

MRI evaluation of the contralateral breast in patients with recently diagnosed breast cancer

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Abstract

Introduction: Contralateral breast cancer can be synchronous and/or metachronous in patients with cancer of one breast. Detection of a synchronous breast cancer may affect patient management. Dynamic contrast-enhanced MRI of the breast (DCE-MRI) is a sensitive technique for detecting contralateral lesions occult on the other imaging modalities in women already diagnosed with cancer of one breast. **Aim:** The aim was to assess the incidence of mammographically occult synchronous contralateral breast cancer in patients undergoing MRI mammography for the evaluation of a malignant breast lesion. **Materials and Methods:** A total of 294 patients with recently diagnosed breast cancer who underwent MRI of the breast were evaluated for lesions in the opposite breast. **Results:** The incidence of synchronous contralateral malignancy detected by preoperative MRI mammography done for evaluation of extent of disease was 4.1%. **Conclusion:** Preoperative breast MRI may detect clinically and mammographically occult synchronous contralateral cancer, and can help the patient avoid an additional second surgery or a second course of chemotherapy later; also, as theoretically these lesions are smaller, there may be a survival benefit as well.

Key words: Bilateral breast cancer; MR mammography; synchronous breast cancer

Introduction

Women with breast cancer have a high risk of either synchronous or metachronous cancer in the contralateral breast. The detection rate with X-ray mammography ranges from 1% to 3% and with clinical examination from 0.2% to 1.0%.^[1] In various published series of women with breast cancer, MRI detected an additional, otherwise occult, cancer in the opposite breast in 3%–24% cases, and this was found to alter the choice of treatment.^[2]

We present a retrospective analysis of 294 patients of newly diagnosed breast cancer who underwent bilateral

breast MRI as part of a preoperative workup for breast conservation surgery. In this paper we would like to study the incidence of synchronous contralateral breast cancer in the Indian context.

Materials and Methods

Records of 294 patients with recently diagnosed breast cancer who underwent MRI of the breast for the purpose of evaluation of the extent of disease in the same and contralateral breast, over a 3-year period from April 2008 to March 2011, were reviewed. All records, including details of clinical presentation, history, and X-ray mammography findings, were correlated with the cytological and histopathological reports.

MRI of the breast was done on a 1.5-Tesla (Magnetom AVANTO™, Siemens Germany) MRI system with a dedicated four-channel dual breast coil (Siemens, Erlangen, Germany) using a standardized protocol. Chest survey was done with STIR and T1W sequences acquired in an axial plane. Precontrast fat-suppressed T1W gradient-echo images were first obtained (DynaView®) and this was

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followed by intravenous contrast injection. Gadodiamide (GdDTPA-BMA, Omniscan), 0.1 mmol/kg body weight, was injected as a bolus, using a pressure injector with a flow rate of 2.0 ml/s, followed by a flush of 20 ml of saline. Gradient-echo images were obtained at 1 minute and 2 minutes, followed by high-resolution Inter-VIEWS (volume imaging with enhanced water signal) and again at 6 minutes and 7 minutes. Postprocessing was done by digitally subtracting the precontrast images from the sequential postcontrast images, along with 2D and 3D maximum intensity projection (MIP) reconstructions and kinetic analysis using the mean curve technique. The MRI breast findings were interpreted in conjunction with the clinical history and other breast imaging studies, including mammograms and USG when available, and reported according to the breast imaging reporting and data system for MRI (MRI-BIRADS) based on the morphologic and kinetic features of the lesion. The extent of disease in the index breast and the contralateral breast was measured in all three planes (anteroposterior, craniocaudal, and transverse planes). The patients in whom a lesion was detected in the contralateral breast underwent a relook USG and their X-ray mammograms were reviewed for lesions in the opposite breasts. If the MRI-detected lesion was retrospectively seen on USG or X-ray mammography, a guided FNAC/biopsy/wire localization and excisional biopsy was done; else, an MRI-guided breast biopsy was planned.

Results

The 294 women who underwent MRI of both breasts for evaluation of extent of disease were in the age group of 22–80 years, with a median age of 51 years. Eleven patients were postmenopausal and seven had grade IV dense breasts on X-ray mammography.

Suspicious contralateral breast lesions (MRI BIRADS IV and above) were seen in 29 of the 294 patients (9.8%). Two patients were lost to follow-up. In two of the 29 patients, a definitive histological proof was not sought for, and they were excluded from the study. A histopathological proof could be obtained in 25 patients. Two patients had a suspicious contralateral lesion on X-ray mammography at the time of diagnosis, one patient had a cluster of microcalcification corresponding to the enhancing lesion on MRI, and another patient had an asymmetrical density corresponding to the MRI-detected lesion seen retrospectively and hence these four patients underwent stereotactic fine-needle aspiration cytology (FNAC) and biopsy. The contralateral breast lesion was a mass in 15/25 patients, with an average size of 1.2 cm, and was a nonmass-like enhancement in 10/25 patients.

In 21/290 (7.2%) patients, contralateral suspicious lesions were detected only on MRI. Fifteen of 21 patients had a USG correlate on second-look USG done after MRI

mammography and USG-guided FNAC was done. Six of 21 patients underwent MRI-guided biopsy/wire localization. A malignant histopathological result from the opposite breast was seen in 16/290 (5.5%) patients; of these, 12 (4.1%) were detected only on MRI. Thus, the incidence of malignant contralateral breast lesions detected by MRI was 4.1%. The histopathology was infiltrating ductal carcinoma ($n=10$), infiltrating lobular carcinoma ($n=3$), ductal carcinoma *in situ* ($n=3$). The 12 mammographically occult cancers were equally distributed among the different age groups. Ten of 12 patients had heterogeneously dense or extremely dense breasts on X-ray mammography (ACR grades 3 and 4). Two of the patients had ACR grade 2 mammographic density. Both of these patients had subcentimeter contralateral lesions not discernable on the X-ray mammograms. The age range of these cancers along with a correlation with X-ray mammographic density is depicted in a histogram in Figure 1.

Benign histopathological results for the lesions detected on MRI were seen in 9/290 (3.1%) patients, with a false positive rate of 2.7%. Of these, two patients had a high-risk lesion (atypical ductal hyperplasia) in the contralateral breast [Table 1].

Discussion

Synchronous contralateral breast cancer may be detected by mammography and/or clinical examination either at the time of diagnosis or within 3–12 months of initial diagnosis in approximately 2% of women.^[3] A subsequent (metachronous) cancer has been reported to develop in the opposite breast in 0.5%–1% of patients per year or in 5%–10% of patients during a 10-year follow-up, which is a significantly higher rate than that in the general population.^[4]

MRI of the breast has high reported sensitivity -- of the order of 94%–100% -- in detecting cancer.^[5] The reported specificity of MRI ranges from 37% to 97% in various studies, which

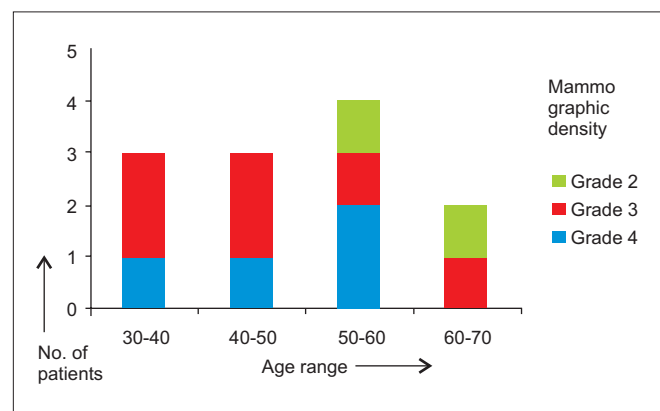


Figure 1: Histogram shows the correlation of the mammographically occult cancers with the age and mammographic density

Table 1: Summary of the characteristics of bilateral breast lesions

Age	Index lesion laterality	Size of C/ lesion	Mass/ nonmass	H/P index lesion	H/P contralateral lesion
45	R	10 mm	M	Adenocarcinoma	Fat necrosis
38	L	-	NM	IDC	IDC
65	R	8 mm	M	IDC	IDC
55	L	25 mm	M	IDC	IDC
38	L	16 mm	M	IDC	ADH, FCD
62	R	10 mm	M	IDC	IDC
38	R	-	NM	IDC	UDH
45	L	10 mm	M	IDC	IDC
62	R	15 mm	M	IDC	BBD
51	L	11 mm	M	IDC	IDC
48	R	10 mm	M	DCIS	ADH
38	R	8 mm	M	IDC	ILC
75	R	-	NM	ILC	ILC
45	L	-	NM	IDC	Adenosis
44	R	-	NM	IDC	ILC
65	L	-	NM	IDC	BBD
54	R	-	NM	IDC	IDC
32	L	10 mm	M	IDC	DCIS
59	R	17 mm	M	IDC	IDC
60	R	-	NM	IDC	DCIS
57	R	-	NM	IDC	Papillomatosis
53	L	8 mm	M	IDC	IDC
48	L	7 mm	M	IDC, DCIS	DCIS
50	L	-	NM	IDC	FCD
60	L	15 mm	M	IDC	IDC

*R: Right, L: Left, M: Mass, NM: Non-mass, IDC: Infiltrating ductal carcinoma, ILC: Infiltrating lobular carcinoma, DCIS: Ductal carcinoma *in situ*, FCD: Fibrocystic disease, ADH: Atypical ductal hyperplasia, BBD: Benign breast disease, UDH: Usual ductal hyperplasia

is due to the overlap of the enhancement characteristics of benign and malignant lesions and can also be ascribed to inconsistent imaging protocols and reporting. A number of clinical indications for breast MRI have been described by the American Cancer Society, and the role of MRI is expanding as physicians and surgeons the world over are increasingly recognizing the value of this highly useful technology. Among its various indications are screening the opposite breast for cancer in patients with proven cancer of one side, therapeutic monitoring, and screening for high-risk patients.

In this retrospective study, we have tried to evaluate the incidence of mammographically and clinically occult synchronous contralateral cancers that were detected with MRI in the Indian clinical context. In various published reports in the literature, the incidence of an otherwise occult contralateral breast cancer detected by MRI is 3%–24%.^[6] In a study led by Libermann *et al.*,^[21] clinically and mammographically occult contralateral breast cancer was detected by MRI in 12 out of 223 women who underwent

breast MRI, yielding an incidence of 5%. In another study involving 969 women that was conducted by Lehman^[6] from the University of Washington in Seattle, MRI detected cancer in 30 of the 969 women, giving an additional diagnostic yield of 3.1%; the authors have stated that the cancers identified on MRI were, in general, at an earlier stage than those identified on other types of examinations. Positive MRI findings led to biopsy recommendation in 13.9% of patients in their study, and 24.8% of these biopsies were positive for malignancy. They have reported a specificity of 88% and a negative predictive value of 99%, with the risk of developing contralateral cancer after 1 year of negative MRI being 0.3%. The authors have also stated that a preoperative MRI might reduce the number of unnecessary contralateral prophylactic mastectomies done in high-risk patients.

In our study, the incidence of synchronous contralateral malignancy detected by MRI done prior to surgery was 4.1%. A biopsy recommendation due to MRI findings was made in 9.8% of patients. Histopathological proofs could be obtained in 25/29 (86%) cases, of which 16/25 were positive (true positives) [Figures 2 and 3]. In our study, the number of false positive cases with MRI was 9/290 (2.7%). In these cases biopsy was recommended but the lesion turned out to be benign on biopsy [Figure 4] (two of these patients had high-risk lesions) [Figure 5]. Unlike the study by Lehman *et al.*, there were no false negative cases in our study since none of our patients underwent a prophylactic mastectomy.

X-ray mammography remains the recommended screening modality for breast cancer detection but may not be as sensitive in the detection of contralateral cancer, which is usually smaller; detection is further hampered by the higher breast density in younger patients who are apparently at a higher risk for synchronous contralateral cancer. Screening of the opposite breast for cancer with MRI in patients diagnosed with cancer of one breast is now the recommended standard of practice according to the American Cancer Society guidelines.^[7] Identifying those patients who might benefit from breast MRI or those who are at greater risk for synchronous bilateral breast cancer is still under clinical investigation and requires large-scale follow-up studies. However, the various risk factors that have been associated with higher probability of synchronous bilateral cancers include younger age, family history of breast cancer, and invasive lobular carcinoma of the primary breast.

Whether or not the detection of a small contralateral cancer focus has significant impact on the overall prognosis and whether this small focus if undetected can be taken care of by a subsequent course of chemotherapy are questions that are still unanswered. However, theoretically at least it appears that as these lesions are smaller there may be a survival benefit.

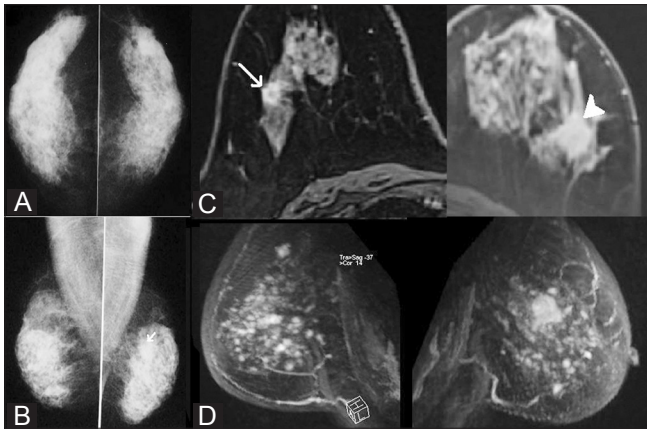


Figure 2 (A-E): A 55-year-old female with proven malignancy in the left breast. X-ray mammography CC (A) and MLO (B) views show dense breasts and an obscured density in the upper outer quadrant of the left breast (arrow). Axial contrast-enhanced high-resolution inter-VIEWS (C) and sagittal oblique 1-minute subtraction MIP image (D) show a spiculated mass in the left breast (arrowhead, proven malignancy) and a subcentimeter size spiculated mass in the right breast (arrow). Subsequent MRI-guided biopsy from the MRI-detected lesion in the right breast revealed IDC. This was a true-positive MRI imaging finding

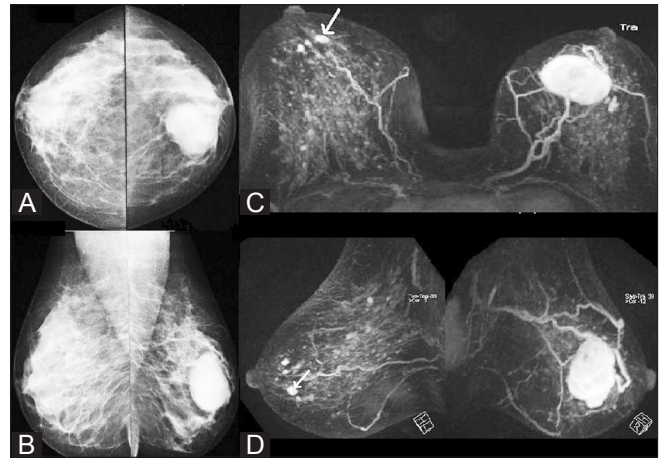


Figure 3 (A-D): A 48-year-old female presented with proven malignancy in the left breast. X-ray mammography CC (A) and MLO (B) views show a heterogeneously dense breast and a large mass in the left breast (proven malignancy). Axial (C) and sagittal oblique (D) 1-minute subtraction MIP images show an enhancing mass in the left breast (proven malignancy) and subcentimeter-enhancing lesion in the retroareolar region of the right breast (arrow). The right breast lesion was surgically excised after MRI-guided wire localization. HPE revealed DCIS. This was a true-positive MRI finding

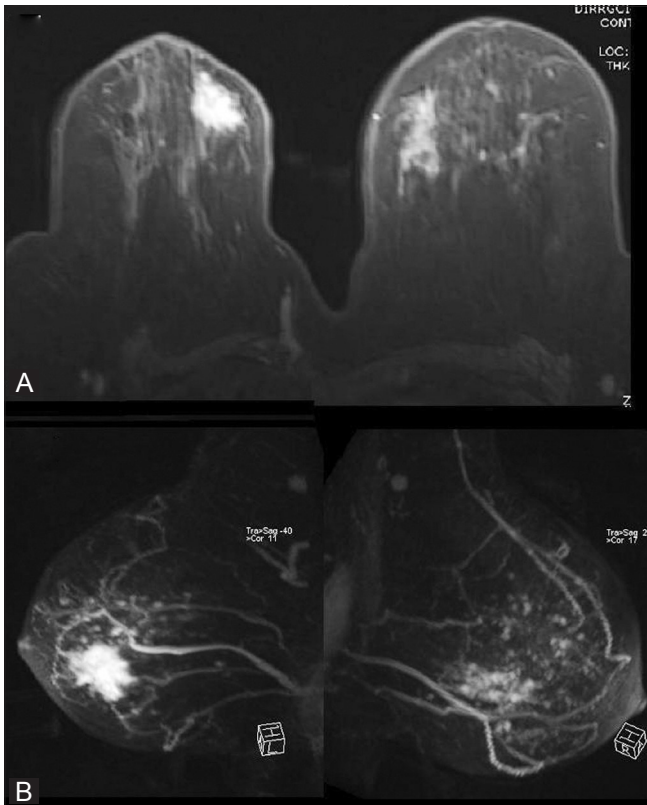


Figure 4 (A-B): A 57-year-old postmenopausal female with proven malignancy in the right breast. Axial fat-suppressed T1W gradient-echo (A) and reconstructed sagittal oblique (B) 1-minute subtraction MIP images show enhancing lesions in the right breast (proven malignancy) and clumped segmental enhancement in the left breast. Histopathology of tissue from the left breast lesion showed papillomatosis

Our figures may not reflect the true incidence in the Indian population because in this study only patients who opted

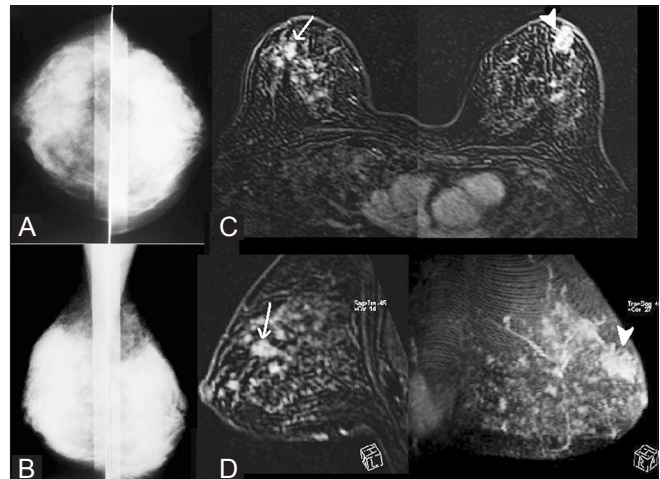


Figure 5 (A-D): A 48-year-old female presented with proven malignancy in the left breast. X-ray mammography CC (A) and MLO (B) views reveal dense breasts. Axial (C) and reconstructed sagittal oblique (D) 1-minute subtraction images show an enhancing left breast mass (proven malignancy, arrowhead) and a right breast lesion (arrow), which was surgically excised after wire localization. Histopathological examination revealed ADH

for breast conservation were referred for MRI. However, our study shows that MRI done prior to surgery can detect additional malignancy in the opposite breast.

Conclusion

Breast MRI detected additional clinically and mammographically occult synchronous contralateral cancer in about 4.1% of the patients in our series and this altered the treatment in these patients. Whether or not the detection of an additional contralateral lesion with MRI

provides a long-term survival benefit is yet to be established. Nevertheless, if a synchronous lesion is discovered, it helps the patient avoid an additional second surgery or a second course of chemotherapy.

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