ORIGINAL RESEARCH

Evaluation of breast lesions using diffusion-weighted imaging and dynamic contrast-enhanced MRI with pathological correlation

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ABSTRACT
Background: In this study, we wanted to differentiate benign and malignant breast lesions using diffusion-weighted imaging and dynamic contrast MRI, derive enhancement pattern curves to differentiate benign from malignant breast lesions and correlate MRI findings with pathological findings.
Methods: This was a hospital-based cross-sectional study conducted among 31 patients who underwent MRI breast examination in the Department of Radio Diagnosis, R.L. Jalappa Hospital and Research Centre, attached to Sri Devaraj Urs Medical College, Tamaka, Kolar, from January 2021 to July 2022 after obtaining clearance from the institutional ethics committee, and written informed consent from the study participants.
Results: 17 (38.6%) out of the 44 lesions showed restricted diffusion and 14 (31.8 %%) did not show restricted diffusion. As per MRI final diagnosis, 16 (36.4%) lesions were diagnosed as malignant and 28 (63.6%) as benign. As per the HPE report, 24 lesions (54.5%) were benign and 20 (45.5%) were malignant in aetiology. By comparing the DWI findings with HPE findings there were 17 (85%) true malignant lesions and 3 were misclassified as malignant lesions. And when DC-MRI was compared with HPE there were 16 (80%) true malignant lesions and 4 were misclassified as malignant lesions. The association between restricted diffusion on DWI and diagnosis by HPE and between DC MRI and HPE modes of diagnosis was statistically significant.
Conclusion: Assessment of breast lesions by multiparametric analysis like morphology of lesions, DWI, dynamic contrast MRI, and kinetic curves has more sensitivity and specificity than single parametric analysis.
Keywords: Breast, Diffusion-Weighted Imaging (DWI), Dynamic Contrast-Enhanced MRI (DCE-MRI)

INTRODUCTION

Evaluation of patients with breast cancer needs a triple assessment using clinical evaluation, imaging, and tissue biopsy. Mammography is a widely used screening approach in the detection of breast cancer and has proven to effectively reduce mortality. Other screening methods such as Magnetic Resonance Imaging (MRI) which is more sensitive than mammography have also been implemented and studied during the last decade. Breast MRI is widely regarded as the most sensitive breast screening technique and is increasingly recommended for high-risk population screening, preoperative staging and therapy monitoring.[1] Multiparametric MRI (mpMRI) protocols include diffusion-weighted imaging (DWI), apparent diffusion coefficient (ADC), and MR spectroscopy, along with DCE-MRI. They can also access regional lymph nodes which have metastasized. These sequences increase the sensitivity and specificity of DCE-MRI and thereby provide better imaging diagnosis. The random water molecular movement within tissue is influenced by the microstructure of tissue, and its cellular density is quantified by DWI. To achieve this, motion-sensitizing gradients (b factors) are used in the T2W echo-planar imaging (EPI) sequence. Because of the increased cell density in cancers, water diffusion is reduced, resulting in higher signal intensity during DWI.[2] To increase breast MRI specificity, diffusion-weighted imaging (DWI) was designed. Since 2002, a lot of studies have revealed the usefulness of breast DWI in the differentiation of benign from malignant lesions of the breast.[3] Dynamic contrast-enhanced magnetic resonance imaging (DCE-MRI) is an in vivo imaging method providing vascular information, which has become an important tool in both preclinical and clinical research.

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Dynamic contrast-enhanced (DCE) MR perfusion, sometimes also referred to as permeability MRI, is one of the main MRI perfusion techniques which calculates perfusion parameters by evaluating T1 shortening induced by a gadolinium-based contrast bolus passing through tissue. The most commonly calculated parameter is k-trans.[4] Multiple studies have demonstrated that assessment of the breast using DCE-MRI and DWI significantly improves the diagnostic accuracy in breast cancer using non-invasive techniques and may reduce unnecessary breast biopsies of benign lesions.

AIMS AND OBJECTIVES

- To differentiate benign and malignant breast lesions using Diffusion-weighted imaging and Dynamic contrast MRI.
- To derive enhancement pattern curves to differentiate benign from malignant breast lesions.
- To correlate MRI findings with pathological findings.

METHODS

This was a hospital-based cross-sectional study conducted among 31 patients who presented with MRI breast examination to the Department of Radio Diagnosis, R. L. Jalappa Hospital and Research Centre attached to Sri Deva raj Urs Medical College, Tamaka, Kolar, from January 2021 to July 2022 after obtaining clearance from the institutional ethics committee and written informed consent from the study participants.

INCLUSION CRITERIA

- Patients with a breast lesion on clinical examination.
- Patients with inconclusive mammography and ultrasonography findings.

EXCLUSION CRITERIA

- Patients with a history of FNAC/ breast biopsy within 3 weeks.
- Patients with cardiac pacemaker and claustrophobia and deranged renal function test.

STATISTICAL METHODS

Collected data was coded into a Microsoft excel data sheet and analyzed using SPSS 22 version software. Categorical data was represented in the form of frequencies and proportions. Chi-square was used as a test of significance for qualitative data and an independent *t*-test was used as a test of significance for quantitative data. *P*-value < 0.05 was considered statistically significant.

RESULTS

Tissue	Frequency	Percent
Almost entirely fat	14	31.8
Scattered fibroglandular tissue	14	31.8
Heterogeneous fibroglandular tissue	13	29.5
Extreme fibroglandular tissue	3	6.8
Total	44	100.0

Distribution of study patients based on the type of breast tissue

Background parenchymal enhancement (BPE)	Frequency	Percentage
Minimal	15	34.1
Mild	13	29.5
Mod	12	27.3
Extreme fibro glandular tissue	4	9.1
Total	44	100.0

Descriptive analysis of breast tissue- background parenchymal enhancement (BPE) in the study population

Shape	Frequency	Percent
Irregular	13	29.5
Oval	17	38.6
Round	14	31.8
Total	44	100.0

Distribution of study patients based on the shape of the lesion

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Margin	Frequency	Percent
Circumscribed	31	70.45
Irregular	9	20.45
Spiculated	4	9.09
Total	44	100.0

Distribution of study patients based on the margin of the lesion

Table 1

The total number of lesions in 31 patients was 44. Among the study population, of the 4 categories of breast composition, 14 (31.8%) were reported to have scattered fibroglandular tissue and almost entirely fat content within the breast with minimal or absent fibroglandular tissue. 13 patients (29.5%) had heterogeneous fibroglandular tissue and the rest 3 (6.8%) patients were reported to have breast with extreme fibroglandular tissue within.

Based on the amount of enhancement of the fibroglandular tissue of the breast after contrast administration, BPE is broadly divided into 4 categories, minimal, mild, moderate or marked enhancement of the breast tissue. We observed 15 (34.1%) patients to have minimal BPE and 13 (29.5%) mild BPE for each respectively, 12 (27.3%) were reported as having moderate BPE and only 4 (9.1%) patients had marked BPE.

Regarding the morphology of the enhancement of breast lesion, out of all the 44 lesions assessed, 13 (29.5 %) lesions had an irregular shape, 17 (38.6 %) were oval and 14 (31.8 %) lesions were round in shape.

The margins of the lesions describe the border and extent of the lesion. The lesions were broadly divided into circumscribed or not circumscribed. The lesions which were not circumscribed were subdivided into two categories: lesions having irregular margins or spiculated margins. As we observed, most of them, i.e. 31 lesions (70.45 %) were circumscribed. 13 lesions had margins which were not circumscribed, out of which 9 (20.45 %) lesions had irregular margins and the rest 4 (9.09 %) were found to have spiculated borders.

Enhancement Pattern	Frequency	Percentages
Homogeneous	19	43.1
Heterogeneous	14	31.8
Rim enhancement	3	6.8
Dark internal septations	8	18.1
Total	44	100.0

Distribution of study patients based on enhancement pattern of the lesion

Type	Frequency	Percent
Type 1	24	54.5
Type 2	9	20.5
Type 3	11	25.0
Total	44	100.0

Distribution of study patients based on the type of kinetic curve

Restricted diffusion on DWI	Frequency	Percentages
Present	17	38.6
Absent	27	61.4
Total	44	100.0

Distribution of study patients based on restricted diffusion on DWI

Axillary Lymph Nodes – Restricted Diffusion	Frequency	Percentage
Absent	30	68.2
Restricted diffusion present	14	31.8
Total	44	100.0

Distribution of study patients based on axillary lymph nodes restricted diffusion

Table 2

Lesions were identified as enhancement either as a mass or if they showed non-mass-like enhancement. All the masses were observed to have either of the 4 types of enhancement- homogenous, heterogeneous, rim enhancement or enhancement with dark internal septations. In our study, majority of the masses (19/43.1 %)

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showed the homogeneous type of enhancement, followed by heterogeneous enhancement 14 (31.8 %), enhancement with dark internal septations was noted in 8 (18.1 %) lesions and 3 of the lesions showed rim like enhancement constituting 6.8 % of the total study population.

Enhancement curves of the breast lesions following contrast administration were divided into type I, II or III following assessment of the signal intensity/ time curve on both the initial and delayed phase. As per the lesions studied, 24 (54.5%) showed type 1 enhancement curves, 9 (20.5%) of them had type 2 and 11 (25.0%) had type 3 Kinetic Curves.

17 (38.6%) out of the 44 lesions showed restricted diffusion and 27 (61.4%) lesions showed no restricted diffusion. Out of 44 lesions studied, 14 (31.8 %) showed axillary lymph nodes –Restricted Diffusion.

MRI Final diagnosis	**Frequency**	**Percentages**
Benign	27	61.3
Malignant	17	38.6
Total	44	100.0
MRI final diagnosis		
Histopathological diagnosis	**Frequency**	**Percent**
Ductal carcinoma	1	2.3
Fibroadenoma	18	40.9
Fibroadenoma with apocrine infiltration	2	4.5
Granulomatous lesion	4	9.1
Infiltrating ductal carcinoma	5	11.4
Intra cystic papillary carcinoma	3	6.8
Invasive ductal carcinoma	5	11.4
Pure Mucinous carcinoma	3	6.8
Squamous cell carcinoma	3	6.8
Total	44	100.0
Descriptive analysis of histopathological diagnosis in the lesions studied		
HPE Diagnosis	**Frequency**	**Percentage**
Benign	24	54.5
Malignant	20	45.5
Total	44	100.0
HPE final diagnosis		
Table 3		

As per MRI final diagnosis, 17 (38.6 %) lesions were diagnosed as malignant and 27 (61.3 %) as benign.

The histopathological type of the breast lesion was assessed and among 44 patients, fibroadenomas (n=18/40.9%) were the most common benign breast lesions followed by infiltrating ductal carcinoma (n=5/11.4%).

As per the HPE report, 24 (54.5%) were benign and 20 (45.5%) were malignant in aetiology.

Restricted diffusion on DWI	**HPE**		**Total**	**Chi**	**p**
	Benign	**Malignant**			
Present	0 (0)	17 (85.0)	17 (38.6)	30.375	0.001
Absent	24 (100.0)	3 (15.0)	27 (61.4)		
Total	24	20	44		
Comparison of restricted diffusion on DWI with HPE					
MRI Diagnosis	**HPE**		**Total**	**Chi**	**P**
	Benign	**Malignant**			
Benign	24 (100.0)	3 (15.0)	28 (63.6)	27.302	0.001
Malignant	0 (0)	17 (75.0)	17 (36.4)		
Total	24	20	44		
Association between MRI and Histopathological diagnosis					
Table 4					

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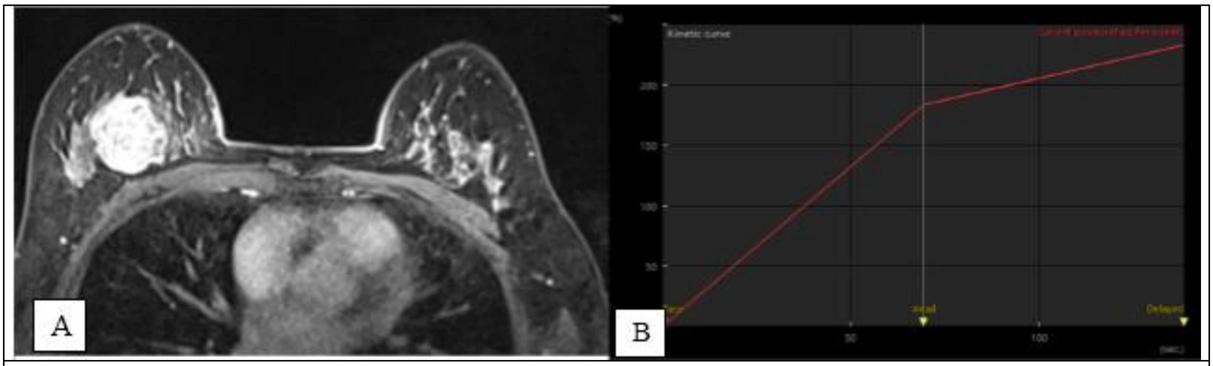

Figure 1: A) MRI breast T1 post contrast fat sat images axial section demonstrating oval shaped lesion with dark internal sepatation – likely fibroadenoma. B) Kinetic curve showing type I enhancement curve

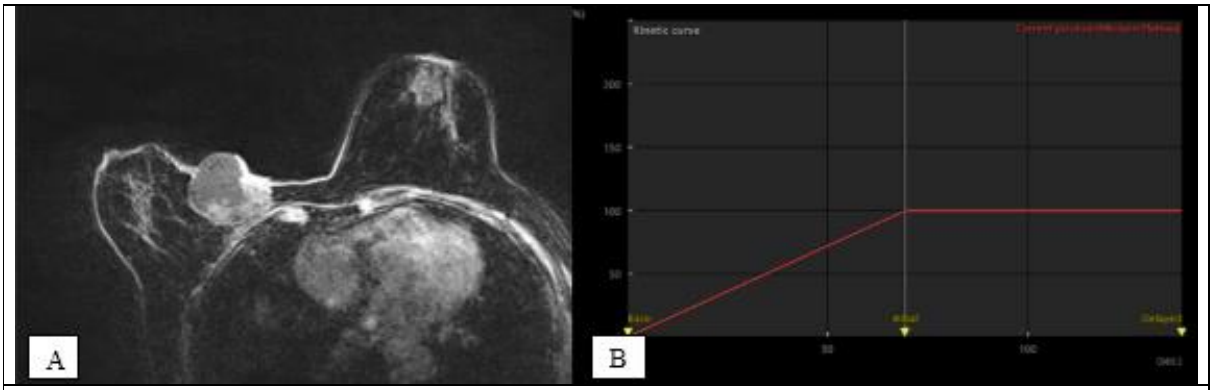

Figure 2: A) MRI breast T1 post contrast fat sat images axial section demonstrating heterogeneously enhancing with central necrosis noted in right inner lower quadrant of right breast. There is loss of fat plane with pectoralis muscle – likely Squamous cell carcinoma. B) Kinetic curve showing type II enhancement curve

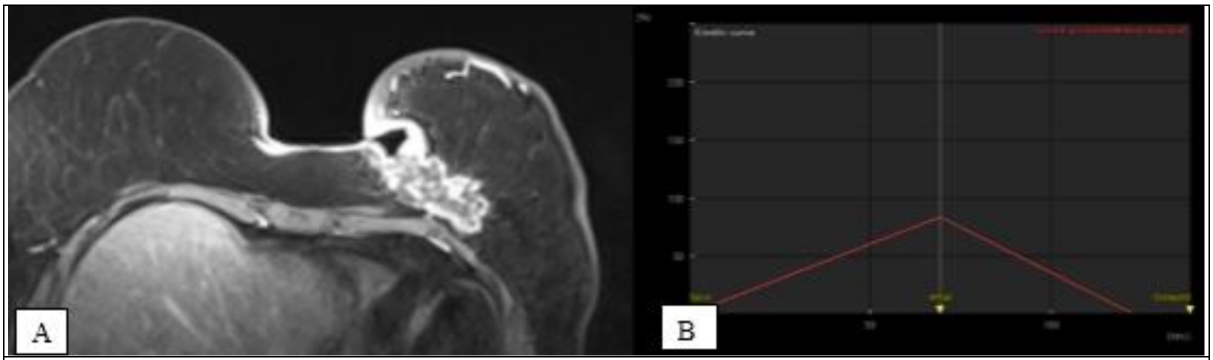

Figure 3: A) MRI breast T1 post contrast fat sat images axial section demonstrating heterogeneously enhancing lesion with spiculated margins noted in lower inner quadrant of left breast – likely Infiltrating ductal carcinoma. B) Kinetic curve showing type III enhancement curve

Out of 20 malignant lesions on HPE, 17 (85.0%) showed restricted diffusion on DWI and findings were consistent. But 3 mucinous carcinomas showed no restricted diffusion which gave false negative results on MRI. The association between restricted diffusion by MRI and diagnosis by HPE was found to be statistically significant.
Among 44 patients, out of 24 benign showed on HPE, 24 (100%) were labelled as benign by MRI. Out of 20 malignant observed on HPE, 3 (20.0%) were labelled as benign by MRI and 17 (80.0%) were labelled as malignant by MRI. The association between MRI and HPE modes of diagnosis was statistically significant.

DISCUSSION
In the present study, it was found that the commonest age groups in the study were 40-59 years and 50 to 59 years (n=9, 39.0%), followed by 30- 39 years (n = 4; 12.9%). Patients with the age group of > 70 years and

above were 9.7% (n = 3) and there was only one patient with age < 20 years and below constituting 3.2% (n = 1). In the study of Singh et al, the mean age of the patients was 49.4 ± 14.0 years (mean ± SD) with a range of 19 to 75 years in the study population. 78 breast lesions among 60 female patients with ages ranging from 25 to 73 years. The mean age of those with benign breast lesions was 31 years and of those with malignant breast lesions was 46 years.[5,6] Ahluwalia et al study consisted of 30 females with the youngest patient being 20 years old and the oldest being 75 years old.[6] In Tezcan et al study, the patients' ages ranged from 21 to 82 years (mean age: 46.5 + 11.4 years).[7]

Out of 31 patients, the majority of the patients were reported to have only one breast lesion 20 (64.5%); 9 patients (29.0%) were reported to have 2 breast lesions and 2 patients had (6.5%) 3 breast lesions in our study. Among the study population of the 4 categories of breast composition, 14 (31.8%) were reported to have scattered fibroglandular tissue and almost entirely fat content within the breast with minimal or absent fibroglandular tissue. 13 patients (29.5%) had heterogeneous fibroglandular tissue and rest 3 (6.8%) patients were reported to have breast with extreme fibroglandular tissue within. Based on the amount of enhancement of the fibroglandular tissue of the breast after contrast administration, background parenchymal enhancement (BPE) is broadly divided into 4 categories: minimal, mild, moderate or marked enhancement of the breast tissue. We observed 15 (34.1%) patients to have minimal BPE and 13 (29.5%) mild BPE for each respectively, 12 (27.3%) were reported as having moderate BPE and only 4 (9.1%) patients had marked BPE. Another similar study by Daimiel et al, analyzed 93 subjects with a mean age of 49 years ± 12 years and benign lesions in 55.8% and malignant in 44.2%. They studied 104 lesions in total and found fibroadenoma or fibroadenomatoid change (histopathological finding) in the majority of the subjects (51.8%) followed by adenosis, stromal fibrosis, ductal ectasia, or normal breast in 17.3% among the benign lesions and invasive ductal carcinoma in 91.6% followed by invasive lobular carcinoma and ductal carcinoma in situ in 4.3% each.[8]

With respect to the morphology of the enhancement breast lesion, out of all the 44 lesions assessed, 13 (29.5 %) lesions had an irregular shape, 17 (38.6 %) were oval and 14 (31.8 %) lesions were round in shape. As we observed, most of them, i.e., 31 lesions (70.45 %) were circumscribed. 13 lesions had margins which were not circumscribed, out of which 9 (20.45 %) lesions had irregular margins and the rest 4 (9.09 %) were found to have spiculated borders.

In a study by Zhang M et al, On DCE-MRI, DCE morphological features associated with breast cancer presented as masses having an irregular shape, irregular/spiculated margins, and heterogeneous/rim internal enhancement pattern (P < 0.0001). The significant morphological features presenting in benign lesions were masses with round/ oval shapes, circumscribed margins and dark/homogenous septations internal enhancement pattern (P < 0.0001). For benign breast lesions presenting as NME, the significant features were focal distribution and homogenous internal enhancement pattern (P < 0.0001).[9] Although, in our study, we found all these features, these descriptions for benign and malignant lesions were not studied and hence such a correlation was not possible. In another study by Tezan et al, in 28 benign lesions, including fibroadenomas (n = 14), fibrocystic disease (FCD; n= 6), intraductal papilloma (n = 3), fat necrosis (n =1), atypical ductal hyperplasia (n =2), adenosis (n = 1), and apocrine metaplasia (n =1), mass enhancement was observed. Among all 14 fibroadenomas, heterogeneous enhancement was observed in 4 cases in which smooth margin and oval or round shape in 3 cases and both irregular margin and irregular shape in 1 case were observed. The remaining 10 fibroadenomas showed homogeneous enhancement with smooth margins and oval or round shapes, except for 2 cases which had irregular margins and irregular shapes. In the present study, it was detected that the mass lesions that had well-delineated and well-defined margins were mostly benign (29.5%), whereas the lesions that had irregular margins (27.3%) and oval (43.2%) were diagnosed to be malignant in most of the cases. These findings were in concordance with the study performed by Macura et al. who concluded that the description of the margin of a focal lesion is one of the most characteristic features of the MRI breast analysis. They also found that irregular margins raised greater suspicion for the lesion to be malignant.[10]

All the masses were observed to have either of the 4 types of enhancement- homogenous, heterogeneous, rim enhancement or enhancement with dark internal septations. In our study, majority of the masses (19/43.1 %) showed the homogeneous type of enhancement, followed by heterogeneous enhancement 14 (31.8 %), enhancement with dark internal septations was noted in 8 (18.1 %) lesions and 3 of the lesions showed rim like enhancement constituting 6.8 % of the total study population. In Tezcan et al study among malignant lesions with mass enhancement, homogeneous enhancement was observed in 8 malignant tumours that were all IDCs (invasive ductal carcinoma). The rim enhancement was observed in 1 patient who had IDC. All remaining malignant tumours showed heterogeneous enhancement. In malignant tumours, smooth margins and round shapes were found in only 2 malignancies, including 1 IDC and 1 ILC.

All remaining malignant tumours had irregular or spiculated margins. Among all 14 fibroadenomas, heterogeneous enhancement was seen in 4 cases of which smooth margin and oval or round shape were seen in 3 cases and both irregular margin and irregular shape in 1 case. The remaining 10 fibroadenomas showed homogeneous enhancement with smooth margins and oval or round shapes, except for 2 cases which had

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irregular margins and irregular shapes. Among all 6 FCDs (fibrocystic disease), heterogeneous enhancement was observed in 2 cases while the remaining cases were homogeneous. Irregular margins and irregular shape were observed only in 2 cases with FCD. In 1 patient with intraductal papilloma, heterogeneous enhancement, smooth margin, and oval shape characteristics were observed while 2 cases with intraductal papilloma showed homogeneous enhancement, smooth margin, and round shape. In a case with fat necrosis, features of rim enhancement, irregular shape, and irregular margin were observed. In all remaining benign lesions with mass enhancement including atypical ductal hyperplasia, adenosis, and apocrine metaplasia, the findings of homogeneous enhancement, smooth margin, and round or oval shape were observed. The mass enhancement pattern was the most common in both malignant and benign lesions; however, the mass enhancement pattern was more likely in malignant tumours. Non-mass enhancement pattern (NME) was more likely in benign lesions, in which the majority of the benign lesions with NME pattern were IGM (Idiopathic granulomatous mastitis), which generally presents the NME pattern, including segmental, diffuse, ductal, or clumped enhancement patterns.[11]

Enhancement curves of the breast lesions following contrast administration were divided into type I, II or III following assessment of the signal intensity/ time curve on both the initial and delayed phase. As per lesions studied, 24 (54.5%) showed type 1 enhancement curves, 9 (20.5%) of them had type 2 and 11 (25.0%) had type 3 Kinetic Curves. This is in agreement with various previous research studies that described and assessed the importance of the various enhancement kinetic curves in differentiating between malignant and benign breast lesions. Imamura et al. reported that the use of enhancement kinetic curves of time–signal intensity resulted in markedly increased differentiation of benign from malignant breast lesions. Roganovic et al. also showed that the enhancement kinetic curve of a persistent type is more in favour of benign changes and a type III wash-in wash-out curve is more in favour of malignancy, as their study showed that 86% of malignant lesions had a wash-out type of enhancement kinetic curve, 14% had a plateau type of enhancement kinetic curve, and none had a persistent type of enhancement kinetic curve.

Most of the patients with triple-negative breast cancer in the research conducted by Azzam et al. also showed malignant-pattern kinetic curves. In Singh et al. study, the Type I enhancement kinetic curve (rising curve) and Type II enhancement kinetic curve (plateau curve) were seen in 22 benign lesions (78.6%). Type III enhancement kinetic curve (rapid wash-in and wash-out curve) was seen in 48 malignant lesions (96%). In a study by Zhang M et al, when they included the kinetic curves in their MRI model, they found that Lesions with a plateau or washout kinetic curves had a 3.7-fold risk of being malignant than lesions with persistent enhancement. Hashem et al studied the kinetic curve analysis of the detected breast lesion. A statistically significant correlation was found between the malignant curves (plateau and wash-out types) and pathological proven malignant lesions, and between the benign curves (rising curve) or no enhancement and benign lesions. In Ahluwalia et al. study 7 out of 10 benign lesions showed type I dynamic curve enhancement (70 %) followed by 3 benign lesions showing type II dynamic curve. On the other hand, 15 out of 20 malignant breast lesions showed type III dynamic curves (75 %) followed by 4 / 20 lesions showing type II dynamic curves. One case of IDC showed a type I curve. Our findings are in concordance with Pinker-Domenig et al. who stated that the final diagnosis of malignancy was positively associated with a type III dynamic curve.

17 (38.6%) out of the 44 lesions showed restricted diffusion. 27 (61.4%) lesions showed no restricted diffusion. Out of 44 lesions studied, 14 (31.8%) showed Axillary Lymph Nodes demonstrating restricted Diffusion. This is in accordance with the results of Youssef et al., which proved that DWI further enhances the capability of the DCE-MRI for diagnosing breast lesions.[12]

By comparing the DWI findings with HPE findings there were 17 (85%) true malignant lesions and 3 were misclassified as malignant lesions. And when DC-MRI was compared with HPE there were 16 (80%) true malignant lesions and 4 were misclassified as malignant lesions. The association between restricted diffusion on DWI and diagnosis by HPE and between DC MRI and HPE modes of diagnosis was statistically significant. According to our results, the diagnostic performance of DWI was higher than DC-MRI and that means that it serves as a better option when trying to solve problematic lesions. This is in accordance with the studies of Daimiel et al, and Singh et al. Daimiel et al. concluded that DWI was more specific but less sensitive and accurate compared to DC MRI for breast cancer detection.[13] Singh et al also found that DWI alone has almost comparable sensitivity as compared with breast DCE-MRI; however, it is more specific.[14] The concomitant use of DWI and DCE-MRI improved the sensitivity and specificity of breast MRI for characterizing benign and malignant breast lesions, compared with DWI and DCE-MRI alone.[15] The relatively higher performance of DWI in our study led us to believe that DW-MRI is a beneficial tool with limitations. Its role can be especially highlighted when there is concern regarding contrast safety or when cost and availability limit the use of enhanced MRI.

CONCLUSION

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Breast MRI has been promoted as a technique for resolving issues with lesions that provide a challenge for other imaging modalities. When comparing the ability of DC-MRI and DWMRI in assessing the lesions with the ultimate aim of reducing unnecessary biopsies, this study concludes that DW-MRI is best delegated to cases where contrast administration is contraindicated. The sensitivity and specificity of multiparametric assessment of breast lesions like morphology of lesions, DWI, Dynamic contrast MRI, and kinetic curves are more accurate than single parametric analysis.

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