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BREAST CANCER - IMPROVEMENT IN EVALUATION, STUDY AND EARLY DETECTION: USEFULNESS OF MRI OVER OTHER MODALITIES AND ITS ASSOCIATION WITH HISTOPATHOLOGICAL FINDINGS OF VARIOUS BREAST LESIONS

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ABSTRACT

Background: Our study included all of the female patients presenting to the OPD of the departments of General Surgery and Radiation Oncolgy with breast masses, that were palpable or either ultrasound or mammography documented. All the patients were worked up as per the set proforma before a contrast MRI of breasts was done on them to see for detection and characterization of breast disease along with assessment of local extent of the disease and guidance for biopsy with further correlation on HPE. **Aim:** To study the morphological characteristics of benign and malignant breast masses using various MR sequences as its safer and has better correlationship with HPE. **Methods:** In our study we performed a prospective study for a total period of two years which included total of 60 patients from varied age groups, ranging from adolescents to elderly. Female patients with breast masses, where worked up as per the set proforma before the contrast MRI of breasts was done. 1.5-Tesla MRI system with a dedicated four-channel dual breast coil was used. Chest survey was done with STIR and T1W sequences acquired in an axial plane. Precontrast fat-suppressed T1W gradient-echo images were first obtained and this was followed by intravenous contrast injection. Gadodiamide (GdDTPA-BMA), 0.1 mmol/kg body weight bolus, using a pressure injector with a flow rate of 2.0 ml/s, followed by a flush of 20 ml of saline was used and dynamic scans were then obtained. All observations where made note of to see for type, extend and staging of breast diseases in these patients and samples sent for histopathological examination (HPE) for correlation. **Results:** We inferred that MRI Showing masses with lobulated or irregular shape and spiculations had more chances of being malignant and on the contrary, masses with round or oval shape with smooth margins were more likely to be benign as reiterated by final biopsy and HPE. Also lesions with heterogenous, rim and central enhancement pattern on MRI in a breast lesion favoured malignancy. While as homogenus internal enhancements were mostly a feature of benign breast masses further reinforced by HPE. **Conclusion:** MRI and subsequent HPE can be a useful tool for detecting type, extend and staging in multifocal breast.

KEYWORDS: MRI, HPE, breast lesions.

INTRODUCTION

Breast releated disease in women have been in a rise over a past few decades now,encompasses a spectrum of benign and malignant disorders. With intensive public education about breast cancer and the growing acceptance of routine breast self-examination (BSE), an increasing number of women can be expected to seek consultation for the evaluation of breast symptoms. Vast majority of lesions that occur within the breast are benign.[1] Skin lesions like sebaceous cysts, epidermal inclusion cysts may sometimes be confused with true breast lesions. Benign lesions of the breast include, lymph nodes, solitary /multiple intraductal papillomas, sclerosing adenosis.[2,3] Radial scars & fat necrosis both, can mimic cancer by producing a palpable mass or a density on mammography that may contain calcifications. A palpable cyst is another common benign lesion of the breast and develops in at least 1 in every 14 women. Because of early detection of breast cancers from widespread screening mammography, HPE and improvements in treatment , the mortality from breast cancer has decreased almost 30 % since 1990.[4] A long list of factors raise a woman's risk for breast cancer including early menarche, late menopause, childbirth after age 30, nulliparity, lactation for <2 years, alcohol ingestion, obesity, low socioeconomic status, particular ethnicity, hormone replacement therapy (HRT), family

history, radiation exposure, and prior history of proliferative breast disease or breast cancer.[5] Fibrocystic disease is the most common, most often bilateral, disorder of the breast. It is the result of distortion and exaggeration of normal menstrual cyclic changes of ductal epithelium and stroma.[6] Atypical hyperplasias, are included in the spectrum of fibrocystic disease, and may be associated with a slight increased risk for cancer.[7,8] Infections of the breast may be, lactational infections and chronic subareolar infections associated with duct ectasia.[9]

The invasive breast carcinomas consist of several histologic subtypes; the estimated percentages are from a contemporary population-based series of 135,157 women with breast cancer reported to the Surveillance Epidemiology and End Results (SEER) database of the National Cancer Institute between 1992 and 2001.[10] :Infiltrating ductal - 76 %, Invasive lobular – 8%, Ductal/lobular – 7 %, Mucinous (colloid) - 2.4%, Tubular - 1.5%, Medullary - 1.2 % and Papillary - 1 %. Other subtypes, including metaplastic breast cancer and invasive micropapillary breast cancer, all account for fewer than 5 percent of cases[11] Because of its high sensitivity and effectiveness in dense breast tissue, MRI can be a valuable addition to the diagnostic work up of a patient with a breast abnormality or biopsy-proven cancer overcoming drawback of standard mammography only.[12,13] The numerous advantages of MRI over conventional breast imaging for the detection of malignancy have become apparent with increasing clinical experience. These advantages include

1. No ionizing radiation
2. All imaging planes possible
3. Capability of imaging the entire breast volume and chest wall
4. Superb 3-dimensional (3D) lesion mapping with techniques such as maximum intensity projection (MIP) slab 3D reconstruction
5. Greater than 90% sensitivity to invasive carcinoma
6. Detection of occult, multifocal, or residual malignancy
7. Accurate size estimation for invasive carcinoma[20]
8. Good spatial resolution
9. Ability to image regional lymph nodes.

Because of its high sensitivity and effectiveness in dense breast tissue, MRI can be a valuable addition to the diagnostic work up of a patient with a breast abnormality or biopsy-proven cancer.[13]

According to ACR practice guidelines for performance of contrast enhanced breast MRI revised in 2013;

A. Current indications for breast MRI include, but are not limited to.

1. Screening

a. For high-risk patients – Clinical trials from the United States and Europe have demonstrated that breast MRI can significantly improve the detection of cancer that is otherwise clinically, mammographically, and sonographically occult.[14,15]

b. For patients with a new breast malignancy - Screening of the contralateral breast with MRI in patients with a new breast malignancy can detect occult malignancy in the contralateral breast in at least 3% to 5% of breast cancer patients.[16] For this reason, it may be used as a diagnostic tool to identify more completely the extent of disease in patients with a recent breast cancer diagnosis.

c. For patients with breast augmentation - Breast MRI using contrast may be indicated in the evaluation of patients with silicone or saline implants and/or free injections with silicone, paraffin, or polyacrylamide gel in which mammography is difficult. The integrity of silicone implants can be determined by non-contrast MRI.

2. Extent of disease

a. Invasive carcinoma and ductal carcinoma in situ (DCIS) – Breast MRI may be useful to determine the extent of disease and the presence of multifocality and multicentricity in patients with invasive carcinoma and ductal carcinoma in situ (DCIS). Multiple clinical trials in the United States and Europe show that on average MRI can detect occult disease in the ipsilateral breast (containing the index malignancy) in approximately 15% of patients, with ranges reported from 12 to 27% and disease in the contralateral breast in 4% of patients.[14,15,17] MRI determines the extent of disease more accurately than standard mammography and physical examination in many patients.

b. Invasion deep to fascia – MRI evaluation of breast carcinoma prior to surgical treatment may be useful in both mastectomy and breast conservation candidates to define the relationship of the tumor to the fascia and its extension into pectoralis major, serratus anterior, and/or intercostal muscles.[18]

c. Postlumpectomy with positive margins – Breast MRI may be used in the evaluation of residual disease in patients whose pathology specimens demonstrate close or positive margins for residual disease.

d. Neoadjuvant chemotherapy – Breast MRI may be useful before, during, and/or after chemotherapy to evaluate treatment response and the extent of residual disease prior to surgical treatment

3. Additional evaluation of clinical or imaging findings

a. Recurrence of breast cancer – Breast MRI may be useful in women with a prior history of breast cancer and suspicion of recurrence when clinical, mammographic, and/or sonographic findings are inconclusive.

b. **Metastatic cancer when the primary is unknown and suspected to be of breast origin –** MRI may be useful in patients presenting with metastatic disease and/or axillary adenopathy and no mammographic or physical findings of primary breast carcinoma. Clinical trials demonstrate that breast MRI can locate primary tumor in the breast in over half of women presenting with metastatic axillary adenopathy and an occult primary.[19] Breast MRI can also define the disease extent to facilitate treatment planning.
c. **Lesion characterization –** In rare cases, breast MRI may be indicated when other imaging examinations, such as ultrasound and mammography, and physical examination are inconclusive for the presence of breast cancer, and biopsy cannot be performed (e.g., possible distortion on only one mammographic view without a sonographic correlate).
d. **Postoperative tissue reconstruction –** Breast MRI may be useful in the evaluation of suspected cancer recurrence in patients with tissue transfer flaps.
e. **MRI-guided biopsy –** MRI is indicated for guidance of interventional procedures such as vacuum assisted biopsy and preoperative wire localization for lesions that are occult on mammography or sonography and demonstrable only with MRI.

Two important technical requirements for breast MRI are the use of a dedicated breast coil and administration of a contrast agent. State-of-the-art breast coils typically consist of multicoil arrays with a geometric design that provides a high signal-to- noise ratio over an area covering both breasts, with extension beyond the chest wall and into the axilla in the majority of patients. Breast MRI examinations are performed with patients lying in the prone position, with both breasts hanging freely in the bilateral openings of the breast coil support. Breast MRI that is performed to evaluate a patient for breast cancer requires the use of a contrast agent. Non-contrast MRI is not sensitive to the presence of breast carcinoma and is not considered to be diagnostic. Breast MRI is most commonly performed using one of the gadolinium based low-molecular-weight MRI contrast agents. The majority of studies reported in the literature use either a single dose (0.1mmol/kg body weight) or double dose (0.2mmol/kg body weight) of contrast agent.

As contrast enhanced breast magnetic resonance imaging (MRI) becomes more ubiquitous, standardization of terminology has become necessary, any abnormal enhancement should be categorised according to ACR BI-RADS lexicon as mass or focus or non masslike enhancement.

A mass is a space occupying lesion in the breast which can be described in three dimensions. These are further described in terms of shape, margin, and internal enhancement characteristics. Shape may be round, oval, lobular, or irregular. Lobular masses have gently undulating contours. Any mass that cannot be described as round, oval, or lobular is considered irregular. Mass margins may be described as smooth, spiculated, or irregular. The term spiculated refers to fine hairlike projections radiating away from the lesion, and is analogous to spiculated margins on mammography. Any margin that cannot be described as smooth or spiculated is described as irregular. Round or oval masses with smooth margins are more likely to be benign, whereas irregular masses or masses with spiculated margins are more likely to be malignant. Enhancement in the mass may be described as homogenous,with smooth uniform enhancement throughout the mass, or heterogenous, with some areas of the mass enhancing to a greater degree than others or not at all. Homogenous enhancement is more suggestive of a benign lesion, whereas heterogenous enhancement is more suggestive of a malignant lesion.[17]

In contrast to masses, foci are not space occupying lesions. They have no mass effect or corresponding abnormality on precontrast images. By definition, these are small dots of enhancement less than 5mm in size with no definable shape.[18]

The non-mass like enhancement is described by morphology and distribution as

Characteristic	Descriptor	Illustration
Distribution:	Linear	Enhancement in a line that may not conform to a duct
	Ductal	Enhancement in a line that may branch , conforming to a duct
	Segmental	Triangular enhancement, with apex at the nipple,
	Regional	corresponding to a duct and its branches
	Diffuse	Enhancement in a large volume of breast, not conforming to a
	Homogenous	ductal distribution
		Enhancement distributed uniformly throughout the breast
	Heterogenous	Confluent uniform enhancement
		Non uniform enhancement in a random pattern
	Clumped	Punctuate dot like enhancing foci
		Cobblestone like enhancement, with occasional confluent
Internal enhancement	Stippled or punctate	areas
		Enhancement with finger-like projections extending toward
pattern:	Reticular or dendritic	nipple

Ductal and segmental distribution patterns have higher associations with DCIS, invasive cancer, atypical ductal hyperplasia, papillary neoplasms or sclerosing adenosis.[20,21]

The analysis of enhancement kinetics is achieved by measuring the signal intensity in a small area of a lesion and tracking its course over the dynamic series to yield the kinetic curve. For adequate kinetic evaluation dynamic imaging acquisition times should be less than 2 minutes. The early phase constitutes the first 2 minutes after contrast, the curve during this phase demonstrates the rate of uptake of contrast by the lesion, which is described in the lexicon as slow, medium, or rapid. Most invasive malignant lesions show rapid, intense uptake of contrast and will have reached their peak enhancement by the end of this phase. The remainder of the curve is considered the delayed phase. Three general types of curves are noted that rely less on the absolute value of the enhancement than on the shape of the enhancement curve.[22,23] A type I curve is continuous enhancement increasing with time. A type II curve reaches a plateau phase where maximum signal intensity is reached approximately 2 to 3min after injection and the signal intensity remains constant at this level. Type III is a washout curve where there has been a decrease in signal intensity after peak enhancement has been reached within 2 to 3min. Benign lesions follow a type I curve and malignant lesions follow a type III curve.A type II curve can be seen with both benign and malignant lesions. As with morphologic analysis, malignant lesions can exhibit benign kinetics and vice versa.[22,23]

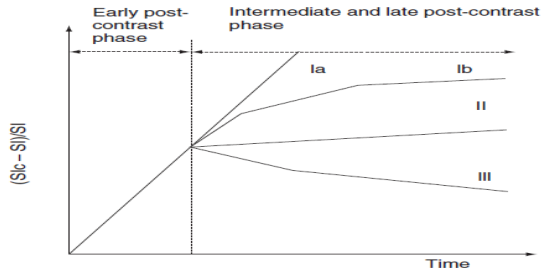


Figure 10.3 *Time–signal intensity curve types (from Kuhl 1999). Type I: straight (Ia) or curved (Ib) line, enhancement increasing. Type II: plateau curve, sharp bend after upstroke. Type III: Washout curve. SI = signal intensity; SIc = signal intensity after intravenous contrast.*

The breast lesions studied on dynamic contrast enhanced MRI are then categorised according to the Assessment Categories based BI-RADS categories which were initially developed for mammography but are now used for MRI also. The BI-RADS categories for MRI are

a. Category 0 (Assessment Is Incomplete)
Finding for which additional imaging evaluation is needed. This is almost always used in a technically unsatisfactory scan, a screening situation in which kinetic imaging has not been done, or when more information is needed to interpret the scan. A recommendation for additional imaging evaluation includes repeating MRI with satisfactory technique, obtaining information from other imaging modalities (mammographic views, ultrasound, etc.), or correlation with prior breast history.

b. Category 1 (Assessment Is Complete) : Negative scan
No abnormal enhancement found; routine follow-up advised. There is nothing to comment on. The breasts are symmetric and no enhancing masses, architectural distortion, or suspicious areas of enhancement are present.

c. Category 2: Benign Finding(s)
The interpreter may describe a benign finding such as hyalinised nonenhancing fibroadenomas; cysts; old nonenhancing scars; fat-containing lesions such as oil cysts, lipomas, and galactoceles and mixed- density hamartomas. The interpreter may describe implants while still concluding that there is no mammographic evidence of malignancy.

Category 3: Probably Benign Finding–Short-Interval Follow-Up Suggested
A finding placed in this category is highly unlikely for malignancy and should have a very high probability of being benign. It is not expected to change over the follow-up interval, but the radiologist would prefer to establish its stability. Data are becoming available that shed light on the efficacy of short-interval follow-up. At the present time, most approaches are intuitive. These will likely undergo future modifications as more data accrue as to the validity of an approach, the interval required, and the type of findings that should be followed.

Category 4: Suspicious Abnormality–Biopsy Should Be Considered
These are lesions that do not have the characteristic morphologies of breast cancer but, do have a definite low to moderate probability of being malignant. The radiologist has sufficient concern to urge a biopsy. If possible, the relevant probabilities should be cited so that the patient and her physician can make the decision on the ultimate course of action.

Category 5: Highly Suggestive of Malignancy–Appropriate Action Should Be Taken: (Almost certainly malignant).These lesions have a high probability of being cancer.

Category 6: Known Biopsy-Proven Malignancy–Appropriate Action Should Be Taken: A cancer diagnosis that has been established by histology and is imaged on the MRI and corresponds to the previously biopsied lesion.

METHODS

This prospective study was conducted in a tertiary hospital institute in north india for a total period of three years. Female patients with breast masses, that were

either palpable or ultrasound or mammographically documented who presented to the OPD of the departments of General Surgery and Radiation Oncolgy were included in the study. Before a contrast MRI of breasts was done all the patients were worked up as per the set proforma that included a detailed history of each patient including age, sex, residence,occupation, presenting complaints.Baseline investigations included CBC, KFT, LFT. 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, Erlangan, 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 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). Biopsies where taken from each suspected case and subjected to HPE. The sensitivity and specificity of the MRI findings were then compared with the final histopathological (HPE) diagnosis, especially so in differentiating malignant from benign lesions.

RESULTS

The minimum age of a patient observed was 18 years and the maximum age observed was 70 years. 10% of the patients were <20 years of age, and all lesions in this age group were proven benign on pathological examination. In the 20 to 45 yr age group, (n=29), 68 percent of the lesions were of malignant aetiology. In the >45 yr age group only 9 out of 25 patients had benign disease. This suggests a statistically significant relation between age and malignancy (p value =0.017), i.e, increasing chances of malignant disease with advancing age of the individual. The results are depicted in the following table and graph.

Table 1: Age distribution of patient population (n=60).

Age group (yrs)	No of patients (%)	HPE benign	HPE malignant
<20	6 (10)	6	0
20 - 35	14 (23.3)	4	10
36-45	15 (25)	5	10
>45	25 (41)	9	16
Total	**60**	**24**	**36**

$x^2 = 10.206$; df = 3; p = 0.017; Significant

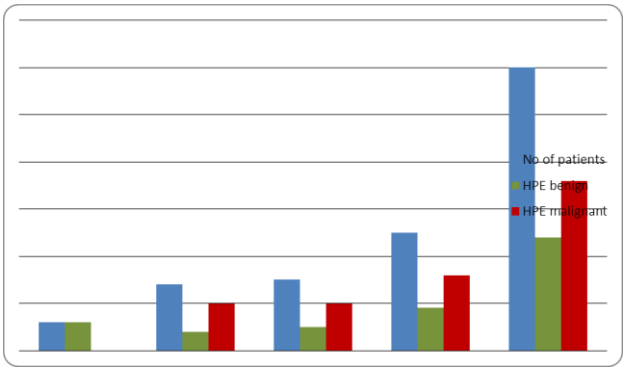


Table 2: Presenting complaints among the patient population (n=60).

Nature of the complaint	No. of patients (%)	HPE Benign	HPE Malignant
Lump	44 (73)	18	26
Pain	20 (33)	15	5
Nipple discharge	11 (18.3)	5	6
Nipple retraction	5 (8.3)	1	4
Upper limb edema	1 (1.6)	0	1
Axillary swelling	3 (5)	0	3
Pathological fracture	1 (1.6)	0	1

Table 3: Distribution according to shape of lesion on MRI (n=60).

Shape	No. of cases (%)	HPE Benign	HPE Malignant
Round	12 (20)	8	4
Oval	12 (20)	10	2
Lobulated	9 (15)	3	6
Irregular	27 (45)	3	24
Total	60	24	36

$x^2 = 22.500$; df = 3; p < 0.001; Highly Significant

The table above depicts that 20% of the patients had round masses on MRI, out of these 66% had benign nature (n=12), same was true of oval lesion.15 % of the lesions were lobulated in shape, out of these 66% were malignant (n=9). Among the irregularly shaped lesions (n =27), 89 % were malignant. This suggested that the relationship between shape of the lesion and its pathological nature was statistically highly significant (p

value <0.001). Masses with lobulated or irregular shape had more chances of being malignant and on the contrary, masses with round or oval shape were more likely to be benign. These results are illustrated in the table below

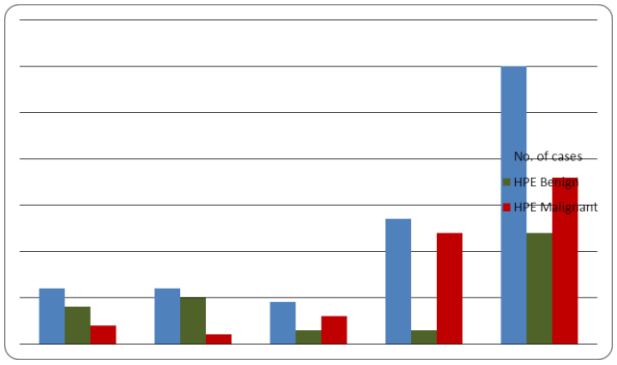


Table 4: Distribution according to margin on MRI (n=60).

Type of margin	No. of cases (%)	HPE benign	HPE malignant
Smooth	21 (35)	18	3
Irregular	29 (48)	6	23
Spiculated	10 (16)	0	10
Total	60	24	36

$x^2 = 29.458$; df = 2; p < 0.001; Highly Significant

The table above shows the relationship between margins of the lesion and the nature of pathology. Out of the 60 cases in our study, 35 % of the lesions had smooth margins, 48 % had irregular and 16 % had spiculated margins. So, 76 % of the lesions with smooth margins (n=21) were benign, whereas, only 20% of lesions with irregular margins (n=29) were benign. All the lesions (n=10) with spiculated margins (n=10) were malignant. This demonstrates a high association of margin irregularity and spiculations with malignancy. On the other hand, lesions with smooth margins were more likely to be benign. These conclusions were statistically highly significant (p value = <0.001).

These observations are illustrated in the graph below

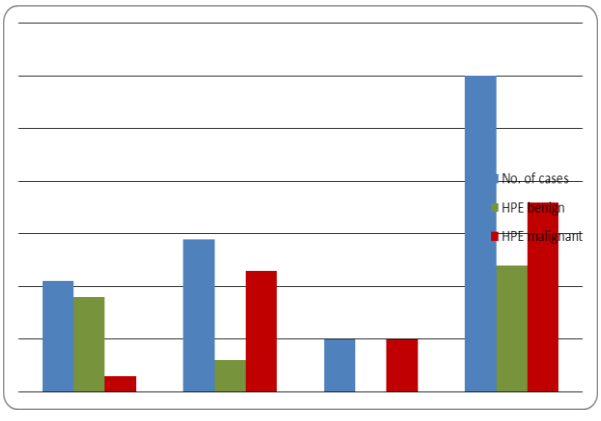


Table 5: Distribution according to signal intensity characteristics on T1 weighted images on MRI (n=60).

Signal intensity	No. of cases	HPE benign	HPE malignant
High signal	5 (8.3)	4	1
Intermediate signal	15 (25)	7	8
Low signal	40 (66)	13	27
Total	60	24	36

$x^2 = 4.549$; df = 2; p = 0.103; Not Significant

The above table shows the distribution of lesions with respect to signal characteristics on T1 weighted images. 66% of the cases were of low signal, 15 % were of intermediate signal intensity and 5 % were of high signal intensity. Out of the 40 lesions that were hypointense on T1W images, 67.5 % were malignant. In the intermediate signal group (iso-intense) (n=15), 53 % were malignant. Out of the 5 cases that were hyperintense on T1W, only 1 was malignant (20%). These findings were statistically insignificant with a p value of 0.103. The following graph depicts the above mentioned findings.

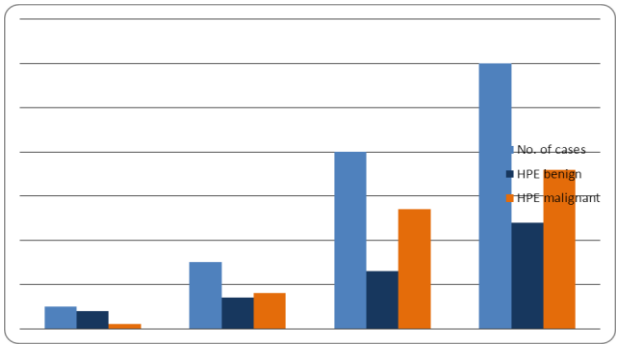


Table 6: Distribution according to T2 characteristics on MRI (n=60).

Signal intensity	No. of cases (%)	HPE benign	HPE malignant
High signal	15 (25)	12	3
Intermediate signal	15 (25)	7	8
Low signal	30 (50)	5	25
Total	60	24	36

$x^2 = 17.083$; df = 2; p < 0.001; Highly Significant

The above table shows the distribution of lesions with respect to signal characteristics on T2weighted images. 50% of the cases were of low signal, 15 % were of intermediate signal intensity and 15 % were of high signal intensity. Out of the 30 lesions that were hypointense on T2W images, 83.3 % were malignant. In the intermediate signal group (iso-intense) (n=15), 53 % were malignant. Out of the 15 cases that were hyperintense on T2W, only 3 were malignant (20%). These findings were statistically significant with a p value of <0.001. The following graph depicts the above mentioned findings.

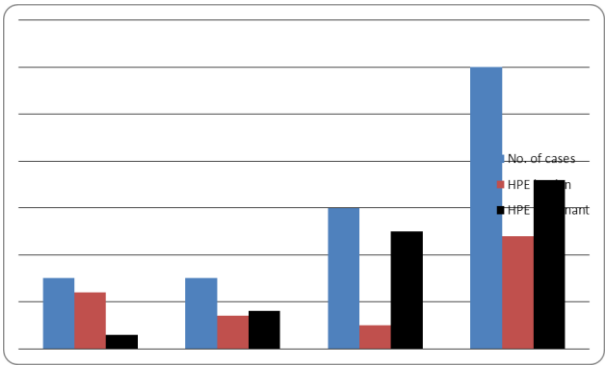


Table 7: Distribution according to enhancement pattern of masses on MRI (n=60).

Enhancement pattern	No. of patients (n=60)	HPE Benign	HPE Malignant
Homogenous enhancement	16 (26)	14	2
Heterogenous enhancement	30 (50)	7	23
Rim enhancement	8 (13.3)	2	6
Central enhancement	6 (10)	1	5
Total	60	24	36

$x^2 = 20.625$; df = 3; $p < 0.001$; Highly significant

In the table above, lesions have been distributed according to the internal enhancement characteristics on MRI .16 lesions showed homogenous internal enhancement, 14 of these turned out to be benign. 30 lesions showed heterogenous internal enhancement and most of these lesions(23) were proven to be malignant of histopathology.8 lesions demonstrated rim enhancement pattern, 6 out of these were malignant (75%,n=8), also 5 out of 6 lesions with central enhancement were malignant (83.3%, n=6).

These findings were statistically highly significant and showed that heterogenous, rim and central enhancement pattern in a breast lesion favoured malignancy. While as homogenus internal enhancement was mostly a feature of benign breast masses.

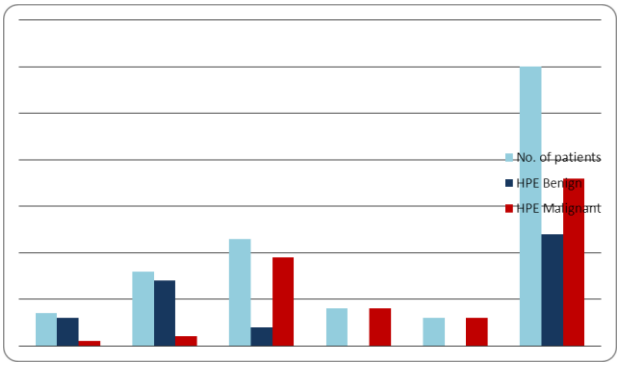


Table 8: Distribution according to type of kinetic curve on MRI (n=60).

Type of curve	No. of patients (%)	HPE Benign	HPE Malignant
Type 1	24 (40)	18	6
Type 2	22 (36)	4	18
Type 3	14 (23)	2	12
Total	60	24	36

$x^2 = 20.471$; df = 2; $p < 0.001$; Highly Significant

The above table shows the distribution of lesions according to the time-signal intensity curve as depicted by the post contrast dynamic T1 images. After optimal region of interest placement, kinetic curves were described for each lesion. Type 1 curve was seen in 24 cases, 75% of these were proven benign. Out of the 22 lesions that demonstrated a Type 2 curve, 81 % were malignant. 12 out of 14 lesions with a type 3 kinetic curve were malignant (85%). These findings were statistically highly significant with a p value of <0.001.

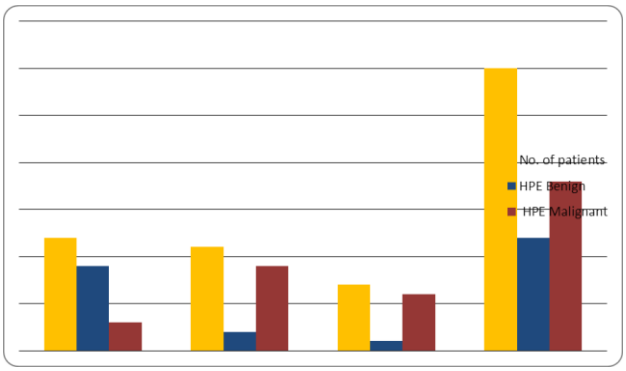


Table 9: Distribution of patients according to MRI and pathological stage N=36.

T stage	MRI Stage (number of patients) (n=36)	Pathological stage (number of patients) (n=36)	Concordant staging	Discordant staging	Number of masses upstaged	Number of masses downstaged
T1	13 (36 %)	20 (55.5%)	13	7	7	none
T2	10 (27.7%)	8 (22.2%)	10	2	2	none
T3	13 (36%)	8 (22.2%)	13	5	5	none

In our study, we made an attempt to assess the usefulness and accuracy of MRI in describing the local stage in malignant masses. Post contrast T1 W images were used for disease assessment. Masses were measured in three dimensions and the maximum diameter was used to describe the stage. For staging we used the TNM system

TX	Primary tumor cannot be assessed
T0	No evidence of primary tumor
Tis	Carcinoma in situ
Tis(DCIS)	Ductal carcinoma in situ
Tis(LCIS)	Lobular carcinoma in situ
Tis(Paget)	Paget disease of the nipple NOT associated with invasive carcinoma and/or carcinoma in situ (DCIS and/or LCIS) in the underlying breast parenchyma. Carcinomas in the breast parenchyma associated with Paget disease are categorized based on the size and characteristics of the parenchymal disease, although the presence of Paget disease should still be noted
T1	Tumor ≤ 20 mm in greatest dimension
T1mi	Tumor ≤ 1 mm in greatest dimension
T1a	Tumor > 1 mm but ≤ 5 mm in greatest dimension
T1b	Tumor > 5 mm but ≤ 10 mm in greatest dimension
T1c	Tumor > 10 mm but ≤ 20 mm in greatest dimension
T2	Tumor > 20 mm but ≤ 50 mm in greatest dimension
T3	Tumor > 50 mm in greatest dimension

In our study, 13 out of 36 cases were staged as T1 disease on MRI, on histopathology, all of these were actually T1 stage, but there were also 7 more T1 stage tumors that were erroneously upstaged to T2 and T3 stage on MRI. Among the 10 lesions that were put in as stage T2 on MRI, only 8 were truly of stage T2, while as 2 lesions were actually T1 lesions on HPE and were therefore, upstaged by MRI. Also MRI classified 13 tumors to be of T3 stage , while on histopathology, only 8 of these were confirmed to be T3 , thereby revealing that the additional 5 lesions had been upstaged from T1 and T2 on MRI.

With these findings in mind, note is made of the strong tendency of erroneous upstaging of disease on MRI.

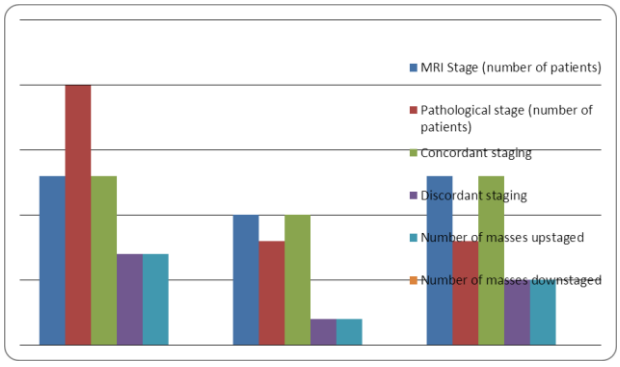


Table 10: Distribution of patients according to N stage (n=36).

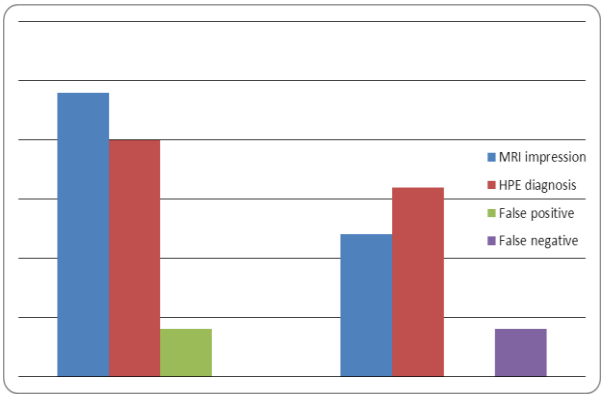
	MRI impression (%)	HPE diagnosis (%)	False positive	False negative
Node positive	24 (66.6)	20 (55.5)	4	0
Node negative	12 (33.3)	16 (44.4)	0	4

The above table shows the distribution of node positive and node negative disease as suggested on MRI in comparison to pathologically confirmed nodal disease.

The criteria used in our study for nodal positivity on MRI were

1. A more rounded contour
2. Eccentric enlargement of the lymph node with focal thickening of the cortex
3. Obliteration of the fatty hilum
4. Heterogeneous enhancement
5. However, if tumor has totally replaced the node, diffuse enhancement can also be seen.
6. Gross speculation and irregularity due to extranodal extension
7. Short axis diameter >1.5 cm

According to the data obtained, 66.6 % of the cases were categorised as node positive on MRI, while as only 55.5 % of the cases were node positive on histopathology. 33.3 % of cases were classified as node negative on MRI, while as 44.4 % were node negative on histopathology. The following graph represents the data obtained in the table above:



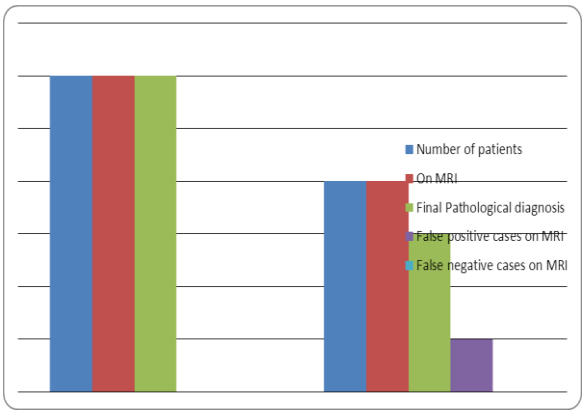
MRI Against HPE: True positive: 20; False positive 4; True negative: 12; False negative: 0.

True Positive	False Positive	True Negative	False Negative	n	Sensitivity (%)	Specificity (%)	Positive Predictive Value (%)	Negative Predictive Value (%)	Accuracy (%)
20	4	12	0	36	100.00	75.00	83.33	100.00	88.89

MRI demonstrated a high sensitivity (100%) for picking up nodal involvement however, it had a lower specificity (75%). The positive predictive value was 83.3 %, however, negative predictive value was as high as 100%. The overall accuracy for detecting nodal disease was 88.89 %. So MRI can emerge as a vital tool in ruling out local node involvement with a high negative predictive value of 100%.

Table 11: additional findings detected on MRI vis a vis histopathological diagnosis (n=36).

Finding	Number of patients (%)	On MRI	Final Pathological diagnosis	False positive cases on MRI	False negative cases on MRI
Chest wall invasion	6 (16.67)	6	6	0	0
Skin involvement	4 (11.1)	4	3	1	0



The data above shows that 6 lesions showed features of chest wall invasion on MRI. The findings were confirmed on surgery and histopathology in all of these cases and found to be consistent with the MR impression.

Skin involvement was suggested on MRI when skin thickness was more than 2mm and it showed abnormal enhancement. A total of 4 cases were considered positive for skin involvement on MRI, 3 of these were confirmed on histopathology while as one case showed no pathological evidence of skin involvement

Table 12: summary of patients with ipsilateral additional breast lesions detected on MRI which were otherwise occult (n=12).

Age of the patient	Index lesion laterality	Size of additional lesion (mm)	HPE of index lesion	HPE of additional lesion
46	R	5	IDC	IDC
36	L	10	IDC	IDC
64	L	20	IDC	IDC
52	R	15	IDC	ADH
37	L	20	IDC	ADH
48	R	5	FA	FA
60	L	8	FA	FN
50	R	9	IDC	FN
48	R	30	IDC	IDC
39	R	20	IDC	ADH
70	L	16	FA	CYST
45	L	8	IDC	CYST

The above data shows that a total of 12 patients out of 60(20%), showed an additional lesion in the ipsilateral breast, 4 of these additional lesions detected were malignant on histopathology, thereby, suggesting multicentricity of disease in these patients. This finding had a definite impact on the pre-op surgical planning of these patients.

Table 13: summary of patients with contralateral breast lesions (n=16).

Age of the patient	Index lesion laterality	Size of additional lesion (mm)	HPE of index lesion	HPE of additional lesion
40	R	10	IDC	FA
46	R	13	IDC	FN
36	R	8	IDC	FA
40	R	9	IDC	CYST
48	R	12	IDC	FA
70	L	15	IDC	IDC
65	L	10	IDC	IDC
34	L	7	IDC	ADH
36	R	9	IDC	FN
28	L	12	FA	CYST
26	R	12	FA	FA
29	L	9	FA	FA
31	L	6	FA	FA
48	L	7	IDC	CYST
50	R	8	ILC	ILC
52	L	15	IDC	CYST

A total of 16 patients revealed a lesion in the opposite breast on MRI, FNAC was performed for all of these lesions. 3 of these lesions turned out to be malignant on cytology, with all three having a diagnosed malignancy in the index breast. Thus MRI is a useful tool for detecting multifocal disease and thereby changing the treatment plan in these patients.

DISCUSSION

Our study was undertaken to evaluate breast masses that were detected clinically, sonographically or mammographically using dynamic contrast enhanced MRI and the findings were interpreted using the standard breast imaging lexicon published by the American College of Radiology that allows a standardized and consistent description of the morphologic and kinetic characteristics of breast lesions. The sensitivity and specificity of the MRI findings were then compared with the final histopathological diagnosis, especially so in differentiating malignant from benign lesions. Final diagnosis was provided by histopathological or cytopathological assessment (whichever relevant) of the breast lesions in all the cases.

In our study we had a total of 60 patients from varied age groups, ranging from adolescents to elderly. The minimum age of a patient observed was 18 years and the maximum age observed was 70 years. All lesions in the 20 yr age group were proven to be benign on pathological examination. In the 20 to 45 yr age group, (n=29), 68 percent of the lesions were of malignant aetiology. In the >45 yr age group 16 out of 25 i.e. 64 % patients had malignant disease. This suggested a statistically significant relation between age and malignancy (p value =0.017), i.e, increasing chances of malignant disease with advancing age of the individual. Masses with irregular borders and rim enhancement were associated with carcinoma, while masses with lobulated borders and internal septations were associated with fibroadenomas. The results are also in keeping with those of Guitterez and colleagues, who in 2009, performed a statistical analysis of 258 lesions and found out that there were higher odds of malignancy in lesions with lobular or irregular shape, or irregular or spiculated margins and heterogenous or rim enhancement.[24] In our study, 10 out of 36 cases were staged as T1 disease on MRI, on histopathology, all 18 were actually T1 stage. Among the 16 lesions that were put in as stage T2 on MRI, 12 were truly of stage T2. Also MRI classified 10 tumors to be of T3 stage, while on histopathology, only 6 of these were confirmed to be T3. This revealed that a total of 12 masses had been upstaged. Four T2 lesions had been upstaged to T2, whereas, eight T1 lesions had been upstaged to T2. In our study, MRI achieved sensitivities of 55.5 %, 66.6 % and 100% for diagnosing T1, T2 and T3 stage disease respectively. Our findings are consistent with those of Davis and coworkers (1996), who examined the accuracy of breast cancer T staging by MR imaging using a 3D fast spoiled gradient echo technique, mammography and ultrasonography. Fourteen carcinomas were examined in 13 patients and the largest diameter of each tumour compared with the pathological findings. MR imaging demonstrated the best correlation with pathology (r = 0.98) and the smallest standard error (0.34), whilst mammography and ultrasonography resulted in correlations of 0.46 and 0.45 and standard errors of 1.04 and 0.78, respectively. The authors noted that the improved accuracy of MR imaging was particularly evident for the larger cancers.Similar findings were reported by various other workers including Esserman et al and Yang and colleagues.[25,26]

Axillary lymph node status is the most important prognostic factor in breast cancer patients and is currently determined by surgical dissection. Magnetic resonance imaging (MRI) has a potential role in imaging the axilla in patients with breast cancer as an alternative

to surgical staging. Axillary lymph node staging is a challenge for any imaging modality and, at present, is only being performed using MRI in the context of research studies.

We also studied made an attempt to study the distribution of node positive and node negative disease as suggested on MRI in comparison to pathologically confirmed nodal disease. The criteria used in our study for nodal positivity on MRI were

1. A more rounded contour
2. Eccentric enlargement of the lymph node with focal thickening of the cortex
3. Obliteration of the fatty hilum
4. Heterogeneous enhancement
5. However, if tumor has totally replaced the node, diffuse enhancement can also be seen.
6. Gross speculation and irregularity due to extranodal extension
7. Short axis diameter >1.0 cm

According to the data obtained, 24 of the 36 cases were categorized as node positive on MRI, while as 20 of the cases were node positive on histopathology. Twelve of cases were classified as node negative on MRI, while as sixteen were node negative on histopathology, thus MRI demonstrated a high sensitivity (100%) for detecting nodal involvement, however, it had a lower specificity (75%). The positive predictive value was 83.3 %, however, negative predictive value was as high as 100%. The overall accuracy for detecting nodal disease was 88.89%. So MRI can emerge as a vital tool in ruling out local node involvement with a high negative predictive value of 100%.

Our results are comparable to those obtained by Murray AD, Staff RT, et al in 2002 who performed a study to assess whether dynamic gadopentetate dimeglumine (Gd) enhanced MRI is an accurate method for non-invasive staging of the axilla. 47 women with a new primary breast cancer underwent pre-operative dynamic Gd enhanced MRI of the ipsilateral axilla. Lymph node enhancement was quantitatively analysed using a region of interest method. Enhancement indices and nodal area were compared with histopathology of excised nodes using a receiver operating characteristic (ROC) curve approach. 10 patients had axillary metastases pathologically and all had > or =1 lymph node with an enhancement index of >21% and a nodal area of >0.4 cm (2) 37 patients had negative axillary nodes pathologically. 20 of these had enhancement indices <21% and nodal areas <0.4cm (2). Using this method, a sensitivity of 100%, a specificity of 56%, a positive predictive value of 38% and a negative predictive value of 100% could be achieved. Using this method of quantitative assessment,they concluded that dynamic Gd enhanced MRI may be a reliable method of predicting absence of axillary nodal metastases in women with breast cancer, thereby avoiding axillary surgery in women with a negative MRI study.[27]

In our study, a total of 12 patients out of 60(20%), showed an additional lesion in the ipsilateral breast on MRI, 9 of these additional lesions were detected in known cases of breast cancer in the same breast. All 9 were subjected to core needle biopsy/FNAC, 4 of these additional lesions were proven malignant on histopathology, two being multicentric and two multifocal. This finding had a definite impact on the pre-op surgical planning of these patients.

Also total of 16 patients revealed a lesion in the opposite breast on MRI, FNAC was performed for all of these lesions. Three of these lesions turned out to be malignant on cytology all three patients already had a diagnosed malignancy in the index breast. Two of these were cases of invasive ductal carcinoma and one was a case of lobular carcinoma in the index breast. Thus MRI is instrumental in detecting contralateral synchronous disease and thereby changing the treatment plan in these patients.

Our findings are consistent with the works of Uwe Fisher(1998) and Mameri CS, Kemp C et al (2008) whose studies showed that breast MRI alters significantly the rate of mastectomy, the approach of axillary chain for staging, and the use of systemic therapy because of its accuracy in evaluating breast cancer local extent and contrast-enhanced MR imaging of the breast imaging may reveal unsuspected multifocal, multicentric, or contralateral breast carcinoma and result in therapy changes.[28,29]

CONCLUSSION

MRI and HPE helps in studying characteristics of benign and malignant breast masses using various sequences. Evaluating contrast kinetics of various breast lesions e.g. In differentiating benign from malignant lesions etc. Discovering additional synchronous breast lesions, not otherwise suspected e.g. as in multicentric carcinomas as well as staging of malignant breast lesions Hence thereby helping in diagnosing, thereafter treatment planning and deciding prognosis of disease in the patients with further help of HPE.

CONFLICT OF INTERESTS

The authors declare that there is no conflict of interests regarding publication of this paper.

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