Reliability and reproducibility of breast MRI as a roadmap to treatment planning of breast cancer

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Aims and objectives

Breast cancer is the second most common cause of cancer deaths among women, exceeded only by lung cancer. However the number of deaths reported have been decreasing mainly contributed by earlier detection through screening mammography and improved treatment strategies(1). Accurate staging of breast cancer is important in treatment planning and radiological findings are being incorporated into clinical staging as a routine protocol (2-5). Screening mammography is used for early detection of breast cancer and Ultrasound is mainly used as a diagnostic modality and for guided biopsies. Contrast enhanced MRI along with Diffusion weighted imaging has come up to play a pivotal role in breast cancer staging in conjunction with mammography and ultrasound and can be used as a roadmap in treatment planning(6,7).

Dynamic contrast enhanced MRI (DCE-MRI) helps in detection of multicentric and multifocal disease in the same breast as well as in identification of synchronous lesions in contralateral breast. Involvement of the chest wall or pectoral muscle and the skin is better demonstrated by MRI which upgrades the disease to T4 (8-10). Identification of non mass like enhancement (NMLE) along with the index lesion increases the total span of the disease in the breast as compared with the clinical examination and may be a predictor of the presence of extra-tumoral DCIS or extensive intraductal component (EIC). DCE MR also helps in the nodal staging of breast cancer by showing the levels of suspicious axillary nodes as well as in detection of internal mammary nodes and supra-clavicular nodes. The metastatic involvement of the axillary nodes is suggested by certain features such as rounding of shape, eccentric cortical thickening, compression or partial or complete effacement of fatty hilum. This information is necessary for treatment decision in choosing between breast conservation and mastectomy, preoperative and post operative chemotherapy or hormonal therapy, sentinel lymph node biopsy and axillary lymph node dissection(1). However with all its capabilities and high sensitivity to identify and stage breast cancer, studies have shown that MRI has a low specificity in terms of high false positive rates and in identifying and specifically characterizing the extratumoral and nonmass forming DCIS.

Our study was aimed -

• To study those interpretation criteria of MRI that serve to increase its specificity in patients with non mass like enhancement and therefore bring down false positive results.

• To determine the accuracy of MRI in evaluating the multicentricity / multifocality of breast cancer and its significance as a roadmap in treatment planning.

• To study its role in predicting the nodal status in patients diagnosed with breast cancer.
Methods and materials

This is a retrospective study, conducted in the Department of Radio-diagnosis, Max Super Speciality Hospital, New Delhi between September 2011 to June 2014.

The study was conducted after the approval of Institutional Review board. The Institutional Ethics committee waived informed consent, this being a retrospective study. 159 female patients with breast cancer, who underwent MRI in our department for assessment of the disease prior to treatment planning and subsequently underwent treatment in the hospital's Cancer Centre were included in our study. These also included 14 post lumpectomy patients operated elsewhere who either had positive surgical margins or were detected with breast cancer on lumpectomy specimen. In these patients MRI was conducted for assessment residual disease and its extent for further treatment planning. There were 11 post neoadjuvant chemotherapy patients in whom MRI was done to take a decision for wide excision or mastectomy depending upon the response.

IMAGING:

MAGNETIC RESONANCE IMAGING (MRI) EQUIPMENT:

MR imaging of the breast was performed on 3.0 Tesla MRI unit (Discovery 750 by GE Healthcare USA). All patients were imaged in the prone position using dedicated 8 channel bilateral breast coils and providing adequate compression.

PROTOCOL FOR BREAST MRI

After adequate positioning of patient on a dedicated phased array breast coil on a 3T scanner, following sequences were acquired -

# Non fat suppressed Axial T1
# Fat suppressed axial T2
# Axial Diffusion-1000B/value
# Axial Diffusion-1500B/value
# Axial T1/Supraclavicular
# Non fat suppressed axial T2
# Sagittal VIBRANT

Following this a dynamic transverse 3D fat suppressed spoiled gradient echo volume acquisition was acquired through both the breasts prior to and six times sequentially
following intravenous administration of 0.1 mmol/kg Gd-DTPA. This was followed by a delayed high resolution contrast enhanced sagittal sequence. These images were then subtracted and reconstructed in multiple planes. Kinetic analysis was done in region of interest. Colour maps were also viewed on the work station using specialized software.

INTERPRETATION OF MRI

Evaluation was done using ACR MRI BI-RADS Lexicon

1. Focus/foci - tiny spot of enhancement, < 5 mm

2. Mass lesion- assessed for its size, morphology in terms of margins, shape signal characteristics, ADC value and enhancement characteristics (homogenous/ internal enhancing or non-enhancing septations/ heterogeneous/ clustered rim enhancement) and kinetic curves. Number of lesions,(> 2 lesions taken as multiple) were also assessed.


4. Lymph nodes - assessed for eccentric cortical thickening/ partial or complete effacement of fatty hilum/ roundening of shape and perinodal fat stranding.

These patients eventually underwent mastectomy of wide decision with sentinel lymph node biopsy or axillary lymph node dissection. The final specimen pathology report was correlated with MRI findings and variables studied were number of lesions reported, size of the largest single tumor reported, intra-tumoral DCIS present/ absent, extra-tumoral DCIS/ LCIS , extensive intraductal component and nodal metastasis.

Results

Our study showed that NMLE seen on MRI had Sn: 79%, Sp: 86%, PPV : 76%, NPV: 88% for detection of Extra-tumoral DCIS on histopathology. There was Sn: 74%, Sp: 76, PPV: 52%, NPV: 89% for NMLE versus extensive intraductal component (EIC) on histopathology. When NMLE was correlated with extra-tumoral DCIS and EIC taken together, we obtained Sn: 89%, Sp:78%, PPV: 50%, NPV: 97%. Multifocal/ multicentric tumors with or without satellite nodules on MRI had Sn: 86%, Sp: 89%, PPV: 60%, NPV: 97% for multiple lesions on histopathology.

We had 36 patients with clumped nodular pattern of NMLE, out of them 33 were malignant on histopathology and 5 out of 8 patients were malignant for ductal nodular pattern of enhancement. Hence clumped nodular and ductal nodular pattern proved to be good predictors of malignancy. Linear spicular and linear ductal pattern proved to have a good predictor rate for nonmalignant involvement.
In 14 post lumpectomy patients, 11 patients had positive margins on histopathology. Residual abnormally enhancing lesions seen as mass or NMLE were seen on MRI all these 11 patients which were proven as residual disease on final histopathology. In 5 of these patients MRI showed clumped nodular NMLE which on histopathology were proven as residual DCIS with or without IDC. One case was false positive on MRI and 2 cases were true negative.

In 11 post NACT (Neoadjuvant chemotherapy), MRI showed residual enhancing mass/NMLE in 10 patients. 4 of these patients had initial clip placement done and were treated with wide local excision. In 6 patients mastectomy was performed. All the 10 patients had residual disease on final histopathology. In one patient MRI did not show any evidence of residual disease. The patient had no residual disease on mastectomy specimen.

For detection of axillary nodal metastasis two criteria were assessed. Results showed effacement of fatty hilum had Sn: 65%, Sp:89%, PPV: 86%, NPV: 73% and eccentric cortical thickening without fatty hilum effacement showed Sn: 86%, Sp: 69%, PPV: 73%, NPV: 84%.

**Abbreviations-**

Sn- Sensitivity  
Sp- Specificity  
PPV- Positive predictive value  
NPV- Negative predictive value

Images for this section:
Fig. 1: Case 1. 46 yr old woman presented with palpable lump in her right breast. DCE MRI done for preoperative staging shows intensely enhancing mass lesion in right breast with type 3 kinetics (a,b,c) with similar smaller lesion also seen in left breast showing type 2 plateau kinetics (d,e,f). USG guided biopsy of both lesions revealed Infiltrating Ductal Carcinoma. The patient also had enlarged suspicious nodes in right axilla which were proven metastatic on final histopathology.
Fig. 2: Case 2. Multicentric lesions (a,b) in the left breast of 40 yr old female patient along with left internal mammary (c-arrow) and axillary nodes (d).
Fig. 3: Case 3. Case of Paget's disease of the nipple, proven on nipple biopsy. Preoperative MRI revealed abnormal enhancement in the nipple (a) with multiple nodular areas of enhancement with type 2 and type 3 kinetics in the underlying breast parenchyma, located at a distance more than 2cm from the nipple areola complex (b,c). Ultrasound guided biopsy revealed IDC with DCIS in one of the larger nodules sampled. Patient was treated with mastectomy. This case highlights the role of MRI in treatment planning of Paget's disease.
Fig. 4: Case 4. Patient with palpable axillary nodes and mild nipple retraction. XRAY Mammogram showed few microcalcific foci in lower inner quadrant of the right breast with axillary adenopathy. DCE-MRI showed a large area of clumped nodular NMLE extending from the upper outer quadrant to the lower inner quadrant showing type 2 kinetics. The enhancement was also involving the nipple with its retraction.
**Fig. 5:** Case 5. Post lumpectomy case with positive surgical margins. Post lumpectomy changes seen in upper outer quadrant of right breast on T2W images (a). On post contrast imaging a large residual area of clumped NMLE seen around the lumpectomy cavity (b,c,d,e). Mastectomy done revealed residual DCIS on final histopathology.
Fig. 6: Case 6. Pre (a and b) and Postchemotherapy (c and d) images show reduction in the tumor volume as well as in the size of the axillary lymphnodes. Histopathology revealed (PR) partial tumor response.
Fig. 7: Case 7. Case of Ca Breast with predominant DCIS. No significant change is seen in the area of involvement, DWI and contrast enhancement after 3 cycles of chemotherapy consistent of poor response.
**Fig. 8:** Case 8. 39 yr female patient with palpable lump in right breast along with vague nodularity in the outer half of the breast. DCE MRI shows an oblong spiculated mass lesions in the upper outer quadrant of the right breast (a) with multiple linear and nodular areas of enhancement extending up to the nipple with involvement of the skin of nipple areola complex (b,c,d). Nodular areas were seen extending to the lower outer quadrant of the breast as well. The patient was treated with neoadjuvant chemotherapy followed by surgery.
**Fig. 9:** Case 9. Lesion detected on screening mammography in right breast (a). On MRI, besides the primary lesion, there is linear nodular NMLE extending further laterally (c,d,e). Mastectomy specimen revealed Infiltrating ductal carcinoma with DCIS with invasive lobular carcinoma with LCIS.
**Fig. 10:** Case 10. Spiculated mass lesion in right breast (a), with adjoining node showing cortical thickening with partial effacement of fatty hilum (b). c and d show enlarged node with complete effacement of fatty hilum and mildly irregular margins.
**Fig. 11:** Case 11. MRI in patient with bloody nipple discharge shows a large area of nonmass like enhancement in lower outer quadrant of the left breast (c,e) with type 3 kinetics. Histopathology revealed high grade DCIS.
Conclusion

Our study concluded that MRI has a high sensitivity in detection of breast cancer including the detection of multicentric/multifocal lesions in the same as well as contralateral breast. It also has a high sensitivity in detection of nonmass like enhancement. This is in concordance with various earlier studies. There was a good correlation seen between the size of the primary tumor detected on MRI and the tumor size on final histopathology. Identification of multiple lesions in different quadrants of the breast helps in treatment decisions in which either the patient is treated with mastectomy or with neoadjuvant chemotherapy. However multiple tumors in the same quadrant within 2cm of the primary lesion can be still treated with wide excision with subsequent whole breast radiation as the protocol followed in our hospital’s cancer centre.

Our study showed that nonmass like enhancement in clumped nodular pattern in ductal/segmental or regional distribution has high specificity in detection of DCIS or extensive intraductal component. Linear spicular enhancement and stippled enhancement along with the tumor had low specificity. Multiple areas of nonmass like enhancement in the same or both breasts is also seen in benign breast disease than in malignancy. Identification of these patterns can help in diagnosing the in situ carcinoma with relatively high specificity. Non mass forming DCIS, Infiltrating Lobular Carcinoma and oestrogen receptor negative invasive ductal carcinoma are the malignant lesions which are more likely to have these patterns on MRI(11,12).

In post lumpectomy patients with positive surgical margins and in post NACT patients MRI is a highly sensitive technique to assess for residual disease seen as enhancing mass/foci or residual areas of DCIS seen as clumped nodular NMLE. Patients with no residual disease can be treated with wide excision while those with residual disease are treated according to its extent.

MRI has a definite role in detection of metastatic involvement of axillary lymph nodes. The features with high positive predictive value for malignancy are roundening of the shape, eccentric cortical thickening of > 3mm, effacement of fatty hilum and effacement of fatty hilum. It also identifies enlarged internal mammary and supra clavicular nodes.

Given the above mentioned potential of MRI in evaluation of breast cancer, MRI should be added to the preoperative imaging work-up of breast cancer patients as an aid in surgical and definitive treatment. Breast MRI has a definite potential to reduce the number of surgical procedures to obtain negative margins of resection or to convert patients from planned breast-conservation therapy (BCT) to mastectomy (13,14). It also has been postulated that the detection of additional areas of cancer in the ipsilateral breast on MRI may result in a lower rate of in-breast recurrence following BCT (15).
One of the major limitations of MRI of the breast in breast cancer staging is false-positive enhancement as seen in fibroadenomas, fat necrosis and fibrocystic changes resulting in being results on biopsy on the MRI detected suspicious lesions. This may result in increased cost, patient anxiety and increased rate of mastectomies. Balancing the known pitfalls of breast MRI and its false positives with the clinical goal of accurate assessment of extent of disease is a subject of continued investigation (16-18).

Personal information

References


