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THE CONTRIBUTION OF DYNAMIC CONTRAST ENHANCED MRI IN THE DIAGNOSIS OF BREAST CANCER

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ABSTRACT

Background: Breast MRI has evolved as a promising complimentary sensitive tool for detection and local staging of breast cancer. In this study our goal was to determine the role of MRI in the preoperative assessment of breast cancer in conjunct with the traditional imaging modalities. **Patients and methods:** This prospective study was performed during the period from November 2012 to December 2013 at the Medical City Teaching Center. A selected sample of 50 female patients aged from 30-74years with a mean age of 51 year having clinical suspicion of breast cancers; were subjected to mammographic and ultrasonic classification in the breast clinic of the Oncology Hospital, confirmed by FNAC and referred to the MRI unit of Baghdad Teaching Hospital where DCE-MRI were done, utilizing a special breast coil and bilateral axial high resolution 3D scan. Histopathological confirmation was obtained from 32 patients of the study sample. **Results:** MRI interpretations in our study depend upon the enhancement pattern but basically on the temporal resolution and kinetic analysis, and patients were classified according to the Breast Imaging Reporting and Data System (BIRADS classification) as BIRADS IV and V with one patient that had a BIRADS VI. Breast MRI provides a more precise evaluation of the size of breast lesions than that obtained by US. It also determines the extent of primary cancer and chest wall invasion as well as local recurrence of a previous lesion more precisely than other imaging modalities. It has the ability to detect multifocal and bilateral lesions that did not be picked up by mammography and ultrasound. Five histopathological types were found in our study. Invasive ductal carcinoma found to be the most common accounting about 65 % of cases. MRI diagnostic yield in correlation with histopathological detection of breast cancer had a sensitivity of 93.75%. It has shown to increase the sensitivity of traditional modalities up to 100 % instead of combined sensitivity by mammography and ultrasound that did not exceed 84%. The sensitivity, specificity, accuracy and positive predictive value of breast MRI based on cytological diagnosis proved to be: 95%, 66% and 86% and 97% respectively. MRI assessment of axillary lymphadenopathy wasn't specific in our study with 61 % false positive cases regarding the kinetic analysis curves. However; morphology, signal intensity and pattern of enhancement may be suggestive about the nature of LAP. Hormonal effect on temporal resolution and the pattern of enhancement of normal breast tissue was found to display false positive type 3 malignant curves in two of our patients whom scan were performed during or shortly after their menstrual cycle. **Conclusion:** This study has revealed that DCE-MRI is the most sensitive modality in detecting breast cancer and has an important role in the preoperative assessment and work - up that can lead to better outcome as it enables the detection of cancers that are occult in other conventional imaging modalities. Most importantly; it's more sensitive in detecting multifocal and bilateral breast cancer and more accurate than US for assessing the size and extent of primary breast cancer presenting as a mass. It has a useful role in detecting local recurrence in addition. **Recommendations:** Because of the world wide promising role of breast MRI; we recommend an establishment of a specialized unit with a well-qualified and expect staff as this will allow proper selection of high risk group population that improves early detection of breast cancer and hence better prognosis Further studies with larger samples are recommended with more detailed evaluation of each of MRI indication to determine the effect of its utilization in planning management and improving the outcome. To increase specificity; proper selection of high risk patients and proper timing for premenopausal patients to perform their breast MRI between day 7and 14 of their menstrual cycles as this period has a relative reduced hormonal effect on the pattern of enhancement and temporal resolution i.e. the least false-positive enhancement.

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INTRODUCTION

Breast MRI has evolved as a promising complimentary tool for detection and local staging of breast cancers and is indicated in:

1. Detection of mammographically occult breast malignant masses in patients with dense breasts as well as detecting the non-mass like lesions that are equivocal on conventional imaging.
2. Problem solving technique:
   A. Clinical / imaging discrepancy; e.g. malignant or suspicious clinical mass, with benign or normal conventional imaging, or size discrepancy.
   B. Assessment of disease recurrence that can be difficult to detect on conventional imaging in the early stages where the appearances of post-operative and radiotherapy changes can both mimic signs of malignancy.

3. Exclude multi focal breast cancer as well as assessing the other breast; influence the multifocality and bilaterality of breast cancer.

4. Assessment of disease extent in cases of
   a) Invasive lobular carcinoma which is often difficult to diagnose on clinical examination and conventional imaging and its extent is notoriously difficult to determine as its likely to be more extensive in MRI; thereby informs the surgeon about the most appropriate surgery to clear the tumor margins in one step operation.
   b) Ductal carcinoma in situ ; in dense breasts it is often difficult to adequately assess disease extent and MRI might be useful before considering wide local excision, especially in cases of high grade cancer.

5. Local staging; including invasion to the deep fascia and pulmonary infiltrate; so the best treatment can be chosen.
6. Look at breast tissue changes during treatment for cancer and assess the response of chemotherapy in advanced cancer; it can change the treatment plan in 15-30% of patients with breast cancer.
7. Post operative assessment; looking for any residual disease after lumpectomy.
8. Patient with metastatic disease and axillary LN with unknown primary
9. Screening high risk group patient for breast cancer such as those who test positive for the BRCA-1 or BRCA-2 gene, or who have two or more close family members who had breast or ovarian cancer before the age of 50.
10. Assessment of breast implants; to evaluate their integrity and looking at a suspicious area of those women (Charles Perou *et al.,* 2012; Meaad Al Attar, 2013; Leonard Glassman, 2009).

Dynamic contrast enhanced MRI interpretation Breast lesions could be displayed as mass or non-mass like lesions.

Masses: Morphology including the shape and margin where an irregular masses that cannot be characterized as round, oval, or lobulated, it has a 32% chance of being malignant. While an irregular or speculated margins has 80% chance of being malignant.

T1-T2 characteristics :

High signal on T1: The pre-contrast T1, non-fat-suppressed sequence can show a high signal due to the presence of fat in a lesion such as hamartoma. Central high signal can be seen in intra-mammary lymph nodes or fat necrosis. Fatty lesions are benign unless, rapidly growing and they should be biopsied.

High signal on T2-fat suppression: Bright lesions on T2 are cysts, lymph nodes and fat necrosis and all are benign. Unfortunately one exception to the rule is the colloid carcinoma

Moderate and low signal on non-contrast enhanced T1 and T2-fat suppression: Usually caused by invasive lobular carcinoma (ILC) and ductal carcinoma in situ (DCIS) display moderate signal while invasive ductal carcinoma (IDC) displays low signal on T2 fat suppression; however fibrocystic changes can also produce moderate signal while scar and sclerotic fibroadenoma display low signal.

Enhancement pattern of a mass: this occurs in six main patterns:

1. Homogeneous enhancement: uniform and confluent enhancement throughout the mass that can be seen in an invasive ductal carcinoma.
2. Heterogeneous enhancement: non uniform enhancement, which varies within the mass may demonstrated an invasive lobular carcinoma.
3. Rim enhancement: mainly peripheral and is frequently a feature of high-grade invasive ductal cancer, fat necrosis and an inflammatory or atypical cyst. This has a 40% chance of being malignant.
4. Dark internal septations refers to non-enhancing septations in an enhancing mass that are typical for fibroadenoma, especially when the lesion has smooth or lobulated margins.
5. Enhancing internal septations are usually a feature of malignancy.
6. Central enhancement is pronounced enhancement of a nidus within an enhancing mass which is associated with high-grade ductal cancer.

Kinetic Analysis and Temporal Resolution (Curves) interpretation: The kinetic analysis takes about six minutes of repetitive scanning in total and can lead to three types of curves (Leonard Glassman, 2009). The initial upslope of the curve in the first 1-2 min of dynamic scan or until first change of curve; can be slow, medium or rapid. Then there is the delayed portion; 2 min. or more after the injection of contrast medium ; can show three patterns: a continued increase enhancement (persistent pattern; type 1 curve), steady enhancement (plateau pattern; type 2 curve) and decrease in signal intensity (washout pattern; type 3 curve). Early washout pattern and plateau pattern are more likely to be associated with malignancy, whereas persistent pattern usually benign lesions and lesions associated with hormonal changes (Erguvan-Dogan *et al.,* 2006).

I, Initial upslope of curve can be slow (1), medium (2), or rapid (3) within 2 min. of dynamic scan or until first change in curve.

II, after first 2 min Continued increase enhancement is persistent pattern; steady enhancement is plateau pattern; and decrease in signal intensity is washout pattern.

Early washout pattern and plateau pattern are more likely to be associated with malignancy, whereas persistent pattern usually benign lesions and lesions associated with hormonal changes (Erguvan-Dogan *et al.,* 2006).

Computer Assisted Diagnosis (CAD): A purely kinetic evaluation that does not evaluate the anatomy but looks at the curves and peak enhancements for the CM (automated kinetics) and has some very nice features such as motion registration during subtraction which can correct for a patient's movement during the exam. It can do multiplanar reconstruction and subtraction very well and quickly and has a good measurement package. In CAD, red is bad: it means type 3 washout and probably cancer. Non Mass like lesions: it is the enhancement without 3D characteristics and it occurs in a significant number of cancers; its distribution, pattern and whether symmetrical or not all should be looked for:

Distribution

Focal: it refers to enhancement in less than25% of a quarter of the breast.

Ductal: enhancement occurs in a duct and is cancer in 60% of cases.

Linear: it doesn`t have a ductal orientation and its cancer in 31% of cases.

Segmental: refers to multiple ducts and has a78%chance of being cancer.

Regional: not ductal or segmental and larger than focal ; 21% ca possibility

Diffuse: this is typically benign.

Internal Enhancement Pattern:
Homogeneous or non-heterogeneous, just as mass enhancement. It could be:

Punctuate; which is usually benign, but when occur focally there is a 25% chance of being a cancer. Clumped this is the most important non-mass enhancing pattern. It has a 60% chance of cancer (typically DCIS). Kinetic Analysis for non-mass enhancement is not very useful especially in low-grades as many cases of DCIS that show no washout and usually there is slow initial enhancement (Gillian Newstead, 2012). A focus 'little bright objects'; enhancing areas of less than 5mm in diameter and are too small to characterize, they have typically stable persistent type 1 curves on follow-up and are considered to be a part of the normal background enhancement pattern in the breast (Leonard Glassman, 2009). To overcome difficulties arising from lack of standardization among radiologists in describing lesions and interpret results to the referring physicians; the BI-RADS-MRI lexicon was published in 2003 as a part of the ACR's Breast Imaging Reporting and Data System Atlas (Leonard Glassman, 2009; Reston Va, 2003). The assessment categories were developed for Mx and later adapted for the MRI and US Atlases. The summary of each category, given below, is identical for all 3 modalities. Category 6 was added in the 4th edition of the Mammography Atlas.

0: Incomplete.
1: Negative.
2: Benign finding(s).
3: Probably benign only 2% malignancy.
4: Suspicious abnormality30-93% malignancy.
5: Highly suggestive of malignancy >95% malignancy.
6: Known biopsy – proven malignancy (Reston Va, 2003).

A BI-RADS classification of 4 or 5 warrants biopsy to further evaluate the offending lesion (ACR, 2009). Some experts believe that the single BI-RADS 4 classification does not adequately communicate the risk of cancer to doctors and recommend a sub classification scheme (Sanders *et al.,* 2010).

4A: low suspicion for malignancy.
4B: intermediate suspicion of malignancy.
4C: moderate concern, but not classic for malignancy as in BIRADS V.

Associated findings: Nipple retraction or inversion, skin retraction, thickening or invasion, pectoralis muscle or chest wall invasion, high signal intensity in ducts on unenhanced images, abnormal signal void, hematoma, edema, LAP and cysts; all should be included in interpretation of a breast MRI report.

Aim of the study

This study is conducted to evaluate the clinical application of dynamic contrast enhanced MRI in breast cancer : describe its value on the diagnostic yield and early detection and find out its role in the preoperative assessment, local staging and management ; in conjunct with the traditional imaging modalities including mammography and ultrasound.

PATIENTS AND METHODS

During the period from November 2012 to December 2013; 50 women with high suspicion of breast cancers referred from the breast clinic at the Oncology Hospital to the MRI unit at Baghdad Teaching hospital in Medical City where breast DCE-MRI was done. The patients' ages range from 30-74 years with a mean age of 51years. Marital state, obstetrical history and breast feeding, relevant family history, previous breast problems, and history of contraceptive pills were added to the data of each patient. Clinical presentation and patients complains, physical breast examinations were performed; the size, location, consistency and mobility of breast masses were noted as well as any previous scar, asymmetry between breasts, nipple discharge, skin changes or discolorations, thickened skin or peau d 'orange and lymph node status were assessed. Mammography and ultrasound were done for all patients and FNAC were done to 47 patients of the suspected malignant masses. MRI for patients with BI-RADS III, IV and V were carried out using Philips- Achevia machine 1.5 Tesla. After assessing the patients' blood urea and serum creatinine to confirm normal renal function; every patient was examined in a prone position on the MR table with her both breasts within a special breast coil and bilateral breasts where examined according to the following protocol: 3 mm slice thickness and 1mm gap was applied in all sequences staring with T2 axial,T1axial, DWI, T2 fat suppression and sometimes coronal T2 (when needed), then a dynamic study with IV contrast;

Dimeglumin Gadopentetate (each ml = 449mg Gado); the dose given to the patient about 1mmol/ kg by manual injection and post contrast sequence (eTHRIV; enhanced T1 high resolution isotropic volume excitation). The examination takes about 40-60 minutes for each patient, then the curve is displayed by choosing the area of maximum enhancement and data were transformed to the work station where they were studied carefully and reported by an expert specialist; Dr. E. A. who described the site, morphology, pattern of enhancement and the type of curve displayed for each detected mass as well as extension of the lesion, any axillary LAP and/ or chest wall invasion and finally gave the conclusion by applying the BIRADS classification. Histopathological studies following excisional biopsies and / or mastectomy were undertaken for 32 of the total 50 women who had imaging diagnosis of breast cancer.

Principles of statistics:

A. Descriptive statistics: Including: tables and figures, numbers and percentages, arithmetic mean and standard deviation.

B. Analytical statistics:

1. Validity The value of a diagnostic test lies in its ability to detect patients with disease; (its sensitivity), and to exclude patients without disease; (its specificity) and accuracy.
2. Predictive values:- Positive Predictive Value (PV^+): Is the probability that person actually has the disease giving that he or she tests positive, it is also called "Yield" of the test:

C. Statistical software

1. Microsoft excel 2007
2. Mini tab version 17

RESULTS

A total number of 50 female patients with clinical suspicion of breast malignancy were included in this prospective analytic study and had mammographic and ultrasonic classification as BIRADS III, IV, V and one case had previous mastectomy (BIRADS VI).

Table 1. Age distribution of breast lesions in the study sample

Group	Age	No	%
1	31-40	14	28
2	41-50	16	32
3	51andabove	20	40
Total		50	100

Mean age 51.4

Table 2. Clinical presentation of breast lesions in the study sample

	Clinical presentation of patient with breast lesions	No	%
1	Painless mass only	34	68
2	Pain +tenderness	5	10
3	Pain +nipple discharge	5	10
4	Skin- nipple changes	3	6
5	Skin–nipple changes +pain	2	4
6	Nipple discharge	1	2
Total		50	100

Table 3. Anatomical distribution of breast lesions in the study sample

	Anatomical site	No	%
1	UOQ	30	60
2	UIQ	4	8
3	LIQ	4	8
4	Retro areolar	4	8
5	LOQ	3	6
6	Lower mid zone	3	6
7	Upper mid zone	2	4
total		50	100

Table 4. MRI enhancement pattern of breast masses in the study sample

	MRI pattern of enhancement	N0	%
1	Homogenous intense	24	48
2	Heterogeneous intense	11	22
3	Heterogeneous moderate	8	16
4	Homogenous moderate	7	14
Total		50	100

Table 5 (A). MRI kinetic analysis and temporal resolution of unifocal lesions

	kinetic analysis and temporal resolution	No	%
1	Type 3 curve	29	72.5
2	Type 2 curve	11	27.5
Total		40	100

Table 5 (B). MRI kinetic analysis and temporal resolution of multifocal lesions

	kinetic analysis and temporal resolution	No	%
1	Type 3 curve	16	70
2	Type 2 curve	7	30
total		23	100

NB. Three patients had three masses and seven patients had two masses.

Table 6. MRI BIRADS classification in the study sample

	BIRAD classification	No	%
1	BIRAD V	44	88
2	BIRAD IV	5	10
3	BIRAD VI	1	2
Total		50	100

Table 7. Comparison between MRI and US in determining the size of breast masses

comparison of size of lesion concerning US and MRI	US	MRI
Mean	19.3	27.5
SD	11	15

Table 8. Histological classification of breast cancer in the study sample

	Histological classification of breast cancer	No	%
1	Invasive ductal ca.	21	65
2	Ductal ca in situ	4	12
3	Mixed invasive lobular and ductal ca.	3	10
4	Invasive lobular ca.	3	10
5	Inflammatory Ca.	1	3
Total		32	100

Table 9. Comparison of MRI sensitivity with traditional imaging modalities according to histopathological diagnosis

Comparative diagnostic sensitivity of imaging modalities	detected by Mx	detected by US	detected by Mx-US	detected by MRI	detected by MRI-US-Mx
Sensitivity of cancer detection	50%	78%	84%	93.7%	100%

Table 10. Show MRI / Cytology validity of study sample

Yield*	Sensitivity	Specificity	accuracy	PV+
MRI	95%	66%	86%	97%

Fig 2. T1 and T2 weighted images

DISCUSSION

MRI accuracy influenced by many factors including the selection of appropriate indications (Sylvia *et al.,* 2001), standardization of technical factors including; field strength, suitable surface coil, thin slices, pulse sequences and CM (Heywang- kobrunner, 1996; Fischer, 1999). It also depends on the image interpretation criteria employed which should be based on morphology and pattern and dynamics of enhancement (Heywang- kobrunner, 1996; Nunes *et al.,* 1997). Patients` selection should be limited to lesions that cannot be adequately evaluated by other imaging modalities (Nunes *et al.,* 1997). In this prospective study, a selected sample of 50 female patients with a mammographic and Ultrasonic classification of indeterminate and suspicious breast lesions; BIRADS III, IV and V were examined with DCE-MRI, in a comparable principles with that of Sylvia H.H et al., who stated that the best results of breast MRI will based on the strict selection of the appropriate indications (Nunes *et al.,* 1997).

Our protocol selection and technical factors adjustment together with the interpretation criteria; describing the lesion and its pattern of enhancement with basic dependency on the kinetic analysis curves, all were relatively comparable to those used by Heywang *el al*. (1996) and Nunes *et al.* (1997). The commonest presentation in our study sample was a painless palpable mass; seen in 68% of cases with a 60% were found in the UOQ; reasonably comparable with Ellsworth et al, who demonstrate an increased levels of genomic instability of outer breast quadrants (Ellsworth *et al.,* 2004) and in agreement with Hadi A.M. study who found that 58.06% of malignant breast lesions situated at the UOQ (Hadi, 1998). The malignant masses displayed either low or intermediate signal intensity on the non-enhanced T1 and T2weighted images (Fig.2) and were enhanced homogeneously and intensely in 48% of patients, heterogeneously and intensely in 22% of patient while moderate heterogeneous and homogenous enhancement displayed in 16% and 14% of patients respectively. The enhancement criteria in our cases fulfilled the criteria of malignant enhancement pattern proved by Leonard Glassman

in his literature about breast MRI (Leonard Glassman, 2005). In our study the kinetic analysis; done to all breast masses where type 3 and type 2 curves displayed in 72.5% and 27.5% respectively in patients with unifocal breast cancerand70% and 30% of masses in multifocal breast cancers. MRI BIRADS classification of our sample showed 88% of patients with BIRADS V which has a high malignant probability (>95%), in a addition to one patient with recurrent cancer (BIRADS VI) corresponds to 2% of patients, while BIRADS IV found only in 10 % of the study sample. MRI-based tumor size has a mean of 27.5mm and standard deviation of 15, while the mean size with US measurement was 19.3 and a standard deviation of 11. About 8.2mm increase of the mean size in MRI and this is relatively in agreement with the other studies made by Wasif *et al.* (2009) and Weatherall (2001) who stated that MRI is more accurate in assessing the size of primary breast cancer. Chest wall invasion was found in two of patients with invasive lobular carcinoma that couldn't be detected by other modalities one of which showed multiple focal liver enhancing masses suggesting secondary metastases. Recurrent breast cancer seen in one patient who had previous mastectomy; presented with pain and tenderness; an intense homogeneous enhancement and type 3 curve on kinetic analysis revealed by MRI.

In FNAC; malignant epithelial cells with marked pleomorphism and glandular proliferation was depicted. Hence breast MRI may help in a more precise evaluation of the extent of breast cancer assisting local staging. It also help in detecting recurrence of previously treated cancer, when other imaging tests have been inconclusive. Those finding were comparable to other studies and literatures (Charles Perou *et al.,* 2012;' Meaad Al Attar *et al.,* 2013 Breast, 2009; Diagnostic Breast Imaging, 2001; Rakha *et al.,* 2010; Abeloff *et al.,* 2012). In 10 cases; more than one mass detected: in 7cases bilateral masses were detected; two were detected in mammography and ultrasound and confirmed by FNAC while in the other five cases, the patients were asymptomatic and no palpable masses were felt on examination; thus detected incidentally during bilateral breast MRI. Multifocal breast cancers were detected in 3 cases of the study sample; in the 1st case ; a large ulcerating mass detected by mammography and ultrasound then confirmed by FNAC, while the 2nd mass was non palpable and can't be detected on conventional modalities ; revealed by DCE-MR; both masses proved to be ILC on histopathology. In the other two cases; small, deeply seated, non-palpable masses were detected incidentally on DCE-MRI that were originally done to a symptomatic ipsilateral masses. It has been claimed that MRI is more sensitive in identifying multifocal and / or bilateral breast cancers. in full agreement with a study by Sardanelli *et al.* who conclude that MRI is more sensitive than mammography for the detection of multiple malignant foci in fibro-glandular or dense breasts and mammography missed larger and more invasive cancer foci than MRI (Charles Perou *et al.,* 2012;' Meaad Al Attar *et al.,* 2013 Breast, 2009; Sardanelli, 2004). DCIS usually found during breast cancer screening mammogram. In our study, we select only symptomatic patients that's why; the four cases of DCIS were found incidentally in patients had presented with other palpable masses in the contralateral breasts in three of cases and displayed as a small deeply seated ipsilateral mass in the fourth patient. IDC found in 21patient, all presented with palpable breast masses. It's found to be the most common histopathological type accounting about 65 % of our sample that is shown to be comparable to the available literatures (Sylvia *et al.,* 2001; Sujana Movva, 2013; Pam Stephan, 2012). ILC found in 3patients out of 32 patients (10%) two of them presented with thickening of skin with nipple retraction and the 3rd was presented with nipple discharge and all with large masses. ILC makes up a small portion of all breast cancers, it typically doesn't form a lump and may cause no signs and symptoms at its earliest stages but as it grows larger, it may result in a mass or thickening of the tissue or an area of swelling and fullness or a change in the texture and appearance of the skin over the lesion, such as dimpling or thickening or it may cause an inverted nipple. Women with ILC tend to be a few years older than women diagnosed with other types of breast cancer. It is more likely to occur in both breasts compared with other types of breast cancer (Rakha *et al.,* 2010; Abeloff *et al.,* 2012). Mixed infiltrative ductal and lobular breast cancer found in 3 cases (10%) of our sample. Inflammatory breast cancer considered as locally advanced cancer with poor prognosis. It is a rare type; found only in one of our cases presented with enlarged, heavy and red breast with a large irregular rigid area that can easily be confused with a breast infection, however dimpling and ridges on the skin of the affected breast similar to an orange peel and multiple ipsilateral axillary lymph nodes; all provide features parallel to the typical criteria of this type of cancer (Dawood *et al.,* 2011). DCE-MRI sensitivity in detecting breast cancer found to be 93.75% in correlation with histopathological diagnosis. It also increased the sensitivity of other modalities up to 100 % versus mammography sensitivity of 50% and ultrasound sensitivity 78% while combined sensitivity by mammography and US together did not exceed 84% in our sample LAP had been found in 23 patients. Malignant infiltration proved pathologically in 9 cases while benign reactive lymph nodes were depicted in 14 of cases. MRI showed type 3; malignant curves, i.e. high false positive rate; about 61%, implying that the kinetic analysis is not useful in determining malignant lymph node infiltration, however the morphology may be of help in suggesting the nature of LAP such as the fatty center in benign reactive enlarged lymph nodes that display a hyper-intense signal on non-enhanced T1 weighted sequence while malignant nodes exhibit peripheral enhancement in dynamic CE MRI Two falls positive results were depicted in our study; the 1st patient presented with a well defined retro-areolar mass with US features of fibroadenoma but slight tenderness together with some reactive breast and skin changes made the overall features indeterminate (BIRADS III US classification) while mammography was inconclusive due to dense breast while the MRI features goes with malignancy. The 2nd patient complaining of bilateral mastalgia and nipple discharge; the mammography features again were non-specific due to dense breast and US shows prominent glandular tissue and diffuse adenosis that shows non homogenous echo-texture and again was classified as BIRADS III. Both of them; displayed malignant curves in DCE-MRI and had no malignancy on cytology. In correlation with clinical data the 1st was at her secretary phase of cycle and the 2nd was at her third day of cycle (proliferative phase); thus false positive results had been explained by the hormonal effect on temporal resolution and the pattern of enhancement of normal breast tissue. Those results fulfill the available literatures that stated false-positive diffuse and nodular enhancement occur especially in 1st and 4th weeks during the menstrual cycle (Christopher *et al.,* 2001). MRI and cytology diagnostic validity including MRI sensitivity, specificity, accuracy and positive predictive value were 95%, 66%, 86% and 97% respectively and is well comparative with related articles It has been claimed that MRI is a very sensitive

method for detecting even small cancers that cannot be detected by conventional imaging modalities in full agreement with most of other studies and literatures (Breast , 2009; Gillian Newstead , 2012; Sylvia *et al.,* 2001; Eliassen *et al.,* 2010).

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