Role of Contrast MRI in Detection of Breast Lesions and Histopathological Correlation

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Abstract

Background: *Breast cancer is the most common cancer in women all over India and accounts for 25% to 31% of all cancers in women in Indian cities. No preventive method for breast cancer has yet been defined. Special attention and control can so far only be planned among the known hereditary cancers. Therefore, to improve survival rate early detection is needed. The application of MRI for diagnosis of breast lesions is increasing rapidly. MRI imaging technique that employs time signal intensity curve, obtained by performing MRI scan after injection of contrast agent has emanated as amicable tool for screening of breast cancer, owing to its high sensitivity for detection of abnormalities.*

Materials and Methods: *Study was conducted at Department of Radio-diagnosis in Andhra Medical College, Visakhapatnam. Study population is 54 patients over duration of 2 years referred from OPD or IPD with clinically palpable breast lesions; non-palpable lesions with inconclusive findings on screening mammogram or screening ultrasonography; and high-risk patients who presented for screening MRI evaluation.*

Results: *The mean age of the patients was found to be 52.3 years. The range was found to be between 26 to 78 years. 11 patients (Approx. 21 %) with almost entirely fat type of fibro glandular tissue had malignant lesions. 32 cases i.e. 61% of patients showed mild background parenchymal enhancement, out of which 24 lesions were found to be malignant and 8 lesions were found to benign. 23 patients (48 %) had masses with irregular margin and 17 patients (35%) had masses with speculated margins, 8 cases (17%) had circumscribed margins.*

Conclusion: *DCE MRI of breast has been found to be an excellent diagnostic and screening tool for detecting and characterizing breast lesions. Evaluation is done based on morphology and enhancement pattern of the margin and an enhancement pattern of washout. Amongst these two, evaluation of morphology has emerged as the most useful and reliable parameter.*

Introduction

The incidence of breast cancer has increased globally over the last several decades. Greatest increase has been observed in Asian countries. Breast cancer is the most common cancer in women all over India and accounts for 25% to

31% of all cancers in women in Indian cities. The age adjusted rate of breast cancer in Indian women is as high as 25.8 per 100,000 women, with mortality 12.7 per 100,000 women.

The most basic technique of assessment is self-palpation of breasts and regional lymph nodes, known as breast self-examination (BSE). However, this being a subjective method has its own limitations. In may be difficult to find very small lesions, which can be completely missed on palpation, especially in bulky breasts. However, in the clinical evaluation a thorough palpation of the breasts and regional lymph node stations holds great significance.

Mammography and ultrasonography have been the traditional imaging modalities for evaluation of breast lesions. But the sensitivity of mammography drops to 48% in high density breasts[1]. Limitations of mammography like incomplete imaging of axillary lymph nodes and blood supply, and underestimation of disease, can be overcome by MRI. The American Cancer Society recommends MRI as an adjunct to mammography for women with lifetime risk of 20-25 % or greater, which include women with strong family history of breast or ovarian malignancy and women who had been treated for Hodgkin's disease[2].

The advent of MRI has significantly added to the diagnostic armamentarium of the breast conditions that cannot be obtained by other imaging modalities, such as mammography or ultrasound. It has emerged as an important new tool in the fight against breast cancer[3].

The application of MRI for diagnosis of breast lesions is increasing rapidly. MRI imaging technique that employs time signal intensity curve, obtained by performing MRI scan after injection of contrast agent has emanated as amicable tool for screening of breast cancer, owing to its high sensitivity for detection of abnormalities[4,5]. As recommended by American and European guidelines. Breast MRI is currently the most sensitive detection technique for breast cancer diagnosis[6,7]. It has been stipulated, that in BRCA1 and BRCA2 mutation carriers, MRI is more sensitive for detecting breast cancers than mammography, ultrasound, or CBE alone[8].

Materials & Methods

It is a Prospective Analytical study. Study was conducted at Department of Radio-diagnosis in Andhra Medical College, Visakhapatnam during February 2017 to October 2018. Study includes 54 patients referred from OPD or IPD with clinically palpable breast lesions; non-palpable lesions with inconclusive findings on screening mammogram or screening ultrasonography; and high-risk patients who presented for screening MRI evaluation.

Inclusion Criteria

1. Patients aged between 18 to 80, coming for contrast MRI of lesion for evaluation or screening.
2. Patients who give a valid consent.

Exclusion Criteria

1. Patients with history of allergy to contrast media.
2. Patients with renal impairment.
3. Non-MRI compatible Cardiac Pacemaker.
4. Non-MRI compatible Metallic Aneurysm clips.
5. Pregnant women.
6. Patients with recurrent breast cancer following chemotherapy or radiotherapy.

Results

54 patients were studied over duration of 21 months from February 2017 to October 2018.

- Data analysed: 51 patients
- 3 cases were lost to follow-up

Table 1: Patient Distribution According to Indication of MRI

			HPE		Total
			BENIGN	MALIGNANT	
INDICATION (Diagnostic/screening)	DIAGNOSTIC	Count	10	30	40
		% within HPE	66.7%	83.3%	78.4%
	SCREENING	Count	5	6	11
		% within HPE	33.3%	16.7%	21.6%
Total		Count	15	36	51
		% within HPE	100.0%	100.0%	100.0%

Chi-Squ		are Tests
	Value	p value(significantif<0.05)
Pearson Chi-Square	1.739	.264
N of Valid Cases	51	
b. Computed only for a 2x2 table		

- 11 patients were a part of screening protocol, whereas 40 patients were evaluated for further diagnostic studies.
- 11 patients (Approx. 21 %) with almost entirely fat type of fibro glandular tissue had malignant lesions
- 41 patients showed symmetrical background enhancement in both breasts and 10 patients showed asymmetric enhancement i.e. different BPE in both breasts.
- 32 cases i.e. 61% of patients showed mild background parenchymal enhancement, out of which 24 lesions were found to be malignant and 8 lesions were found to benign.

Table 2: Distribution According to Amount of Fibroglandular Tissue (On MRI) with Histopathology Correlation

			HPE		Total
			BENIGN	MALIGNANT	
Amount of Fibroglandular tissue on MRI	Almostentirely fat	Count	0	11	11
		% Within HPE	0.0%	30.6%	22.0%
	Scattered fibroglandular tissue	Count	5	13	18
		% Within HPE	35.7%	36.1%	36.0%
	Heterogenous fibroglandular tissue	Count	3	7	12
		% Within HPE	35.7%	19.4%	24.0%
	Extreme fibroglandular tissue	Count	4	5	9
		%nWithin HPE	28.6%	13.9%	18.0%
Total		Count	14	36	50
		% Within HPE	100.0%	100.0%	100.0%

Chi- SquareTests		
	Value	p value (significant if<0.05)
Fisher's Exact Test	7.233	.058
of Valid Cases	50	

Table 3: Distribution of Mass Shape

MASS SHAPE	DISTRIBUTION	Valid Percent
IRREGULAR	34	69.3
OVAL	8	16.3
ROUND	7	14.4
Total	49	100

Table 4: Distribution of Mass Enhancement and Its Correlation to histopathology

			HPE		Total
			BENIGN	MALIGNANT	
MASS ENHANCEMENT	HETEROGENOUS	Count	1	7	8
		% within HPE	9.1%	20.0%	17.4%
	HOMOGENOUS	Count	6	28	34
		% within HPE	54.5%	80.0%	73.9%
	HOMOGENOUS WITHIN DARK SEPTATIONS	Count	3	0	3
		% within HPE	27.3%	0.0%	6.5%
	RING ENHANCEMENT	Count	1	0	1
		% within HPE	9.1%	0.0%	2.2%
Total		Count	11	35	46
		% within HPE	100.0%	100.0%	100.0%

| Chi-Square		Tests	
	Value	P value (significant if<0.05)	
Fisher's Exact Test	10.968	.005	
N of Valid Cases	46		

- 49 cases with mass morphology were evaluated and regrouped into respective categories accordingly Remaining cases showed non mass like enhancement and were assessed separately.
- 23 patients (48 %) had masses with irregular margin and 17 patients had masses with speculated margins. (35%) 8 cases (17%) had circumscribed margins. Strong correlation was observed. (p<0.001).
- 28 patients with homogenous mass enhancement were found to be malignant and 1 benign lesion depicted smooth ring like enhancement.
- 59 % of patients showed rapid rise in early phase dynamic contrast, out of which 32 patients were found to be malignant. Estimated p value was found out to be <0.001 suggesting very strong correlation.
- 65 % of the lesions showed washout on delayed scan out of which 89% were found to be malignant on histopathology with

estimated p value to be around <0.001 suggesting significant correlation.
- Type III enhancement curve was demonstrated by 30 malignant lesions and 1 benign lesion whereas type I curve was seen in 6 benign lesions.p<0.001 suggest significant correlation.
- 14 out of 16 BIRADS IV and 24 BIRADS V patients were found to be malignant on histopathology.
- 33 % patients (17) were diagnosed with invasive ductal carcinoma on histopathology lobular carcinoma (12 %) of the total patients and 21 % patients were found to be having ductal carcinoma.
- 10 % patients (5) had fibroadenomas, being the most common benign pathology in our study.
- BIRADS IV and above according to MRI Lexicon were considered to be malignant. 40 lesions (74%) were diagnosed as malignant and 14 as benign.
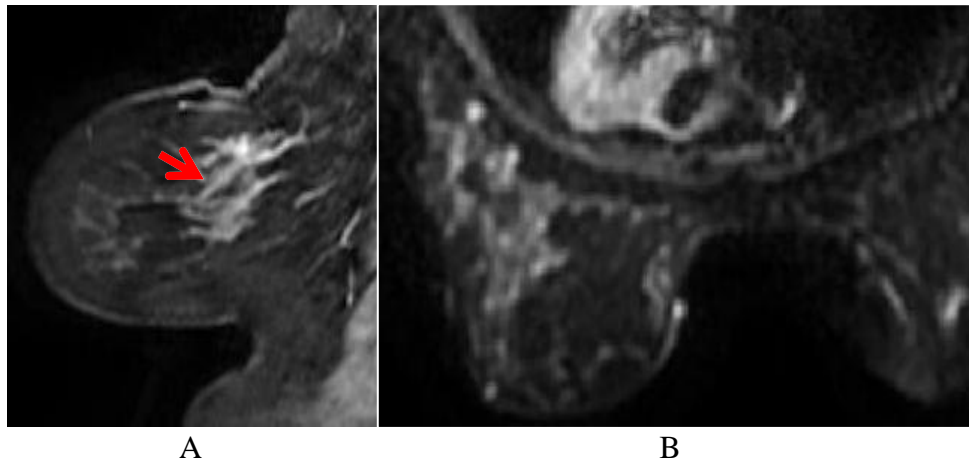
Figure 1: A Sagittal dynamic post contrast image shows heterogeneous regional non mass like enhancing area in upper half of right breast. **B** T2 Axial DWI image shows subtle increased intensity in corresponding area.
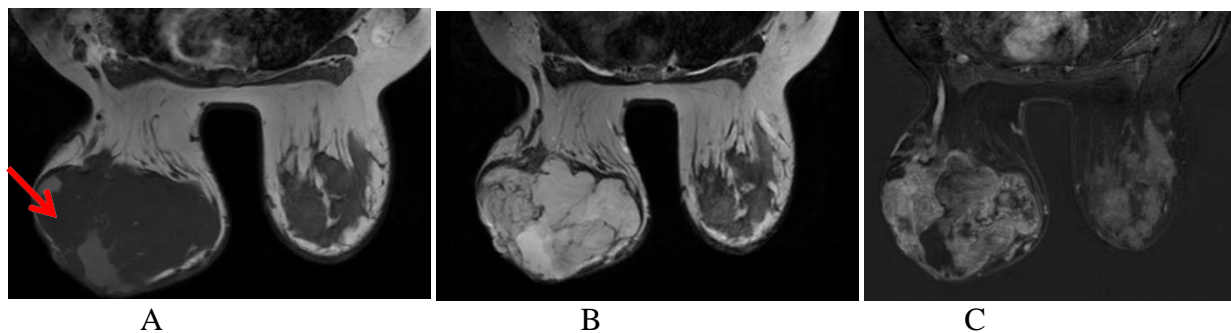
Figure 2: A Axial T1WI images. **B** Axial T2WI.**C**Axial dynamic contrast enhanced image.

Discussion

The present study was carried out in 54 cases referred from OPD or IPD of King George Hospital, Visakhapatnam, with clinically palpable breast lesions, non-palpable lesions seen in mammography or ultrasound according to the inclusion and exclusion criteria.

Among the 54 cases 3 were lost to follow up. So, total 51 cases were characterized on dynamic contrast enhancement characteristic and correlated to histopathology. In our study mean age was 52.37 years ranging from 26 years to 78 years. Out of 54 cases, 12 lesions were diagnosed as a part of screening protocol out of which 6 cases had malignant aetiology. Brennan S et al.[9] emphasized the importance of screening with breast MRI and detected cancer in 12% of women with a history of prior breast cancer and in 39% of women who had biopsies prompted by MRI findings.

Morphological Parameters
Fibroglandular Tissue

In our study, 11 cases had almost entirely fatty type of fibro glandular tissue and all of them were found to have malignant lesions. Whereas, 9 cases had extreme fibro glandular tissue, out of which 5 were found have malignant mass. Fibro glandular tissue type was not found related to lesion detection or pathology of mass in our study.

Similarly, Blumke D et al.[10]and Brennan et al.[9] also concluded in their study that MRI performance was not significantly affected by breast density, tumor histology or menopausal status. Sardanelli et al.[11] in their study, reported that sensitivity for malignancy detection in fatty type of fibro glandular tissue was about 80% for MRI and the PPV was 65% (not significant). In breasts with fibro glandular or dense pattern, the sensitivity was 81% ($p < 0.001$) and the PPV was 71% (not significant).

Background Parenchymal Enhancement

In our study, 24 malignant lesions showed mild background parenchymal enhancement, 9 malignant lesions showed moderate enhancement and 1 malignant lesion showed marked enhancement. p value was estimated to be around 0.10 (p>0.05) and no significant correlation was obtained.

Similar results were demonstrated by Baiti et al.[12] who assessed background parenchymal enhancement and its correlation with BIRADS in non-high-risk patients and reported that age showed a moderate negative correlation with FGT (r = -0.43, p<0.001) and a weak negative correlation with BPE (r = -0.28, p<0.001). FGT and BPE correlated moderately (r =0.35, p<0.001). Final diagnosis of breast cancer displayed very weak negative correlations with FGT (r = -0.09, p= 0.046) and BPE (r = -0.156, p<0.001) and weak positive correlation with age (r = 0.353, p<0.001). On multivariate logistic regression analysis, the only independent covariate for prediction of breast cancer was age (OR 1.032, p<0.001).

Mass Shape

In our study, 30 cases had irregular mass shape distribution out of which 28 lesions were found to be malignant with strong correlation. (p=0.01).Remaining 2 cases with irregular mass were found to be benign on histopathology, one being necrotizing inflammation, and the other being fibroadenoma.

Shape of the lesion and its association with malignancy has been studied by Liberman et al.[13] and similar results were found .According to their study, the feature with the highest PPV was irregular shape (32% carcinoma) and there was a significantly higher frequency of carcinoma among irregular masses as opposed to lobular shape (32% vs. 13%, p = 0.17).One important point to be noted is that, as per latest ACR BI-RADS (5th edition, 2013)[14], the term lobular has been eliminated from the MRI lexicon ,and has been encompassed with oval.

Mass Margin

In our study, masses in 23 cases were found to have irregular margins, out of which 19 were malignant. 17 cases had mass with spiculated margins, all of which were found to be malignant on histopathology, and a strong correlation was observed; p value was estimated to be <0.001.

Liberman et al.[13] also concluded the same, with significantly higher frequency of malignancy in masses with spiculated margins (80% vs 20%, p = 0.01). In their study, they found that carcinoma was present in 22% of masses with irregular margins and in 17% of smoothly marginated masses.

7 out of 8 lesions with circumscribed margins, in our study, were found to be benign on histopathology.1 case of malignant mass, diagnosed as mucinous carcinoma on histopathology was found to have circumscribed margins.

Nunes et al.[15] also concluded in their previous studies that the MR imaging features with the highest PPV were spiculated margin (77–95% cancer) and smooth borders were associated with benignity in 97–100% of cases in their prior reports.

Mass Enhancement Characteristics

In our study, 34 cases showed homogenous enhancement and 8 showed heterogeneous enhancement out of which 28 and 7 were found to be malignant on histopathology, respectively.

3 cases showing homogenous enhancement with dark septations, were found to be fibroadenoma on histopathology.1 case showed peripheral rim enhancement, which on histopathology, was found to be an abscess.

Out of 5 cases with non-mass like enhancement patterns, regional non-mass like enhancement was seen in 3 cases with biopsy proven fibrocystic breast disease. Diffuse heterogeneous and homogenous pattern was seen in 2 cases which turned out to be lobular carcinoma in-situ on biopsy.

Nunes et al.[15] and Liberman et al.[13] concluded that irregular shape and rim enhancement were associated with a higher frequency of carcinoma than other shape and enhancement features. These differences, however, did not achieve statistical significance.

Dynamics of Contrast Enhancement

The two components of time intensity curve, i.e. initial phase kinetics and delayed phase kinetics were evaluated.

Initial phase kinetics was regrouped into slow, medium and rapid rise. Rapid rise was found in 30 lesions (59%), all of which turned out to be malignant on histopathology. $p < 0.001$ signified good correlation.

Medium rise was found in 16(31.4%) cases, out of which 11(73.3%) were benign and 5(13.99%) were malignant on histopathology.

Slow rise was found in 5(9.8%) cases, out of which 4(26.7%) 4 were proven to be benign and 1(2.8%) was found to be malignant on histopathology.

The most common type of pattern observed in delayed phase kinetics in our study was rapid washout pattern amounting to 64.7 % of all the cases. Persistent and plateau types of delayed enhancement was seen in 8 and 11 cases respectively.

Rapid washout was seen in 32 malignant lesions and 1 benign lesion with strong correlation. ($p < 0.001$).

33 cases (61% approximately) demonstrated Type III Kuhl's curve (Time Intensity curve/ enhancement curve), 14 cases exhibited Type II and 7 cases showed Type I enhancement curve patterns.

Out of the 33 cases with Type III curve, 30 were found to be malignant on histopathology with significant correlation ($p < 0.001$). 2 cases were lost to follow up and 1 case was found to be fibroadenoma on histopathology.

Houserkova et al.[16] also evaluated the level of enhancement and found slow initial peak in 6 % enhanced DCIS, medium peak in 27 % and rapid peak in 67 % of them. In only 3 % case with low-grade DCIS persistent enhancement pattern was found. In delayed phase, 67 % of the DCIS patients were found to have plateau enhancement pattern, and in 30 % DCIS cases there was washout enhancement pattern.

Lesion Histology and Types

Out of 51 lesions evaluated in our study, the most common lesion identified was invasive ductal carcinoma (33 %; 17). 11 cases (21.6 %) had ductal carcinoma in-situ on histology.

Similar results and prevalence of lesions were demonstrated by Kinkel K et al.[17] who evaluated dynamic contrast MRI in breast lesions and found 12 invasive, 3 ductal carcinomas in situ and 19 mixed cancer in their study group.

In our study, amongst benign lesions, fibrocystic breast disease (total number 6) and fibroadenoma (total number 5) were the most common lesions.

1 abscess, 1benign phyllodes, 1fibroadenomatosis and 1 case of bilateral papilloma were identified.

Conclusion

In conclusion, DCE MRI of breast has been found to be an excellent diagnostic and screening tool for detecting and characterizing breast lesions. Evaluation is done based on morphology and enhancement pattern of the margin and an enhancement pattern of washout. Amongst these two, evaluation of morphology has emerged as the most useful and reliable parameter.

Kinetic curve assessment, however, adds significantly in increasing the sensitivity of this modality. Imaging parameters for the characterization of suspicious breast lesions were also assessed. This modality proved to have excellent histopathology correlation.

The following salient features have been concluded by our study:

- Breast MRI finding are impendent of the composition of fibro glandular parenchyma.

- Type III curve is most frequently associated with malignancy (61%) in our study.
- Most of the malignant masses are associated with rapid enhancement
- Presence of internal non enhancing septations is almost always suggestive of fibroadenoma.
- Lobular carcinomas often show a non-mass like enhancement.
- Malignancies that are occult on Mammogram or ultrasonography can be picked up on DCE MRI
- DCE MRI proves to be a very useful tool in screening of high-risk cases

With the help of a multimodality approach, making use of DCE MRI along with ultrasonography and mammography, we can go a long way in screening and early detection of breast lesions.

In fact, with a sensitivity of as high as 100% (as in our study) DCE MRI breast holds the potential to alleviate the need of a biopsy which is an invasive procedure.

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