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# The Role of Magnetic Resonance Imaging in Surgical Decision Making of Suspicious Breast Lesions in Dense Breast

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## ABSTRACT

**Background**: Presurgical Magnetic Resonance Imaging **(**MRI) is increasingly used for staging patients with breast cancer. If breast-conserving surgery (BCS) is required, MRI evaluation has to be carried out to cases with suspected breast cancer, in particular those with dense breast parenchyma, in which the sensitivity of ultrasonography and mammography is low. **Objective**: The aim of the current study is to evaluate the validity of MRI in surgical decision making in women with dense breast who are provisionally diagnosed to have breast cancer by sono-mammography and are considered suitable for BCS with pathological correlation of MRI findings.

**Patients and methods**: A prospective case series was conducted on females with dense breast admitted at Mansoura Oncology Center, during the period of 2 years. The study included patients with dense breast (mammography ACR C & D) who are provisionally diagnosed to have breast cancer by sono-mammography and are considered suitable for BCS. All cases underwent breast sonography and MRI. **Results**: The study was carried out on a total of 30 female cases, with mean age 43 years old. All cases show abnormal sono-mammographic findings. MRI displayed additional suspicious findings in the form of non-mass enhancement in 50%, multifocal lesions in 10%, multicentric lesions with non-mass enhancement and deep fascia infiltration in 3.33%. Concordance and discordancy between MRI additional findings and pathology displayed true positive in 95.2%. Only 1 (4.8%) non-mass enhancement was false positive (4.8%). **Conclusion**: Regarding BCS for cases with dense breast, preoperative breast MRI provides more information in detecting multifocal, multicentric, and extension of lesions which is necessary for determining the management plan.

**Keywords**: Breast cancer, Invasive ductal carcinoma, Ductal carcinoma in situ.

## INTRODUCTION

Breast cancer is the most frequent cancer diagnosed in females, representing more than one out of ten new cancer diagnoses annually. It is the second most common etiology of death from cancer among females globally [1]. Age, familial history of breast disease, genetic and environmental factors have been accompanied by a higher possibility for the development of breast cancer [2]. Early diagnosis is required for proper choice of therapeutic strategy. Although mammography and ultrasound (US) are the most frequently radiological approached utilized for the diagnosis of breast alterations, the comparatively low sensitivity and specificity of such approaches (especially among cases with dense breast tissue) resulted in a demand for recent imaging approaches [3].

Breast density has implications for breast screening and risk. Dense breast tissue obscures tumors on a mammogram and has been considered as an independent predisposing factor for breast cancer development. Since dense breasts are frequently detected and not abnormal, it is identified that mammograms are of minimal efficiency as regards dense breasts and additional screening could help the recognition of the early stages of breast cancer among cases with dense breasts [4].

The primary diagnostic value of Magnetic Resonance Imaging (MRI) depends on detection of foci of multifocal, multicentric or contralateral disease unrecognized on traditional evaluation (clinical examination, mammography and US), identification of invasive components in ductal carcinoma in situ (DCIS), evaluating the response to neoadjuvant chemotherapy (NAC) and detection of an occult primary breast cancer in cases with manifestations of metastasis in axillary lymph nodes (LNs) as well as identification of cancer in dense breast tissue [3].

Surgeries for breast cancer are composed of 2 primary methods: breast-conserving surgery (BCS), only the tumour and an area of normal tissue adjacent to it are excised. Mastectomy, entire breast tissue is excised [5,6]. In recent years, BCS with radiation therapy has been considered as the traditional therapy in the context of cases with low grade breast cancer. It is safe and favored therapeutic approach in all early detected breast cancers, as it offers comparable efficiency of overall survival as mastectomy by a lot of researches. In addition, BCS offers a better esthetic appearance, in comparison with radical management, a considerable gain for cases [7]. The aim of the current study is to evaluate the validity of MRI in surgical decision making in women with dense breast who are provisionally diagnosed to have breast cancer by sono-mammography and are considered suitable for BCS with pathological correlation of MRI findings.

## PATIENTS AND METHODS

A prospective case series was conducted on females with dense breast admitted at Mansoura Oncology Center, during the period of 2 years. The study included patients with dense breast (mammography ACR C & D) who are provisionally diagnosed to have breast cancer by sono-mammography and are considered suitable for BCS. Cases with sono-



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mammographic suspicious multifocal and multicentric lesions, patients who have contraindications to MRI examination such as with cardiac pacemaker or cardiac defibrillator, renal function impairment, pregnancy and severe claustrophobia were excluded.

**Methods**:

Entire cases were subjected to complete medical history, physical examination by our colleagues in Mansoura Oncology Center, reviewing of any previous radiological data (if available), radiological investigation in the form of (revision of included mammographic images followed by repeated sonography and breast MRI examination), and ultrasound True-cut guided biopsy for pathological conformation.

**Radiological Investigation**

***Mammography:*** Cranio-caudal (CC) and medio-lateral (ML) views were performed for entire cases and then evaluated in the context of the breast composition, masses (shape, border, density and location), calcifications (classically benign, suspicious and distribution), structural distortion, asymmetries, solitary dilated duct, intramammary LNs, skin lesion, axillary adenopathy and accompanying features (such as skin retraction, and thickening).

***Ultrasound (US):*** Breast US was carried out for entire cases by utilizing high frequency probe (5-12 MHz) with comment on, tissue component, masses, calcifications (in a mass, outside of a mass and intraductal), accompanying signs (architecture distortion, duct alterations, skin thickening, skin retraction, edema and vascularity (absent, internal and rim)), and LNs.

***Post contrast MRI examination:*** Bilateral breast examination was carried out for entire cases using 1.5T machine (Philips) at MRI unit at Diagnostic Radiology Department of Mansoura University Hospitals.

❖ **Image Acquisition:**

1. Localizing sagittal protocol (scout view).
2. T1-weighted pulse sequence: By utilizing fast spin echo (FSE) with the following imaging parameters: repetition time (TR) 500ms, time to echo (TE) 8ms, slice thickness 3 mm, field of view (FOV) 400-500 mm, matrix 256×256 and flip angle (FA) 90 degree to obtain axial non-fat saturated T1WI.
3. T2-weighted pulse sequence: By utilizing FSE with the next imaging parameters TR 2500ms, TE 120ms, slice thickness 3mm, FOV 400-500 mm, matrix 256×256 and FA 90 degree to obtain axial non-fat saturated T2WI.
4. Short T1 inversion recovery (STIR): By utilizing TR 3700ms, TE 65ms and inversion time (TI) 150ms, slice thickness 3mm with inter-slice gap 1mm, FOV 400-500mm, matrix 256×256 and FA 90 degree to get STIR images.
5. Dynamic study: A bolus of Gd DTPA- magnevist was injected in a dosage of 0.2mmol/kg by utilizing an automated injector at a rate of 2ml/sec. One pre contrast and 5 post contrast series were acquired in dynamic study, each of them is about 1.16 minute with a break between the non-contrast and post contrast study approximately 20sec. Entire dynamic studies were made in the axial plane with fat suppression via the application of fat saturated pulse. The used sequence was gradient GRE-T1 weighted images with the next parameters: TR 3-4ms, TE 1.5ms, slice thickness 2mm without inter-slice gap, FOV 450mm, matrix 256×256 and flip angle 10 degree.

❖ **Image Post-Processing**

1. Image subtraction: Pre-contrast images were subtracted from each post-contrast images.
2. Maximum intensity projection (MIP) views were acquired across all orthogonal plane, producing sagittal, coronal and axial projections.
3. Morphological analysis was done for the presence of lesions and was categorized for (mass, non-mass enhancement and enhanced focus).

**Ethical Consideration:**

**This study was ethically approved by the Institutional Review Board of the Faculty of Medicine, Mansoura University. Written informed consent was obtained from all participants. This study was executed according to the code of ethics of the World Medical Association (Declaration of Helsinki) for studies on humans.**

***Statistical Analysis***

The collected data were introduced and statistically analyzed by utilizing the Statistical Package for Social Sciences (SPSS) version 20 for windows. Qualitative data were defined as numbers and percentages. Chi-Square test and Fisher's exact test were used for comparison between categorical variables as appropriate. Quantitative data were tested for normality by Kolmogorov-Smirnov test. Normal distribution of variables was described as mean and standard deviation (SD), and independent sample t-test was used for comparison between groups. P value $\leq 0.05$ was considered to be statistically significant. Sensitivity and predictive values are assessed using cross tabulation with detection of true positive cases.

**RESULTS**

The study was carried out on a total of 30 female cases with suspicious breast cancer, referred from Mansoura Oncology Center. The mean age was 43 years; most of the cases were within the age from 40-45 years (50%), followed by 45-50 years (30%) and 36-40 years (20%).

The clinical presentations were breast lump (56.67%), both breast and axillary lumps (20%), mastalgia and axillary lump (16.67%) and only axillary lump (6.67%). Lesions were observed at right side in 19 (63.67%) patients and left side in 11 (36.3%) patients.

**Table 1** demonstrates pathological types of the 30 lesions of the studied women with BCS.

**Table (1): Pathological types of lesions of studied patients.**

| Type | No | % |
|---|---|---|
| ▪ **IDC** | **(28)** | **(93.33)** |
| ○ **No definite DCIS component** | **(5)** | **(16.66)** |
| • Lympho-vasculer embolization (LVE) | 2 | 6.66 |
| • Focal atypical hyperplasia (FAH) | 1 | 3.33 |
| ○ **DCIS component <5%** | **(17)** | **(56.66)** |
| • Low grade | 6 | 20 |
| • Low grade with lympho-vasculer embolization (LVE) | 5 | 16.66 |
| • Intermediate grade with cancerization of lobules (COL) and lympho-vasculer embolization (LVE) | 3 | 10 |
| • High grade (comedo type) with lympho-vasculer embolization (LVE) | 3 | 10 |
| ○ **DCIS component >20%** | **(6)** | **(20)** |
| • Intermediate grade | 3 | 10 |
| • High grade (comedo type) | 3 | 10 |
| ▪ **Others** | **(2)** | **(6.66)** |
| ○ Sclerosing adenosis | 1 | 3.33 |
| ○ Chronic abscess | 1 | 3.33 |
| **Total** | 30 | 100 |

**Table 2** demonstrates radiological findings of suspicious lesions and MRI lymph nodes evaluation. Up to 80% of cases displayed abnormal mammographic findings.

**Table (2): Sono-mammographic findings and MRI additional findings.**

| **Mammography results** | **No. (24)** | **%** |
|---|---|---|
| ▪ Suspicious Unifocal lesion | **17** | **56.66** |
| ▪ Focal asymmetry | **6** | **20** |
| ▪ Retro-areolar increased density | **1** | **3.33** |
| **US results** | **No. (30)** | **%** |
| ▪ Suspicious unifocal lesion | **30** | **100** |
| **MRI results** | **No. (21)** | **%** |
| ▪ Suspicious unifocal lesions with occult extended non-mass enhancement | **(15)** | **(50)** |
| ○ Segmental enhancement | **7** | **23.3** |
| ○ Linear ductal enhancement | **6** | **20** |
| ○ Clumped enhancement | **2** | **6.66** |
| ▪ Suspicious multifocal/daughter/satellites occult lesions | **(3)** | **(10)** |
| ▪ Suspicious multicentric occult lesions with non-mass enhancement and deep fascia infiltration | **(1)** | **(3.33)** |
| ▪ Increase size of unifocal lesion | **(2)** | **(6.66)** |
| **MRI lymph nodes evaluation** | **No. (30)** | **%** |
| ▪ Suspicious looking axillary lymph nodes | **29** | **96.6** |
| ▪ Suspicious looking axillary, retro & inter-pectoral "rotter" lymph nodes | **1** | **3.33** |
| **Total** | 30 | 100 |

**Table 3** demonstrates concordant and discordant results between sono-mammographic findings and pathology.

**Table (3): Concordant and discordant between sono-mammographic findings and pathology.**

| **Sono-mammographic findings** | | **Pathology** | | | | **Sensitivity** | **Positive predictive value (PPV)** |
|---|---|---|---|---|---|---|---|
| **Suspicious looking** | | **Malignant** | | **Benign** | | **100%** | **93.3%** |
| **No.** | **%** | **No.** | **%** | **No.** | **%** | | |
| **30** | **100%** | **28** | **93.3** | **2** | **6.7%** | | |
| **Total** | | **30** | | | | | |
| **Test of significance** | | **$x^2$= 2.06** | | | | | |

$x^2$: Chi-Square test

**Table 4** demonstrates concordant and discordant results between MRI additional suspicious findings and pathology.

**Table (4): Concordant and discordant between MRI additional findings and pathology.**

| MRI additional suspicious findings | | | | | | | | Pathology | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Non-mass enhancement | | Multifocal | | Multicentric with non-mass enhancement | | Increase size of unifocal lesion | | Malignant | | Benign | |
| No. | % | No. | % | No. | % | No. | % | No. | % | No. | % |
| 15 | 71.4 | 3 | 14.3 | 1 | 4.8 | 2 | 9.5 | 20 | 95.2 | 1 | 4.8 |
| Total | | | | 21 | | | | | | | |
| Sensitivity | | | | 100 | | | | | | | |
| Positive predictive value (PPV) | | | | 95.2 | | | | | | | |
| Test of significance | | | | $x^2$= 1.02 | | | | | | | |

$X^2$=Chi-Square test

**Table 5** demonstrates MRI findings of 5 patients post neoadjuvant therapy "NAT" (only 1 patient with good response and no residual lesion "pathologically proved", 2 cases with partial response and two cases with stable disease.

**Table (5): MRI findings of 5 patients post neoadjuvant therapy "NAT".**

| Item | MRI findings pre NAT | MRI findings post NAT |
|---|---|---|
| ▪ **Lesions** | | |
| ○ Unifocal (increased size) | **1** | **0** |
| ○ Multi focal | **1** | **1** |
| ○ Multicentric with non-mass enhancement | **1** | **1** |
| ○ Non-mass enhancement | **2** | **2** |
| ▪ **Lymph nodes** | | |
| ○ Malignant looking | **5** | **3** |
| ○ Benign looking | **0** | **2** |
| ▪ **RECIST** | | |
| ○ Complete response (CR) (no residual) | **-** | **1** |
| ○ Partial response (PR) (>=30% decrease) | **-** | **2** |
| ○ Stable disease (SD) | **-** | **2** |
| ○ No definite progressive disease (PD) or new lesions | **-** | **0** |
| **Total** | **5** | |

RECIST means response evaluation criteria in solid tumors. Stable disease (SD) means <20% increase or <30% decrease. Partial response (PR) means >=30% decrease. Progressive disease (PD) means >=20% increase.

**Table 6** demonstrates a positive role of MRI (N=20, 66.66%) at surgical plan according to the type of surgery after pathological correlation (MRI have no additional findings at 8 malignant cases, one of them has good response on neoadjuvent therapy "NAT" with subsequent converted to breast conserving surgery).

**Table (6): Impact of MRI at surgical management.**

| Surgical plan | According to sono-mammographic findings | | According to MRI additional occult findings | | | | |
|---|---|---|---|---|---|---|---|
| | No. | % | No. pre NAC | % | No. post NAC | % | Impact of MRI |
| ▪ **Breast conserving surgery (BCS)** | 9 | 30 | 0 | 0 | 1 | 3.33 | 66.66% |
| ▪ **Breast oncoplastic technique** | 14 | 46.66 | 3 | 10 | 3 | 10 | |
| ▪ **Extreme oncoplastic technique or mastectomy** | 5 | 16.66 | 25 | 83.33 | 24 | 80 | |
| ▪ **Excision** | 2 | 6.66 | 2 | 6.66 | 2 | 6.66 | |
| **Total** | **30** | | | | | | |
| **Test of significance** | **$x^2$=30.0, P<0.001*** | | | | | | |

$x^2$=Chi-Square test, *Statistically significant.

**Table 7** demonstrates multivariate analysis of 28 cases with breast cancer.

**Table (7): Multivariate analysis of malignant cases.**

| Variable | Patients with MRI additional findings | | Patients without MRI additional findings | | P-value |
|---|---|---|---|---|---|
| | No.=20 | % | No.=8 | % | |
| Age <45y | 17 | 85 | 4 | 50 | 0.05* |
| IDC | 20 | 100 | 8 | 100 | 1.0 |
| Definite in situ component | 20 | 100 | 3 | 37.5 | <0.001* |
| Positive lympho-vascular embolization | 11 | 55 | 2 | 25 | 0.15 |
| Suspicious looking lymph node | 20 | 100 | 8 | 100 | 1.0 |
| Positive estrogen and progesterone receptors (ER and PR) | 20 | 100 | 8 | 100 | 1.0 |
| Positive Human epidermal growth factor receptor2 (Her2/neu) | 16 | 80 | 7 | 87.5 | 0.63 |

*Statistically significant.

**CASE PRESENTATION**

A 44 years old female patient complaining from left breast lump (**Figure 1**).

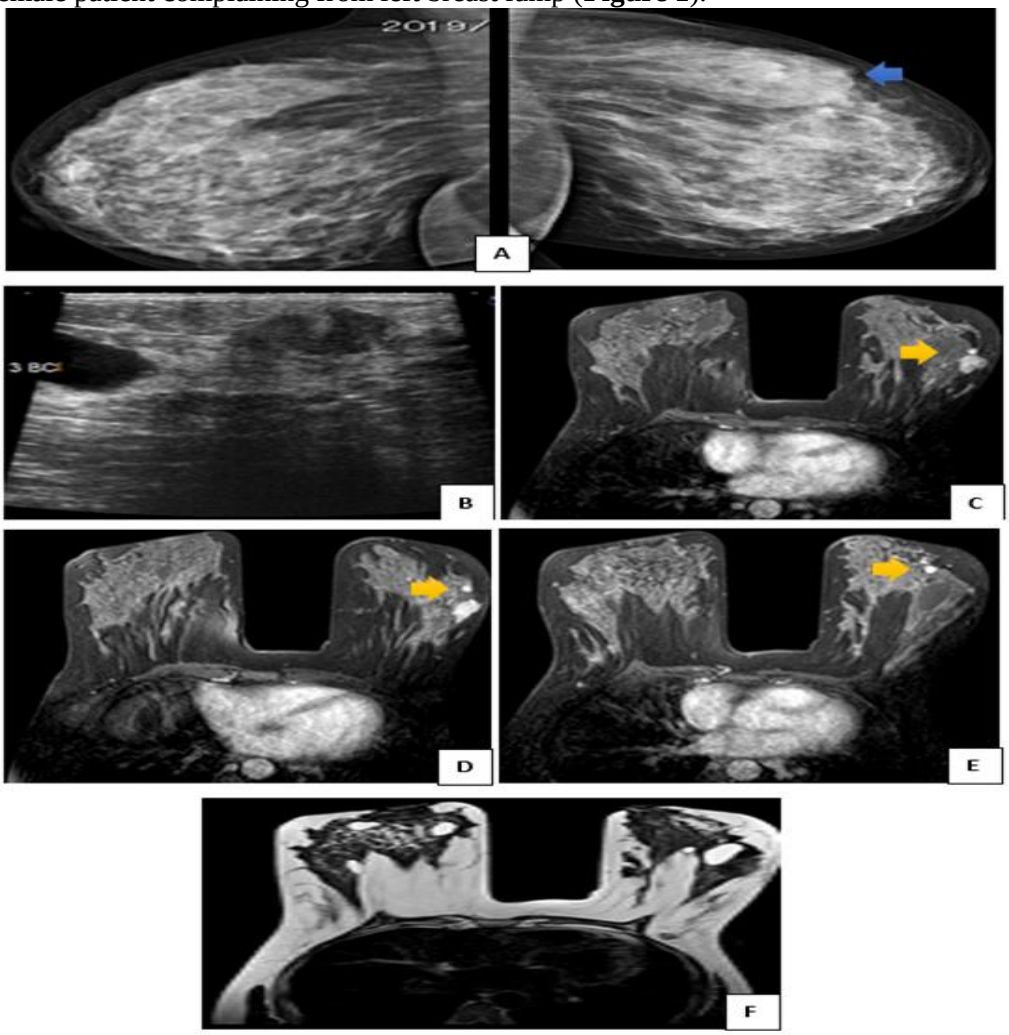


**Figure (1): (A):** Standard mammographic views (MLO) on both breasts show upper left side isodense lesion with indistinct posterior margins (arrow). **(B):** Ultrasound of left breast shows hypoechoic lesion with irregular indistinct margins and posterior shadowing. Adjacent anechoic cyst with posterior enhancement is seen. **(C, D & E):** Post-contrast dynamic MRI study shows irregular shaped speculated lesion seen at the left breast outer quadrant (3 o'clock zone 2). Three adjacent nearby satellites/daughter nodules are seen (yellow arrows) … suspicious breast lesion with multifocal suspicious process. **(F):** T2 weighted images show bilateral fibrocystic changes. Pathologically proved invasive ductal carcinoma (IDC) with ductal carcinoma insitu (DCIS) with cancerization of lobules (COL) and lympho-vasculer embolization (LVE).

## DISCUSSION

The aim of current study was to evaluate MRI role in surgical management of suspicious breast lesions in women with dense breast considered suitable for BCS. The study was a prospective study over a period of 24 months, conducted on a total of 30 cases with dense breast (mammography ACR C & D), admitted at Mansoura University Hospitals "oncology center", with suspicious breast cancer by sono-mammography and are considered suitable for conserving breast surgery.

This matches with **Duygulu and Colleagues [8],** who have reported that, if BCS is required, MRI evaluation has be carried out on all ages of women with suspected breast lesions, in particular cases demonstrating dense or heterogeneously breast parenchyma, in which the sensitivity of US and mammography is low. Also come in the same line with **Brennan and Colleagues [9],** who have concluded that MRI indications are: clinically dense breast tissue difficult to be assessed, discordant clinical/conventional imaging assessment, invasive carcinoma in clinically dense breast tissue and palpable/mass-forming DCIS. **Sharma and Colleagues [5],** also have reported that MRI allows for evaluation of the pectoral muscle and chest wall invasion. In addition, it permits for the evaluation of levels 1, 2, and 3 axillary and internal mammary LNs, that have influence on staging and therapeutic planning as well as it has been considered as the most essential factor with regard to breast cancer prognosis.

In current study, the average age of the enrolled cases was 43 years. The majority of cases were within the age from 40-45 years (50%), followed by the age (45-50 years) and (36-40 years) which represented 30% and 20% respectively. This matches with **Duygulu and Colleagues [8],** who have reported that mean age was 40.2 years (age ranged from 26 to 60 years).

In current study, IDC was in (93.33%) with accompanying DCIS component <5% at 56.66% and accompanying DCIS component >20% at 20%. In addition, benign lesions (fibroadenosis and chronic abscess) were detected at 2 (6.66%) cases. **Brennan's [9] Study,** proved that 155 (86.6%) patients has invasive cancer, and 26 (14.3%) had DCIS.

In current study, MRI displayed additional suspicious findings in the form of occult non-mass enhancement in 50% (23.3% segmental enhancement, 20% linear ductal enhancement and 6.7% clumped enhancement), multifocal occult lesions in 10%, multicentric occult lesions with non-mass enhancement and deep fascia infiltration in 3.33%. In addition, increase size of unifocal lesion in 6.66%. This came in the same line with **Liu and Colleagues** study **[10],** who have concluded 118 non-mass enhancement lesions (NME) (62 benign and 56 malignant) were included in 118 cases. They demonstrated a segmental distribution, clustered ring enhancement were accompanied with malignant tumor. Also, in agreement with **Aydin and Colleagues** study **[11],** who have proved MRI results of 129 non-mass enhancement lesions (NME) that were retrospectively evaluated. Segmental and diffuse distribution besides clustered ring internal enhancement were significantly accompanied by malignancies, in contrast, linear distribution and homogeneous enhancement pattern were accompanied by benign tumor. **Haraldsdóttir and Colleagues [12],** have reported that, MRI plays an essential role in the context of the diagnosis of contralateral and multifocal lesions.

In current study, regarding concordance and discordancy between MRI additional suspicious findings and pathology, sensitivity was 100% and PPV 95.2% with true positive represented 95.2% and false positive represented 4.8% (one non-mass enhancement was pathologically proved sclerosing adenois). **Duygulu and Colleagues [8],** have displayed that, the sensitivity, specificity, PPV, and negative predictive value (NPV) of MRI for additional malignant lesion detection and identification were 85%, 98%, 92%, and 96%, correspondingly. The agreement test demonstrated 86% agreement (very good) between the other features noticed on the MRI and the histopathologic results. **Kuhl and Colleagues [13],** have reported that MRI has been demonstrated to be associated with a significant increase in sensitivity (91%) and specificity (97.2%). In addition, the sensitivity in the higher risk groups was 100%.

In current study, MRI findings of five patients post neoadjuvant therapy "NAT" (only one patient with full response, two cases with partial response and two cases with stable disease. **Gezer and Colleagues [14],** have reported that MRI identified type of NAC response correctly in 32 (84.2%) of 38 patients as compared to pathology. Dynamic contrast-enhanced breast MRI seems to be of great efficiency in comparison with mammography or US in the assessment of NAC response. **Abedi and Colleagues [15],** have stated that MRI has greater sensitivity and lower specificity in comparison with clinical examination for identification of residual tumour following NAC in locally advanced breast carcinoma. In addition, the tumour size measured by MRI demonstrated a positive correlation with the histological findings.

In current study, there is a positive role of MRI at surgical plan (66.6%) at surgical plan according to the type of surgery after pathological correlation by identifying additional occult malignant findings (20 cases are converted from breast conserving surgery and oncoplastic technique to extreme oncoplastic technique or mastectomy). Likewise, another recent study conducted by **Lee and Colleagues [16],** on a total of 1113 cases with breast cancer who were undergone mammography, US, and breast MRI prior to surgical procedure. They have concluded that, changes (either by increase or by decrease) in surgical approaches were very common in the ductal carcinoma in situ group in comparison with the invasive ductal carcinoma group, subsequent to increase in the size of suspicious lesions on breast MRI, recognition of further daughter nodules,

multifocality or multicentricity, and suspicious signs on mammography or US but benign signs on breast MRI. As a result, they have revealed that, pre-surgical breast MRI could provide additional data as regards the determination of the surgical strategy for cases with DCIS compared to cases with IDC. This came in the same line with **Brennan and Colleagues [9],** who have proved that the further data from MRI changed the treatment in 69/181 (38.1%), with extensive unilateral surgery (broader excision or mastectomy) in 53/181 (29.3%), change to bilateral surgery in 12/181 (6.6%), minimal surgery in 4/181 (2.2%). Also, in agreement with **Mukherjee and Colleagues [17],** who have displayed that, the commonest alteration in surgical plan following breast MRI was from BCS to a mastectomy. Following reviewing the pathological outcomes and comparing them with the breast MRI outcomes, they concluded that breast MRI has been demonstrated to be associated with a positive outcome in 13/32 (41%) cases. In addition, breast MRI was associated with no changes in surgical strategy in 15/32 (47%) cases and resulted in a negative change in surgical strategy in 4/32 (13%) cases. Bilateral breast MRI identified a contralateral breast cancer in 2/32 (6%) cases. **Houssami and Colleagues [18],** have proved the accuracy and surgical impact of presurgical breast MRI on breast cancer cases of whole ages in formerly reported data with conversion from wide local excision (WLE) to mastectomy was 8.1% and from WLE to more extensive surgery was 11.3% in multifocal/multicentric lesions with increased the mastectomy rate by about 15%-20% in cases of all ages.

In the same line, **Schelfout and Colleagues [19],** have demonstrated in their research that breast MRI changed the treatment modality in 30.6% of breast cancer cases, with no recorded cases of unwarranted mastectomy.

## CONCLUSION

In the context of BCS for patients with dense breast, preoperative breast MRI provides more information in detecting multifocal, multicentric, and extension of lesions which is necessary for determining the management plan. According to multi-varied analysis of our study, preoperative MRI is high recommended for young patients <45 years and accompanying insitu component. Finally, more research is needed especially with our limited cases.

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