPV: 93.94%.
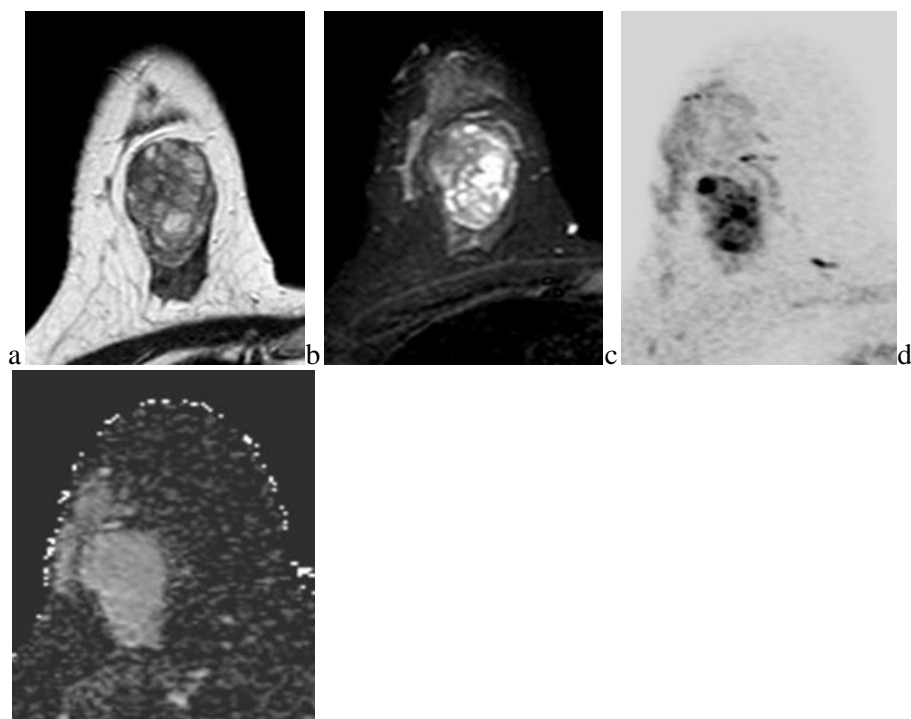
Fig4: (a) T2W, (b) STIR showing a well defined oval lesion that have regular smooth outline, heterogeneous intermediate signal with areas of increased signal on T2W and heterogeneous bright signal intensity on STIR sequence, the lesion was categorized as BIRADS IVa owing to the heterogeneity of the lesion, (c) the DWI revealed high signal lesion (d) ADC map: ADC values ranging from1.4 to 1.9 x 10^{-3} mm^2/s which is in favoring of a benign entity which on biopsy turned out to be fibroadenoma with myxoid degeneration.
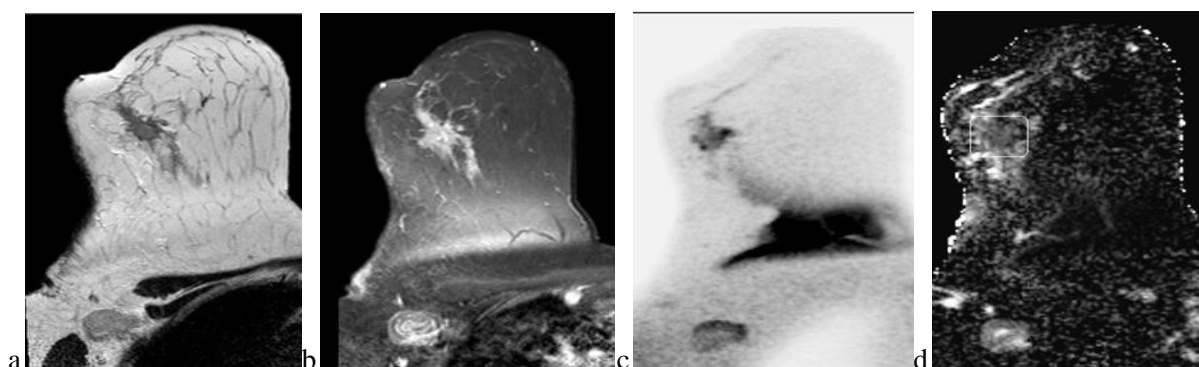

Fig5:(a)T2W: an area of architectural distortion was seen at about 11 o'clock position in the right breast along the pathway of a previous biopsy needle which had intermediate signal intensity enlarged adenopathies showing increased cortical thickness (b)T1W post-contrast fat suppression sequence: showing non mass appreciable enhancement,(c)DWI: revealed an irregular area of high signal on DWI and (d) corresponding ADC map: showing a small lesion of about 1.8cm with low ADC signal giving a low ADC value of 0.734 x 10^{-3} mm^2/s "which is coinciding with malignant values" amidst an area of increased signal that likely represent post-biopsy changes. Also, the right axillary nodes yielded high signal on DWI with low signal on corresponding ADC maps giving values as low as 0.706 x 10^{-3} mm^2/s which suggest malignant infiltration. This patient upon the MRI data and diffusion study had an excisional biopsy which revealed an invasive ductal carcinoma "grade2".

DISCUSSION

As, MR imaging of the breast known for its inherently high sensitivity but only moderate specificity for the characterization of breast lesions. Thus, efforts have been directed toward developing new pulse sequences and evaluation methods that improve lesion characterization[1].

Use of diffusion-weighted (DW) imaging is an approach that may improve MR imaging lesion characterization. High cell

proliferation in malignant tumors increases cellular density, creating more barriers to the extracellular water diffusion, reducing the ADC, and resulting in signal loss. This sequence appears to be a useful tool for tumor detection and characterization, as well as for monitoring and predicting treatment response[8].

This study included a wide range of lesion sizes. We found no association between lesion size and ADC. Therefore, difference in ADC values between different types of lesions couldn't be attributed to lesion difference in size. This is agreeing with Partridge et al. [9], who found no differences in ADC between small and large malignant lesions or between small and large benign lesions and the mean differences in ADC between benign and malignant lesions were similar for both size groups. And hence, no association between lesion size and ADC and reported that DWI isn't significantly limited by lesion size.

In our study, DWI could accurately diagnose 3 cases out of the 17 patients had recurrence , in which there was increased signal on DWI and corresponding low signal on ADC map, with lower ADC values with a mean of 0.88×10^{-3} mm^2/s while in scar tissue the mean ADC value was: 2.07×10^{-3} mm^2/s.

Our results agree with Rinaldi et al. [4], who studied the value of diffusion in differentiation between scar tissue post-surgery and tumor recurrence using a cut value of 1.4×10^{-3} mm^2/s and found that ADC strong predictor of tumor recurrence and adding diffusion sequence to contrast MRI increase diagnostic value in the evaluation of scar in patients operated for breast cancer

The obtained diffusion results were keeping with the pathology/ follow up final data for non-mass-like lesions. The mean ADC for malignant lesions presenting with non-mass-like pattern was 0.86×10^{-3} mm^2/s. For non-mass-like benign lesions, the mean ADC value was 2×10^{-3} mm^2/s.

These results were in agreement with Yabuuchi et al.[10], who evaluated the diagnostic accuracy of a combination of dynamic contrast-enhanced MR imaging (DCE-MRI) and diffusion-weighted MR imaging (DWI) in characterization of lesions showing non-mass-like enhancement on breast MR imaging and found that the combination of DCE-MRI and DWI showed high diagnostic accuracy in characterization of non-mass-like enhancement lesion on contrast-enhanced breast MR images. Segmental distribution, clumped internal enhancement and an ADC value less than 1.3×10^{-3} mm^2/s were the strongest indicators of malignancy.

Although type II curve is more going with malignant lesions as described by Kuhl [1] yet, About 40% of those presented with type II curve pattern in this study, had benign lesions on pathology/ follow up. So in cases having type II curve, further assessment by another technique "such as DWI" may be required to help in further confirmation of the nature of the lesion.

From our results, we had in 2 cases of those presented with type II curve were having false negative results on diffusion in which DWI, in one case it was negative with no lesion detected and the other one had ADC value going with benign lesion that later turned out to be malignant. From above mentioned data, we can see that DWI could be a valuable additional tool in cases with inconclusive dynamic MR results.

The results mentioned above are in agreement with Partridge et al[11] who found that ADC was significantly higher for lesions exhibiting predominantly persistent enhancement (mean ADC, $1.64 \pm 0.44 \times 10^{-3}$ mm^2/s) compared with those exhibiting predominantly washout or plateau enhancement (mean ADC, $1.39 \pm 0.30 \times 10^{-3}$ mm^2/s, P = 0.006).

There was a highly significant difference in the conspicuity between malignant and benign lesions on the DWI (P < 0.0001). Most malignant lesions were circumscribed and displayed strong signals on DW images. Margin characteristics, such as the appearance of being speculated, could not be displayed on DW images for inferior spatial resolution and partial-volume effect. Most benign lesions displayed mild to moderate signal with indistinct or definite margins on DW images. However, DW imaging cannot detect all lesions detected by other conventional MRI. This has been detailed above in the case which was negative on the diffusion study while shown on post-contrast study.

Malignant lesions had significantly lower ADC values that benign lesions "P<0.001". The mean ADC values for malignant and benign lesions were: 0.897 ± 0.183 and $1.83 \pm 0.462 \times 10^{-3}$ cm^2/sec respectively.

Using different ADC cut values, different studies showed variation in DWI sensitivity and specificity. Tozaki and Maruyama [3] using the two-step method of visual assessment of high b-value images and a cutoff ADC value of 1.13×10^{-3} mm²/s, achieved a specificity of 67% and sensitivity of 97% for mass lesions, regardless of the lesion size. Partridge et al. [12] studied the value of DWI as adjunct to conventional MRI to improve PPV and by applying an ADC threshold of 1.81×10^{-3} mm²/s for 100% sensitivity produced a PPV of 47% versus 37% for DCE-MRI alone. Pereira et al. [8] studied the utility of diffusion-weighted magnetic resonance imaging in the differentiation between benign and malignant breast lesions and stated that Diffusion-weighted imaging showed high sensitivity and specificity (both, 92.3%) in the differentiation between the entities. In their study, Palle and Reddy [5] used 2 different cut values for the malignant and benign lesions which were: 0.89 and 1.41×10^{-3} mm²/s respectively and reported a sensitivity of 97.22%, specificity of 100%, PPV was 100% and NPV was 99%. Kul et al. [13] were studying the contribution of DWI to DCE- MRI in characterization of breast tumors. They used a cutoff value of 0.92×10^{-3} mm²/s for ADC that provided 91.5% sensitivity and 86.5% specificity. DCE-MRI alone showed 97.9% sensitivity and 75.7% specificity. The specificity of breast MRI improved by 13.5% (p = 0.063) without a significant decrease in the sensitivity (p = 1.000). While, Gouhar and Zidan[14] stated that the sensitivity and specificity of DWI in the differentiation between benign and malignant breast tumors were 92.6% and 98%, respectively.

The calculated ADC value is clearly affected by the scanning parameters of TR, TE, and b value used for DWI[15]. That is the reason for the different cutoff values found for the discrimination of the malignant from benign lesions in the previous studies and in the current study. We think that all MRI sites should determine their own cutoff values according to the DWI sequence used for breast imaging[13].

There are some limitations in the present study. Firstly, there was some difficulty in categorization of breast lesions because of the limited capacity to recognize small lesions (< 1 cm) on the ADC map. So, for optimal lesion localization and ROI placement on ADC maps, we had co-registration and synchronization of the ADC maps with contrast-enhanced images and diffusion-weighted images can be helpful. Another limitation is the alteration of the ADC value if cystic or necrotic components were included in the ROI. So, during drawing ROI we excluded area of necrotic or cystic regions.

One of the most important limitations, this study didn't include a variety of malignant pathological entities i.e. mucinous carcinomas and pure DCIS were not represented in our study.

Finally, like in other studies, the sample of the present study is relatively small, and future studies with greater populations should be considered, and this is one of the next steps of the authors.

CONCLUSION

DWI is a short unenhanced scan that can be inserted easily into standard clinical breast MRI protocols as a potential adjunct that can be added routinely to conventional breast MRI, and ADC values derived from it can accurately differentiate benign from malignant breast lesions with high sensitivity and specificity.

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