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EXPERIENCE ON EVALUATION AND CORRELATION OF SUSPICIOUS BREAST LESION ON SCREENING DIGITAL MAMMOGRAPHY AND ULTRASOUND WITH HISTOPATHOLOGY AND MRI

Radiodiagnosis

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ABSTRACT

Breast cancer is a leading cause of cancer mortality among women with 12.5% lifetime risk for developing breast cancer by 85 years of age (1). The incidence is also increased by about 4% per year since 1980's. However Surveillance, Epidemiology, and End Results (SEER) programme reported decrease in the breast cancer mortality rate from 3.1 % to 9.3 % during the period of 1989 to 1992 across all age groups.(2) This decrease in mortality was at least partially attributable to the benefits gained by early detection through screening mammography. The high prevalence and need for early treatment of breast malignancy emphasizes the need for early and accurate diagnosis.

The radiological examination of breast is an integral part of modern multidisciplinary approach for effective management of breast disease (3). The aim of breast imaging is to assess the probability of a lesion being benign or malignant. Currently digital mammography, ultrasound, color Doppler and MRI are being utilized for detection of breast cancer.

The suspicious lesion has to be evaluated with tissue diagnosis as well as MRI as the MRI has advantage of evaluation of whole breast with dynamic curve and diffusion weighted imaging, if needed spectroscopic evaluation.

KEYWORDS

CAD - Computer aided detection, DCEMRI - Dynamic contrast enhanced Magnetic Resonance Imaging, Gd-DTPA - Gadolinium diethylenetriamine pentacaetic acid, MRI - Magnetic resonance imaging, Mammo - Mammography, PPV - Positive predictive value, PET - Positive emission tomography, SEER - Surveillance, Epidemiology, and End Results, Sen - Sensitivity, Sp - Specificity

INTRODUCTION:

Mammography is a specific type of imaging that uses low dose x-rays for examination of breast. It is of great importance due to its ability to detect micro calcifications which often are earliest sign of malignancy. It is the standard investigation for routine screening of the patients for breast diseases. It has high specificity in detecting invasive breast carcinomas.

Breast Ultrasound is real time imaging modality and has invaluable role in characterizing a mass as cystic or solid. It is the preferred modality employed during pregnancy and lactation and in painful conditions where compression of breast is not desired. It is also valuable for evaluation of post surgical and irradiated breasts. Ultrasound can also be used to evaluate lumps that are hard to see on a mammogram. Sometimes, ultrasound is used as part of other diagnostic procedures, such as needle biopsy or aspiration

Dynamic contrast material–enhanced magnetic resonance (MR) imaging of the breast with gadolinium-based contrast agents now is accepted widely as a potential adjunct to conventional imaging modalities such as mammography and ultrasonography (US) The diagnosis in dynamic contrast-enhanced breast MR imaging is based primarily on contrast material enhancement velocity. Breast carcinomas generally show a faster and stronger signal intensity increase after a bolus injection of gadolinium-basedcontrast agent than most benign lesions and normal breast tissue.

Dynamic Contrast Enhanced MRI of Breast is a very sensitive method and is capable of detecting even small lesions not visualized by other methods. Excellent results have been achieved when contrast enhanced MRI was used as an additional modality in cases with significant risk of breast cancer and where assessment by conventional imaging is equivocal. Early contrast enhanced breast MR imaging studies showed marked increased signal intensity in cancers compared to surrounding fibro glandular tissue, with sensitivities of almost 100 % for invasive disease (5). Initial reports regarding use of dynamic contrast enhanced MR imaging to measure increased uptake of contrast in suspicious breast lesion revealed specificity of 30-85 % and sensitivity of 90-99 % (6). The lesion can be further evaluated with diffusion weighted imaging and spectroscopy after contrast study.

With this background this study has been carried out to explore usefulness of Dynamic Contrast Enhanced MRI as compared to X ray and sonomammography in evaluation of a suspicious malignant breast lesion.

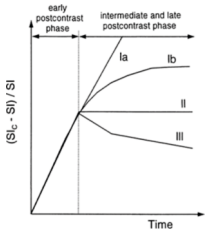
Dynamic contrast-enhanced MRI of the breast is becoming increasingly useful in the detection, diagnosis, and management of breast cancer. To overcome difficulties arising from lack of standardization among radiologists in describing lesions and communicating results to referring physicians, the American College of Radiology in 2013 developed the BI-RADS–MRI lexicon, published as a part of the American College of Radiology's *Breast Imaging Reporting and Data System Atlas* (49).

METHOD:

The prospective study included fifty patients who were referred for screening digital mammography and they were found to have suspicious lesion or inconclusive findings, they were taken for USG, MR mammography and followed by tissue biopsy if required. They were evaluated for detailed morphologic features according to MRI BI-RADS lexicon in combination with dynamic kinetic analysis of time/signal intensity curves for lesion characterization as benign or malignant.

Standard dynamic contrast-enhanced subtracted breast MRI of both entire breasts was performed using 1.5 Tesla MR System 'Siemens', Somatom Germany. All patients were imaged in the prone position in a dedicated double breast coil. No compression device was used. The MR sequences done were transverseT1-weighted spin-echo sequence for localization purposes ;Sagittal fat-suppressed T2-weighted fast spin-echo sequence with the following parameters: TR/TE, 4500/85; field of view, 34 cm; matrix size, 256 x 192; slice thickness, 5 mm with gap of 1mm and three-dimensional axial fat suppressed T1-weighted fast gradient-recalled echo sequence was obtained before, and 5 sets of images after a bolus injection of 0.1 mmol/kg of gadopentetate dimeglumine (Magnevist, Berlex Laboratories, NJ) with an acquisition time of 90 seconds for each set of 74 images. The following parameters were used: TE, minimum PREP time 40;flip angle 10degree, field of view, 34 cm; matrix size, 256 x 192; slice thickness, 4.2 mm with no gap. Fat suppression and subtraction of precontrast from first set of post contrast images was done. Bilateral imaging was done for all sequences.

Morphologic analysis was done on post processed subtracted images. Detailed morphologic analysis was done using MRI BI-RADS Lexicon proposed by American college of radiology(25).



Type I is typically seen with benign findings.

Type III is a washout curve, found in malignant lesions.

Type II is a plateau curve that is a combination of a Type I and Type III curve and can be seen with both benign and malignant lesions. In these patients help was taken from morphologic analysis to categorize a lesion as benign or malignant.
Depending on various parameters (shape, margin type, enhancement pattern, and kinetics), each lesion was assigned a score that is analogous to one of the following BI-RADS categories.

Normal (category 1), benign finding (category 2) , probably benign finding (category 3), suspicious abnormality (category 4) or highly suggestive of malignancy (category 5) .

OBJECTIVES:
The objective of the study is to perform mammography in all patients reporting to hospital either for screening or with clinically suspicious breast lumps and perform Dynamic contrast enhanced MRI of breast in all patients with suspicious breast lesion detected on digital mammography. The findings of digital mammography and contrast enhanced MRI of breast were correlated with histo pathological examinations in all patients with positive imaging.

FINDINGS AND RESULTS
The age incidence in the study was from 30yrs to 82 yrs. The age distribution of patients is shown in fig1.

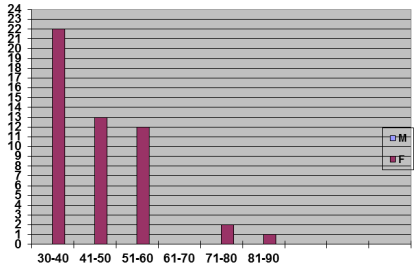


Fig1 Age and sex distribution of patients who underwent breast MRI.

MRI DESCRIPTION OF LESIONS USING BI-RADS LEXICON

LESION	NO OF PATIENTS
MASS	35
NONMASS	15
FOCUS	-

MASS MORPHOLOGIC DESCRIPTORS

DESCRIPTOR	NO OF PATIENTS
MARGIN	
SMOOTH	6
IRREGULAR	8
SPICULATED	21
SHAPE	
OVAL	2
ROUND	3
LOBULATED	11
IRREGULAR	19
INTERNAL ENHANCEMENT	
HOMOGENOUS	5
HETEROGENOUS-	22
RIM	3
DARK INTERNAL SEPTATION	5
ENHANCING INTERNAL SEPTATION	-
CENTRAL ENHANCEMENT	-

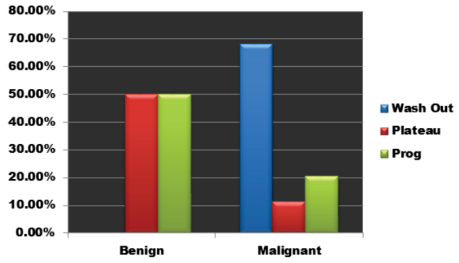
NONMASS MORPHOLOGIC DESCRIPTORS

DESCRIPTOR	NO OF PATIENTS
LINEAR/DUCTAL	8
REGIONAL	3
SEGMENTAL	-
DIFFUSE	4

FREQUENCY OF VISUALLY ASESSED KINETIC PATTERNS

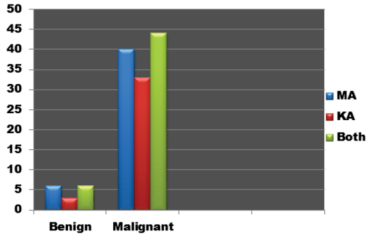
DESCRIPTOR	NO OF PATIENTS
WASHOUT	33
PLATEAU	7
PROGRESSIVE	10

Bargraph Showing Distribution Of Time Signal Intensity Curve In Benign And Malignant Lesions (fig- 2)



In our Study group of 50 patients, 6 patients with histopathological diagnosis of fibroadenoma breast when analyzed by time signal intensity curves showed plateau and progressive pattern. In malignant group all 44 pts had histopathological diagnosis of invasive ductal carcinoma (26), invasive lobular carcinoma (11) and non invasive carcinoma (7) , out of which 30 showed washout curve(68.18%) and 5 had plateau (11.36%) and 9 had progressive pattern (20.45%).

Comparison Of Benign And Malignant Lesion On Basis Of Morphology, Kinetic Analysis And Combination Of Both In Reference To Histopathological Diagnosis(fig- 3)



Morphologic analysis alone was sufficient for categorizing the breast lesion into benign and malignant in 46 patients (92%).

Kinetic analysis alone could categorize correctly in only 3 out of 6 benign lesions (50%),33 out of 44 malignant lesions(75%).

HISTOPATHOLOGY OF PRIMARY LESIONS

HISTOLOGY	NO
INVASIVE BRAEST CANCER	11
DUCTAL	26
LOBULAR	11
MEDULLARY	-
MUCINOUS	-
NON-INVASIVE CANCER	7
BENIGN	
FIBROADENOMA	6

BENIGN VS MALIGNANT

TYPE OF LESION	NO OF PATIENTS
BENIGN	6
MALIGNANT	44

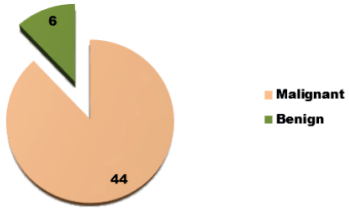


Fig-4 Distribution of patients on basis of Histopathology

BENIGN LESIONS
Six patients had histopathological diagnosis of fibroadenoma out of fifity patients. Two lesion had oval shape with smooth margin and other had round shape with lobulated margin. All had non enhancing internal septations.

In analysis of time Intensity curve one case showed progressive pattern

and other showed plateau pattern of enhancement.

All patients with diagnosis of benign lesion, fibroadenoma could be diagnosed only on basis of morphology alone. One patient showed progressive pattern and other had plateau pattern of time signal intensity.

MALIGNANT LESIONS

Forty four patients had histopathological diagnosis of malignancy. Twenty six patients had diagnosis of Infiltrating Ductal carcinoma, 11 patients had diagnosis of lobular carcinoma and seven patients had diagnosis of non invasive ductal carcinoma.

Thirty five patients had mass like enhancement; all 21 Patients had spiculated and irregular margin.

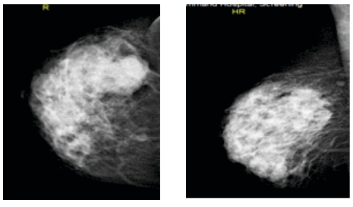
Fifteen patients had non mass pattern of enhancement. Eight patients had ductal, three patients had regional pattern and four patients had diffuse pattern of enhancement. Twenty two patients had heterogeneous and 3 patients had rim pattern of enhancement.

Out of 44 patients with malignancy 33 had wash out pattern, 7 had plateau and 10 had progressive pattern of signal intensity curve.

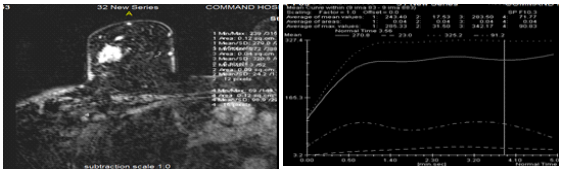
Out of 44 patients with malignant lesion 41 had associated findings of skin infiltration, retraction of nipple and chest wall invasion, 2 had only skin infiltration helping in staging of malignancy and 1 had only ulcerated lymph node involvement.

CASE 1

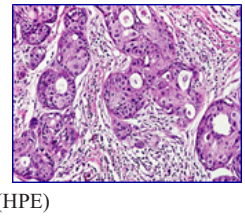
A 34 yrs old female presented with painless, hard, mobile lump in the lateral quadrant of right breast The lump was detected 3 mths from the date of presentation.



Mammogram showing spiculated soft tissue density at superolateral quadrant of right breast



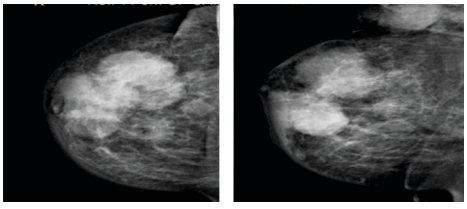
DCEMRI showing type III kinetic curve at the lesion



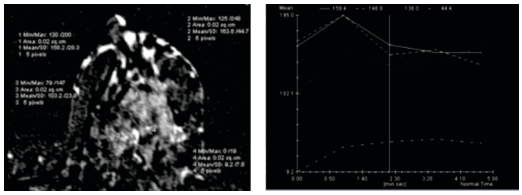
Ductal Carcinoma (HPE)

CASE 2

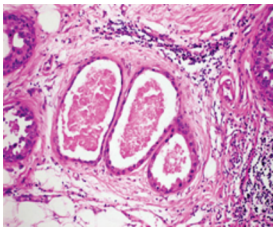
A 53 yrs old lady presented with multilobulated hard, fixed lump at the lateral quadrant of left breast with overlying skin edema and retraction of nipple. She presented after 2 ½ mths of detection of the lump.



Mammogram showing lobulated soft tissue density at lateral quadrant of left breast with pectoral infiltration



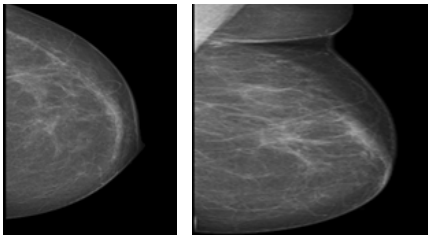
DCEMRI showing type III kinetic curve at the lesion



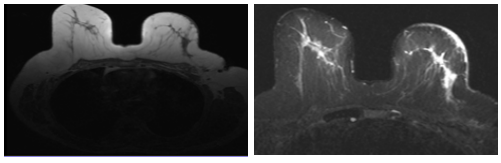
Ductal Carcinoma (HPE)

CASE 3

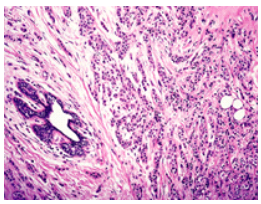
A 53 yrs old female post lumpectomy for carcinoma, presented for screening



Mammogram showing large irregularly marginated soft tissue density at superolateral quadrant of left breast



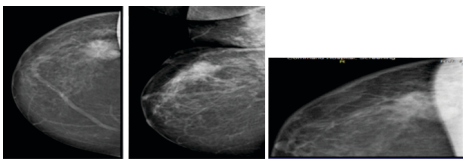
Multiple enhancing axillary lymphnodes
DCEMRI showing type III kinetic curve at the lesion



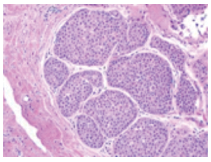
Ductal Carcinoma (HPE)

CASE 4

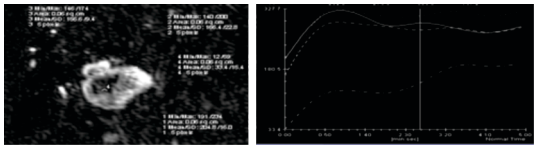
A 42 yrs old female presented with well defined, hard, small, mobile lump at the upper outer quadrant of right breast. It was painless and she noticed it 3 mths before the date of presentation.



Mammogram showing a well defined spiculated soft tissue density at superolateral quadrant of left breast Mag Spot view showing? muscle invasion



Infiltrative ductal Carcinoma (HPE)



DCEMRI showing type III kinetic curve at the lesion

DISCUSSION:

Breast MRI is gaining increasing clinical acceptance in multiple applications, including assessing indeterminate lesions on physical examination, mammography, and sonography; staging biopsy-proven breast cancer and detecting contralateral disease .The excellent sensitivity of MRI for invasive breast cancer detection is beneficial, but its varying specificity has proved problematic.

The American College of Radiology in 2003 developed the BI-RADS–MRI lexicon, published as a part of the American College of Radiology's Breast Imaging Reporting and Data System Atlas (49).

Our study group consisted of 50 patients chosen for breast MRI, for lesions suspicious of malignancy and for pre-operative evaluation in diagnosed cases of carcinoma breast.

In our study, we successfully used MRI –BI RADS lexicon for describing lesion morphology. The morphologic criteria based on MRI BI-RADS were effective for differentiating between benign and malignant breast lesions in high-spatial-resolution images regardless of their histological variability. In our study, in majority of cases we were able to correctly diagnose breast lesions based on certain morphologic features(92%).Six patients had histopathological diagnosis of fibroadenoma out of 50 patients. Two lesions had oval shape with smooth margin and other had round shape with lobulated margin. All had non enhancing internal septations.

Forty four patients had histopathological diagnosis of malignancy. Thirty five patients had mass like enhancement, all 21 Patients had spiculated and irregular margin.15 patients had non mass pattern of enhancement. Eight had ductal and three had regional pattern. 22 Patients had heterogeneous and 3 patients had rim pattern of enhancement. Similar results have been shown in study by Orel GS et al and Nunes LH et al. In study by Nunes et al of One hundred ninety-two patients with mammographically visible or palpable findings who underwent breast MRI and subsequent excisional biopsy for histopathological confirmation, showed that smooth and lobulated borders in a focal mass were highly predictive of benign disease: NPVs were 100% (21 of 21) for smooth borders and 87% (39 of 45) for lobulated borders. Irregular and spiculated borders were more characteristic of malignant disease and had PPVs of 81% (22 of 27) and 88% (28 of 32), respectively. The presence of nonenhancing internal septations was associated with benign disease. The presence of peripheral rim enhancement was highly predictive of malignancy, with a PPV of 79% (37 of 47).

In study by Orel et al of Forty-one patients with mammographic and/or palpable lesions which were imaged and all patients underwent excision biopsy. Of the 16 carcinomas that were identified at MR imaging, the borders were irregular in 13, five demonstrated inhomogeneous enhancement and four demonstrated rim enhancement. Internal septations in five of the nine visualized fibroadenoma were seen. This morphologic characteristic was seen only in fibroadenoma and could be correlated histologically with fibrous septa between adjacent lobules of the fibroadenoma.

Our study revealed that the enhancement kinetics as shown by time signal intensity curves differ significantly for benign and malignant enhancing lesions, so can be used as aid in differential diagnosis. In breast cancers washout and plateau curves prevail and benign lesions show progressive enhancement. In our Study group of 50 patients, histopathological diagnosis of fibro adenoma breast when analyzed by time signal intensity curves showed plateau and progressive pattern in each(50%). In malignant group all 44 pts had histopathological diagnosis of infiltrating ductal carcinoma out of which 30 showed washout curve(68.18%) and 5 had plateau (11.36%) and 9 had progressive pattern (20.45%).

The study supports the potential value of washout suggested by Susan et al (72). In their study group 83% of the benign lesions exhibited a steady or curved time–signal intensity curve. In contrast, 57% of malignant lesions exhibited a washout time–signal intensity curve. Using the shape of the time–signal intensity curve alone, the authors report a sensitivity of 91% (92 of 101), a specificity of 83% (137 of 165), a positive predictive value of 77% (92 of 120), a negative predictive value of 94% (137 of 146), and a diagnostic accuracy of 86% (229 of 266). The likelihood of breast cancer associated with a type I, II, or III time course was 6% (nine of 146), 64% (34 of 53), and 87% (58 of 67), respectively.

Similar results were also shown in a study by Kuhl et al (73), two hundred sixty-six breast lesions were examined with a two-dimensional dynamic MR imaging series and subtraction post processing. There were 101 malignant and 165 benign lesions. The distribution of curve types for breast cancers was type I, 8.9%; type II, 33.6%; and type III, 57.4%. The distribution of curve types for benign lesions was type I, 83.0%; type II, 11.5%; and type III, 5.5%. The distributions proved significantly different ({chi}2 = 139.6; P < .001). The diagnostic indices for signal intensity time course were sensitivity, 91%; specificity, 83%; and diagnostic accuracy, 86%. The diagnostic indices for the enhancement rate were sensitivity, 91%; specificity, 37%; and diagnostic accuracy, 58%.

In our study morphologic analysis was almost sufficient for the correct diagnosis of the lesions. Kinetic analysis showed minimal additional benefit that it increased the confidence of diagnosis. Morphologic analysis alone was sufficient for categorizing the breast lesion into benign and malignant in all our patients (96%). Kinetic analysis alone could categorize correctly in only 3 out of 6 benign lesions (50%), 30 out of 44 malignant lesions (68.18%).As compared to study done by Liu et al (74) which showed that combined qualitative and quantitative analysis yielded higher sensitivity, specificity and accuracy of 93%,74% and 85% when compared to qualitative morphologic analysis alone. This difference in results can be explained by the fact that our study sample was very small and majority of the patients were diagnosed cases of carcinoma breast and were referred for pre-operative evaluation. Similar results have been shown by Kuhl et al (73) in their study which describes such an integration of kinetics and architecture . The authors make the very important point that there must be concordance between the kinetic information and the morphologic features.

Evaluation of tumor spread to adjacent structures is important preoperative information for the surgeon . In our study we detected chest wall involvement and nipple retraction and skin infiltration in 3 out of 9 cases with diagnosis of malignant disease. (33.33%) of cases. Similar results were shown by Morris EA et al (74), Orel SD et al (52), where MR imaging was able to contribute important local staging information for those with posterior breast tumors.

Our study has some limitations that need to be discussed. First, the subjects may not directly reflect the general population due to small study group, and some sampling bias may have occurred because majority of our cases were diagnosed cases of breast cancer for pre-operative evaluation. As a result, a large percentage of the lesions were malignant, and there were many invasive cancers and few benign lesions

CONCLUSION

MR imaging could possibly be an important breast imaging modality. Both malignant and benign lesions are identified with high-resolution MR imaging.

- The identification of specific morphologic features can aid in the differentiation of malignant from benign lesions. Cancers tend to have irregular and spiculated margins and demonstrated heterogeneous and peripheral rim enhancement. Fibroadenomas consistently have lobulated, and well defined borders with non enhancing internal septations as specific morphologic feature.
- Morphologic Analysis of dynamic contrast enhanced MRI scores over Kinetic analysis of time signal intensity curves. Analysis of time course kinetics should be done after the evaluation of the lesions' morphology in post contrast images. If morphology is indeterminate or suggests a benign lesion, performing a time–signal intensity curve analysis is recommended.
- MRI offers superb visualization of the posterior breast tissue , axillary lymph node involvement , multiplicity in the same as well as opposite breast and can assess contiguous involvement better than conventional imaging, so helps in pre-operative staging of malignant lesions.

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