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Original Article

Radiology Section

Role of DCE and DWI in Differentiating between Benign and Malignant Breast Masses using 3T MRI: A Cross-sectional Study

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ABSTRACT

Introduction: Dynamic Contrast-enhanced Magnetic Resonance Imaging (DCE-MRI) imaging is the mainstay of breast MRI techniques in characterising breast masses. Diffusion-weighted Imaging (DWI) is an adjunct MRI technique to differentiate between benign and malignant breast masses.

Aim: To evaluate the diagnostic efficacy of breast MRI by combining DCE-MRI and DWI to differentiate benign from malignant breast masses and compare it with histopathology.

Materials and Methods: The present cross-sectional study was conducted in the Department of Radiology and Imaging, Bharat Scans private limited, Chennai, India, from July 2013 to April 2015. A total of 51 patients with suspicious breast masses detected by mammography and/or ultrasonography were evaluated by DCE-MRI and DWI using General Electric (GE) 3 Tesla Magnetic Resonance Imaging. The results were compared with histopathology. Sensitivity, specificity, Positive Predictive Value (PPV) and Negative Predictive Values (NPV) were calculated for DCE-MRI and for the combined method using DCE-MRI with DWI. Statistical analysis was done using Statistical Package for the Social Sciences (SPSS) software version 17.0 and Open Epi software. A p-value <0.05 was considered statistically significant.

Results: Out of the 51 masses, 26 were benign and 25 were malignant on histopathology. DCE-MRI showed a type I curve in 17 masses, type II curve in 11, and type III curve in 18, with a sensitivity of 88% and specificity of 73.08% in differentiating benign from malignant masses. In DWI, 26 masses showed diffusion restriction with a mean Apparent Diffusion Coefficient (ADC) value of 1.108×10^{-3} mm^2/s and 25 masses showed the absence of diffusion restriction with a mean ADC value of 1.656×10^{-3} mm^2/s. In the combined evaluation (DCE-MRI+DWI), 27 masses were classified as malignant and 24 masses were classified as benign with improved sensitivity of 96% and specificity of 88.46% as compared with DCE-MRI or DWI alone.

Conclusion: Dynamic contrast-enhanced magnetic resonance imaging has high sensitivity in differentiating benign from malignant breast masses, but has low specificity. Multiparametric MRI combining DWI with DCE-MRI increases the sensitivity and specificity, hence improving the diagnostic efficacy for breast mass evaluation.

Keywords: Breast cancer, Dynamic contrast-enhanced, Diffusion-weighted image, Histopathology, Magnetic resonance imaging, Mammography

INTRODUCTION

Breast cancer is the most common malignancy in women, with more than 2.3 million newly diagnosed cancer cases in 2020 [1]. Also, now it has become the world's most prevalent cancer among women in developed and developing countries, with 7.8 million women alive by the end of the year 2020, who was diagnosed to have breast carcinoma in the past five years [1].

Early detection plays a pivotal role in the management, thereby reducing morbidity and mortality due to breast cancer [2]. Ultrasound and mammography are the most common imaging tools for the evaluation of breast masses, but the diagnostic sensitivity and specificity are low, especially in patients with dense breast parenchyma and postsurgical scars [3,4]. Because of this limitation, efforts have been made to develop several adjuvant imaging techniques. Magnetic resonance imaging is increasingly being used to evaluate breast masses. Dynamic Contrast-enhanced Magnetic Resonance Imaging (DCE-MRI) has been the mainstay of breast MRI with excellent sensitivity. However, the moderate specificity leads to unnecessary biopsies of many benign lesions [5-9]. To increase the specificity of breast MRI, additional MR techniques have been incorporated into conventional MRI examination, in particular Diffusion-Weighted Imaging (DWI). Increasing numbers of studies are evaluating the diagnostic accuracy of combined DCE-MRI with DWI [10-12]. However, the clinical value and potential benefits of a multi-parametric approach are still unclear and need further studies to clearly establish a practical, cost and time-effective MRI protocol [10-12].

The aim of the present study was to evaluate patients with breast masses using Dynamic Contrast Enhancement (DCE) kinetics and compare with histopathology. Other objectives of the study were to evaluate diffusion-weighted MRI findings with Apparent Diffusion Coefficient (ADC) values in patients with breast masses and compare with histopathology, to assess the role of ADC values in differentiating benign from malignant breast masses and to compare the diagnostic performance of DCE-MRI and DWI for characterisation of breast masses.

MATERIALS AND METHODS

A cross-sectional study was conducted in the Department of Radiology and Imaging, Bharat Scans private limited, Chennai, India, from July 2013 to April 2015. The sample size of the study was 51 cases. All patients who met the eligibility criteria and underwent MR imaging of the breast during the above-mentioned period were enrolled in the study after obtaining informed consent. The study was approved by the Institutional Ethical Committee (Reg. No. 140-41113-131-107117).

Inclusion criteria:

- Patients with suspicious breast masses at mammography or breast ultrasound.
- Mass lesions measured 1 cm or larger on MRI.
- Patients who were willing to undergo image-guided biopsy or needle localisation for a breast mass.

Exclusion criteria:

- Patients not willing to undergo the entire MR examination and patients not willing for contrast injection.
- Patients with claustrophobia.
- Patients who were unable to lie down in a prone position.
- The presence of a breast haematoma adjacent to the suspicious lesion (from either recent surgery or biopsy).
- Patients with breast lesions <1cm in size (or) non mass enhancement.
- Patients who were not willing to undergo a biopsy.

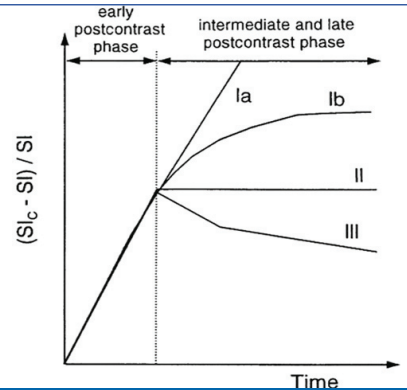
MRI Imaging Protocol

The study was done in 3 Tesla Magnetic Resonance Imaging General Electric (3T MRI GE) SIGNA HDx, (GE Healthcare, Milwaukee, USA) using a high resolution 16 channel breast coil. Standard MRI protocol includes

1. Axial T2 FSE with TR: 4280 ms, TE: 100.1 ms, MATRIX: 384×256, slice thickness: 5 mm, spacing 1.5 mm.
2. Axial STIR with TR: 7220 ms, TE: 32 ms, MATRIX: 384×224, slice thickness: 5 mm, spacing 1.5 mm.
3. Axial T1 with TR: 620 ms, TE: 90 ms, MATRIX: 384×256, slice thickness: 5 mm, spacing 1.5 mm.
4. DWI sequences were acquired using a dual spin echo EPI (Echo planar imaging) sequence with a parallel imaging factor of 2. The matrix size was 96×160, the Number of excitations: 16, the slice thickness was 5 mm with a gap of 1 mm, TR: 2800 ms, TE: 80 ms. The b value pairing used was 500 and 1000 s/mm^2. The ADC maps were created automatically and the calculation of ADC values was done by placing the ROI well within the confines of lesions. The average size of ROI was 0.003 cm^2. The cut-off ADC value for differentiating between benign and malignant lesions was considered as 1.2×10^{-3} mm^2/s. The ADC calculations were done retrospectively by post processing software, FuncTool™, GE healthcare.
5. DCE-MRI was done by using a commercially available VIBRANT™ (Volume Imaging for BReast AssessmeNT) sequence by GE healthcare, which is a fat-suppressed three dimensional T1 Weighted (W) sequence, with flip angle of 100, 1 mm^3 isotropic voxel. The sequences were acquired using a 320 x 320 matrix. One unenhanced and five contrast-enhanced acquisitions were made. The contrast used was gadolinium-DTPA, with a dosage of 0.1 mmol/kg of bodyweight, at a rate of 2 mL/sec, using an MR compatible power injector, followed by a bolus of 15 mL isotonic saline.

The image viewing and postprocessing was done using CAD stream™ version 4.3 workstation (GE Healthcare). Time to signal Intensity Curve (TIC) was created for suspicious enhancing masses.

Time Intensity Curves (TIC): In DCE-MRI following types of enhancement kinetic curves were possible as described by Kuhl CK et al., [Table/Fig-1] [5].



[Table/Fig-1]: Patterns of Time-signal Intensity Curves (TIC) in breast lesions according to Kuhl CK et al., [5]

Type Ia (persistent enhancement)

- Shows slow and progressive enhancement over almost the entire dynamic period. Peak enhancement is achieved in the late postcontrast phase
- Considered as benign

Type Ib (persistent with bowing)

- It shows slow and progressive enhancement over the entire dynamic period. Peak enhancement is achieved during the late postcontrast phase, following which it attains plateau or shows a very slow decline that starts in the late postcontrast phase.
- Considered as benign.

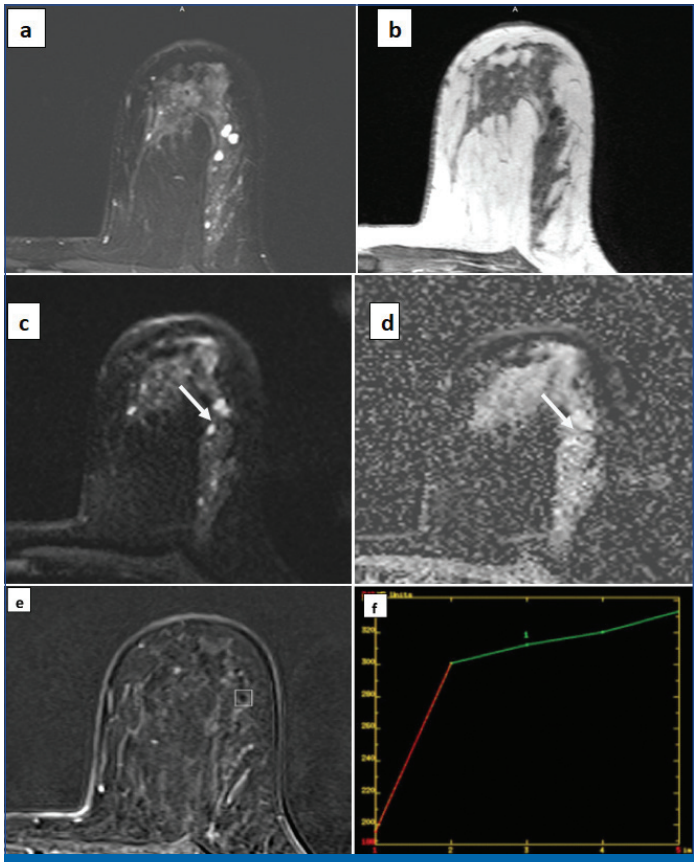
Type II (plateau curve):

- Shows initial rapid enhancement following which the signal intensity reaches peak almost immediately after the early postcontrast phase.
- In intermediate and late postcontrast phase, it attains a plateau (Not much signal intensity variation during the intermediate and late postcontrast phases).
- Considered as malignant.

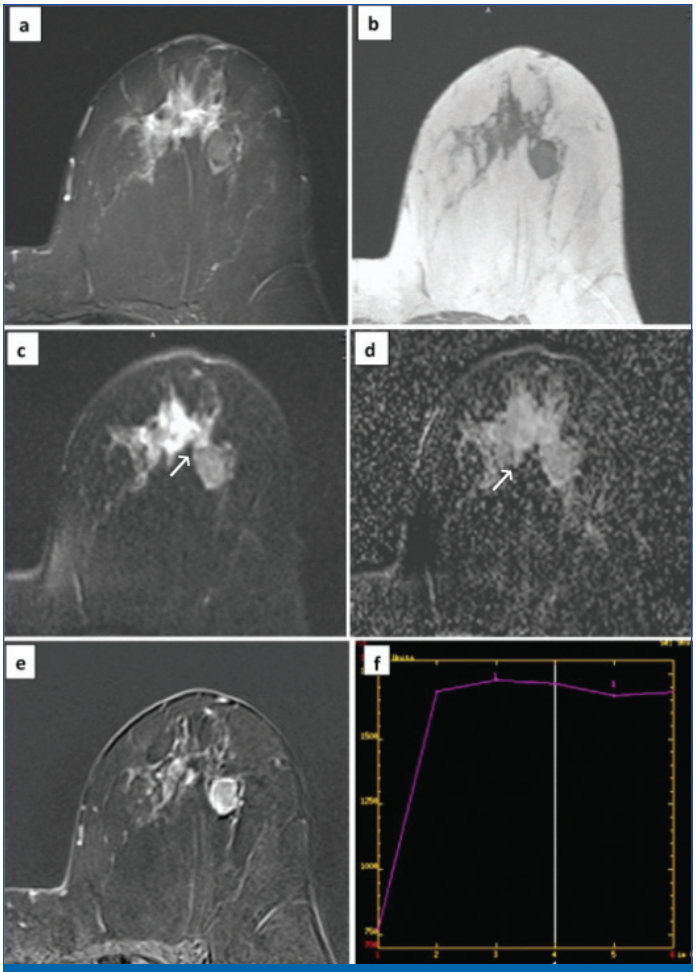
Type III (washout curve):

- Shows initial rapid uptake with peak enhancement almost immediately after the early postcontrast phase.
- The signal intensity starts declining in the intermediate and late postcontrast phase (Wash out).
- Considered as strongly malignant.

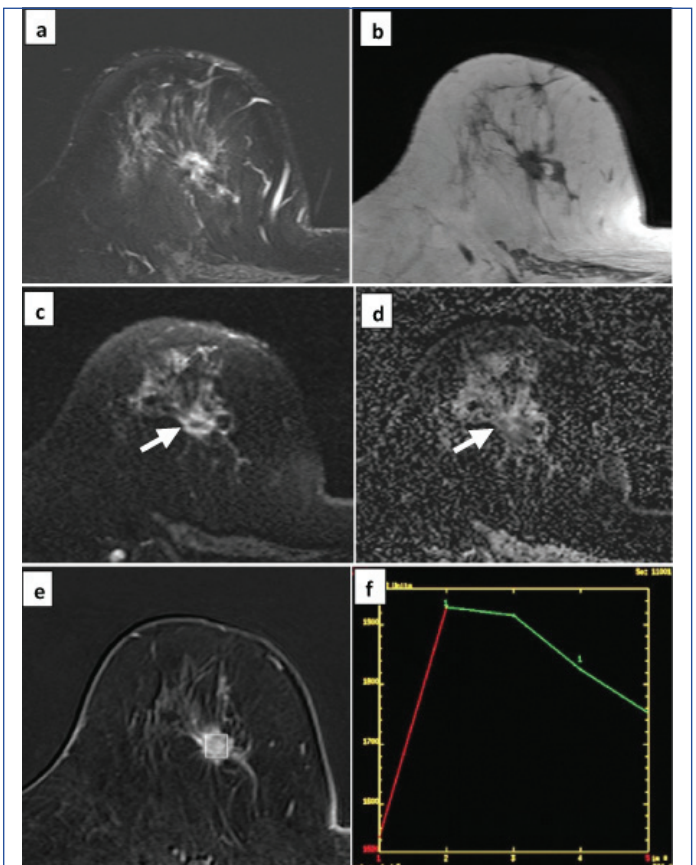
Based on qualitative assessment of the TIC, the lesions showing Type I (Ia and Ib); TIC [Table/Fig-2] were considered as benign; The lesions with type II [Table/Fig-3] and type III TIC [Table/Fig-4] were considered as malignant. Histopathologic diagnosis remained the standard of reference for this study.



[Table/Fig-2]: Case of fibrocystic disease: (a) hyperintense on STIR images; (b) hypointense on T1 weighted images; (c,d) DWI and ADC images shows no evidence of restricted diffusion (white arrow); (e,f) DCE images showing Type I kinetic pattern.



[Table/Fig-3]: Case of fibroadenoma: (a,b) STIR and T1 weighted images shows well defined hypointense lesion; (c,d) DWI and corresponding ADC images shows no evidence of restricted diffusion (white arrow); (e,f) DCE images showing Type II kinetic pattern.



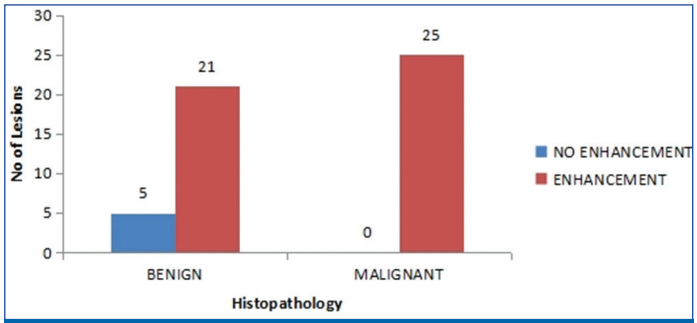
[Table/Fig-4]: Case of fibroadenoma: (a,b) Irregular spiculated lesion appearing hyperintense on STIR and hypointense on T1 weighted image; (c,d) DWI and ADC images shows evidence of restricted diffusion (white arrow); (e,f) DCE images showing Type III kinetic pattern.

STATISTICAL ANALYSIS

Sensitivity, specificity, Positive Predictive Value (PPV) and Negative Predictive Value (NPV) were calculated using the standard of reference. Data was analysed using Statistical Package for the Social Sciences (SPSS) software version 17.0 and Open Epi software. A p-value <0.05 was considered statistically significant.

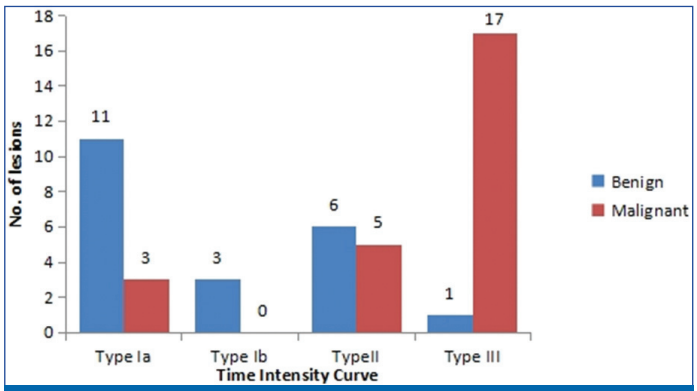
RESULTS

Dynamic contrast-enhanced MRI versus Histopathological Examination (HPE): In the evaluation of 51 breast masses, five did not show any enhancement after contrast injection and were considered benign. The rest of the 46 enhancing masses were assessed by DCE TIC [Table/Fig-5].



[Table/Fig-5]: Contrast enhancement in breast lesions, correlated with HPE.

Out of 46 enhancing masses, 17 showed type I (Ia and Ib) TIC and were categorised as benign. Similarly, 29 were considered as malignant as they showed type II or type III TIC enhancement patterns [Table/Fig-6].



[Table/Fig-6]: Distribution of Time Intensity Curves (TIC) in benign and malignant lesions.

In 17 masses with type I curve: 14 were benign and three were malignant; In 11 masses with type II curve: six were benign and five were malignant; In 18 masses with type III curve: one was benign and 17 were malignant [Table/Fig-7].

TIC curves	Total no. of cases	Histopathology	
		Benign	Malignant
Type I	17	14	3
Type II	11	6	5
Type III	18	1	17

[Table/Fig-7]: Enhancement kinetics of breast lesions as compared with histopathology.

Diffusion weighted imaging with ADC values versus HPE: Out of the total 51 masses, 26 were showing diffusion restriction with a mean ADC value of 1.108×10^{-3} mm^2/s (Standard deviation: ±0.24). Twenty-five were showing no restriction of diffusion with a mean ADC value of 1.657×10^{-3} mm^2/s (Standard deviation: ±0.49). The difference in ADC values obtained between benign and malignant lesions was significant (p-value <0.001).

Out of 26 masses with restricted diffusion, 23 were malignant and three were benign. The histopathologic diagnosis of benign masses with restricted diffusion included granulomatous mastitis in one patient and abscess in two patients. Out of 25 masses with no restriction of diffusion, 23 were benign and two were malignant. The histopathologies of malignant masses with absence of diffusion restriction were mucinous adenocarcinoma and invasive ductal carcinoma [Table/Fig-8].

DWI	Total number of cases (n)	Histopathology	
		Benign (n)	Malignant (n)
Present	26	3	23
Absent	25	23	2

[Table/Fig-8]: DWI findings as compared with histopathology.

Diffusion weighted imaging with ADC combined with DCE-MRI versus HPE:

On combining DWI with DCE-MRI, the masses were classified as malignant (positive) if:

- Type III TIC on DCE-MRI with/without diffusion restriction (or)
- Type I/type II TIC with diffusion restriction.

The masses were considered as benign (negative) if:

- No enhancement on DCE-MRI (or)
- Type I/type II TIC with the absence of diffusion restriction.

Out of 27 masses positive on the combined evaluation, 24 were malignant and three were benign on histopathology. Out of 24 masses classified as benign on combined evaluation, 23 were benign on histopathology and one was malignant [Table/Fig-9]. Out of the three false positive cases, two cases were abscesses and one was granulomatous mastitis. One false negative lesion was an infiltrating ductal carcinoma.

DCE-MRI+DWI	Total number of cases	Histopathology	
		Benign	Malignant
Positive	27	3	24
Negative	24	23	1

[Table/Fig-9]: DCE-MRI+DWI findings as compared with histopathology.
PPV: Positive predictive value; NPV: Negative predictive value

In the combined evaluation (DCE-MRI+DWI), the sensitivity was 96% and the specificity was 88.46% as compared with DCE-MRI or DWI alone [Table/Fig-10].

Parameters	DCE-MRI	DWI	DCE+DWI
Sensitivity	88%	92%	96%
Specificity	73.08%	88.46%	88.46%
PPV	75.86%	88.46%	88.89%
NPV	86.36%	92%	95.83 %

[Table/Fig-10]: Sensitivity and specificity of Dynamic Contrast-Enhanced MRI (DCE-MRI), Diffusion-Weighted Imaging (DWI), and combined MRI as compared with histopathology.

DISCUSSION

In DCE-MRI, enhancement characteristics of the 51 breast masses were analysed from the postcontrast subtracted images. This agreed with Kvistad KA et al., who used subtracted images for detecting an enhancing lesion [13].

Prior studies have shown that DCE-MRI is more sensitive and less specific for breast cancer detection. Similarly, in this study, authors found a sensitivity of 88% and a specificity of 73.08%. These results are discordant with those of Kul S et al., who reported higher sensitivity of 97.9% and specificity of 75.7% [14]. The present study results are also in discordance with those of Yabuuchi H et al., in which the reported sensitivity was 92% and specificity was 86% [6]. This study can be compared with the results of Huang W et al., who reported low specificity of DCE-MRI (62.5%), despite high sensitivity (100%) [7].

In the present study, the ADC values of malignant masses were significantly lower (<0.001%) than the ADC values of benign lesions which correlated with the results of Partridge SC et al., [15]. The current study was also in agreement with the study done by Min Q et al., who obtained a mean ADC value of $1.66\pm0.90\times10^{-3}$ mm^2/s for benign lesions and $1.1\pm0.37\times10^{-3}$ mm^2/s for malignant lesions (ADC cut-off used 1.23×10-3 mm^2/s) with resultant sensitivity of 82.8% and specificity of 90% [16].

The DWI as a standalone procedure is not a complete method of diagnosis as stated by Kuroki Y and Nasu K [17]. Hence, in this study authors evaluated DWI in conjunction with DCE-MRI to increase the diagnostic efficacy. Tan SL et al., analysed 44 breast lesions on 3T MRI by combined DCE and DWI [18]. For DWI, they used a cut-off ADC value of 1.22×10^{-3} mm^2 for b value of 1000. They reported sensitivity of 90.6% and specificity of 100%. The present study was in agreement with Tan SL et al., where we used the same ADC threshold was used with the same b value, and we obtained sensitivity of 96% and specificity of 88.46% for the combined method [18].

In the current study, an increased specificity from 73.08% to was reported and improved PPV from 75.86% to 88.89% by combining DWI with DCE-MRI, as compared to DCE-MRI alone. Sensitivity also slightly improved from 92% to 96%. These results agreed with Kul S et al., who reported improved specificity (86.5%), sensitivity (91.5%), PPV (89.6%), NPV (88.9%) and accuracy (89.3%) after combined DCE-MRI and DWI [14]. The present results also agreed with that of Singh A et al., who reported a sensitivity of 98% and specificity of 86% for the combined evaluation method [Table/Fig-11] [10-12,14,19].

Studies	DCE-MRI		DCE-MRI+DWI	
	Sensitivity	Specificity	Sensitivity	Specificity
Kul S et al., 2011 [14]	97.9%	75.7%	95.7%	89.2%
El Bakry MA et al., [10] 2015	91.7%	84.2%	97.2%	94.7%
Zhang L et al., 2015 [11]	93.2%	71.1%	91.6%	85.5%
Sharma U et al., 2019 [12]	83.9%	NA	96.4%	NA
Singh A et al., 2021 [19]	96%	78.5%	98%	86%
Present study	88%	73.08%	96%	88.46%

[Table/Fig-11]: Comparison of the diagnostic accuracy of DCE-MRI and DCE-MRI+DWI in various studies [10-12,14,19]. (NA-Not available).

Limitation(s)

Small sample size as few patients were not willing to undergo MRI examination due to cost factor. Benign appearing Breast Imaging-Reporting and Data System (BI-RADS) 2 lesions on ultrasonography and mammogram were not included in the study.

CONCLUSION(S)

Dynamic contrast enhanced MRI has high sensitivity but low specificity for characterising breast masses. Multiparametric MRI combining DCE-MRI and DWI techniques had higher sensitivity, specificity and PPV than DCE-MRI and DWI alone, hence improving the diagnostic accuracy and thus can be incorporated in the standard MRI protocol of breast mass evaluation.

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