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Comparative evaluation of mammography, Sonography and magnetic resonance imaging in diagnosing malignant breast lesions

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Abstract
Objective: The purpose of this study is to assess the role of magnetic resonance imaging (MRI) in detecting malignant breast lesions and to compare it to mammography and sonography.
Subjects and Methods: 25 females with breast complaints were subjected to mammography, sonography and MRI. The breast lesions were classified as benign and malignant on the imaging features of these modalities. The reference standard was considered on the basis of histopathologic confirmation of these lesions.
Results: The sensitivity and specificity of MRI was superior to mammography and sonography in detecting malignant breast lesions.
Conclusion: MRI has improved the diagnostic efficacy in early detection of breast cancer with additional advantage of detecting lesions in dense breast and in determining the exact extent of the lesion which guides treatment plan.

Keywords: Mammography, sonography, magnetic resonance imaging, malignant

Introduction
The incidence of breast cancer is on rise in every country and it presents a great challenge to the entire health care system. The importance of timely differentiation and early diagnosis of breast lesions is crucial to achieve a successful treatment. At present various imaging modalities are available for evaluation of breast lesions i.e. mammography, sonography, color Doppler, galactography and Magnetic resonance imaging (MRI).
Mammography is an excellent screening modality for detecting breast cancer at clinically occult stage. A remarkable advantage of mammography is detection of microcalcifications. However, it is nonspecific and the nature of lesions may not be fully ascertained in many cases. The extent of the tumor is often underestimated on mammography [1]. Lesions may not be detected in dense breast and in cases following breast-conserving surgery and radiotherapy due to distortion, scarring and calcification.
Ultrasonography (US) is the most widely used adjunctive tool in breast diagnostics. The most important role of US has been to determine whether a lesion is solid or cystic. The diagnostic accuracy in solid lesions is considerably low, although some morphologic criteria have been presented for classifying solid lesions as benign or malignant [2]. The value of US in differentiating benign and malignant lesions is still controversial because of overlapping sonographic features and the high interobserver variability [3]. It is more accurate than mammography for determining actual tumor size.
Recently MRI has been added to the list of imaging modalities for evaluation of breast lesions. MRI is ideal for breast imaging because it is noninvasive, non-irradiating and 3-dimensional modality with its excellent ability to depict soft tissue contrast. It is also used to assess axillary lymph nodes. MRI has been found to be more accurate in detection of lesions within dense breast and in better differentiation of malignant and benign lesions. It better defines the extent and the presence of multifocal and multicentric lesions. In dealing with lesions that remain equivocal after mammographic and sonographic evaluation, MR imaging could be a problem solving modality [4]. MRI caters the need of breast conservation surgery by defining the exact margins of tumor thus decreasing the recurrence rate. It is the best method for detecting an otherwise occult primary breast carcinoma in patients with axillary

node metastases [5, 6]. MR imaging is also the most sensitive tool for preoperative staging and treatment planning [7, 8, 9]. It is a diagnostic modality of choice in post treatment surveillance in conservatively treated breasts with suspected recurrence and in evaluation of tumor response to chemotherapy [10, 11].

The purpose of this study was to evaluate the role of MRI in comparison to sonography and mammography in detecting carcinoma breast. The various imaging features of these malignant breast lesions have also been enumerated.

Subjects and methods

This prospective study included 25 females who presented with the following complaints: pain /discomfort in breasts, discharge from nipple, palpable breast lesions, non palpable suspicious lesions on mammography, non specific axillary lymphadenopathy or family history of breast carcinoma. The age of patients ranged from 26 to 63 years. A detailed clinical history and physical examination were followed with mammography, sonography and MRI. The diagnosis was confirmed on histopathology in all patients.

Image Acquisition

Mammography was done on "Melody B" villa Systemimedicali" mammography unit. Two standard views i.e. craniocaudal and mediolateral oblique views of both the breasts were obtained.

The patients were then subjected to sonography on "Toshiba Core Vision PRO" machine using 8 MHz linear array transducer. The breasts and axilla were scanned in supine position with arm raised above the head.

This was followed by MRI on "Siemens Magnetom Avanto 1.5 Tesla" machine using a double CP breast array coil. T2W TRIM(TR 9000 and TE 69 ms)followed by post contrast dynamic vibe sequences {3-D fat suppressed gradient-recalled echo (GRE) VIBE sequence}were obtained before and 35s, 60s, 100s, 3 min and 5min after the start of intravenous injection. After the dynamic series, image subtraction was performed and enhancing lesions were identified on the subtracted images. The enhancing lesions on the subtracted images were also identified on the non subtracted images in order to exclude subtraction artifacts or other normal enhancing structures. Kinetic analysis and time signal intensity (SI) curve of the lesion was obtained. Time signal intensity curve was classified as: Type I - progressive enhancement, with a continuous increase in signal intensity on each successive contrast-enhanced image (benign in 83%). Type II - plateau pattern, in which an initial increase in signal intensity is followed by a flattening of the enhancement curve (sensitivity of 42.6% and specificity of 75% for the detection of malignancy). Type III - a washout enhancement pattern, involves an initial increase and subsequent decrease in signal intensity (malignant lesions) [12].

Image Analysis

On mammography, breast density was classified according to BI-RADS (Breast Imaging Reporting and Data System) i.e. Type 1-fibroglandular tissue being less than 25% and the breast component is almost entirely fatty, Type 2- 25-50% scattered fibroglandular tissue, Type 3 - 51-75% fibro glandular tissue and Type 4 -highest category of breast density with fibroglandular tissue occupying more than 75% of breast tissue [13].

On mammography the size, shape, margins, density of the mass were documented. In addition microcalcifications and lymphadenopathy were noted. The lesions having irregular margins were categorized as malignant.

On sonography the size, shape, echogenicity, sound transmission, depth/width ratio, lymphadenopathy and microcalcifications were documented.

On MRI, the morphology and enhancement patterns of the lesions were noted. The lesions having irregular margins and type II or type III SI curve on dynamic MRI were grouped as malignant.

Statistical Analysis- The sensitivity and specificity of mammography, sonography and MRI individually and in combination, to detect malignant breast lesions were obtained.

Results

The histopathologic examination (HPE) revealed 13 malignant lesions out of total 25 lesions.

On the basis of mammographic features, 8 lesions (true positive) were categorized as malignant while 2 were wrongly diagnosed as benign (false negative). Three lesions could not be assessed due to increased breast density (BI-RADS density 3 & 4) and hence were labeled as inconclusive. Lymphadenopathy (LAP) was detected in only one patient with malignant breast lesion. The lymph nodes were round in shape. No calcification was seen in any of these 8 malignant cases.

Sonography detected 11 true positive malignant lesions and 2 false negative lesions. LAP was detectable in 8 patients with malignant lesions.

MRI detected 12(true positive) out of 13 malignant lesions, while one was wrongly diagnosed as benign (false negative). LAP was seen in 11 malignant cases. Pectoralis muscle involvement was detected in 6 patients and skin thickening was noticed in three cases.

The mammographic, sonographic and MRI features of these malignant lesions have been enumerated in table1. Table 2 gives the comparative sensitivity and specificity of these three modalities in diagnosing malignant breast lesions.

Table 1: Mammographic, Sonographic and MRI features of malignant breast lesions.

S. No.	Features	Mammographic features (n=13)	Sonographic features (n=13)	MRI features (n=13)
1	Size			
	a) <2cm	1	2	2
	b) 2-5 cm	8	10	7
	c) >5cm	1	1	4
	d) No mass assessable*	3	-	-
2.	Shape			
	a) Oval/ Round	9	10	7
	b) Irregular	1	3	6
	c) No mass assessable*	3	-	-
3.	Margins			
	a) Well defined	1	1	1
	b) Ill-defined/ Spiculated	9	12	12
	c) No mass assessable*	3	-	-
4.	Density			
	a) Water	10	-	-
	b) Mixed	0	-	-
	c) No mass assessable*	3	-	-
5.	Depth/width ratio			
	a) <1	-	10	-
	b) >1	-	3	-
6.	Echogenicity			
	a) Hypoechoic	-	10	-
	b) Mixed	-	3	-
	c) Hyperechoic	-	0	-
7.	Sound Transmission			
	a) Edge Shadowing	-	5	-
	b) Posterior enhancement	-	2	-
	c) Posterior shadowing	-	4	-
	d) Neutral	-	2	-
8.	Signal intensity A) T1WI			
	a) Hypointense	-	-	8
	b) Hyperintense	-	-	2
	c) Isointense	-	-	1
	d) Heterogeneous	-	-	2
	B) T2W1			
	a) Hypointense	-	-	1
	b) Hyperintense	-	-	11
	c) Heterogeneous	-	-	1
9.	Contrast enhancement pattern			
	a) Homogeneous	-	-	5
	b) Heterogeneous	-	-	8
10.	Signal intensity curve			
	a) Type- I	-	-	0
	b) Type-II	-	-	8
	c) Type- III	-	-	5

* Due to dense breast

Table 2: Comparison of sensitivity, specificity of mammography, sonography and MRI in diagnosis of malignant breast lesions.

	Sensitivity	Specificity
Mammography	61.5%	75.0%
Ultrasonography	84.6%	83.3%
MRI	92.3%	91.6%

Discussion

Early detection of breast cancer is the primary goal of breast imaging. Breast MRI has gained immense clinical acceptance in early detection and assessing lesions which are indeterminate on physical examination, mammography or sonography.

In our study 13 out of 25 breast lesions were malignant, and these patients presented with the commonest clinical complaint of painless lump. The mean age of presentation was 45 years, which is consistent with Park's statement that the mean age of breast cancer in India is 42 years [14].

Mammography

Mammography had a sensitivity of 61.5%. 2 lesions were false negative. Out of these two false negative cases, 1 had smooth margins and the other showed calcification hence was diagnosed as benign on mammography. Mammography was inconclusive in 3 patients who had BIRADS density grade 3/4 (Figure 1). According to Leconte *et al.* [15] as the BIRADS density grade increases the sensitivity of mammography for detecting lesions decreases. In grades 3 and 4 dense breasts, sensitivity of mammography for lesion detection was 56%, whereas in grade 1and 2 density the sensitivity increased to 80% [15].

In our study the most sensitive mammographic parameter for diagnosing malignancy was ill-defined margins of the mass. The lesion margins were ill-defined or spiculated in 9 and well defined in 1 lesion. Sickles [16] found that 90% of breast cancers are seen as poorly defined masses with irregular contour which was similar to our series.

Sonography

On sonography malignant lesions were correctly diagnosed in 11 patients with a sensitivity of 84.6%.Two lesion were wrongly diagnosed as benign out of which one had well defined margins and the other one showed calcification hence was labeled as benign.

The most sensitive parameters on sonography were ill-defined margins and hypoechogenecity. The margins of the malignant masses were irregular in all 12 patients and well defined in one lesion in our study. Soo *et al.* [17] analyzed that malignant lesions of the breast were irregular in 89% cases. Our findings were also in agreement with these observations that irregular margin of the mass is one of the most important sonographic features suggestive of carcinoma.

Out of 13 malignant lesions, 10 were hypoechoic and 3 showed mixed echogenicity. No malignant lesion was hyperechoic. Skaane *et al.* [18] found that carcinomas were hypoechoic in 92% cases; they observed that hypoechogenicity is a prominent feature of malignancy.

The sonographic size of malignant lesions in all 11 patients was smaller than the palpable size because of desmoplastic reaction due to which the lesions appear larger on clinical examination. Fornage [19] observed that sonography yields the most accurate pre-operative cancer size.

Depth/width ratio was <1 in 10 and >1 in 3 malignant lesions. This is not in accordance to other studies in which depth to width ratio >1 was more in favor of malignancy. However, it is in accordance to a study conducted by M. Kubota *et al.* in 1999 in which majority of malignant and benign lesions had Depth/Width ratio of <1. They suggested that Depth/Width ratio is influenced by many complex factors including the growth pattern and hardness or elasticity of the breast tumors. Soft tumors are easily compressible by ultrasound transducer thereby decreasing Depth/Width ratio [20].

MRI

MRI had a sensitivity of 92.3%. Only 1 lesion was wrongly diagnosed as benign. This mass was heterogeneous on both T1 and T2 WI and had heterogeneous post contrast enhancement. Although its signal intensity curve was type II, the lesion was diagnosed as benign phyllodes tumor because of its well defined margins. This signifies the importance of signal intensity curve which in our case was type II thereby suggesting the possibility of malignancy (Figure 2).

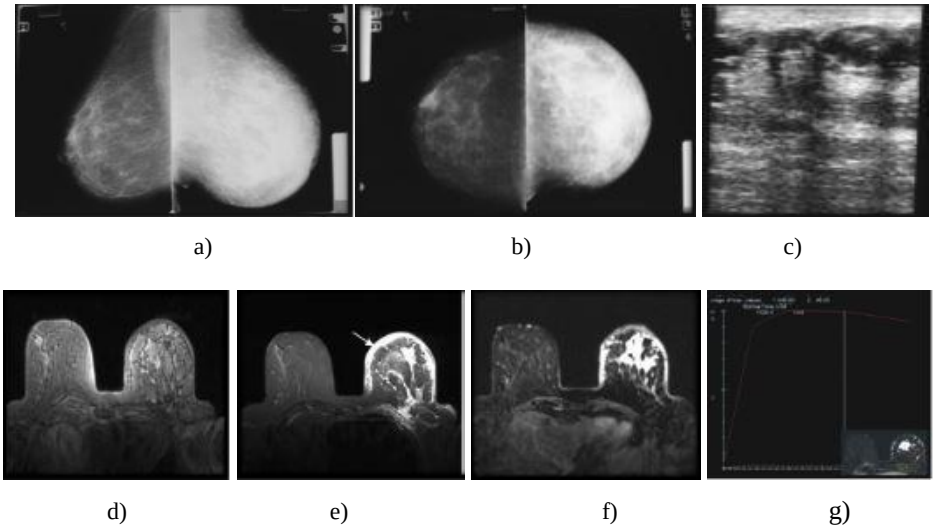
The sensitive parameters on MRI for diagnosing malignancy were ill-defined margins, hypointense signal on T1 and hyperintense signal on T2 and type II and type III signal intensity curves. The size of lesion or post contrast enhancement pattern carried no significant differentiating feature between malignant and benign lesions.

The margins of masses were ill-defined in 12 lesions. Mitsuhiro Tozaki *et al*. stated that the most frequent type of lesion shape and margin among the malignant lesions were irregular (47%) and spiculated (43%) [21].

On T1W fat saturation sequence 8 lesions were of low signal intensity (less than fibroglandular tissue), 2 (17%) showed high signal intensity and 1(8%) showed isointense signal. The remaining 2 lesions showed heterogeneous signal. On T2W (TIRM) sequence 11 lesions had intermediate to hyperintense signal, 1 was hypointense and 1 showed heterogeneous signal. Orel *et al*. found that all cancers were of low signal intensity (less than or equal to that of fibroglandular tissue) on TI-weighted images similar to our finding and on T2-weighted images were intermediate to high in 86%, low in 7% and intermediate signal intensity in 7% [22].

In our study all malignant lesions showed Type-II (8/13) or type - III (5/13) (Figure3) signal intensity curve which is similar to other studies [12]. The pathophysiology of these patterns of enhancement is not clear, however, the washout phenomenon suggests increased vessel density in lesion with arterio-venous anastomosis. This leads to rapid outflow of contrast from the lesion [23].

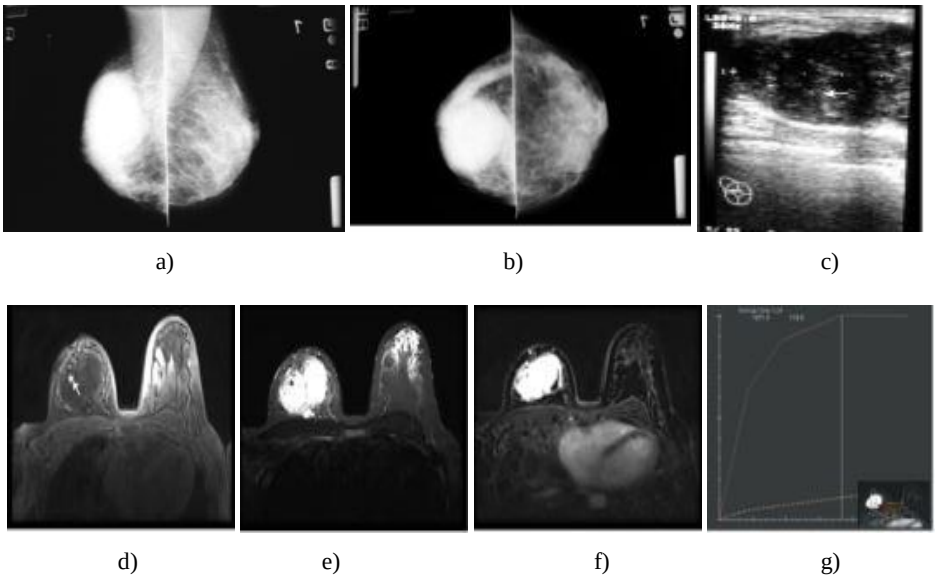
MRI had the additional advantage of detecting pectoralis muscle infiltration (6/13), features of invasive carcinoma (3/13) and axillary lymphadenopathy (11/13).



a) b) c)

d) e) f) g)

Fig 1(a-g): 50-years-old female with lump and diffuse enlargement of left breast.
Mammography bilateral MLO & CC views (a, b) show BIRADS grade 4 density and increased size of left breast as compared to right breast. Ultrasonography (c) shows heterogeneous echogenicity of mass with irregular margins. The skin of the breast is thickened.
MRI (d-g) On fat saturation T1W sequence (d) hypointense mass with irregular margins is present in all quadrants. On T2W TIRM (e) mass is hyperintense with multiple hyperintense strands in the adjacent parenchyma. Skin is also hyperintense and thickened. Post contrast dynamic subtraction image (f) shows exact margins of the mass with its intense enhancement. The lesion shows type II SI curve (g). Features suggested malignant mass (inflammatory carcinomatosis) later confirmed on histopathology.



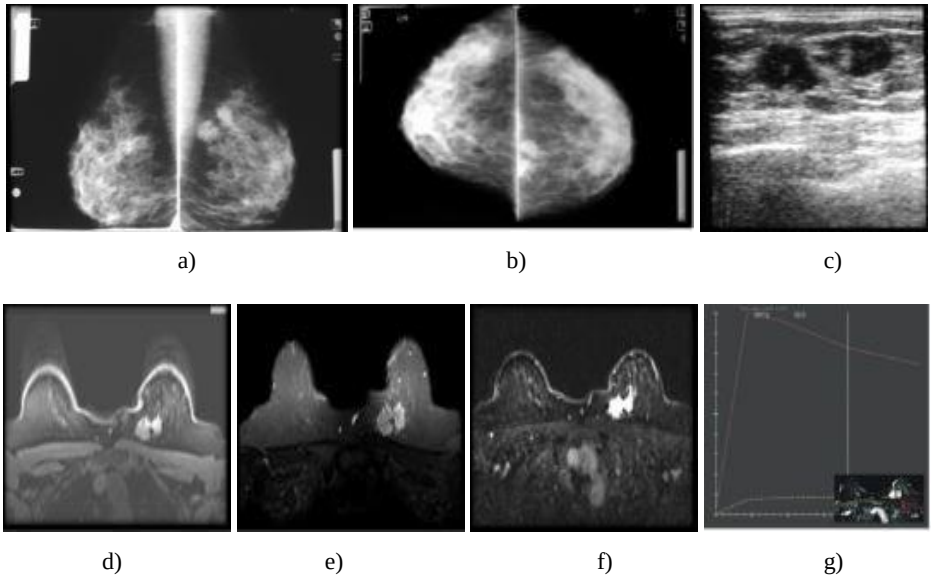
a) b) c)

d) e) f) g)

Fig 2(a-g): 29-years-old female with lump right breast for 1 month and prior history of lump excision from the same breast 6 months back.

Mammography bilateral MLO & CC views (a&b)show oval, water density mass well defined margins present in right breast occupying all quadrants. Ultrasonography (c) reveals mixed echogenicity mass i.e. hypoechoic mass with isoechoic areas within. The margin of the mass is lobulated.

MRI (d-g) On fat saturation T1W sequence (d), hypointense mass with foci of hyperintensities within is seen.T2W TIRM image (e) shows this mass to be heterogeneously hyperintense with hypointense foci and internal septa.Post contrast dynamic subtraction image (f) shows heterogeneously enhancing mass with no enhancement of septa. The lesion shows type II SI curve (g). Features suggested Phyllodes tumor (benign type). However, the histopathologic diagnosis was malignant phyllodes tumor.



a) b) c)

d) e) f) g)

Fig 3(a-g): 30-year-old female with lump left breast.

Mammography bilateral MLO & CC views (a&b) show two rounded water density lesions having irregular margins present in upper and inner quadrant.

Ultrasonography (c) shows two hypoechoic lesions with irregular margins.

MRI (d-g) On fat saturation T1W sequence (d), a bilobed mass is seen which is hyperintense in signal. T2W TIRM image (e) shows that this mass is hyperintense with irregular margins. Post contrast dynamic subtraction image (f) shows intensely enhancing mass with normal adjacent pectoralis muscle. The lesion shows type III SI curve (g). Features suggest malignant mass confirmed as duct cell carcinoma on histopathology.

Conclusion

MRI due to its noninvasive, non-irradiating and multiplanar capability has significantly improved the diagnostic efficacy in early detection of breast cancer. The combined interpretation of morphological features and signal intensity curve pattern is of immense value in characterizing breast lesions. MRI has the additional advantage in detecting lesions in dense breast (BI-RADS density grade 3 and 4) where mammography is inconclusive, also it can determine the exact extent, multicentricity, multifocality, intraductal spread of carcinoma and pectoralis muscle involvement, which is helpful in treatment planning.

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