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Role of MRI in evaluation of residual tumor burden following neoadjuvant therapy in patients with breast cancer

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ABSTRACT

Objectives: To correlate the accuracy of MRI with pathology in assessing the response of neoadjuvant chemotherapy (NACT) in patients with breast cancer and assessment of factors affecting the accuracy of MRI.

Materials and Methods: Twenty-five patients (with 33 tumors) having biopsy-proven breast cancer were included to undergo dynamic contrast-enhanced MRI, mammography, and ultrasound prior to NACT and after completion of NACT before undergoing surgery. Tumor morphological features and receptor subtypes were compared between complete and non-complete responders, and the accuracy of MRI in estimating residual disease was assessed with respect to histopathology. The performance of MRI was also compared with ultrasound and mammography, wherever feasible.

Results: The sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracy of MRI for predicting pathological complete response (pCR) were 100%, 70%, 83.3%, 100%, and 88%, respectively, which were significantly better ($p = 0.02$) in the triple-negative subtype. Size measured in preoperative MRI had a significant positive correlation with pathological size ($r = 0.76$, $p < 0.001$) with the lowest mean size difference in triple negative subtype and in tumors showing a concentric pattern of shrinkage. Among the baseline morphological features on MRI, significant difference was seen in the shape ($p = 0.02$) and enhancement ($p = 0.036$) of the tumors between complete and non-complete responders. Also, MRI had the highest overall accuracy in predicting pCR and residual tumor size as compared to mammography and ultrasound.

Conclusion: MRI is a sensitive modality for predicting pCR and residual tumor size with better accuracy for triple-negative tumors as compared to other subtypes.

Keywords: Breast MRI, Breast cancer, Neoadjuvant chemotherapy, Response assessment

INTRODUCTION

Breast cancer is a heterogeneous disease with different subtypes and different risks for progression and recurrence and with variable treatment outcome.[1] The incidence of breast cancer has been increasing in the past few decades, and it has now become the most common cancer in women worldwide, with a lifetime risk of 12.4%.[2]

Breast cancer management requires a multipronged approach. Neoadjuvant chemotherapy (NACT) is primarily administered in the preoperative setting with the main goal of downstaging tumors and eradicating micrometastases. Apart from locally advanced breast cancer, NACT is

Table 1: Imaging protocol used for dynamic post-contrast MRI.

Sr. No.	Sequence	Plane	TR (ms)	TE (ms)	Section thickness	Flip angle	Additional
1	T2	Axial	4,437	60	3 mm	90	
2	STIR	Axial	4,506	60	3 mm	120	IR-150 ms
3	Dynamic post-contrast T1 (THRIVE)	Axial	7.4	3.6	3 mm	10	Using 0.1 mmol/kg of gadolinium dimenglumine
4	SSh (single shot) DWI	Axial	13,846	71	3 mm	90	b values of 0, 500, and 1000

STIR: Short tau inversion recovery, THRIVE: T1 weighted high resolution isotropic volume examination, DWI: Diffusion weighted imaging, MRI: Magnetic resonance imaging, TR: Repetition time, TE: Echo time, IR: Inversion recovery time.

increasingly being used in early-stage cancer to facilitate better outcomes in breast conservation surgery (BCS).[3] It aims at downstaging the tumor prior to surgery and improving long-term disease-free survival.[4,5]

The decision to opt for NACT is driven more by tumor biology rather than tumor size and is tailored according to hormone receptor status.[6] According to hormone receptor status, various breast cancer subtypes are:

- Luminal A (ER PR+, HER2−)
- Luminal B (ER+, PR+/−, HER2+/−)
- HER2 enriched (ER PR−, HER2+)
- Basal like (triple negative).

Neoadjuvant therapy may decrease the tumor load and make BCS more feasible; however, because of the variable patient response to NACT, an accurate assessment of the residual disease is imperative for surgical planning. Patients who experience pathologic complete response after NACT have significantly higher survival rates than the patients with residual tumor.[7] Therefore, post-NACT tumor assessment can help in both treatment planning and prognosticating a patient.[8]

Physical examination has been historically used to assess response; however, it has low accuracy of 57% with limited use in tumors less than 2 cm in size and dense breasts.[9] Mammography and ultrasound have variable accuracy due to the development of fibrosis and fragmentation of mass. Magnetic resonance imaging (MRI) has been shown to be superior to other imaging modalities in assessing residual disease and response to NACT with a sensitivity and specificity of 86–92% and 60–89%.[10,11] However, the accuracy of MRI has been shown to be variable depending on the molecular subtype of cancer and tumor phenotype.[6,12]

This prospective study was planned to correlate MRI with pathology in assessing response to NACT in patients with breast cancer. The performance of MRI was also compared with ultrasonography and mammography.

MATERIALS AND METHODS

The study was conducted prospectively after institutional ethical clearance and duly informed consent, over 2 years on consecutive women planned to receive NACT for histopathologically proven breast cancer followed by surgery. Patients were evaluated for mass size, number, location, fixity to the chest wall, skin involvement, axillary lymph node status, etc.

Image Acquisition and Analysis

1. Digital mammographic acquisition was done on the machine Selenia dimensions (Hologic, Germany), and standard mediolateral oblique and cranio-caudal views were taken for both breasts.
2. Ultrasonography was done on the Aixplorer ultrasound system (Supersonic Imagine, France) using high-frequency (7–12 MHz) linear probe.
3. Dynamic contrast-enhanced magnetic resonance imaging (DCE-MRI) was performed using a dedicated breast radiofrequency coil on a 1.5 Tesla MRI scanner (Achieva, Philips).

The imaging protocol for DCE breast MRI has been provided in Table 1.

The first post-contrast acquisition was started during the saline flush, and then five subsequent post-contrast images were acquired at 77-second interval with a field of view (FOV) sufficient to cover the entire breasts. Subtracted post-contrast images and maximum intensity projection (MIP) images were obtained from the dynamic post-contrast images.

Mammographic Analysis

The longest dimensions of the tumor after NACT were assessed on both craniocaudal and mediolateral oblique views, and the longest dimension of the two was taken as the residual tumor size on mammography. Complete disappearance of mass/asymmetric density present in region

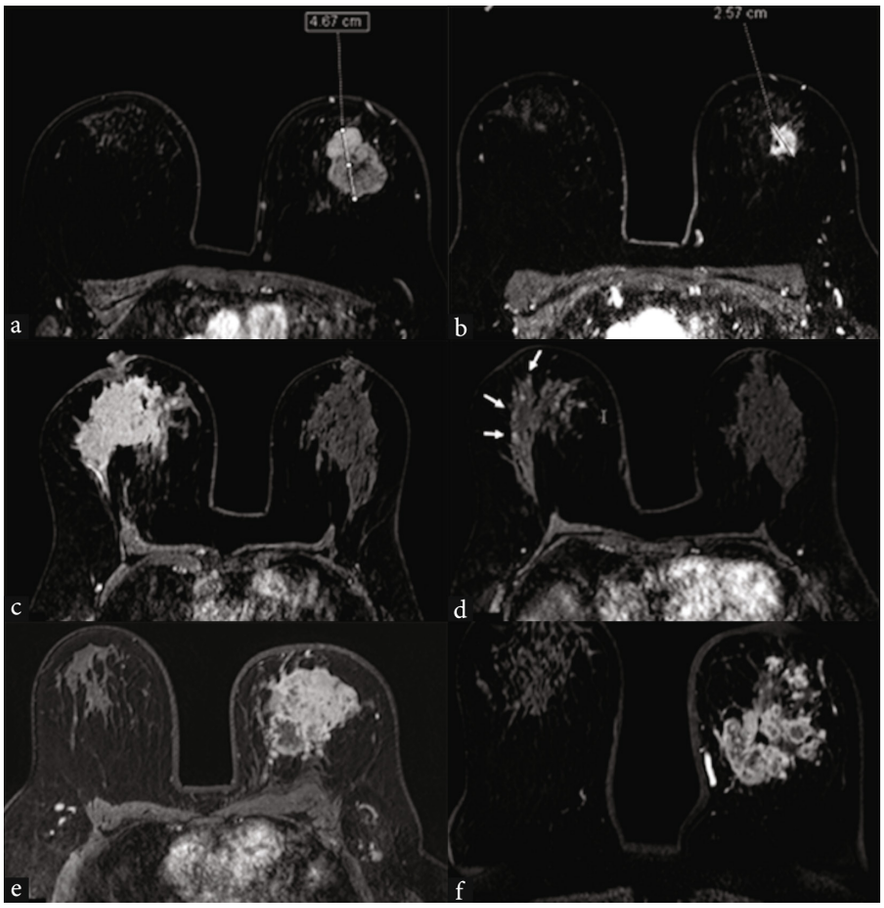

Figure 1: Post chemotherapy shrinkage patterns (a) Axial post contrast image before neoadjuvant therapy shows mass in left breast measuring 4.6cm (dashed line). (b) Post neoadjuvant chemotherapy axial image shows concentric shrinkage of mass. The longest dimension of residual mass is measured to be 2.5cm (dashed line). (c) Axial post contrast image showing enhancing mass in right breast. (d) Post chemotherapy image shows fragmented pattern of shrinkage with mass breaking down into multiple small enhancing lesions (white arrows). (e) Axial post contrast pre neoadjuvant therapy image of a 45 year old female shows heterogenously enhancing mass in left breast. (f) Post neoadjuvant chemotherapy scan showing mixed pattern of shrinkage with mass with posterior part of the mass showing concentric shrinkage with rest of the mass breaking down into smaller fragments.

of pre-NACT mammographic abnormality was interpreted as a complete response on post-NACT mammogram.

Ultrasound Analysis

The longest diameter of the mass was measured on both pre- and post- NACT studies. Complete disappearance of the mass on post-chemotherapy scan was interpreted as a complete response, whereas the presence of residual mass was considered as a non-complete response.

MRI Analysis

Maximum cross-sectional diameter of the mass was measured on the post-contrast images in both pre- and post-NACT MRI. Any mass showing enhancement in early or late post-contrast images in the region of the mass seen in pre-NACT MRI was taken as a residual tumor. Kinetic curve and peak enhancement were measured by drawing multiple regions of interest (ROI) over the most enhancing regions of the mass seen in color overlay images as red areas. ROI showing the worst curve was used for interpretation.

Mean apparent diffusion coefficient (ADC) was measured by drawing five ROIs on the largest enhancing areas of the mass in the post-contrast images and copying the ROI onto the ADC image. In addition to the above characteristics, shrinkage pattern was assessed for all residual masses and was defined as concentric for masses showing concentric

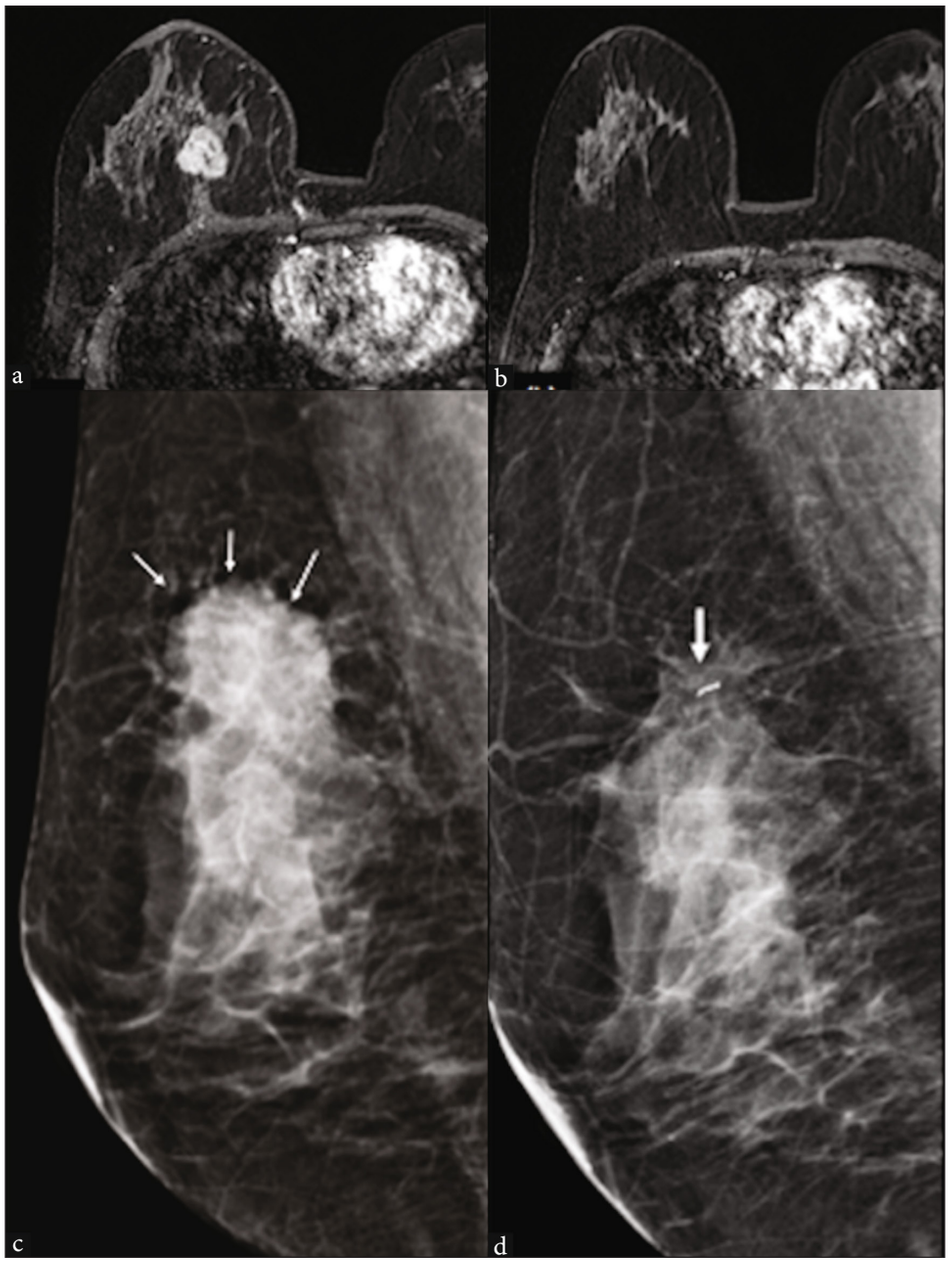

Figure 2: Infiltrative ductal carcinoma showing complete response: (a) Axial post contrast image showing an enhancing mass in the left breast with (b) complete disappearance of the mass post 8 cycles on neoadjuvant chemotherapy. (c) Mammogram (MLO view) of the same patient showing irregular hyperdense mass in right breast (white arrows) with no residual density on mammogram post neoadjuvant chemotherapy (d) with clip in situ (white arrow). MLO: Mediolateral oblique view.

shrinkage; scattered for masses which broke down into multiple smaller lesions; and mixed for masses in which some part showed concentric shrinkage but the rest of the mass showed breakdown [Figure 1].

The patients were categorized as either complete responders [Figure 2] or non-complete responders [Figure 3] on the basis of the absence or presence of any residual tumor, respectively, on the second MRI. The longest diameter of the residual mass was measured in all cases and compared with the longest diameter measured on pathological analysis of the surgical specimen.

In addition, morphological features observed on the pre-treatment MRI were compared between complete responders and non-complete responders as stated on post-operative pathology.

Table 2: Comparison of baseline morphological MRI characteristics of tumors between complete and non-complete responders (n = 25).

Variable		CR	NCR	p-value
Fibroglandular tissue	Dense	5 (50)	5 (50)	0.442
	Non-dense	5 (33.33)	10 (66.67	
Background enhancement	Mild/minimal	9 (39.13)	14 (60.87)	0.99
	Moderate/marked	1 (50)	1 (50)	
Non-enhancing findings	Present	3 (50)	3 (50)	0.653
	Absent	7 (36.84)	12 (63.12)	
Side	Right	7 (50)	7(50)	0.414
	Left	3 (27.27)	8 (72.73)	
Type	Mass	7 (46.67)	8 (53.33)	0.678
	Mass with NME	3 (30)	7 (70)	
Number	Single	9 (42.9)	12 (57.1)	0.626
	Multiple	1 (25)	3 (75)	
Margins	Circumscribed	4 (66.67)	2 (33.33)	0.239
	Irregular	1 (16.67)	5(83.33)	
	Spiculated	5 (38.46)	8 (61.54)	
Internal T2 hyperintensity	Present	5 (41.67)	7 (58.33)	0.99
	Absent	5 (38.46)	8 (61.54)	
Shape	**Oval**	**4 (57.14)**	**3 (42.86)**	**0.02**
	Round	3 (100)	0 (0)	
	Irregular	3 (20)	12 (80)	
Enhancement	**Homogeneous**	**4 (80)**	**1 (20)**	**0.036**
	Heterogeneous	4 (23.53)	13 (76.47)	
	Rim	2 (66.67)	1 (33.33)	
Peritumoral edema	Present	9 (37.50)	15 (62.50)	0.4
	Absent	1 (100)	0 (0)	
Lymph nodes	Absent	2 (50)	2 (50)	0.65
	Present	8 (38.1)	13 (61.9)	

CR: Complete responder, NCR: Non complete responder, NME: Non mass enhancement, MRI: Magnetic resonance imaging. Bold values indicate statistically significant p-values.

Images of patients were analyzed by two experienced radiologists according to the American College of Radiology Breast Imaging Reporting and Data System (ACR BIRADS) lexicon, fifth edition, for mammography, sonography, and MRI, both before commencement of chemotherapy and pre-operatively in an independent manner.

NACT Regimen

Each patient was subjected to 6–8 cycles of NACT, each cycle lasting for 21 days. Drugs used were 5-fluoro-uracil, epirubicin, and cyclophosphamide (FEC) with or without taxanes and trastuzumab. An MRI-compatible metallic marker clip made of nitinol was inserted in solitary masses which did not show microcalcifications on mammogram prior to the start of NACT for lesion localization.

Histopathological Analysis

All patients underwent surgery after NACT in the form of either BCS or modified radical mastectomy (MRM). The resected surgical specimen was fixed in 10% formalin and prepared as 5 mm slices. Any residual tumor, if present, was measured along its longest diameter. If no evident tumor was found, the clip marker (if present) was identified, and slides were prepared from the region adjacent to it. Assessment of pathological response was done in accordance with

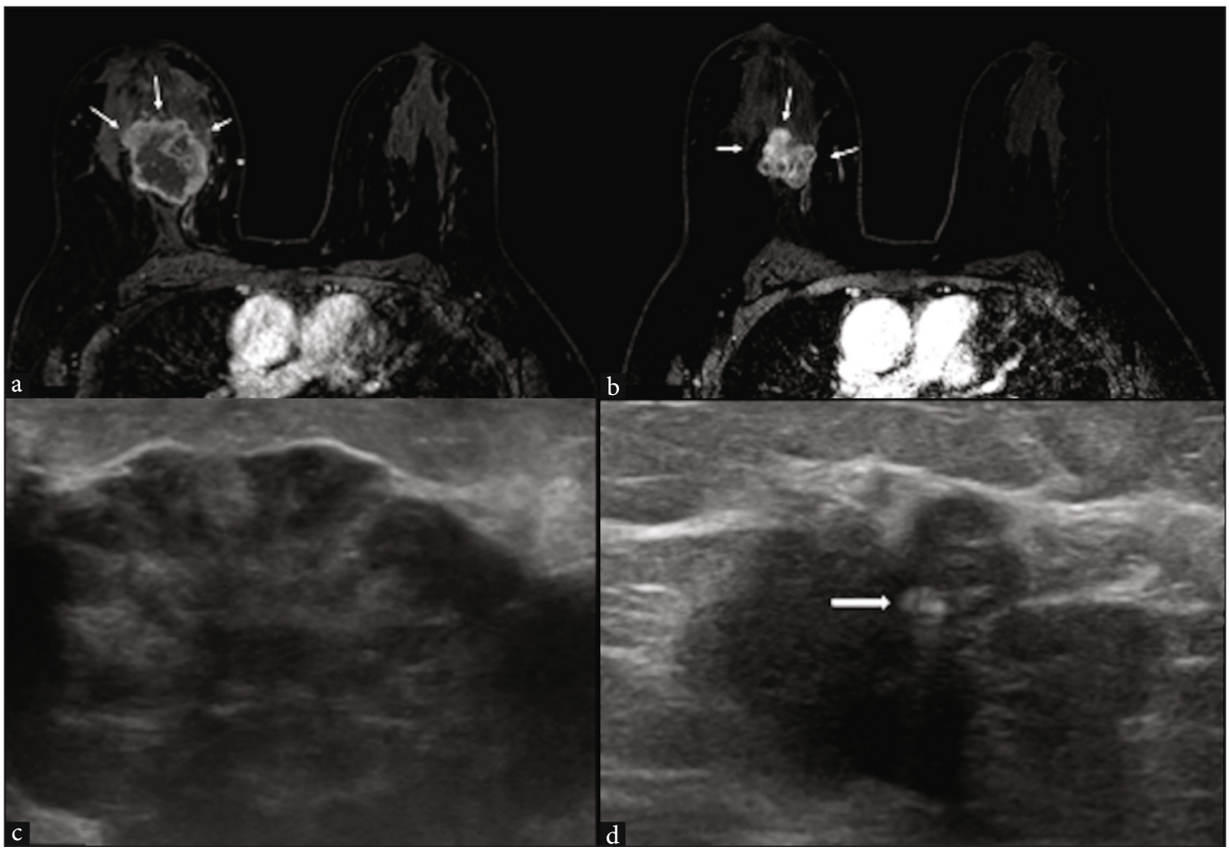

Figure 3: Infiltrative ductal carcinoma showing non complete response. (a) Axial post contrast image showing a heterogenously enhancing mass in the right breast (white arrows). (b) Post 8 cycles of neoadjuvant chemotherapy the mass has reduced in size, however residual mass is seen (white arrows). (c) Pre chemotherapy ultrasound images of the same patient showing irregular hypoechoic mass in right breast. (d) Residual hypoechoic mass seen post neoadjuvant chemotherapy with echogenic clip within the mass (white arrow).

Miller and Payne criteria.[5] Grade 1–4 was categorized as a pathological non-complete response (pPR) and grade 5 as a pathological complete response (pCR).

Statistical Analysis

Statistical data were analyzed by using the Statistical Package for Social Sciences (SPSS) version 23. Statistical comparisons of various MRI, mammography, and ultrasound categorical parameters were performed between the complete and non-complete responders using chi-square and Fisher's exact test. Comparison of quantitative MRI parameters was done between complete and non-complete responders using a two-sample t-test. The value of significance (*p*-value) was calculated using the Mann-Whitney test in the case of skewed data. Comparison of residual tumor size measured by imaging was done with pathological size using a paired sample t-test and Wilcoxon signed rank test, and correlation coefficients were calculated. A *p*-value of less than 0.05 was considered significant.

RESULTS

Forty-seven patients with biopsy-proven breast cancer were enrolled during the study duration who were planned to receive NACT followed by surgery and underwent pre-NACT imaging. Out of these, 3 patients discontinued chemotherapy before its completion due to toxicity and poor general condition, 5 patients died while on chemotherapy, and 14 patients did not undergo surgery after NACT and were lost to follow-up. Subsequently, 25 patients were finally analyzed in the study who completed 6–8 cycles of NACT and underwent post-NACT MRI followed by surgery.

Twenty out of 25 subjects also underwent post-chemotherapy mammograms and ultrasonography. 21 patients out of 25 had a single mass, whereas 4 patients had multiple masses in the same breast. Hence, 25 patients had 33 tumors. Histological subtype was invasive ductal carcinoma in all patients.

The majority of patients were triple negative (12/25). Three patients (12%) had the luminal A hormonal subtype, six patients (24%) had luminal B cancer, and four patients (16%) had HER2-enriched subtype.

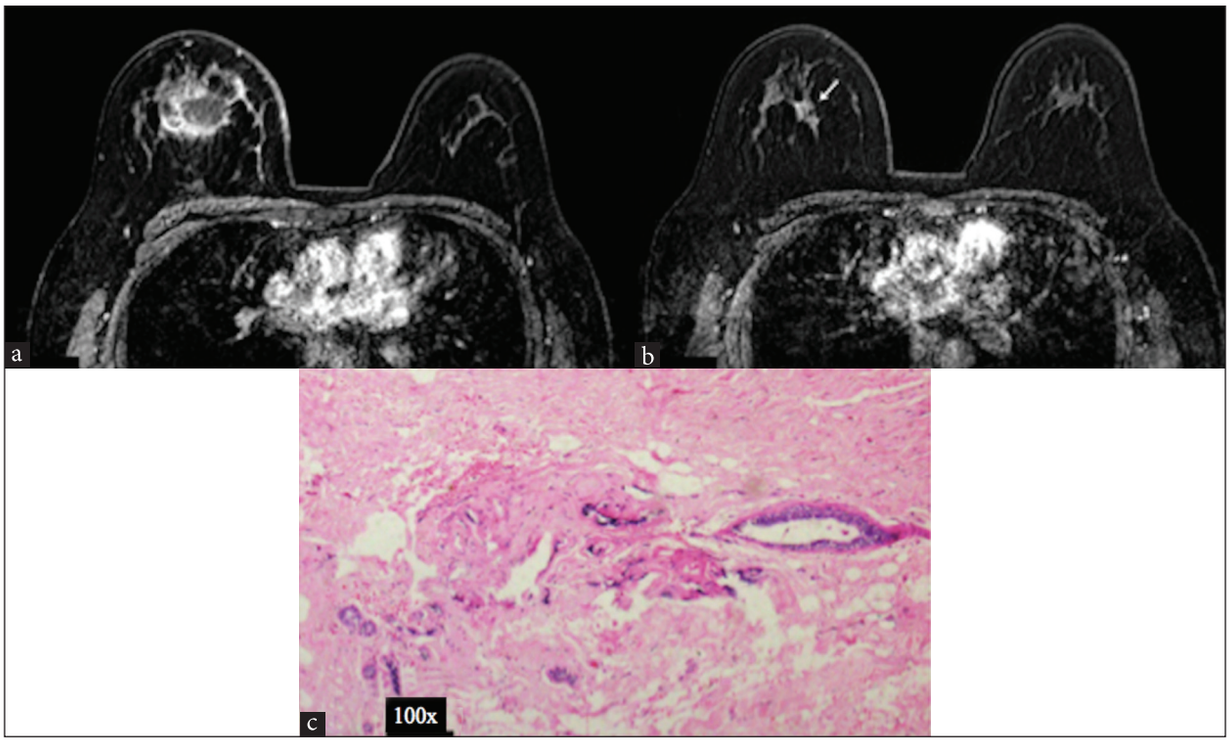

Figure 4: (a) Baseline MRI showing malignant mass in the right breast. (b) Post NACT MRI of the same patient showing residual enhancing tissue (white arrow) in the tumor bed. (c) Histopathology image of the same patient showing complete disappearance of tumor cells with residual fibro vascular stroma suggestive of false positive case. MRI: Magnetic resonance imaging, NACT: Neoadjuvant chemotherapy.

Out of these 25 patients, 12 underwent BCS, and the remaining 13 patients underwent MRM.

On analysis of surgical specimen, 12 patients out of 25 were Miller Payne grade 5, and 13 were grade 1–4.

Comparison of Baseline Morphological and Quantitative MRI Characters between Complete and Non-Complete Responders

A significant difference (p = 0.02) was seen in the shape of the tumors between complete and non-complete responders. Oval (4/10) and round shapes (3/10) were more commonly seen in complete responders, whereas irregular shape was more common in non-complete responders (12/15). Similarly, homogeneous enhancement was more common in complete responders with a statistically significant difference (p = 0.036) [Table 2].

Mean initial size of tumor, peak enhancement, and mean ADC of tumors were similar in complete and non-complete responders with no statistically significant difference.

Prediction of pCR by Post-NACT MRI

MRI predicted complete response in 7 (28%) patients and non-complete response in 18 (72%) patients. Whereas pCR was observed in 10 (40%) patients and pPR in 15 (60%) patients. Three false positive cases showed residual tumor on MRI, but no invasive carcinoma was found on post-op histopathology [Figure 4]. The sensitivity, specificity, positive likelihood ratio, negative likelihood ratio, accuracy, positive predictive

Table 3: Diagnostic performance of MRI in relation to hormonal subtype.

Subtype		pNCR	pCR	*p*-value
Luminal A	iNCR	2	1	
	iCR	0	0	
Luminal B	iNCR	5	0	
	iCR	0	1	0.167
TNBC	iNCR	5	2	
	iCR	0	5	0.028
HER2 E	iNCR	3	0	
	iCR	0	1	0.25

TNBC: Triple negative breast cancer, pNCR: Pathological non complete response, pCR: Pathological complete response, iNCR: Imaging non complete response, iCR: Imaging complete response, HER2 E: Human epidermal growth factor receptor 2 enriched, MRI: Magnetic resonance imaging.

Table 4: Comparison of diagnostic performance of MRI, ultrasound and mammography.

Variable	MRI (95% CI)	Mammogram (95% CI)	USG (95% CI)
Sensitivity	100 (73.5–100)	83.3 (51.5–97.9)	100 (73.5–100)
Specificity	87.5 (47.3–99.6)	62.5 (24.4–91.4)	62.5 (24.4–91.4)
Positive likelihood ratio	8 (1.28-50)	2.22 (0.8–5.6)	2.67 (1.09–6.52)
Negative likelihood ratio	0	0.27 (0.07–1.05)	0
Accuracy	95 (75.1–99.8)	75 (50.9–96.3)	85 (62.1–96.7)
PPV	92 (65.7–98.6)	76.9 (56.8–89.4)	80 (62.05–90.7)
NPV	100	71.4 (38.7–90.8)	100

PPV: Positive predictive value, NPV: Negative predictive value, MRI: Magnetic resonance imaging, CI: Confidence interval, USG: Ultrasonography.

Table 5: Comparison of size measured on imaging and pathology (n = 23).

Modality	Size	Size path	p-value	DIFF	Corr Coeff (p-value)
Mammography	1.574 ± 1.77	1.83 ± 2.05	0.52	−0.256 (−1.06, 0.57)	0.53 (0.03)
USG	1.565 ± 1.62	1.83 ± 2.05	0.32	−0.265 (−0.86 ,0.33	0.73 (<0.001)
MRI	1.913 ± 2.15	1.83 ± 2.06	0.97	0.08 (−0.6, 0.76)	0.74 (<0.001)

DIFF: Difference, Corr Coeff: Correlation coefficient, USG: Ultrasonography, MRI: Magnetic resonance imaging.

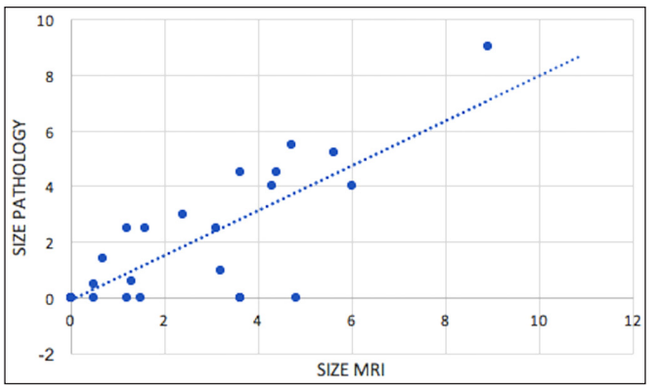

Figure 5: Scatter plot of residual tumor size measured on MRI and pathology (n = 25). MRI: Magnetic resonance imaging.

value (PPV), and negative predictive value (NPV) of MRI in predicting pCR were 100, 70, 3.33, 0, 88, 83.3, and 100, respectively.

In relation to hormonal subtype, MRI more accurately predicted pCR in triple-negative tumors as compared to other subtypes with a statistically significant difference (p = 0.028) [Table 3].

Prediction of Size of Residual Tumor Mass By MRI

Mean residual tumor size predicted by MRI was 2.04 cm, whereas mean tumor size observed on pathology was 1.65 cm. The mean difference between the two measurements was 0.38 cm. Size measured on MRI had a significant positive correlation with size measured on post-operative histopathology (r = 0.76, p < 0.001) [Figure 5]. MRI also overestimated the disease in the majority of the cases, likely due to reactive inflammation caused by tumor response and subsequent healing, surrounding sclerosis and necrosis, and accompanying ductal carcinoma in situ (DCIS).[3]

Prediction of Size of Residual Tumor According to Hormone Status

The mean size difference between MRI tumor size and post-op pathological tumor size was maximum in the luminal A subtype (2.6 cm) and minimum in the triple-negative subtype (0.12 cm). However, no significant difference between radiological and pathological size was seen in any subgroup.

Prediction of Pathological Size According to Shrinkage Pattern

The mean tumor size measured on MRI and post-operative histopathology was 2.57 ± 1.64 cm and 2.159 ± 2.01 cm for tumors showing concentric shrinkage, whereas it was 5.3 ± 3.06 cm and 4 ± 3.55 cm for tumors showing a fragmented/mixed pattern of shrinkage, respectively. The difference between the mean size measured by MRI and post-op pathology was more in tumors having fragmented or mixed shrinkage patterns (1.3 cm) as compared to tumors showing concentric shrinkage (0.41 cm). However, no

statistically significant difference was found between MRI and pathological size in either category.

Comparison Between MRI, Mammogram and Usg for Predicting pCR

Post-chemotherapy mammograms and USGs were done in 20 patients. In this cohort of patients, the findings of pathological response were compared to imaging findings on mammography, ultrasound, and MRI. Eight patients had a pCR out of 20 patients, and 12 had a non-complete response.

Mammogram showed specificity and sensitivity of 62.5% and 83.3%. NPV%, PPV%, and overall accuracy of mammograms were 71.4%, 76.9%, and 75%, respectively. Whereas overall sensitivity, specificity, NPV, PPV, and accuracy of ultrasound were 100%, 62.5%, 100%, 80%, and 85%, respectively. However, among the three imaging modalities, MRI had the highest overall accuracy in predicting pCR [Table 4].

In comparison of size measured by imaging and size measured on pathology, the minimum difference was seen for size measured by MRI (0.08 cm) and the maximum difference was seen for USG (−0.265 cm), which was marginally more than mammogram (−0.256 cm) [Table 5]. Linear positive correlation was seen with all three imaging modalities, which was maximum for MRI ($r = 0.74$).

DISCUSSION

NACT is an important therapeutic option which is increasingly being used not only to reduce the disease burden in advanced disease but also to reduce the size of tumors in early-stage breast cancer to improve the possibility of BCS and get better cosmetic outcomes following the surgery.

pCR in breast cancer varies according to the hormonal status of the tumour. Tumors which are negative for hormone receptors, i.e., triple negative and positive for HER2 receptors, are usually aggressive with rapid proliferation as compared to hormone receptor-positive cancers and are thus more susceptible to antiproliferative and antiangiogenic effects of chemotherapeutic agents.[13] Therefore, pCR is more common in these subgroups.[14]

Comparison between Complete and Non-complete Responders

Baseline MRI Characteristics

In our study, among the baseline morphologic features on MRI, a significant difference was seen in the shape and enhancement pattern of complete and non-complete responders, with round and oval shapes and homogenous enhancement being more common in complete responders, whereas irregular shape was more common in non-complete responders. Similar results were observed by Eom *et al.* in their study of 73 triple-negative breast cancer patients, where irregular shape and heterogeneous enhancement ware significantly more common in non-complete responders.[15] Our study has a high percentage of triple-negative cases (48%), which might have contributed to similar results.

No significant difference was seen in mean ADC and pretreatment size of tumor between complete and non-complete responders. This was similar to results obtained by Liu *et al.*[13] and Bufi *et al.*[16] in their studies. However, they found a significant difference in the pre-treatment ADC of complete responders and non-complete responders in the triple-negative subgroup of patients, which was not observed in our study.

Performance of MRI in Predicting Pathological Response

In our study, 10/25 (40%) of patients achieved a pCR after NACT. This was higher as compared to previous studies.[15,17] This could be due to a higher percentage of triple-negative (48%) and HER2-positive (16%) patients in our study, as pCR is more common in these subgroups.[14]

The sensitivity of MRI for predicting pCR in our study was 100%, specificity was 70%, NPV was 100%, and the overall accuracy was 88%. Previous meta-analyses by Marinovich *et al.*[11] and Cheng *et al.*[18] showed that MRI had good performance in predicting pCR, especially when the absence of invasive cancer with or without DCIS was taken as pCR.[11] A similar definition of pCR (absence of invasive cancer with or without DCIS) was used in our study. Gonzalez-Cortijo *et al.*, using the same definition, also found MRI to have 100% NPV in detecting pCR to NACT in breast cancer.[19]

Areas of fibrosis with giant cell reaction were seen on histopathological analysis of false-positive cases, which could be because of reactive and inflammatory changes induced by chemotherapy resulting in false enhancement in the region of the tumor bed on MRI. Also, the interval between second MRI and surgery in these three patients was 46, 58, and 74 days, which was more than overall mean of 28 days observed in the entire cohort. Therefore, we may speculate that enhancement due to early fibrosis and inflammation might have been reduced if the MRI had been done closer to the time of surgery.

Among the hormonal subtypes, the accuracy of MRI in predicting pCR was significantly greater ($p = 0.028$) in triple-negative patients as compared to other subtypes. Similar results were obtained by Eun *et al.*[20] in their study of 221 patients.

Performance of MRI in Predicting Residual Tumor Size

Positive correlation ($r = 0.76$) was observed between mean size predicted by MRI and histopathology with a mean

difference of 0.38 cm. MRI overestimated the size in the majority of cases, which could be due to reasons like reactive inflammation caused by response and healing, surrounding sclerosis and necrosis, multiple scattered lesions, and the presence of accompanying DCIS. In their study of 87 patients, Williams *et al*. obtained a correlation coefficient of 0.78 between post-NACT size of MRI and pathology with a mean difference of 0.6 cm, which was similar to that obtained in our study.[2] In another similar study conducted by Rezkallah *et al*., a strong correlation (r = 0.859, p = 0.01) was observed between residual tumor calculated by MRI and histopathology.[21] Also, the lowest mean size difference was seen in triple-negative tumors in our study, similar to the study conducted by Bouzón *et al*.[22] This can be attributed to the unifocal presentation, the concentric pattern of shrinkage, and the absence of surrounding nonmass enhancement, which is more commonly associated with triple-negative tumors as compared to hormone-positive tumors.[15]

The mean discrepancy between the size of MRI and histopathology in our study was more in tumors showing fragmented or mixed patterns of shrinkage (1.3 cm) as compared to tumors showing concentric shrinkage (0.4 cm); however, the difference was not statistically significant. This was due to better observation of margins of tumors that showed concentric shrinkage. On the contrary, tumors that showed a fragmented shrinkage were split into a number of small nodules with areas of non-mass enhancement. Histopathology in tumors showing fragmented pattern of shrinkage showed surrounding by foci of DCIS in two cases and areas of fibrosis with reactive inflammation in one case, which could not be differentiated on MRI, leading to overestimation of size on imaging.

Comparison between MRI, Mammogram and Ultrasound

20 patients in our study underwent mammograms and ultrasounds in addition to MRI. In comparison between MRI, mammogram, and ultrasound in this cohort of 20 patients, the highest sensitivity, specificity, PPV, NPV, and accuracy for predicting pCR was seen with MRI, followed by ultrasound and mammography. Similarly, the mean difference in size measured by pathology and imaging was least in MRI. Also, correlation between the sizes on imaging and histopathology was highest for MRI (r = 0.74), closely followed by ultrasound (r = 0.73) and least for mammogram (r = 0.53). This is similar to results seen in previous studies by Shin *et al*.[23] and Scheel *et al*.[24]

The accuracy of mammograms is limited due to the limited ability to visualize the margins in dense breast, and due to the superimposition of tissues in 2D images. Also, residual fibrosis can be seen as asymmetrical density, which is difficult to differentiate from residual tumor. Further, the difficulty increases in case the tumor shrinks and fragments into multiple small foci.

Ultrasound also has limited ability to differentiate residual fibrosis from viable tumor, leading to false positive results. Also, tumors with a fragmented pattern of shrinkage which have tiny foci of invasive carcinoma may not be seen separately on ultrasound. MRI provides three-dimensional analysis of the tumor with ability to pick up small enhancing lesions. Therefore, it allows better appreciation of the size of residual disease.

Limitations of Study

The majority of patients in our study belonged to the triple-negative subgroup; therefore, the accuracy of MRI in predicting complete response and residual tumor size in each hormonal subcategory could not be calculated. All participants had infiltrating ductal carcinoma, so tumor histology causing variation in chemotherapy response could not be assessed. In the study, the operative specimen was sectioned into 5 mm slices. If these sections did not show residual tumor, no further sectioning was performed. Therefore, presence of smaller residual tumors might have been missed.

CONCLUSION

MRI is a sensitive modality for estimation of post-NACT residual tumor size with a good correlation (0.76) between the size measured by MRI and pathology. It is also a useful modality for estimation of pCR in breast cancer post-NACT with high sensitivity, specificity, and accuracy. Hormonal subtype of cancer affects the accuracy of MRI for predicting pCR and residual tumor size, which is better for triple-negative tumors as compared to other subtypes.

As compared to mammography and ultrasound, MRI has higher accuracy in predicting pCR as well as higher correlation with the pathological size in the surgical specimen.

Ethical approval

The research/study approved by the Institutional Review Board at All India Institute of Medical Sciences, number 331/29.06.2016, dated 29/06/2016.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

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Conflicts of interest

There are no conflicts of interest.

Use of artificial intelligence (AI)-assisted technology for manuscript preparation

The authors confirm that there was no use of artificial intelligence (AI)-assisted technology for assisting in the writing or editing of the manuscript and no images were manipulated using AI.

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