



IS ROUTINE MRI AN ALTERNATE TO BREAST MRI IN RESPONSE ASSESSMENT AFTER NEOADJUVANT CHEMOTHERAPY IN LOCALLY ADVANCED BREAST CANCER

Oncology

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ABSTRACT

In recent days the use of Breast coil MRI is on increasing trend, even though it is not of much useful in early detection and disease mapping, it is widely used in screening in High risk cases and recently in response assessment evaluation in locally advanced breast cancer patients. **Materials And Methods:** We evaluated 34 patients with locally advanced breast cancer with routine MRI which was taken during the time of initial presentation and after the completion of neoadjuvant chemotherapy and analyzed those with standard histopathological examination. **Results:** In 34 patients we did modified radical mastectomy for 32 patients and in those patients the MRI prediction rate is about 34.3 percent. Only 11 patients final histopathological examination correlated with the findings of response assessment MRI. **Conclusion:** The use of routine MRI in assessing the response evaluation after the neoadjuvant chemotherapy lacks to reproduce the results of breast MRI and it is not recommended to go for routine MRI instead of breast MRI for response assessment in LABC.

KEYWORDS

INTRODUCTION:

In 2020, 2.3 million women were diagnosed to have carcinoma breast and about 685000 patients were died due to carcinoma breast worldwide. By the end last decade, there were 7.8 million women alive whom diagnosed to have carcinoma breast(1). Recent studies have shown that overall burden of carcinoma breast will cross more than 2 million by the end of 2030[2]. In India, gynecological cancers, including breast cancer, accounts for more than 50 percent of all cancers in women. Around 25.4% of these patients belongs to carcinoma breast (3). For early stage carcinoma breast surgery in the form of mastectomy / breast conservative surgery followed by with or without chemotherapy and radiotherapy is the treatment of choice. For locally advanced disease, neoadjuvant chemotherapy followed by surgery is the standard of care (4).

In neoadjuvant chemotherapy the response assessment after chemotherapy can be determined by clinically as well as by radiologically by means mammogram ultrasound and breast MRI, more accurately by breast MRI (5 to 7). With the help of breast MRI, the response assessment for neoadjuvant chemotherapy can be measured using size and shrinkage patterns of tumor. Based on RECIST 1.1 criteria the response of tumor can be determined.

Breast MRI (breast coil MRI) is considered as best imaging modality for assessing the malignant breast lesions.(8) In this study we are going to evaluate the effectiveness of the routine MRI (without breast coil) in assessing the response rate after a neoadjuvant chemotherapy, to determine whether in a peripheral setup can we use a routine MRI Instead of standard breast MRI for response assessment.

MATERIALS AND METHODS

All cases of locally advanced carcinoma breast satisfying the inclusion criteria are included in the study. Those patients are evaluated using routine blood investigation, digital mammogram, MRI breast, core needle biopsy and metastatic work up. After complete evaluation patients are planned for neoadjuvant chemotherapy. After completion of four cycles of chemotherapy patients are subjected to an MRI for response assessment. If operable, those patients are planned for surgery. If inoperable, those patients are subjected to another four cycles of chemotherapy. After completion of 8 cycles, those patients are subjected to another MRI. All patients are planned for modified radical mastectomy. After surgery the size of the tumor is measured by standard histopathological examination and this is compared with the response MRI to determine the response assessment nature of MRI.

Design of the study:

All locally advanced (T3, T4/N1-3) breast cancer patients who are all planned for neoadjuvant chemotherapy who got admitted from February 2021 to June 2022 are enrolled in this study. Totally during

that period 34 patients are enrolled in the study. Informed written consent were obtained from those patients.

Exclusion Criteria

1) Patient with contraindication for MRI (cochlear implants, pacemakers bone plates and screws) 2) Patients who all are not fit for chemotherapy 3) Bilateral breast cancer

This prospective study included 34 patients of locally advanced Breast cancer patients who are all subjected NACT.

Period of study – 18 months.

DATA COLLECTION

Out of 34 patients who enrolled in the study 18 patients had partial response and 14 patients had complete response. One patient defaulted treatment. One patient died (not directly related to cancer). In the 34 patients 14 patients belong to T4b N1 disease, 8 patients were under T4b N2a disease. 8 patients belong to T3N1 and 2 patients with T3N0 disease, 2 patients with T2N1.

Among these patients 10 patients belongs to ER PR HER2 positive category, 6 patients in triple negative, 9 patients showed ER PR positive with HER2 negative and 7 patients in HER2 enriched category.

RESULTS

In this 32 patients, whom we did modified radical mastectomy 11 patients showed pathological correlation of size in final histopathological report as that of the response assessment MRI (+/- 3mm). In this study the response assessment predicting rate of routine MRI is about 34.3 percent. In Axilla, out of 32 patients 10 patients showed nodal metastasis in final histopathological examination. In those 10 patients response assessment MRI showed nodes in 5 patients.

Table 1

TOTAL NUMBER OF PATIENTS	34
PATIENTS UNDERWENT MRM	32
PATHOLOGICAL CORRELATION WITH MRI	11
PATHOLOGICALLY NOT CORRELATED WITH MRI	21

Hormonal Status: Table 2

ER PR POSITIVE HER 2 POSITIVE	10
ER PR POSITIVE HER 2 NEGATIVE	9
ER PR NEGATIVE HER2 ENRICHED	8
TRIPLE NEGATIVE BREAST CANCER	6

Nodal Response : Table 3

TOTAL NUMBER OF PATIENTS UNDERWENT MRM	32
NUMBER OF PATIENTS WITH NODES (MRI)-PRECHEMO	27
NUMBER OF PATIENTS WITH NODES(MRI) - POSTCHEMO	13
NUMBER OF PATIENTS PATHOLOGICALLY POSITIVE NODES after MRM	10
NUMBER OF PATIENTS FINAL PATHOLOGICAL FINDING CORRELATED WITH MRI	5

Shrinkage Patterns :

Out of 32 patients, we are able to made out shrinkage patterns only in 19 patients. 7 patients belong to type 1 pattern, 3 patients to type 2 pattern. 5 patients on type 3 pattern and 4 patients belong to type 4 pattern.

DISCUSSION:

In breast magnetic resonance imaging (MRI), surface coils are used which gives us high quality as well as higher spatial resolution images. This can be used to stage the disease in more prompt manner (15, 16). Dedicated breast coils should be used to acquire high resolution images (17- 19). MRI with field strength of 1.5 T can give high spatial resolution (25-27). Breast coil should contain a minimum of four channels, but recently more modern designs are being used with sixteen or more channels. Some centers are even using specially dedicated channels for axillary imaging. The coils with high number of channels obtain a higher signal-to-noise ratio (SNR). If more channels are used it can speed up image acquisition time (28 29).

Most of the meta analysis shows the sensitivity and specificity for response assessment rate in breast coil MRI were 0.63 (range, 0.56–0.70) and 0.91 (range, 90.89–0.92), respectively(9). In addition to the response assessment using size the shrinkage patterns can be also determined by the breast coil MRI. Breast MRI is the most accurate modality when compared with clinical examination, digital mammogram, ultrasonography in diagnosing residual disease with an accuracy of about of 92%. Breast MRI findings correlates with pathological response after neoadjuvant chemotherapy in 90% of cases (20-24). In our study, the response assessment rate of routine MRI is 34.3 percent only.

The shrinkage patterns are categorized into four types: I (concentric shrinkage without surrounding lesion), II (concentric shrinkage with surrounding lesions), III (shrinkage with residual multinodular lesions, and IV (diffuse contrast enhancement in whole quadrants)(12). In routine MRI the assessment of shrinkage patterns weren't able to made out clearly.

Recent studies shows the shrinkage patterns determined by MRI correlates with responders pattern. In general, patients with shrinkage patterns close to type 1 and 3 have more pathological response compared to other types. Patients with type 4 patterns were observed in pathologically non responder group. Patients with type 2 shrinkage pattern usually have response in between these two groups.

The response assessment patterns are classified into two types lesions based on RECIST1.1 responders and non responders. The responders are again classified into complete responders and partial responders. The term partial responders is used when the lesion showing atleast 30% reduction along the long axis. The non responders are categorized into patients with stable disease or progressive disease. When the lesion shows more than 20% increase in size along the long axis or any appearance of new lesions, those patients are termed as progressive disease. The stable disease is defined when the lesion doesn't show any measureable change in size.(13). In carcinoma breast the size of malignant lesion is measured along the longest dimension of lesion, before and after NACT. The size difference before and after NACT helps in determining the response for chemotherapy which was categorized based on RECIST 1.1.

Recent studies shows the breast MRI prediction rate about the residual lesion and about the pathological complete response depends on subtypes of breast cancer (ie) the hormonal receptor status. Breast MRI predicts the pathological complete response more precisely in HER-2 enriched tumors than her-2 negative disease. In HER-2 negative patients, the false-negativity rates are high(10).

HER2-negative and estrogen/progesterone-positive disease shows

non-mass-like enhancement lesions which usually show residual tumor as small foci or scattered cells after neoadjuvant chemotherapy. This eventually leads to underestimation of disease extent in MRI imaging (11). MRI for detecting the pathological complete response tends to be more accurate in patients whom having good response to NACT(14).

In breast coil MRI, the patient should be placed in prone position with nipples pointing down and a bilateral breast coil is used with both breasts hanging into the loop of coils as deeply as possible. This avoids motion artifacts and especially there should not be any undue compression over the breasts. For patients with larger breast in order to obtain the coverage the arms should be placed at the side of the body rather than above the head of patient (31).

At our institution, we calculated the tumor size by measuring the largest diameter of the enhancing lesion in three dimensions along with axillary nodal status. We did not took the tumor volume into account. Moreover, we are able to categorize the shrinkage patterns in only 59.37 percent of patients.

In MRI without breast coils there might be uneven distribution of magnetic fields which might hamper the image quality. Both breasts are in adequate support in coils, in MRI without coils there might be a lack of support to breast which can lead to motion artifact. Due to the inappropriate positioning and lack of support to breast, in routine MRI without breast coils it is difficult to assess the exact size of tumor and its shrinkage patterns and hence the predictive nature might be less when compared to breast coil MRI (31).

CONCLUSION

The use of routine MRI Instead of BREASTCOIL MRI fails to detect the exact pathological response after the neoadjuvant chemotherapy in most of the patients in locally advanced breast cancer patients. It adds additional financial burden to the patient and also leads to wastage of resources. So use of routine MRI is not warranted in response assessment for neoadjuvant chemotherapy.

REFERENCES:

- 1) <https://www.who.int/news-room/fact-sheets/detail/breast-cancer>
- 2) DeSantis C, Siegel R, Bandi P, Jemal A. Breast cancer statistics, 2011. CA Cancer J Clin 2011; 61: 409-418 [PMID: 21969133 DOI: 10.3322/caac.20134]
- 3) National Cancer registry program , clinicopathological profile of cancers in India - A Report of hospital based cancer registry.
- 4) Kaufmann M, Hortobagyi GN, Goldhirsch A, Scholl S, Makris A, Valagussa P, Blohmer JU, Eiermann W, Jackes R, Jonat W, et al. Recommendations from an international expert panel on the use of neoadjuvant (primary) systemic treatment of operable breast cancer: an update. J Clin Oncol. 2006;24(12):1940–9.
- 5) Scheel JR, Kim E, Partridge SC, et al. MRI. Clinical Examination, and Mammography for Preoperative Assessment of Residual Disease and Pathologic Complete Response After Neoadjuvant Chemotherapy for Breast Cancer: ACRIN 6657 Trial. AJR Am J Roentgenol 2018;210(6):1376–1385.6)
- 6) Mann RM, Cho N, Moy L. Breast MRI: State of the Art. Radiology 2019;292(3):520–536.6.
- 7) Reig B, Heacock L, Lewin A, Cho N, Moy L. Role of MRI to Assess Response to Neoadjuvant Therapy for Breast Cancer. J Magn Reson Imaging 2020. 10.1002/jmri.27145. Published online March 29, 2020
- 8) <https://healthmanagement.org/c/healthmanagement/issuearticle/breast-mri-the-new-standard-in-breast-imaging>
- 9) Accuracy of MRI in Prediction of Pathologic Complete Remission in Breast Cancer After Preoperative Therapy: A Meta-Analysis Ying Yuan L, Xiao-Song Chen2, Shi-Yuan Liu1 and Kun-Wei Shen2
- 10) Lobbes M, Prevors R, Smidt M, Tjan-Heijnen V, van Goethem M, Schipper Ret al (2013) The role of magnetic resonance imaging in assessing residual Disease and pathologic complete response in breast cancer patients receiving neoadjuvant chemotherapy: a systematic review. Insights Into Imaging. 4(2):163–175.
- 11) Chen JH, Bahri S, Mehta RS, Kuzucan A, Yu HJ, Carpenter PM et al (2011) Breast cancer: evaluation of response to neoadjuvant chemotherapy with 3.0-T MR Imaging. Radiology 261(3):735–743
- 12) Kim TH, Kang DK, Yim H, Jung YS, Kim KS, Kang SY (2012) MRI patterns of tumor regression after neoadjuvant chemotherapy in breast cancer patients: correlation with pathologic response grading system based on tumor cellularity. J Comput Assist Tomogr 36(2):200–206
- 13) Eisenhauer EA, Therasse P, Bogaerts J, Schwartz LH, Sargent D, Ford R et al (2009) New response evaluation criteria in solid tumours: revised RECIST guideline (version 1.1). Eur J. Cancer. 45(2):228–247
- 14) Assessment and Prediction of Response to Neoadjuvant Chemotherapy in Breast Cancer: A Comparison of Imaging Modalities and Future Perspectives Valeria Romeo, Giuseppe Accardo, [...], and Marco Salvatore , Cancers (Basel). 2021 Jul; 13(14): 3521.
- 15) 1. Kaiser WA. MR-Mammographie [in German]. Radiologe. 1993;33(5):292-299.
- 16) Vaughan JT, Adriani G, Snyder CJ, et al. Efficient high-frequency body coil for high-field MRI. Magn Reson Med. 2004;52(4):851-859.
- 17) Hendrick RE. High-quality breast MRI. Radiol Clin North Am. 2014;52(3):547-562.
- 18) Zhang M, Horvat JV, Bernard-Davila B, et al. Multiparametric MRI model with dynamic contrast-enhanced and diffusion-weighted imaging enables breast cancer diagnosis with high accuracy. J Magn Reson Imaging. 2019;49(3):864-874.
- 19) Kuhl C. The current status of breast MR imaging. Part I. Choice of technique, image interpretation, diagnostic accuracy, and transfer to clinical practice. Radiology. 2007;244(2):356-378.
- 20) Partridge SC, Gibbs JE, Lu Y, Esserman LJ, Sudilovsky D, Hylton NM. Accuracy of MR imaging for revealing residual breast cancer in patients who have undergone

- neoadjuvant chemotherapy. *AJR Am J Roentgenol.* 2002;179(5):1193-1199.
- 21) Wu LM, Hu JN, Gu HY, Hua J, Chen J, Xu JR. Can diffusion weighted MR imaging and contrast-enhanced MR imaging precisely evaluate and predict pathological response to neoadjuvant chemotherapy in patients with breast cancer? *Breast Cancer Treat.* 2012;135(1):17-28.
 - 22) Furman-Haran E, Nissan N, Ricart-Selma V, Martinez-Rubio C, Degani H,
 - 23) Camps-Herrero J. Quantitative evaluation of breast cancer response to neoadjuvant chemotherapy by diffusion tensor imaging: initial results. *J Magn Reson Imaging.* 2018;47(4):1080-1090.
 - 24) Marinovich ML, Sardanelli F, Ciatto S, et al. Early prediction of pathologic response to neoadjuvant therapy in breast cancer: systematic review of the accuracy of MRI. *Breast.* 2012;21(5):669-677.
 - 25) Santamari'a G, Bargallo' X, Fernandez PL, Farru's B, Caparro's X, Velasco M. Neoadjuvant systemic therapy in breast cancer: association of contrast-enhanced MR imaging findings, diffusion-weighted imaging findings, and tumor subtype with tumor response. *Radiology.* 2017;283(3):663-672.
 - 26) Kuhl CK, Mielcareck P, Klaschik S, et al. Dynamic breast MR imaging: are signal intensity time course data useful for differential diagnosis of enhancing lesions? *Radiology* 1999;211(1):101-110.
 - 27) Daniel BL, Yen YF, Glover GH, et al. Breast disease: dynamic spiral MR imaging. *Radiology* 1998;209(2):499-509.
 - 28) Partridge SC, Stone KM, Strigel RM, DeMartini WB, Peacock S, Lehman CD. Breast DCE-MRI: influence of postcontrast timing on automated lesion kinetics assessments and discrimination of benign and malignant lesions. *Acad Radiol* 2014;21(9):1195-1203.
 - 29) Marshall H, Devine PM, Shanmugaratnam N, et al. Evaluation of multicoil breast arrays for parallel imaging. *J Magn Reson Imaging* 2010;31(2):328-338.14.
 - 30) Hancu I, Fiveland E, Park K, Giaquinto RO, Rohling K, Wiesinger F. Flexible, 31-channel breast coil for enhanced parallel imaging performance at 3T. *Magn Reson Med* 2016;75(2):897-905.
 - 31) Eren D, Yeh et al. *Radiographics.* 2014 Jan-Feb ;34(1):E1-17. doi: 10.1148/rg.341125193. Eren D, Yeh I, Dianne Georgian-Smith, Sughra Raza, Lisa Bussolari, Jacqueline Pawlisz-Hoff, Robyn L Birdwell.