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ROLE OF CONTRAST MRI IN EVALUATION OF BREAST LESIONS WITH HISTOPATHOLOGICAL CORRELATION -A PROSPECTIVE ANALYTICAL STUDY

Radiodiagnosis

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ABSTRACT

AIM AND OBJECTIVE : The main aim was to evaluate the role of dynamic contrast enhanced MRI in detection of breast lesions and correlate the result to histopathology as gold standard. The primary objective was to ascertain the differential characteristics of various breast lesions, so as to establish a diagnosis of benign or malignant lesions. This correlation was determined to evaluate the accuracy of contrast MRI as a primary screening and diagnostic tool in breast imaging .

METHODOLOGY: Patients referred from OPD or IPD were further evaluated by contrast MRI. Prospective study of 54 patients was done over a span of two years. The MRI finding were confirmed by histopatholy as gold standard. Multivaraiate analysis was performed and interpretation was done by assessment of kappa value and 'p' factor for establishing agreement.chi square and Fischer's test was performed to evaluate dynamic contrast enhancement` and its histopathological correlation was assessed.

RESULTS AND 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. Breast MRI finding are independent of the composition of fibro glandular parenchyma. With the help of a multimodality approach, we can go a long way in screening and early detection of breast lesions.

KEYWORDS

Breast, MRI , cancer, Dynamic contrast enhancement.

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.

In Asia, breast cancer incidence peaks among women in their forties, whereas in the United States and Europe, it peaks among women in their sixties. Premenopausal patients constitute about 50% of all Indian patients. It is expected that in the coming decades, Asian countries would account for majority of new breast cancer patients diagnosed globally. [1][2][3]

The term “benign breast diseases” encompasses a heterogeneous group of lesions including developmental abnormalities, inflammatory lesions, epithelial and stromal proliferations, and neoplasms that may present with a wide range of symptoms or may be detected as incidental microscopic findings. Much concern is given to malignant lesions of the breast because breast cancer is the most common malignancy in women in western countries; however, benign lesions of the breast are far more frequent than malignant ones.[4]

The practice of breast imaging has transitioned through a wide variety of technologic advances from the early days of direct-exposure film mammography to xeromammography to screen-film mammography to the current era of full-field digital mammography and digital breast tomosynthesis.[5]

Magnetic resonance imaging uses a powerful magnetic field, radio frequency pulses and a computer to produce detailed pictures of organs, soft tissues and virtually all other internal body structures.

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. [5]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 [6] 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. [7]

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[8][9].As recommended by American and European guidelines. Breast MRI is currently the most sensitive detection technique for breast cancer diagnosis[10][11]. 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[12].

The margin characteristics of a lesion and the intensity of its enhancement at MR imaging two minutes or less after contrast material injection are currently considered the most vital features for breast lesion diagnosis[13].

The most recent American College of Radiology (ACR) practices guidelines for the performance of breast MRI outline 12 indications for DCE-MRI. These are [14][15][16]:

1. Lesion Characterization2. Neoadjuvant chemotherapy3. Infiltrating lobular carcinoma4. Infiltrating ductal carcinoma5. Axillary Adenopathy, primary unknown6. Post-operative tissue reaction7. Silicone and non-silicone breast augmentation8. Invasion deep to the fascia9. Contralateral breast examination in patients with breast malignancy10. Post lumpectomy for residual disease11. Surveillance of high risk patients

12. Recurrence of breast cancer

Factors that influence accuracy of MRI include: [17]

(1) Technical factors that influence accuracy, e.g. slice thickness (partial volume effect), motion reduction, reduction of (cardiac) artifacts, dosage of contrast agent, choice of pulse sequence and echo time, and choice of the method for elimination of fat signal. (2) Hormonal factors (timing of the examination with reference to the menstrual cycle, hormonal replacement therapy). They influence accuracy and must be taken into account. (3) Interpretation guidelines-their choice influences sensitivity and specificity mostly inversely and the use of information from conventional imaging appears necessary. Interpretation is done by two independent radiologists. (4) Patient selection influences accuracy for statistical and for biological reasons. Dynamic contrast enhanced MRI is highly sensitive for characterization of breast lesion breast lesion, allowing detection of malignancy that is occult on physical examination, mammography, and sonography.[18] [19]

Study was conducted at our hospitals for patients referred from OPD/IPD with clinically palpable lesions; non-palpable lesions with inconclusive screening mammogram/ sonomammogram; and high risk patients presenting for screening for a duration of 2 years. Patients with allergy to contrast media, renal impairment, Non compatible Cardiac Pacemaker or Aneurysm clips, Pregnancy with recurrent breast cancer following chemotherapy or radiotherapy were excluded.

Local examination, history taking and informed consent were obtained .Data was acquired using 1.5 Tesla (GE-Optima-360) scanner. Patients lied in prone position on a four channel phased array surface Breast Matrix Coil enabling evaluation of both breasts in one image. T1 axial without fat sat Fat/Glandular morphology, T2 axial without and with FatSAT, Diffusion Weighted Imaging (DWI) and VIBRANT (Volume Image Breast Assessment).were attained Total of seven volumes for DCE-MRI sections were acquired, while injection was started at the beginning of second phase. Intravenous bolus injection of Gadolinium based contrast (0.1 mmol/kg body weight) manually at a rate of approximately 2.5 ml/sec followed by 20 ml of saline wash was given.

Breast composition on MRI

According to ACR 2013 guidelines [20] there are four categories of breast composition based on visual estimation of content of fibroglandular tissue (FGT) within the breasts. In case the two breasts have unequal amounts of FGT, the breast with the more FGT is to be used for categorization of breast composition. Categorizing based on percentages is not recommended.

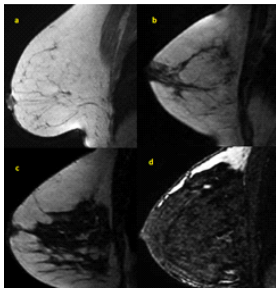


Figure 1 :T1w Sagittal images depicting breast fibroglandular tissue .

a- fatty breast, b- upto 25 – 50% density, c- 50 -75 % ; d- > 75 % fibroglandular parenchyma.

The amount of background parenchymal enhancement in the image are divided into four categories, based on visually estimated enhancement of the FGT of the breast(s). Currently, BPE refers to the volume of enhancement and the intensity of enhancement.

OBSERVATION AND 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 were a part of screening protocol, whereas 40 patients were evaluated for further diagnostic studies. All lesions were classified as benign or malignant (invasive carcinoma and DCIS) using histo-pathology results. Each imaging parameter was analyzed separately for its association to the benign or malignant nature of the lesion using the chi-square test and Fischer's t test.

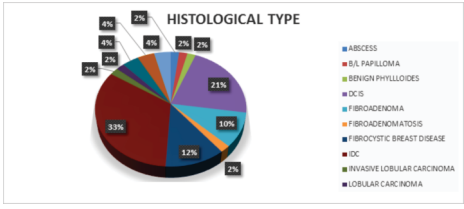


Table 1: Histopathological distribution.

BIRADS (CUTOFF >=IV) * HPE Cross tabulation					
			HPE		Total
			BENIGN	MALIGNANT	
BIRADS (CUTOFF >=IV)	I-III	Count	13	0	13
		% within BIRADS (CUTOFF >=IV)	100.0 %	0.0%	100.0%
		% within HPE	86.7%	0.0%	25.5%
	IV-V	Count	2	36	38
		% within BIRADS (CUTOFF >=IV)	5.3%	94.7%	100.0%
		% within HPE	13.3%	100.0%	74.5%
Total		Count	15	36	51
		% within BIRADS (CUTOFF >=IV)	29.4%	70.6%	100.0%
		% within HPE	100.0%	100.0%	100.0%

Symmetric Measures						
		Value	Asymp. Std. Errora	Approx. Tb	Approx. Sig.	Exact P value
Measure of Agreement	Kappa	.902	.068	6.471	**<0.001**	**<0.001**
N of Valid Cases		51				

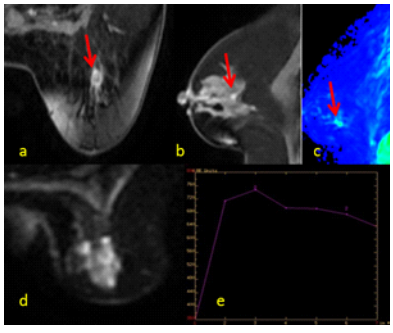
a. Not assuming the null hypothesis.

b. Using the asymptotic standard error assuming the null hypothesis.

Table 2: Histopathological and radiological correlation

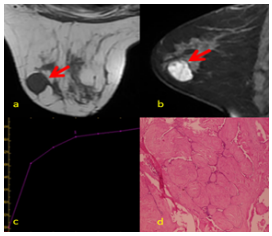
DISCUSSION

Breast radiologists use a myriad of imaging for decision making on procedures like invasive biopsies using plain radiography, ultrasound and all its varieties and with dynamic contrast-enhanced magnetic resonance imaging (DCE-MRI).



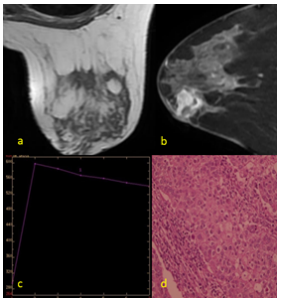
Case 1 Fig.A: Axial VIBRANT post contrast. Right breast-Irregular non mass like enhancing area in central quadrant Fig.B: Post dynamic contrast reformatted sagittal image- early phase venous enhancing area with gradual washout (all images not shown) (BIRADS IVB) Fig.C: Mild DWI restriction. Fig.D: Type II/III kinetic curve. Fig.E:HPE- Lobular Carcinoma

In our study, 11 cases had almost entirely fatty type of fibroglandular tissue and all of them were found to have malignant lesions. Whereas 9 cases had extreme fibroglandular tissue, out of which 5 were found to be malignant. In our study, 24 malignant lesions showed mild background parenchymal enhancement, 9 malignant lesions showed moderate enhancement and 1 malignant lesion showed marked enhancement.



CASE 2 : 48 year old female with complaining of lump in left breast **Fig. A:** Axial T1W image-Well cirmuscribed T1 Isointense(Also T2 isointense)mass in lower outer quadrant of left breast(arrow). **Fig.B:** Sagittal Dynamic Post contrast left breast-Intensely enhancing mass with few non enhancing areas(BIRADS 4A)**Fig. C:**.Type I curve-left breast mass **Fig.D**:HPE of left breast mass-**Fibroadenoma**

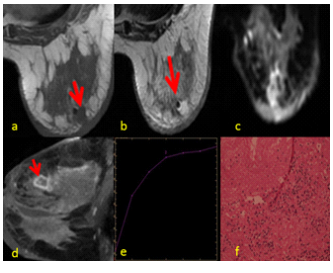
2 cases in our study had irregular mass but were found to be benign on histopathology as tubercular abscess and fibroadenoma respectively. 30 cases had irregular mass shape distribution out of which 28 lesions were found to be malignant with strong correlation. (p=0.01).



Case 3: 43 year old female, complaining of lump in left breast. Fig. A: Axial T1W image Well circumscribed T1 Isointense(T2 heterogeneous) mass in Inferior outer quadrant of right breast(arrow)**Fig.B :**Sag Dynamic Post contrast-Intense homogenously enhancing mass with early enhancement and early wash out with adjacent areas of architectural distortion and overlying skin thickening(BIRADS V) **Fig. C:** Type III curve **Fig. D:HPE -Idc**

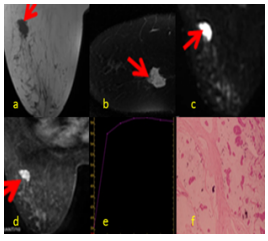
In our study, masses in 23 cases were found to have irregular margins, out of which 19 were malignant. 17 cases had mass with spiculated margins, all of which were found to be malignant on histopathology, and a strong correlation was observed ; ***p value was estimated to be <0.001***.

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. 1 case showed peripheral rim enhancement, which on histopathology, was found to be a tubercular abscess.



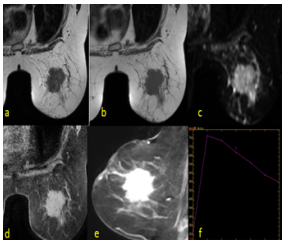
CASE 4 :36 year old female with swelling & pain in right breast .USG showed hypervascular heterogeneously hyperechoic lesion **Fig.A**:Axia l T1W;**Fig B**:Axial T2W –Irreguar T1 hypointense ,T2 Heteregenously hyperintense lesion in upper outer quadrant of right breast with marked skin thickening . **Fig.C**:DWI- Central restricted diffusion in the lesion**Fig D:**Post contrast –Smooth ring enhancing lesion.No enhancement in thickened skin **Fig.E:** Type I kinetic curve **Fig.F**: **HPE- Nectrotizing inflammation/abscess**

Out of 5 cases with non mass like enhancement patterns, Regional non-mass like enhancement was seen in 3 cases with fibrocystic breast disease. Diffuse heterogeneous and homogenous pattern was seen in 2 cases which turned out to be lobular carcinoma in-situ. 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. Rapid washout was seen in 32 malignant lesions and 1 benign lesion with strong correlation. (p<0.001).33 cases (61% approx) demonstrated Type III Kuhls curve(Time Intensity curve/enhancement curve), 14 cases exhibited type II and 7 cases showed type I enhancement curve patterns.



CASE 5 Fig. A: Axial T1W well circumscribed lobulated isointense mass in inferior outer. Quadrant left breast. **Fig.B:** T2 Sag Fat Sat - Mass is heterogeneously hyperintense **Fig C**.Axial DWI shows restriction in the mass. **Fig D**.Dynamic Post Contrast –Homogenous progressive gradual enhancement(BIRADS IVA) **Fig E:**Type II kinetic curve **Fig F**:**HPE-Mucinous carcinoma**

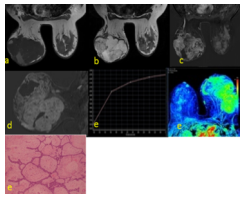
Out of the 33 cases with Type III curve, 30 were found to be malignant on histopathology with significant correlation (p<0.001) .Out of 51 lesions evaluated in our study , the most common lesion identified was invasive ductal carcinoma (33 %; 17). 11 cases (21.6 %) had ductal carcinoma in-situ on histology.



Case 6 Fig. A: Axial T1W image shows a spiculated hypointense mass in the central retro areolar region of right breast extending into all quadrants **Fig. B**: Axial pre contrast VIBRANT image of the same shows that the lesion stands out as hyper intense mass in the background of suppressed parenchymal fat Fig**. C**. Sagittal post contrast image shows intense homogenous enhancement with mild architectural distortion. **Fig D**. Axial DWI image shows restricted diffusion **Fig E:** Kinetic curve shows rapid uptake and rapid washout **Fig F**: HPE-Ducts filled with tumor cells surrounded by myoepithelial layer, no invasion seen. Suggestive of **Ductal carcinoma in situ**.

In our study, amongst benign lesions, fibrocystic breast disease(6) and fibroadenoma (5) were the most common lesions. In our study ,based on the morphological features and kinetic curves of MRI ,14 cases were reported as BIRADS IV, out of which 12 were malignant on histopathology. Amongst the 24 BIRADS V lesions , all were found to be malignant on histopathology.(Fisher's exact test;p<0.001)

On comparison of the test group BIRADS (CUTOFF target =IV) with the Gold standard of Histopathology the test group has a sensitivity of 100 % and specificity of 86.7%. The test has a positive predictive value of 94.7% and Negative predictive value of 100%. The test and the gold standard agree on 49 out of 51 having a diagnostic accuracy of 96.1 . The Kappa value of 0.902 indicates excellent agreement with a p value of <0.001.



CASE 7 : 33 year old female with complaining of mass in left breast. **Fig A**: Axial T1WI images **Fig B** : Axial T2WI **Fig C**: axial dynamic contrast enhanced image **Fig D** sagittal left breast DCE images reveal multi-lobulated, well circumscribed mass in left breast with internal septations , clefts and cystic areas within showing smooth wall **Fig E:**Type II kinetic curve **Fig. F:** Perfusion image-showing increased perfusion in the lesion Fig G: **HPE: BENIGN PHYLLODES.**

CONCLUSION

- DCE MRI of breast is found to be an excellent diagnostic and screening tool in breast imaging.Evaluation is done based on morphology and kinetic curve. Amongst these two, evaluation of morphology has emerged as the most useful and reliable parameter. Kinetic curve assessment, however, adds significantly in increasing sensitivity. This modality proved to have excellent histopathology correlation and is independent of parenchymal composition.
- Rapid enhancement and Type III curve are most frequently associated with malignancy .

Presence of internal non enhancing septations is almost always suggestive of fibroadenoma.

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