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Radio Diagnosis

# ROLE OF MAGNETIC RESONANCE IMAGING OF BREAST IN MAMMOGRAPHICALLY SUBTLE LESIONS

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**ABSTRACT** **BACKGROUND:** MR breast is used either as a problem-solving tool or for staging in cases with mammogram and ultrasound subtle lesions. Majority of these cases present with non-mass enhancement in MRI breast. The objective is to study the distribution of different types of non-mass enhancement and role of diffusion weighted imaging in MRI breast in patients with subtle mammographic findings. **METHODS:** The study included 115 patients with non-mass enhancement in MRI breast assessed between June 2014 to June 2020. Imaging interpretations and ultrasound guided core biopsies was based on BIRADS lexicon 5th edition and histopathological diagnosis of the same was obtained. Categorical variables were expressed using frequency and percentage. Chi-square test was used to test the statical significance. A p value of <0.05 was considered to be statistically significant.**RESULTS:** Overall segmental distribution and clumped internal enhancement pattern where the most common types of non-mass enhancement. Of which segmental distribution was seen in 28/48 cases(58.3%) with calcifications, 14/18 cases(77.7%) with asymmetry and about 15/28 cases(53.6%) with architectural distortion. Whereas in internal enhancement, clustered-ring enhancement was seen in 20/48 cases(41.7%) with calcifications, 4/18 cases(22.2%) with asymmetry and about 14/28 cases(50%) with architectural distortion. Among the distribution pattern malignancy was 79.7% in segmental distribution and among the morphology, it was higher in clustered-ring and clumped pattern about 88.6% and 85.7% respectively. Diffusion restriction aided in diagnosing malignant cases with a PPV of 75.76% and accuracy of 71.65% and p value of 0.001.**CONCLUSION:** Segmental distribution, clumped and clustered-ring morphology has highest prevalence of malignancy with subtle mammographic finding, hence warranting MRI in these situation. Multimodality and multi-parametric evaluation of breast lesion is essential for lesion characterization accurately.

**KEYWORDS :** Mammogram, Magnetic resonance Imaging, Breast, Cancer

## INTRODUCTION:

Among Indian females breast cancer ranks one with high age-adjusted rate of 25.8 per 100,000 women and mortality 12.7 per 100,000 women (1). Breast MR(Magnetic Resonance) has emerged as a highly sensitive modality for the imaging of breast tumours (2). According to the EUSOMA guidelines, dynamic contrast enhanced MR represents an important diagnostic tool for preoperative local staging, for monitoring the treatment response, for surveillance of high-risk women, for post treatment follow up (3). According to recent studies, MRI demonstrates a specificity of about 72%, and a sensitivity of about 90% (3). Background parenchymal enhancement due to hormonal effect paralleling the menstrual cycle can be minimized by scheduling the study during 7 to 14 days of the menstrual cycle and hence the false positive rate can be reduced (4). Goals of proper positioning include minimizing skin folds and including maximum area of breast tissue with homogeneous fat suppression and non-deformed breast parenchyma (5). Non-mass enhancement (NME) is defined as an area of enhancement which did not have any mass in the pre contrast sequence. Several studies have reported NME can also be seen in invasive cancers, though the prevalence of NME is low when compared to mass enhancement. When NME lesions are concerned, BI-RADS is insufficient in distinguishing between benign and malignant lesions. Thus, image interpretation and important findings can be determined better by assessing the MRI characteristics of NME lesions (6). Non-mass enhancement are categorized as Focal, linear, segmental, regional, multiple, diffuse and internal enhancement as Homogeneous, heterogenous, clumped, clustered ring (7).Compared to MRI-guided biopsy, US-guided biopsy is better tolerated, less expensive, and faster, and it allows greater access to lesions in certain locations (8). The knowledge about prevalence of malignancy among different types of non-mass enhancement aids in determining the further management.

## METHODS:

Institutional review board approval was taken for this prospective study. Informed consent was taken from all patients before they underwent mammogram and MRI. The study period was from 2014 to 2020.

### Study population:

All patients who were referred for mammogram breast to the Department of radiology, Amrita institute of medical sciences were assessed and those patients who were having subtle findings in mammogram were referred to MRI Breast. Among those patients who had non-mass enhancement in MRI breast were considered for the study. These patients further underwent core biopsy or excision biopsy to obtain the histopathological correlation. Those patients with normal mammogram or definitive finding in mammogram were excluded from the study. And also those patients who could not undergo MRI breast due to claustrophobia, abnormal renal function tests, metallic implants, and pacemakers were excluded from the study. Totally 115 patients were included in the study.

## TECHNIQUES:

Mammomat inspiration (Siemens AG,Berlin,Germany) was used for mammogram. Both mediolateral (MLO) and craniocaudal (CC) views were obtained along with tomosynthesis in CC and MLO view. The images were interpreted at Barco 5.0-megapixel monitors. An ideal CC view should demonstrate maximum tissue on both medial and lateral aspects of the breast with the retromammary space and some

pectoral muscle. MLO view should demonstrate axilla, axillary tail, and inframammary fold with all the breast tissue (9). MRI was done in Siemen's 1.5T (HDXT Machine, GE Medical systems, Milwaukee, Wisconsin) with dedicated 8 channel breast coils and gadolinium-based contrast medium, Clariscan at a dose of 0.5 mmol/kg is used. The patient is positioned in prone and image acquisition is made. Axial T1, axial T2, axial STIR fat saturation, diffusion weighted imaging on b values 0, 500 and 1000. Then contrast is given using power injector and dynamic axial T1 fat saturation subtraction images are acquired at 90 seconds, 3 minutes and 5 minutes. Post contrast sagittal T1 fat saturated images are also acquired. Maximum Intensity Projection (MIP) image reconstruction is done for all cases. Ultrasound guided core biopsies were done in Philips IU22 system x Matrix (Bothell WA, USA) with High frequency linear 12MHz transducer by a dedicated breast imaging radiologist having more than 10 years of experience with a 14G automated spring-loaded BARD biopsy gun. Imaging interpretations and ultrasound guided core biopsies was performed by a Fellowship qualified breast imaging radiologist having more than 10 year experience in breast imaging. Mammographic findings and areas of non mass enhancement were categorised based on BIRADS lexicon 5th edition.

**Image Interpretation:**

Mammographic interpretation: Calcifications are categorised as typically benign-skin, vascular, popcorn like, large rod like, round, rim, dystrophic, milk of calcium and suture, Suspicious - Amorphous, coarse heterogenous, fine pleomorphic, fine linear or fine linear branching and Distribution - Diffuse, regional, grouped, linear, segmental. Asymmetry can be focal asymmetry, global asymmetry or developing asymmetry (7). Architectural distortion on mammography, defined as distortion of the breast parenchymal architecture without a definable mass (10).

Non-mass enhancement interpretation: Distribution of non mass enhancement can be focal, linear, segmental, regional, multiple and diffuse.Focal area of a NMLE(Non-mass Like Enhancement) would be defined as a single, small and confined abnormal enhancing area occupying less than 25% of any given breast quadrant. Linear is enhancement along a line', but one not conforming to a ductal pattern.Segmental is triangular area of enhancement with apex pointing towards nipple suggesting duct and its branches. Regional is large volume of enhancement not conforming to a ductal distribution. Multiple enhancement is in at least two large volumes of tissues not conforming to a ductal distribution, multiple geographic areas and patchy areas of enhancement. Diffuse enhancement is uniformly distributed throughout the breast (11,12). Internal enhancement patterns are Homogenous, heterogenous, clumped and clustered ring like.Homogenous means confluent uniform enhancement. Heterogeneous is nonuniform enhancement in a random pattern.Clumped is punctate dot-like enhancing foci. Clustered ring like minute ring enhancements are clustered (11,12). Using triangulation, the area of non-mass enhancement is localized in ultrasound and biopsied using 14G core biopsy gun under ultrasound guidance. The histopathology result is compared with the final excision biopsy histopathology result. In our study we studied different types of non-mass enhancement in patients with subtle mammographic findings.

**Statistical Analysis:**

Statistical analysis was performed using IBM SPSS version 20.0 software. Categorical variables were expressed using frequency and percentage. Numerical variables were presented using mean and standard deviation.To test the statistical significance of the association of diffusion weighted imaging with histopathology, Chi-square test was used. Diagnostic measures such as predictive value positives and negatives and accuracy were also calculated. A p value of $<0.05$ was considered to be statistically significant.

**RESULTS:**

Total of 115 cases were taken for the study. The mean age of the patient involved in the study was 48.27 ± 10.41 years. In our study 42 cases (38%) were premenopausal, 16 cases (13.9%) were perimenopausal and the remaining 57 cases (49.5%) were postmenopausal. Of the 115 cases whose mammogram was done, 16 cases(13.9%) had mass, 48 cases (41.7%) had calcifications in mammogram, 18 cases (15.7 %) had asymmetry in mammogram and 28 cases (22.0 %) had architectural distortion in mammogram and 5 cases had no definitive finding in mammography with clinical symptoms. Patients with mammographic abnormalities and also those for whom mammography was not possible technically were then proceeded to CE-MRI as problem solving MR and targeted second look ultrasound examination.

MR findings taken into consideration for the study includes mass, non-mass enhancement and diffusion restriction. Out of the total cases, mass was seen in MR in 24 cases(20.8%) and the remaining 91 cases(79.2%) did not show any mass in MR. Non-mass enhancement was studied in detail based on their distribution and internal enhancement pattern. Non mass enhancement was classified into four types of distribution and four internal enhancement patterns(Table 1).

**Table 1: Frequency of non mass enhancement cases based on distribution pattern and internal enhancement pattern**

| | Calcifications n= 48 | Asymmetry n= 18 | Architectural distortion n=28 |
|---|---|---|---|
| NME-Distribution | | | |
| i) Focal | 14 (29.2) | 2 (11.1) | 12 (42.8) |
| ii) Linear | 5 (10.4) | 1 (5.6) | 0 (0.0) |
| iii) Segmental | 28(58.3) | 14 (77.7) | 15 (53.6) |
| iv) Regional | 1 (2.1) | 1 (5.6) | 1 (3.6) |
| NME-Internal Enhancement | | | |
| i) Homogeneous | 2 (4.2) | 1 (5.6) | 7 (25) |
| ii) Heterogenous | 19 (39.5) | 7 (38.9) | 4 (14.3) |
| iii) Clumped | 20 (41.7) | 4 (22.2) | 14 (50) |
| iv) Clustered-ring | 7 (14.6) | 6 (33.3) | 3 (10.7) |
| Diffusion Restriction | | | |
| i) Present | 40 (83.3) | 15 (83.3) | 17 (60.7) |
| ii) Absent | 8 (16.7) | 3 (16.7) | 11 (39.3) |
| *HPE | | | |
| i) Benign | 11 (22.9) | 5 (27.8) | 10 (35.7) |
| ii) Malignant | 37 (77.1) | 13 (72.2) | 18 (64.3) |

#Numbers with parenthesis are percentage
*HPE - Histopathology Examination

The association pattern between mammogram findings and the types of non-mass enhancement were analysed.

Distribution pattern and internal enhancement pattern of non-mass enhancement in different mammogram findings are described in table 2.

**Table 2 : Summary of MRI characteristics, histopathology and mammogram findings**

| TOTAL SAMPLE SIZE | 115 |
|---|---|
| Non-mass enhancement : Distribution pattern | |
| (i) Focal | 34 (29.5%) |
| (ii) Linear | 8 (7.0%) |
| (iii) Segmental | 69 (60.0%) |
| (iv) Diffuse | 4 (3.5%) |
| Non - mass enhancement : Internal enhancement | |
| (i) Homogenous | 11 (9.5%) |
| (ii) Hetrogenous | 39 (33.9%) |
| (iii) Clumped | 44 (38.2%) |
| (iv) Clustered ring | 21 (18.3%) |

**Histopathology:**

After biopsy 36 cases(31.3%) turned out to be benign and the remaining 79 cases (68.6%) were malignant. Focal enhancement pattern was seen in 34 cases of which 18 cases (52.9%) were malignant and the remaining 16 cases (47.1%) were benign. Eight cases had linear enhancement pattern which were distributed as three cases (37.5%) as malignant and five cases (62.5%) as benign. Then segmental enhancement pattern was seen in 69 cases and of which 55 cases (79.7%) were malignant and the remaining 14 cases (20.3%) were benign. Diffuse enhancement pattern was seen in four cases and in that three cases (75%) were malignant and the remaining one case (25%) was benign.

Homogenous enhancement was present in 11 cases and all were benign. None of them with homogenous enhancement turned out be malignant. Heterogenous enhancement were seen in 39 cases and in them 22 cases (56.4%) were malignant and 17 cases (43.6%) were benign and. 44 cases were showing clumped enhancement and out of them 39 cases (88.6%) were malignant and five cases (11.7%) were benign. 21 cases were showing clustered-ring pattern of enhancement. Out of which 18 cases (85.7%) were malignant and the remaining three cases (14.3%) were benign.

**Diffusion Weighted imaging:**

Of the 92 cases which were showing diffusion restriction in MRI, 69 cases (75%) were malignant and 23 cases (25%) were benign. 23 cases did not have diffusion restriction and among them 13 cases (56.5%) were benign and the remaining 10 cases (43.5%) were malignant (Table 2),(Table 3).

**Table 3: Diagnostic measures of Diffusion restriction and malignancy**

| | Positive predictive value | Negative predictive value | p value |
|---|---|---|---|
| DWI Restriction | 75.76% | 57.14% | 0.001 |

**DISCUSSION:**

MRI has become an essential tool to identify non-palpable and additional cancer foci that would otherwise remain undetected by clinical assessment combined with mammography or ultrasound. There are various patterns of non-mass enhancements in MRI breast which are classified based on their distribution pattern and their internal enhancement morphology. The objective of the study was to analyse the role of MRI breast in mammographically subtle lesion with special interest in non-mass enhancement and diffusion restriction images. In our study a total of 115 patients met the inclusion criteria. The mean age of the patients involved in the study was 48.27 ± 10.41 years. Maximum of 57 cases (49.5%) were post-menopausal.

Additional mammographic views like spot compression or magnification views along with tomosynthesis has increased the rate of cancer detection (13). In a study by Skaane et al., the cancer detection rate was significantly increased with combination of tomosynthesis with digital mammogram by 27% than by using digital mammogram alone(p value - 0.001) (14). In our study, maximum of 48 cases(41.7%) had calcifications in mammogram followed by 28 cases (22%) with architectural distortion. According to the study conducted by Liberman et al., among the different types of calcification linear type has the positive predictive value for malignancy (15). Among those cases with architectural distortion, tomosynthesis(73%) has increased rate of detection of architectural distortion when compared to 2D mammography alone(21%) (16).

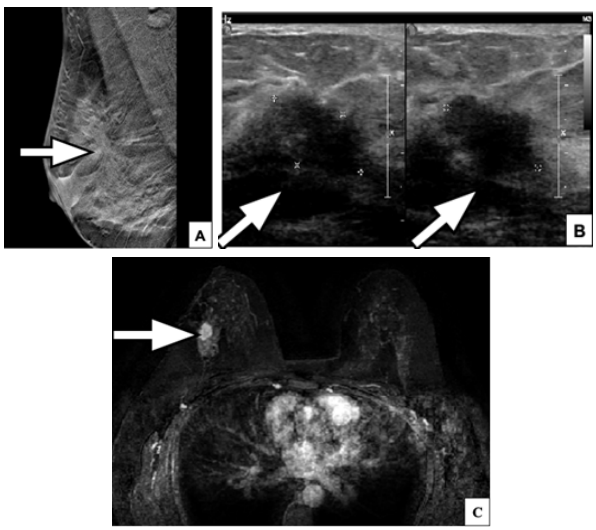


**Figure 1:** 45-year-old lady with right breast mass came for mammography A) Mammogram(3D tomosynthesis) in MLO view shows an area of architectural distortion(arrow) in right breast in upper outer quadrant B) Ultrasound shows hypoechoic solid mass with irregular margins(arrows) C) Dynamic contrast enhanced MRI-MIP image shows clumped pattern of non-mass enhancement(arrow) in upper outer quadrant extending upto pectoralis muscles posteriorly. HPE: Invasive lobular carcinoma mixed classical and pleomorphic type

In cases with inconclusive mammographic findings which were negative on ultrasound also, MRI can be used as a problem solving tool. As most of these lesions are non-palpable, MRI is also used for staging and further surgical planning incase of malignancy. In another study by Taskin et al., out of the 79 cases with architectural distortion, non-mass enhancement was seen 47 cases(59.4%) and among those 28 cases with asymmetry, non-mass enhancement was seen in 7 cases(25%). 28% of the architectural distortions and 11% of the asymmetries with positive findings in MRI turned out be malignant (17). As there is significant proportion malignancy in cases with inconclusive mammographic findings, MRI examination plays a crucial role further management. Also in the above mentioned study by Taskin et al., none of the MRI negative patients had progressive findings on tomosynthesis and no malignancy was detected on follow up (17).

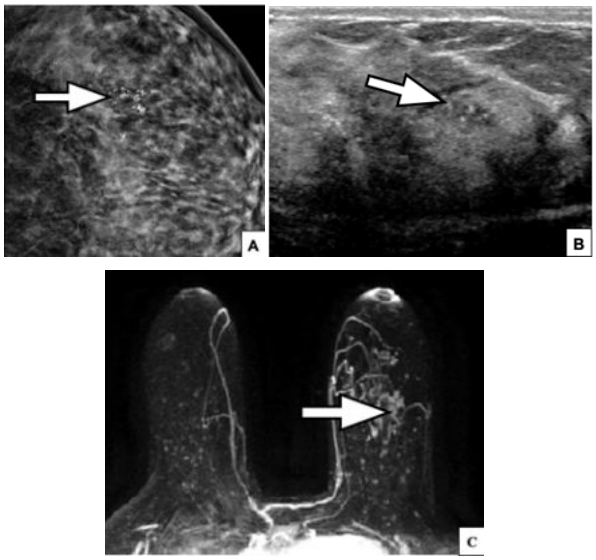


**Figure 2 :** 44 year old asymptomatic patient, came for screening mammography. A) Mammogram CC view shows clusters of amorphous calcifications(arrow) without any associated discrete mass in upper outer quadrant. B) US : Heterogeneous area showing multiple specks of calcifications(arrow) C) Dynamic contrast enhanced MRI-MIP image shows segmental area of clustered ring non-mass enhancement(arrow) in upper quadrant middle third of left breast. HPE : Ductal carcinoma in situ.

Second-look ultrasound after MRI breast is important and helps in localisation of the lesion in ultrasound and aid in ultrasound guided biopsy. If the lesion is ultrasound negative, either MR guided biopsy or incase of non-availability of MR guided biopsy stereotactic biopsy can be used. After biopsy in our study, 36 cases(31.3%) turned out to be benign and the remaining 79 cases (68.6%) were malignant. In a study by Taksin et al., the cancer detection rate by MRI was 13.3% in patients with inconclusive findings on conventional imaging[18]. And in other study by Giess et al., 40 out of 294 patients had malignancy in cases with equivocal mammographic findings and out of the 40 cases, 11 cases had non-mass enhancement[19]. In our study malignancy was seen in 79 cases(68.6 %) with non-mass enhancement. The variations in cancer detection rate maybe attributed to the heterogeneity of the general population and sample selection.

Our study is different from the above studies in that the different types of non-mass enhancement were not categorised separately and also their prevalence in malignancy. Among the different types of non-mass enhancement, overall maximum of 69 cases(60%) belong to segmental distribution pattern and maximum of 44 cases(38.2 %) belong to clumped morphology. With respect to the distribution pattern of NME, the features with highest prevalence for malignancy was segmental 79.7% followed by diffuse enhancement, 75%. This was similar to the frequency for segmental enhancement(67%) in a similar study done by Liberman et.al[20].Similarly, with morphological parameters of NME, the features with the highest prevalence for malignancy was clumped architectures(88.6%) and clustered ring enhancement (85.7%). This is higher than the PPV in a study conducted by Sakamoto et al., in which the PPV for clustered- ring were 67% and clumped pattern was 20%[2]. The clustered-ring internal enhancement pattern has been reported by several studies to be a reliable predictor of malignancy which was correlating in our study also. In our study homogenous enhancement shows 100% benignity which is also reported in a similar study conducted by Aydin et al., with a PPV for homogenous enhancement was 100%(p value - 0.03) with regards to benign category (6). Based on our observations segmental enhancement pattern was consistently associated with malignancy in our study and in several other studies without much discrepancies.

When considering the internal enhancement pattern clustered-ring and clumped pattern had consistent association with malignancies. Other enhancement patterns did not show consistent association when reviewing multiple other studies.

Diffusion restriction is another important parameter used in MRI breast to characterize the nature of the lesion. In our study 92 cases showed diffusion restriction. Based on histopathology the PPV was 75.76% and accuracy was 71.65% for malignancy (p-value 0.001). Similar result was also seen in a study done by Aydin et al., whose PPV was 70.0 % and p-value was 0.01[6]. In the current study, diffusion restriction was evaluated as a categorical variable and the presence of diffusion restriction was significantly more frequent in malignant lesions ($p < 0.01$). This may suggest that instead of using ADC values for benign/malignant differentiation, the presence or absence of diffusion restriction may sufficiently provide better distinction between benign and malignant lesions.

## CONCLUSION:

Segmental distribution of enhancement, clumped and clustered ring morphology of enhancement has highest the prevalence in patients with subtle mammographic finding.The patients with subtle mammographic findings has to undergo further evaluation as there is higher prevalence of malignancy in patients with non-mass enhancement. Multimodality and multi-parametric evaluation of breast lesion is essential for lesion characterization accurately.

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