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The Role of Pre-Operative Magnetic Resonance Mammography In Obese Women With Suspected Breast Cancer

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ABSTRACT
OBJECTIVE: To high-lighten the role of MR mammography as a pilot pre-operative modality in the staging of breast cancer and its impact on surgical planning and management; aiming to decrease morbidity and mortality of this increasingly spreading cancer. In addition, to clarify the assessment of the relationship between the types of obesity and staging breast cancer. Moreover, to evaluate the diagnostic validity of breast MRI in discriminating benign from malignant lesions in women with suspected breast cancer histopathologic findings used as the golden standard.

PATIENTS AND METHODS: Contrast-enhanced bilateral breast MRI was performed on 60 women with suspected breast cancer with indeterminate imaging findings by mammography and/or ultrasonography. Lesions detected by MRI that could represent potential malignancies in both breasts were evaluated. Morphologic assessment and kinetic analysis (contrast enhancement) were performed on each lesion using dedicated postprocessing and display software. Functional MR tools were used in few cases (6 cases) to help in the differential diagnosis between malignant and benign of suspicious lesions detected at conventional MRI. All patients underwent clinical and radiological evaluation followed by Contrast-enhanced bilateral breast MRI using 1.5-tesla superconductive Philips scanner and General Electric Medical Systems. The diagnostic images were evaluated as regard lesion morphology (size, shape, margin type, enhancement pattern), signal intensity parameters (time to peak enhancement, maximum slope of enhancement curve, washout), and the BIRADS categories. Results of the contrast enhanced bilateral breast MRI of the 60 patients were all reported and compared with the histopathalogical biopsy.
RESULTS: A total of 60 patients presented with suspected breast cancer were included in the study with age ranging from 38 to 75 years old. 22 of the studied population had benign findings, while 38 of the patients were diagnosed as malignant. (18 patients IDC, 6 patients Invasive Lobular Carcinoma, 3 patient Mucinous carcinoma, no patients Medullary carcinoma and 4 patients Insitu cancer). In this study population the sensitivity, specificity, positive and negative predictive values of mammography were found to be 51.6%, 88.4%, 66.7%, and 80.3% respectively. Overall accuracy of mammography was 77%. Among the 38 cases diagnosed by sonomammography as malignant or with irregular densities, 16 turned out to be benign by histopathological evaluation (false +ve), while among the 22 cases diagnosed by sonomammography to be benign lesions or non-conclusive studies (dense), 7 were proved to be malignant by histopathological evaluation (false –ve). The sensitivity, specificity, positive and negative predictive values of MRI for occult breast lesions in high risk patients included in the study, were found to be 100%, 93%, 86%, and 100% respectively. Overall accuracy of MRI breast was 95%. Among the 38 cases diagnosed by MRI as malignant, there was no false +ve, while among the 22 cases diagnosed by MRI to be benign lesions, 7 cases were proved to be malignant by histopathological evaluation (false –ve). Therefore breast MRI had higher sensitivity than specificity but general speaking it is considered highly valid with high specificity also. Due to the limited number of cases in this study, there was a trend in relation of obesity (BMI) to breast cancer, malignancy rate 55.3% in obese women and 44.7% in non-obese women.
CONCLUSION: From our study, we conclude that MR imaging of the breast in obese women , is a rapidly evolving modality of excellent sensitivity in detection of breast cancer. The basic drawback of this modality was its low specificity for breast malignancy. However, multiple studies including this study have shown that with the improvement in equipment and technique there is gradual increase in specificity.

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Generally speaking breast MRI is highly effective in detection and characterization of occult breast lesions in high risk population, with excellent sensitivity and high specificity. This is attributed to the advance most in equipment, technique, development and implementation of interpretation guidelines and development of functional MRI tools which contributed to the improving validity of this modality. Also the superiority of MRI compared to mammography, supports the use of MRI as an important tool in screening of asymptomatic women with high risk factors.

INTRODUCTION

Breast cancer is the most common malignancy that affects women worldwide and is a significant health care problem (1). Methods such as X-ray mammography, ultrasound and physical examination are often limited in sensitivity and specificity, especially in young women. MRI is increasingly being used for preoperative local staging, localization of multiple lesions and screening of high-risk patients, and it is an area of intense research (2).

When added to the standard evaluation in patients thought to have breast cancer, contrast-enhanced MRI using both a kinetic and morphologic analysis will often result in changes in recommended patient management, better treatment planning and detect many occult cancers (3).

Breast MRI has a very high sensitivity of greater than or equal to 90% for breast cancer and near 100% sensitivity for invasive breast carcinoma. Breast MR imaging has been successfully used to help detect sonomammographically suspected breast cancer in women (4).

PATIENTS AND METHODS: Contrast-enhanced bilateral breast MRI was performed, at Ain Shams University hospitals and National Cancer Institute, on 60 female patients with suspicious breast lesions: 30 normal control individuals and 30 obese individuals. Their mean age was 45 (age range, 15-77 years). All patients were with suspicious looking imaging findings by Mammography and/or Ultrasonography. Lesions detected by MRI that could represent potential malignancies in both breasts were evaluated by morphologic assessment and kinetic analysis (contrast enhancement) was performed using dedicated post-processing and display software.

• Inclusion Criteria:

a. Patient presenting with breast pain/lump/nipple discharge

b. Obese patients included in the stud" with BM1 > 30kg/m2

c. Women above the age of 25 years

d. Serum Creatinine not more than > 1.4 mg/dl.

• Exclusion Criteria:

a. Previous breast intervention

b. Breast augmentation facilities

c. Mulricenrricity diagnosed by U/S

d. Serum Creatinine more than> 1.4mg/dL

All patients were subjected to complete clinical, radiological and anthropometric evaluation assessment. This involved thorough history taking including personal history, especially with respect to previous breast cancer or biopsies with benign histology, family history of breast or ovarian cancer, abnormalities suspicious of malignancy (e.g., palpable mass, skin retraction, nipple discharge), hormonal status and previous allergic reaction after administration of MR contrast material. Previous imaging studies such as mammography and/or sonography, and their findings were evaluated and recorded. Then contrast-enhanced bilateral breast MRI was performed and results of MRI examination were compared to the findings from histopsthology and/or follow up.

Patient preparation: There is no specific preparation for different MR imaging such as fasting.

- MRI examination of the breast in premenopausal women performed in the second or third week of the cycle, unless urgent.
- Complete screening for Ferromagnetic objects, implanted devices (cosmetics/ surgical). All metallic objects were removed.
- Before starting the MRI, a brief explanation about the procedure was

given to the patient with the prevention of entire movement during the process

A venous line (18–20 G) was inserted prior starting the examination for contrast material administration.

Scan protocol: MR imaging was performed with Philips superconductive magnet system operating at 1.5 Tesla using breast surface coils. The patient lies prone on the examination couch with her breast(s) positioned dependent in the receiver breast coil(s) and the arms placed along the body. Appropriate IV anesthetic agents were given to some patients who feared the MRI machine when needed. IV contrast (gadolinium chelates) was given for assessment of tumor kinetics. Dose given was about 0.2 ml/kg body weight. Spine-echo T1W1 was performed after contrast administration. The routine protocol applied in this study included Axial T1, T2, Axial T2 fat suppressed, STIR or SPAIR ± Sagittal STIR, Axial Post-contrast T1 WI fat suppressed ± Sagittal Post-contrast 3D TFE (T1 WI). Dynamic 3D multiphase post-contrast study was done in 6-8 minutes with MIP reconstruction (once before contrast and 4-5 times after contrast, each around 1 minute). For any region of interest (ROI), Time-Signal intensity curves were performed. Signal intensity measurements were performed prior to as well as following contrast administration in this region of interest (ROI). ROIs are drawn at the point of maximum enhancement. Diffusion weighted imaging + ADC calculation were utilized in 59 cases. The field of view (FOV) typically ranged from 280 to 340 mm, depending on the breast size. The slice thickness was 3 mm or sometimes 2mm, and without gaps.

Table (1) Physical parameters of different pulse sequences.

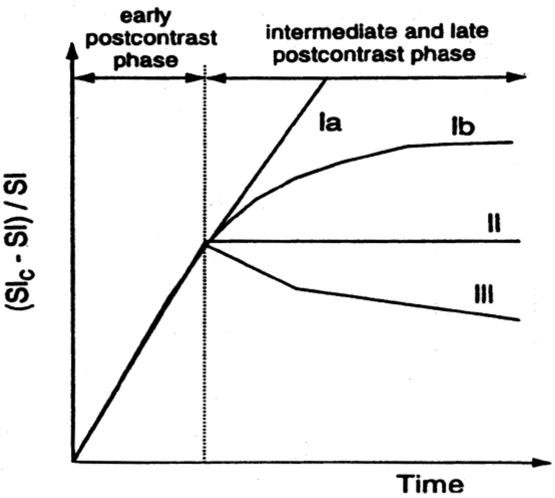
	Axial T1WI	**Axial T2WI**	**Axial/ Sagittal STIR**	**Axial/ Sagittal +c T1WI Fat sat**
TR	540	4000-4800	2000-7500	485
TE	10	120	55-170	10
NEX	1	1	1	1
ST	3mm	3mm	3mm	3mm
Gap	0	0	0	0
FOV	34x34cm	34x34cm	34x34cm	34x34cm
Matrix	256x160 or 256x192	256x160 or 256x192	256x160 or 256x192	256x160 or 256x192

TR: Repetition time TE: Echo time NEX: Number of acquisition FOV: Field of view STIR: Short time inversion recovery Fat sat: Fat saturation ST : Slice thickness.

Data interpretation: All lesions or areas of abnormal enhancement detected by MRI that could represent potential malignancies in both breasts were evaluated, by experienced MR radiologist, as regard:

- Morphology
- Exact Location
- Extent of involvement
- Signal intensity on different pulse sequences
- Kinetics; Enhancement pattern and time/intensity curves
- Vascularity of the lesion

ACR BI-RADS–MRI Lexicon was used as a guideline for data collection. According to the BI-RADS Lexicon of the American College of Radiology, suspicious enhancing areas in the breast are differentiated into (a) focus/foci, (b) masses, or (c) areas of non-mass-like enhancement. Moreover, associated findings are described (10). Masses and areas of non-mass like enhancement are subjected to careful analysis of their morphology, enhancement kinetics, and signal intensity patterns on T1- and T2-weighted images. A focus is a small isolated spot of enhancement, generally less than 5 mm in size, that is so tiny that no definitive morphologic descriptors can be applied. A mass is a three-dimensional space-occupying lesion that may or may not displace or otherwise affect the surrounding normal tissue. For the evaluation of masses, different criteria are described. Criteria include shape, margin, endotumoral type of contrast internal enhancement, and the initial and post-initial signal behavior in relation to the precontrast signal. Non-mass-like lesions on MRI of the breast are enhancing areas that are neither a focus nor a mass. Non-mass-like enhancement descriptions included distribution, internal enhancement and symmetry. It is described as a focal area, linear, ductal, segmental, regional, multiple regions, or diffuse. Internal characteristics of the enhancing area, like homogeneous, heterogeneous, stippled/punctuate, clumped, or reticular/dendritic, is evaluated. Associated findings (such as edema, adenopathy, cysts, and skin or chest wall involvement) are reported and kinetic curve assessment of all lesions described. The analysis of enhancement kinetics included initial peak (Early phase) enhancement and delayed-phase enhancement analyses, by measuring the signal intensity in region of interest (ROI), and tracking its course over the dynamic series (time–signal intensity curve). ROIs were placed into the area that exhibits strongest enhancement on the first postcontrast image. Early Post -contrast Phase enhancement describes the steepness of the first part of the kinetic curve, indicating the velocity and degree with which enhancement occurs and may be slow, medium, or rapid. Delayed phase enhancement refers to signal intensity changes that occur immediately after the early signal intensity increase which may (a) decline again; (b) exhibit a sharp bend and plateau; or (c) continue to rise after the early phase, yielding persistent enhancement. Enhancing nodules were assumed to be almost malignant when they showed early intense enhancement and progressive signal loss over time (washout), whereas lesions showing progressive enhancement over time were assigned to be more likely benign (13). (Fig. 1)



(Fig. 1) : Schematic drawing of time-signal intensity curve types. Type I (persistent or steady curve) corresponds to a straight (Ia) or curved (Ib) line. Type II (plateau curve). Type III (Washout curve) (37).

Using ACR BI-RADS–MRI Lexicon, lesions were categorized into seven categories according to the findings of the breast MRI. MRM-BI-RADS 0 describe an incomplete assessment and the category MRM-BIRADS 6 is given to a histological verified breast carcinoma. The other five categories include: Category MRM-BI-RADS 1: "negative" No abnormal enhancement is found. Category MRM-BI-RADS 2: "benign" MRI shows a benign finding, for example a hyalinized nonenhancing fibroadenoma, cysts, and old nonenhancing scars, fat-containing lesions such as oil cysts, lipomas, galactoceles, or mixed-density hamartomas. Category MRM-BI-RADS 3: “probably benign” Changes that are highly unlikely to be malignant, i.e., those that have a very high probability of being benign, are placed in this category. Category MRM-BI-RADS 4: “suspicious” These are lesions that do not have the characteristic morphology of breast carcinoma, but do have a definite low to moderate probability of being malignant. Category MRM-BI-RADS 5: “highly suggestive of malignancy” Lesions categorized as MRM-BI-RADS 5 have a high probability of being cancerous. They show the typical findings of a malignant breast tumor

DISCUSSION

Breast cancer is the most common cancer, and is the second leading cause of cancer-related mortality in women. Thus, prevention and screening have become important health issues. Early detection and treatment at proper time lead to good prognosis. (5)

The sensitivity of mammography to detect breast cancer decreases in women with dense breast. This disadvantage of mammography has become more important in the recent years which have witnessed a substantial increase in the incidence of malignancy in the young women (6).

One of the major limitation of mammography is the overlap in the appearance of benign and malignant lesions .Some of the abnormal densities on the mammograms are actually caused by superimposition of normal densities ,not all patients with suspected densities on mammography would have breast cancer (7).

The overlap in the mammographic appearance and physical examination findings of benign and malignant lesions results in a relatively high number of benign breast biopsies, unnecessary patient anxiety and morbidity related to biopsy (8).

The high benign biopsy rate has generated significant interest in adjunctive imaging tests that would improve the positive predictive value of the diagnostic work up. The classic example of an adjunctive modality that has been successfully used to improve specificity is sonography .

US has never been important in breast disease management as it is today. Its historical role as an adjunct modality to mammography in differentiating cystic from solid lesions has been widely expanded. US guided sampling procedures represent a widely accepted modality in lesion evaluation .Preoperative localization under US guidance is one of the methods of choice for non palpable solid lesions. However, the main limitation of US is its operator dependent nature , and many other factors.(9).

The role of MRI in evaluating breast disease has been studied and debated since contrast enhanced MRI was introduced in 1985.Interset has grown steadily as evidence of its usefulness has accumulated (10).

Breast magnetic resonance imaging is emerging as an important tool for the detection and characterization of breast cancer .The value of breast MR imaging is derived primarily from the high sensitivity of contrast material enhancement in the detection of breast cancer .The characterization of lesions as benign or malignant on the basis of MR imaging characteristics remains a challenge (8).

Breast MRI is continually recognized for its high sensitivity in breast cancer detection, which in some studies approaches 100%. Although not currently recommended for routine screening, breast MRI may benefit women with high-risk factors including genetic predisposition, dense breast composition, personal history of breast cancer, atypia, lobular carcinoma in situ, and family history. MRI can provide additional information for evaluating the extent of disease in women diagnosed with breast cancer, including identification of multicentric and multifocal disease in the ipsilateral breast and additional sites of cancer in the contralateral breast. Patients who have undergone a lumpectomy, patients with positive axillary nodes and unknown primary carcinomas, and patients with breast implants may also benefit from breast MRI. (11)

In this study, we attempted to investigate the validity of MRI in characterization of suspected breast lesions and to verify the improvement in its validity, particularly specificity, achieved by implementing combined qualitative and quantitative MR tools.

This study included 60 patients (15 to 75 years) with suspected breast lesions, among which 38 patients turned out to be malignant.

Mammographic evaluation of the lesions was based on Breast Imaging Reporting and Data System (BI-RADS) with classification of these lesions into BI-RADS 0 which was assigned for seven lesions with very dense breast, their further classification was based on US findings. BI-RADS II were included in our study as being accidently discovered in association with suspicious findings or being up graded after US evaluation and they represented three lesions. BI-RADS III and BI-RADS IV were our main concern in this study respectively.

Although increasing age is the single most important risk factor for developing breast cancer (12), yet the rate at which risk rises declines significantly around age 50 years. Therefore breast cancer incidence is higher in relatively younger age groups than in the general population. (13) This was reflected among the studied population who were presented with suspicious lesions of breast cancer, around 85% of cancer cases were presented in the 38-75 years age group.

A projection of the future health and economic burden of obesity in 2030 estimated that continuation of existing trends in obesity will lead to about 500,000 additional cases of cancer in the United States by 2030. This analysis also found that if every adult reduced their BMI by 1 percent, which would be equivalent to a weight loss of roughly 1 kg (or 2.2 lbs) for an adult of average weight, this would prevent the increase in the number of cancer cases and actually result in the avoidance of about 100,000 new cases of cancer.

The relationship between obesity and breast cancer may be affected by the stage of life in which a woman gains weight and becomes obese. Many studies revealed that weight gain during adult life, most often from about age 18 to between the ages of 50 and 60, has been consistently associated with risk of breast cancer after menopause.
(13)

The evidence for anthropometric factors influencing breast cancer risk is accumulating, but uncertainties remain concerning the role of fat distribution and potential effect modifiers. Study performed by Lahmann PH et al.,2011 for 5 years duration; 73,542 premenopausal and 103,344 postmenopausal women from 9 European countries, taking part in the study; categorized by cohort-wide quintiles; and expressed as continuous variables, adjusted for study center, age and other risk factors. Weight, BMI and hip circumference were positively associated with breast cancer risk (p < or= 0.002); obese women (BMI > 30) had a 31% excess risk compared to women with BMI < 25.

In this study, by One- Sample Test study revealed that there was statistically non-significance difference of benign to malignant relation in correlation to height (P value 0.345), mid-upper (P value 0.758), waist (P value 0.349) and hip (P value 0.933) circumferences. However, mid- arm circumference showed statistically significance <0.001, mimnimum 23.0 and maximum 77.0.

Due to the limited number of cases in this study, there was a trend in relation of obesity (BMI) to breast cancer , malignancy rate 55.3% in obese women and 44.7% in non obese women.

Lahmann PH et al., (14) revealed that the hip circumference in the premenopausal women was the only measureable significantly related to breast cancer (p = 0.03), after accounting for BMI. In postmenopausal women not taking exogenous hormones, general obesity is a significant predictor of breast cancer, while abdominal fat assessed as waist-hip ratio or waist circumference was not related to excess risk when adjusted for BMI. Among premenopausal women, weight and BMI showed nonsignificant inverse associations with breast cancer.

The factor of pre- and post- menopausal effect on obesity in relationship to breast cancer was not discussed in this study, that was a drawback.

Until recently, the use of breast MR imaging for screening was greatly discouraged. This has changed, mthat MR is increasingly used for screening in selected subsets of women with an increased lifetime risk for breast cancer. An increased risk for breast cancer can be due to (a) a personal history of breast cancer; (b) a history of a breast biopsy, with "borderline" biologic behavior such as radial scar, lobular carcinoma in situ, or atypical ductal hyperplasia; (c) a history of mediastinal irradiation for Hodgkin disease; or (d) a familial clustering of breast and/or ovarian cancer. For all of these subgroups, breast MR imaging has been successfully used to help detect mammographically and sonographically occult breast cancer. (15)

In the current study, we included patients who are at high risk of developing breast cancer with indeterminate imaging findings by mammography and/or ultrasonography and their MRI examination revealed occult breast lesions not seen by other imaging modalities or helped in determining the nature of previously detected equivocal lesions.

The histopathalogical types of the 38 malignant biopsies (in our study were as following: 18 cases IDC (47.4%), 6 cases invasive lobular carcinoma (15.8%), 3 cases mucinous carcinoma (7.9%) and 2 cases DCIS (5.3 %). No cases with medullary carcinoma was detected. The commonest location of the malignant masses within the breast tissue was in the multi- quadrants 34.20 % and upper outer quadrant 28.90%, of the lesions were located.

Our findings agree with Bleiweiss et al (16). They stated that the two main histologic types of invasive carcinoma of the breast are invasive duct carcinoma and invasive lobular carcinoma. Together they constitute the vast majority of infiltrative malignancies that will be encountered in routine practice. Van de Vijver(17) mentioned the estimated frequency of each histologic type of invasive breast cancer; Invasive Ductal carcinoma (not otherwise specified) 70%, Invasive Lobular carcinoma 10%, Tubular carcinoma 5%, Mucinous carcinoma 5%, Medullary carcinoma 3%, Atypical Medullary carcinoma 3% and others 4%. These frequencies are also however reflected in our study.

Of all breast imaging techniques that are currently available, including mammography, breast US, positron emission tomography, and scintimammography, MR offers the highest sensitivity for invasive breast cancer. Published sensitivity levels range between 89% and 100%. In all studies that can be found in the literature, the sensitivity of MR imaging was higher than that of mammography. The degree to which the sensitivities of mammography and breast MR imaging differ in the same patients depend on the mammographic breast density and the type of breast cancer: The difference increases with increasing breast density and for cancers that are difficult to diagnose on the basis of mammographic findings. The latter is the case, for example, in cancers with a diffuse growth pattern, such as invasive lobular cancers, and in cancers that exhibit benign morphologic features, such as medullary cancer. The sensitivity of breast MR imaging is not impaired by the amount or density of the fibroglandular tissue. (15)

Overlooking invasive breast cancer on MR images is rare, but it certainly does happen. Non-enhancing invasive breast cancers are exceedingly rare. More often, the reason for failure to diagnose invasive cancer with breast MR imaging is early and strong enhancement in the surrounding normal fibroglandular tissue that may mask the enhancing cancer. (15)

In this study, we compared the results of MRI and sonomammography in the study population to the findings of histopathology. Mammographic examination of the breast lesions yielded an overall sensitivity of 66.7%, a specificity of 93.8 % and accuracy of 74.1%.Our result is comparable to previous studies that reported the sensitivity of mammography ranged from 63 % (18) to 81.8 % (19) .On the other hand, specificity of mammography ranged from 70% (18) to 99% (19).

This studied agreed with Bassett and Kim, 2001 that the breast density is one of the most important factors limiting the sensitivity of mammography and that was encountered in seven cases in our study.

However, the high specificity of mammography in our study may be attributed to selection of our cases unlike studies which evaluated general population and healthy women who undergo periodic screening.

The results of the sonomammographic examinations of the patients were; 38% of the studied cases had dense breasts in sonomammography which hindered proper assessment of the breast masses, normal sonomammography 11.67% were detected, 6.67% were categorized as BIRADS II (probably benign), 33.33% were categorized as BIRADS III and 48.33% BIRADS IV (probably malignant).

Among the 38 cases diagnosed by sonomammography as malignant or with irregular densities, 16 turned out to be benign by histopathological evaluation (false +ve), while among the 22 cases diagnosed by sonomammography to be benign lesions or non-conclusive studies (dense), 7 were proved to be malignant by histopathological evaluation (false –ve). Among the 28 cases that had dense breasts, 7 cases turned out to have underlying malignant masses, 15 cases had underlying benign pathologies and the rest were free. All these lesions were readily identified in MRI.

Therefore our results agree with Morrow et al,(20) who stated that, compared with mammography, MRI has a higher sensitivity for the detection of breast cancer and is not affected by breast density.

The overall calculated US sensitivity, specificity and accuracy were 83.7%, 87.5% and 84.8 % respectively.

Most of the previous studies showed that the sensitivity of MR imaging for detection of breast cancer is very high, and approaches 100% for invasive carcinoma. However the specificity is lower and varies widely between different studies. The factors associated with this wide range of specificity are differences in the study population, strength of magnet, imaging protocols, and interpretation criteria. (21)

In a study done by Baltzer et al(22), they stated that false positive findings occur and lead to unnecessary biopsy and concluded that non-mass lesions were the major cause of false-positive breast MRI findings.

Some studies were done to improve specificity. A study done by Khatri et al(23)showed that improved specificity could be obtained by quantification of lesion enhancement. This method involved complex mathematical analysis. Another Study done by Siegman et al(24) showed that both qualitative and quantitative lesion characteristics were required for lesion differentiation.

Therefore the basic drawback of this modality was low specificity for breast malignancy. Multiple studies have shown that with the improvement in equipment and technique there is gradual increase in specificity. (5)

The growing role of MRI in the evaluation of breast cancer in symptomatic women has identified that MRI may provide a sensitive method for screening women for breast cancer. (25)

The data regarding the specificity and positive predictive value for screening MR are less concordant: A higher rate of false-positive diagnoses for MR imaging than for mammography has been reported in several studies (26), (27), (5). The study by Warner et al (27) provides a possible explanation for this: Whereas the rate of false positive MR diagnoses was high at the beginning of the breast MR screening project, the rate decreased from year to year to reach the same level as that for mammography, where mammography and MR exhibited equivalent positive predictive values. This observation, as well as the results from other studies (28),(15),(29) suggests that a high rate of false-positive diagnoses is not inherent to the technique of breast MR imaging. Rather, it is due to limited experience with breast MR in a screening setting. (15)

In our study the sensitivity, specificity, positive and negative predictive values of MRI for suspected breast lesions included in the study, were found to be 100%, 93%, 86%, and 100% respectively. Overall accuracy of MRI breast was 95%.

Among the 38 cases diagnosed by MRI as malignant, 0 turned out to be benign by histopathological evaluation (false +ve), while among the 15 cases diagnosed by MRI to be benign lesions, 7 were proved to be malignant by histopathological evaluation (false –ve)

It is becoming increasingly clear that while most investigators have used either enhancement kinetics or lesion morphology in an attempt to differentiate malignant from benign lesions on contrast–enhanced MR imaging studies, the integration of both kinetic and morphologic information may ultimately be needed to achieve optimal discrimination (7).

In general margin and shape analysis should be performed on first post contrast image to avoid wash out and progressive enhancement of the surrounding breast tissue (30).

Macura et al.,(31)found that the description of the margin of a focal mass is the most predictive feature of the breast MR image interpretation. Speculated margins are suspicious for carcinoma, having 91% positive predictive value (PPV) for malignancy.

In concordance with Macura et al.,(31)speculated margins in our study, having (100% specificity and 100% PPV) being encountered only in malignant lesions The calculated P value, sensitivity and specificity of mass margin in differentiating benign from malignant was 0.001, 93.1% and 52.17% respectively .

Moreover, Kuhl(15)found that some of the most powerful diagnostic criteria for the differentiation of benign and malignant tumors belong to internal enhancement of focal mass . He reported that dark septations if present within a lobular or oval mass are typical of fibroadenomas

Also, we found in our study, that non enhancing internal septa were only found in benign lesions (3 lesions) proved to be fibroadenomas by histopathology. The calculated P value of non enhancing internal septa was statistically significant (< 0.005).

Tozaki et al,(32)reported that the most frequent morphological findings among the malignant lesions was heterogeneous internal enhancement.

In our study 11 benign lesions exhibited heterogeneous enhancement, their pathological diagnosis was mastitis and fibroadenomas. Ring enhancement was found in 5 benign cases proved to be fibroadenosis with fibroadenomatoid and cystic changes. Homogenous enhancement was found in 20 lesions, 11 were benign and 9 were malignant.

Thus in our study, there was no statistical correlation between the pathologically proven benign and malignant lesions regarding their enhancement pattern except the non enhancing internal septa and this may be attributed to the small number of studied patients, however all our pathologically proven benign cases did not show enhancing internal septa (100 % specificity) and all lesions showed enhancing internal septa were malignant (100%PPV).

We encountered seven lesions of non mass like enhancement, 5 of them showing ductal enhancement and were interpreted as suspicious MRI findings,2 of them proved to be benign (duct ectasia with periductal mastitis) and 3 were malignant (invasive duct carcinoma).The remaining 2 lesions were of regional enhancement and proved pathologically to be invasive cancer with insitu component ,in which tumor extension was well delineated by MRI examination.

Kuhl,(33) reported that the lesion enhancement rate in the early post contrast period serves as a differential diagnostic criterion with malignant lesions exhibiting stronger and faster enhancement than benign changes do. Yet, a considerable number of benign proliferative changes and benign solid tumors demonstrate enhancement rates comparable to those of malignant lesions, thus reducing the technique specificity.

In this study, there was an overlap in the enhancement rate of benign and malignant lesions ranging from 25 to 120 % (in benign lesions) and from 30 to

280% (in malignant lesions). Our calculated P value was insignificant (>0.005), this is comparable with the study of Kuhl et al, 2005 who reported that enhancement rates proved to be not diagnostically relevant because of the broad overlap between benign and malignant lesions and were therefore of only limited diagnostic use in the individual patient.

The variability of quantitative methods and the overlap in the enhancement kinetics in the early post contrast enhancement period of benign and malignant lesions have led investigators to seek a qualitative approach to lesion enhancement, in which the shape of the entire time -signal intensity curve is qualitatively assessed. Use of these time-signal intensity curves resulted in dramatically higher specificity (83%) and accuracy(86%) than were obtained when enhancement rate specificity (37%) and accuracy (58%) was used (7).

We calculated the P value of each type of time signal intensity curve and we found that progressive (type I) and the wash out (type III) curves were found in 7 and 4 pathologically proven benign lesions compared to 4 and 38 malignant lesions respectively. So their calculating P value was significant (<0.005) in differentiation benign from malignant lesions with progressive type curve more observed in benign findings and wash out curve more with malignant findings . On the contrary ,the P value of plateau (type II) was insignificant (>0.005) being present in 11 benign lesions compared to 4 malignant lesions.

In this study, the calculated MRI sensitivity was 90.7%, specificity was 68.8%, NPV and PPV was 73.3% and 88.6% respectively .This was based on the combination of morphologic and kinetic criteria (34)

We observed that three pathologically proven malignant lesions were falsely classified as probably benign findings based on BIRADS Lexicon system. For example one of those lesions was invasive lobular carcinoma that exhibited regular shaped, well-defined mass of homogenous enhancement as morphologic criteria, 37% enhancement rate and wash out curve as kinetic criteria .So its scoring system was 3 consisting with BI-RADS III category .In order to increase the sensitivity and specificity of MRM we followed the guidelines described by Kuhl et al,(15) concerning MRI BI-RADS category stated classification of lesion as BI-RADS IV with a wash out time curve, irrespective of its morphology or lesion with suspicious morphology irrespective of its kinetics.

Our results were comparable with the study of Seely et al, 2007 who reported that BI-RADS categorization in breast MRI had the highest combination of specificity and sensitivity(77.1%and 81.8%)..

An assessment of probably benign is clinically helpful when used for a lesion that is not definitely benign and that can be followed safely with short term imaging surveillance rather than biopsy (35).Leung 2010 (36) stated that MR imaging has a high negative predictive value in excluding breast cancer, so it plays a role in the evaluation of selected clinical and imaging findings of the breast, especially when biopsy is not technically feasible. Case selection is very important in ensuring the efficacy of this use of MR imaging because of potential false-positive and false-negative results.

Concerning BI-RADS III lesions our calculated NPV of MRM was high (90.9%) compared to that of sonomammography (77.8%).With 9.1% false negative rate, which dose not obviate completely further need for tissue biopsy or recommendation for follow up after MRI examination

Therefore, breast MRI had higher sensitivity than specificity but generally speaking it is considered highly valid with high specificity also. We found that combining qualitative assessment of morphological appearance of lesion on post contrast study and time signal intensity curves with functional MR tools, which were utilized in about few (6 cases) of the study population, was useful for achieving high validity for breast MRI.

Therefore, we agree with Liberman(37) who claimed that MRI can detect otherwise suspected breast cancer.

Lord et al.(38)considered the value of adding MRI to mammography or mammography plus ultrasound and or clinical breast examination, concluding that adding MRI results in the detection of additional cancers, but that any mortality benefit is unknown. The overview of five studies calculated an overall sensitivity of 80.7% for MRI and 39.5% for mammography (38). Bermejo-Perez et al.(39) reported similar conclusions. An older review by Liberman (37) stated that in 3 studies that supplemented mammography with both MRI and ultrasonography, MRI had a higher sensitivity and specificity than ultrasonography and was superior in detecting ductal carcinoma in situ.

Yoshikawa et al (40) performed a study to investigate breast cancer-detecting ability of diffusion weighted magnetic resonance imaging (DW-MRI) by comparing the breast cancer detection rates of DW-MRI and mammography (MMG) in 48 women. The breast cancer detection rates by MMG and DW-MRI were 84.9% and 94.3% (statistically significant $P < 0.001$), respectively. In each classification of histology and size, the detection rate by DW-MRI was higher than that by MMG. In relation to the mammary gland density, the detection rates of fatty, scattered, heterogeneously dense, and extremely dense mammary glands were 100%.

Our results agreed well with these studies mainly as regard the high sensitivity of MRI. This could be attributed to using functional MRI tools, mainly diffusion weighted images which was done in few (6 cases) and helped to a great extent in highlighting the pathology among the normal enhancing glandular tissues.

This explains the excellent sensitivity of MRI that we achieved in this study (100%) and the ability of MRI, including DWI, to detect the lesions which were none visualized in mammography particularly in dense breasts.

Metastases to the breast from non-mammary primary tumours are uncommon and account for 0.5-2.0% of all breast malignancies. In this study, 8% of the cases were secondary metastasis ; Non-Hogkin Lymphoma and Thyroid cancer.

MRI systems at 3.0 T are now available from several major MRI manufacturers. 3.0 T machines have the advantage of higher signal-to-noise ratios (SNR) which can be traded for higher spatial resolution, higher temporal resolution, or both. New techniques, such as hydrogen spectroscopy, would also benefit from the use of 3 T systems in terms of increased spectrum resolution and higher SNR. (41)Therefore the introduction of these high field systems into clinical practice is expected to contribute further in the improvement of the validity of MRI making it more superior in comparison to other available imaging modalities.

Because investigators of breast MR imaging have reported higher sensitivities and specificities for MR imaging compared with those for mammography, it has been suggested that MR imaging could be used to further characterize indeterminate lesions detected at mammography, US or physical examination(7) The reported sensitivity of MRI for the visualization of invasive breast cancer have approached 100% in several studies, while the reported specificities have been very variable, imaging from 37%to 97%(7)

Therefore, Breast MRI is highly valid; however its disadvantages include cost, variations in technique and interpretation, variation in parenchymal enhancement during the menstrual cycle, exclusion criteria (e.g., the presence of pacemakers or aneurysm clips or a patient’s claustrophobia), and an unproved survival benefit.(37)

Hiwatsch et al, (18)reported that although MR imaging is most sensitive for detection of breast tumor, routine preoperative MR appears to be unnecessary for most patients if combination of mammography and whole breast sonography is used.

All breast imaging modalities have either "blind spots" or specific strength and weakness .It is unlikely that the diagnostic accuracy of an imaging technique will be superior to that of another in each and every clinical scenario

. Accordingly, rather than compare overall negative predictive values of imaging modalities ,one should identify specific clinical situations for which it may well be feasible to use MR imaging for problem solving and others for which the same is not attainable because the NPV is high enough (15)

Although our results are comparable to most of the previous studies, still there are a few limitations. The number of patients included in the study was limited by the relatively short duration of the study and limited number of patients who undergo breast MR examinations and fit to our inclusion criteria. This is because of the cost factor and relative lack of awareness regarding usefulness of MR imaging for the diagnosis of breast cancer.

At the end of our study, we conclude that MR imaging of breast is a rapidly evolving modality of excellent sensitivity in detection of breast cancer especially in obese patients. The basic drawback of this modality was low specificity for breast malignancy and the limitation of the coils size (extremely large breasts). However, multiple studies including this study have shown that with the improvement in equipment and technique there is gradual increase in specificity.

Generally speaking breast MRI is highly effective in detection and characterization of suspected breast lesions, with excellent sensitivity and high specificity. This is attributed to the advance in equipment, technique, development and implementation of interpretation guidelines and development of functional MRI tools which contributed to the improving validity of this modality. Also the superiority of MRI compared to mammography, supports the use of MRI as an important tool in screening of asymptomatic high risk women.

We suggest that further studies are needed to develop confidence in this emerging imaging modality should include implementation of the Multiparametric concept and utilize the functional MRI tools, which is expected to aid for better patient management and to avoid unnecessary biopsies by eliminating the false positive results that sometimes occur when using breast MRI.

Case (1)

Obese 43 years old patient

Clinical presentation

Left breast painless lump

and bloody nipple discharge

Anthropometric parameters

Wt:98kg

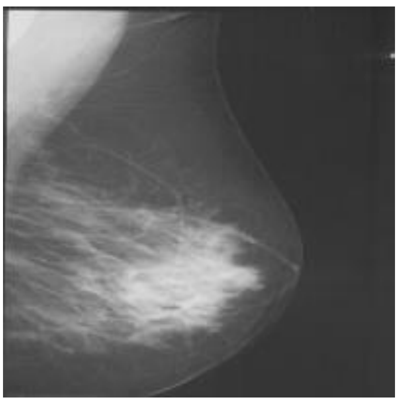
Ht:160m

Circumferences;

- Mid upper arm:47cm
- Waist:110cm
- Hip:150cm
- BMI:38.28

Mammographic findings

(Fig.a):Medio-lateral view of the left breast showing LIQ dense central architectural distortion (BI-RADS III-IV).



(Fig.a):MLO view mammogram of the left breast

Sonographic findings

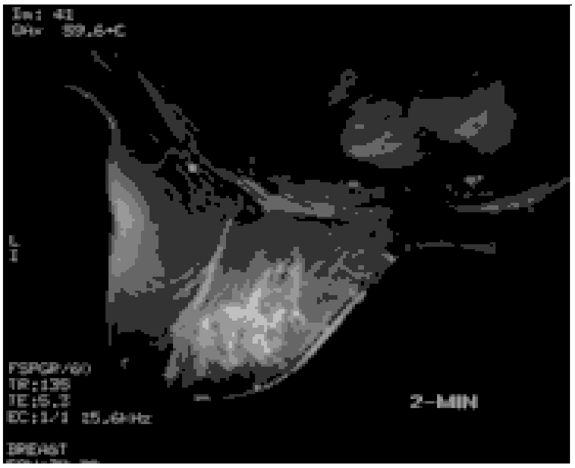
(Figs.b,c):A speculated heterogenous mass at 3 o'clock region casting posterior shadowing with ipsilateral retro-areolar ductectasia (BI-RADS III/IV).

(Fig.b):Left speculated heterogenous mass

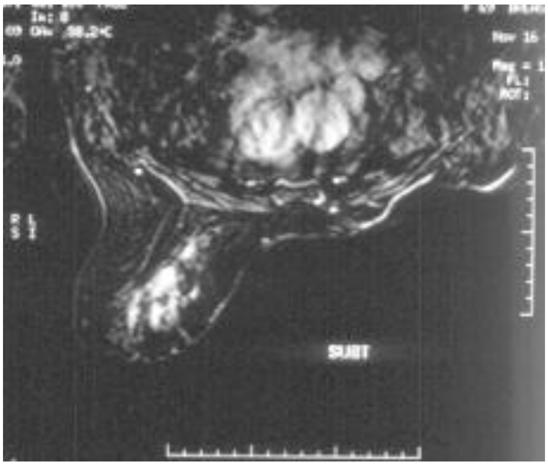
(Fig.c):Left retro-areolar ductectasia

Dynamic MRM findings

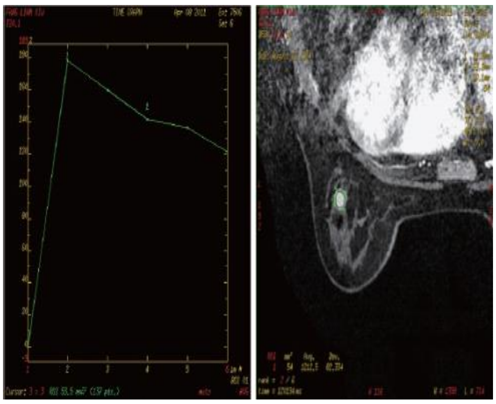
(Figs.d,e):Post contrast T1 WI fat suppression and Subtracted WI images at the same axial plane showing LIQ non mass ductal enhancement with deep extension. (Fig.f) Time signal intensity Type III malignant Wash out curve (BI-RADS IVc).



(Fig.d): Post contrast T1WI of the left breast



(Fig.e):Subtracted MR image of the left breast



(Fig.f):Time- signal intensity Type III curve Wash out

PathologyInvasive duct carcinoma grade III.

Case (2)

Non obese 56 years old patient

Clinical presentation

Right breast multiple painful lumps

Anthropometric parameters

Wt:89kg

Ht:182m

Circumferences;

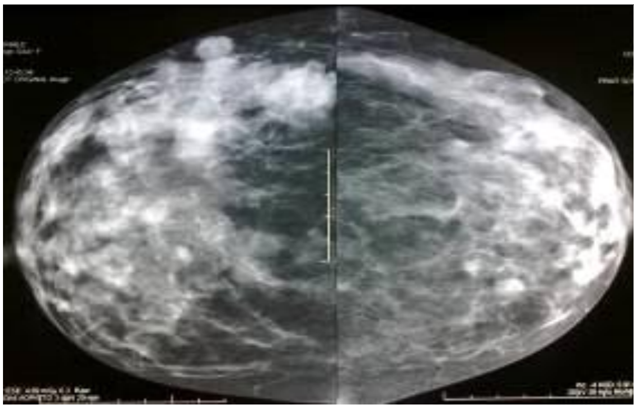
- Mid upper arm:40cm
- Waist:88cm
- Hip:94cm

BMI:26.87

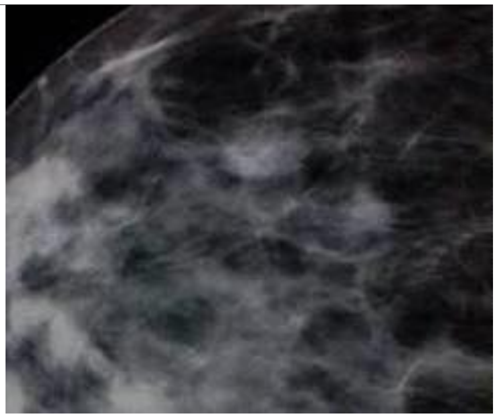
Mammographic findings

(Fig.a):Cranio-caudal view of both breasts and magnified image of the left breast showing right UOQ multiple variable in size and shape dense masses with partially ill defined margins in some (BI-RADS IVa). (arrows)

(Fig. b):Left breast LIQ suspicious looking microlobulated mass with few peripheral microcalcifications (BI-RADS III/IVa). (arrow)



(Fig.a):CC view of both breasts

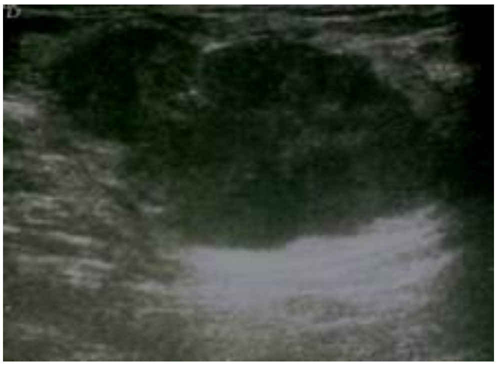


(Fig.b): Magnified image of left breast mass

Sonographic findings

(Fig.c):US of the one of the right UOQ masses showing marco lobulated broad and tall hypoechoic mass casting posterior shadowing with lower border partially ill defined margin (BI-RADS IVa).

(Fig.d): US of the left breast showing well-defined taller than wider isoechoic to hypoechoic small mass with wall enhancement(BI-RADS III).

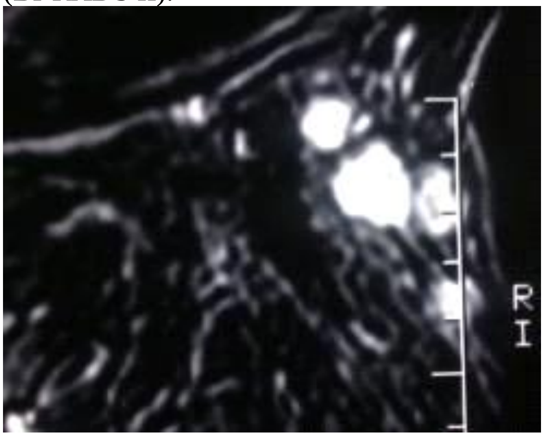


(Fig.c):US of right UOQ mass

(Fig.d):US of the left breast mass

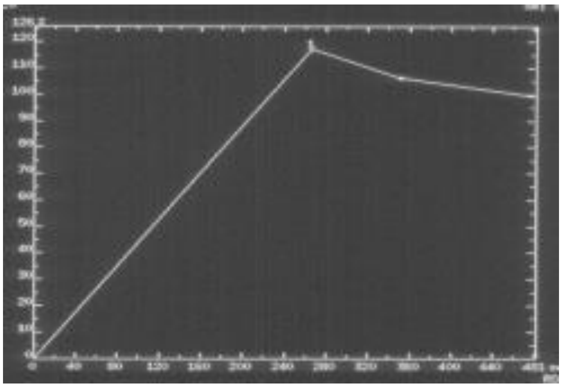
Dynamic MRM findings:

(Fig.e): Subtracted MR image showing right UOQ indistinct heterogeneously enhancing masses, some of them show fine spicules .
(Fig.f): Post contrast T1 WI fat suppression at 1 minute showing left IQ small defined lobulated intense homogenously enhanced mass.
(Fig.g,h): Time /signal intensity curves of the right breast masses are malignant type III curves with initial signal increase >100% and rapid wash out ,while the left breast mass exhibiting benign rising curve (type I). Right breast masses (BI-RADS V), left breast mass (BI-RADS II).

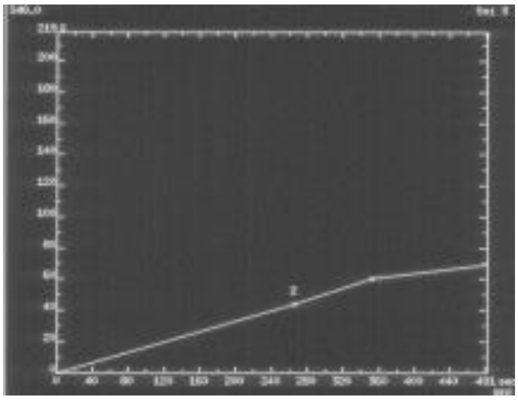


(Fig. e):Subtracted T1WI images showing multiple right UOQ enhancing masses

(Fig. f): Post contrast T1WI showing left IQ small mass



(Fig g):Time /signal intensity curve type III Wash out



(Fig.h):Time /signal intensity curve type I Progressive rise

Pathology
Right breast invasive ductal carcinoma Grade II.
Bilateral fibroadenoma.

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