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Multiparametric Magnetic Resonance Imaging in Evaluation of Benign and Malignant Breast Masses with Pathological Correlation

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Keywords
Breast neoplasms, Magnetic resonance imaging, Diagnostic accuracy, Pathological correlation, Multiparametric imaging

Abstract
Objective: In a cohort of 45 patients, this study sought to evaluate the diagnostic efficacy of multiparametric magnetic resonance imaging (MRI) in discriminating benign from malignant breast masses with pathological association.
Methods: For this prospective investigation, 45 female patients with suspect breast tumors were enrolled. All patients had multiparametric MRI scans, including diffusion-weighted, dynamic contrast-enhanced, T1-weighted, and T2-weighted scans. All patients had a biopsy or a surgical excision after an MRI to check for pathological association. Each imaging parameter's diagnostic performance metrics, such as sensitivity, specificity, and accuracy, as well as the combined multiparametric MRI findings, were calculated.
Results: The individual MRI parameters and the overall multiparametric MRI findings' sensitivity, specificity, accuracy, PPV, and NPV were computed. The findings showed that the best diagnostic accuracy for distinguishing between benign and malignant breast masses was achieved by combining dynamic contrast-enhanced MRI with T2-weighted imaging.
Conclusion: When assessing benign and malignant breast masses, multiparametric MRI, particularly the union of T2-weighted imaging and dynamic contrast-enhanced MRI, shown promising diagnostic accuracy. These results imply that multiparametric MRI may be a useful tool in clinical practice for increasing the precision of the diagnosis of breast cancer, hence assisting in the planning of the patient's care and treatment.

1. Introduction –

The breast is a modified apocrine gland. Breast ailments have piqued medical interest since 3000 B.C. From Egypt's great civilization during the age of the pyramids (3000–2500 B.C.), there have been numerous reports of women suffering breast tumors. Most likely, malignant breast tumors in females were the first human cancers to be recognized and separated from other non-malignant illnesses. In India as well as other countries, breast cancer affects more women than any other type of cancer. (Dhruva et al., 2015)

It has already surpassed cervical carcinoma in terms of prevalence, which is continually rising. According to the World Health Organization (WHO), 2.3 million women will receive a breast cancer diagnosis globally in 2020, and 685,000 of them will pass away as a result of the condition. Widespread metastases are the main reason for the high mortality rate in breast cancer. With more than 7.8 million new cases of breast cancer reported between the most recent five-year figures and 2020, it is currently the most prevalent disease in the world. Breast cancer can occur after puberty at any age, but the risk increases with advancing age. Over time, the mortality rate has decreased because to the early diagnosis made possible by mammography,

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sonomammography, MRI, and early treatment. ("WHO Fact Sheet on Infertility," 2021).

Breast cancer is the most frequent malignancy among Indian women, with an age-adjusted death rate of 12.7 per 100,000 women and a rate as high as 25.8 per 100,000 women.2 In India, 1,62,468 new cases and 87,090 fatalities of breast cancer were reported in 2018. (Dhruva et al., 2015)

Breast cancer can be classified histologically as either in-situ or invasive depending on whether the basement membrane has been pierced or not. Examples of in-situ tumors include lobular carcinoma in situ and ductal carcinoma in situ. Invasive ductal, invasive lobular, invasive medullary, invasive tubular, and invasive mucinous carcinomas are examples of invasive carcinomas. Examples of uncommon primary breast tumours include squamous cell carcinoma, mucoepidermoid, and adenoid cystic carcinoma. Treatment is influenced by the stage of breast cancer.

The most widely used staging system was developed by the American Joint Committee on Cancer (AJCC) and Union Internationale Contre le Cancer (UICC), and it is based on the Tumour, Node, Metastasis (TNM) classification of tumours. Breast cancer can be surgically treated with mastectomy or breast conserving surgery (BCS). The final surgical pathological staging determines the prognosis and the requirement for adjuvant therapy.

Breast conserving surgery can be done in conjunction with sentinel node biopsy to evaluate the condition of the axillary lymph node in cases of small tumors. (Arriagada et al., 1996)

Prior to surgery, breast imaging is utilized to accurately determine the tumor's size and rule out multifocal/multi-centric sickness in the same or opposite breast. Surgery to preserve the breast is improper due to a number of disorders. A few of mammography's limitations include its inability to accurately examine dense glandular tissue, regions close to the chest wall or the axilla, or to detect occult lesions. Microcalcifications can be easily seen with mammography. Inaccurate preoperative assessment and delayed diagnosis of multifocal disease might result in local treatment failure, which may result in recurrence or accelerate the disease course. (Orel et al., 1994, Boetes et al., 1995)

Breast MRI has been utilized for pre-operative local staging of breast cancer in comparison to mammography and ultrasonography (US). Orel et al.5 claim that MRI can discover tumors that are missed by mammography. Boets6 showed that whereas MRI found 100% of the additional malignant breast lesions that mammography missed by 31% (which were not clinically diagnosed), in his comparative study of mammography, US, and MRI in the preoperative evaluation of breast cancer. Furthermore, MRI accurately linked with the pathological tumor size while mammography overstated the tumor's size. Breast MRI reportedly changed the anticipated patient care for 14% of patients, according to Fischer et al. (Boetes et al., 1995)

The present study aims to evaluate the role of whole-breast US and dynamic contrast MRI in clinically suspected breast masses.

2. Materials and Methodology –

A 45-patient observational comparison study was conducted to assess the sensitivity of dynamic contrast breast MRI and ultrasound in classifying breast lesions as benign or malignant in those with BI-RADS categories 3, 4, and 5.

Patients who met the inclusion criteria listed below and presented to Krishna Institute of Medical Sciences' surgical departments with suspicious breast masses were included.

Those who have a clinically detectable breast lump, according to an ultrasonography evaluation, patients in BI-RADS categories 3, 4, and 5 Patients who have a family history of Ca breast cancer who patients with an unidentified primary axillary lymph node cancer.

BI-RADS US Category	Assessment and Management
0	Incomplete: additional imaging evaluation needed
1	Negative

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2	Benign
3	Probably benign
4	Suspicious: biopsy Low suspicion Moderate suspicion High suspicion
5	Highly Suggestive of Malignancy (Recommendation removed)
6	Known Biopsy-Proven Malignancy Recommendation removed)

The patients were excluded in the study because of patient falling under categories 0, 1, 2, and 6 of the BI-RADS, patients who have already had contrast reactions, who have renal failure or chronic kidney disease.

Method of collection of data –

Data were collected from patients who participated in the baseline evaluations of the research. Whole-breast sonography was used to perform axial and sagittal scans of both breasts utilizing the GE LOGIQ P 5 USG VER R- 4.0583037201043012 and, in a few instances, the SIEMENS ACUSON JUNIPER using a high frequency (12MHz) linear probe. The patient was turned slightly to the side of interest during a supine examination in order to flatten the breast equally on the chest wall. The opposite arm was behind the head. Additionally, palpable and non-palpable sonographic anomalies as well as suspicious locations were looked at in both radial and anti-radial orientations.

All 45 patients underwent an MRI assessment on a 1.5 T scanner (MAGNETOM AVANTO 1.5 -TA Tim + Dot MR SYSTEM (SIEMENS)). EPISODE 16 An individual SIEMENS breast array coil was given to each patient. Prior to the injection of contrast, each breast had its axial T1 and T2 images, axial fat saturation photos, STIR images, and sagittal images taken. The next step was a dynamic axial/sagittal series that included pre-contrast scanning of both breasts, contrast and saline injection, and six post-contrast scans. The sequence, which comprised both breasts, was obtained using the axial plane. We were unable to perform MR spectroscopy or diffusion-weighted imaging in this study.

Procedure –

Patients were selected according of the inclusion criteria. Informed written consent was taken from each patient under the study. A thorough clinical history was taken followed by physical examination. Clinically or ultrasonographically detected suspicious breast lesions were subjected to MRI and correlated histopathologically.

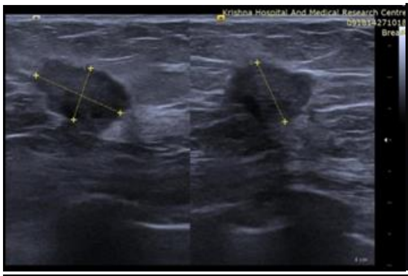

Image 1 - On USG: Irregular hypoechoic lesion with spiculated margins at its superior aspect, transmitting echoes noted in upper outer quadrant.

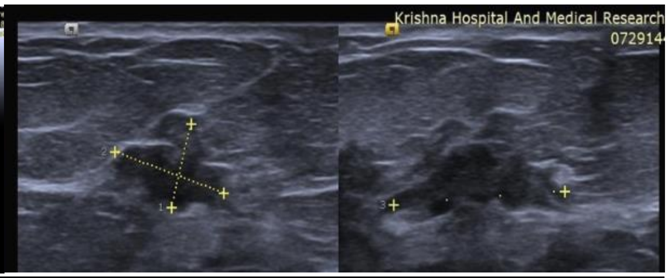

Image 2 - On USG: Hypoechoic irregular lesion with angular margins & adjacent dilated ducts was noted in retro areolar area.

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3. Results –

Following a clinical examination, 45 female patients with breast lesions that were suspected clinically or ultrasonographically underwent US and MRI. Excel and the statistical program R 3.5.3 were both used to analyse the data.

One study participant had unfavourable results for many of the findings that were listed as NIL.

19 participants in the study were in the 40–49 age group, followed by 9 participants in the 30-39 and 50–59 age groups. There were 8 patients who were older than 60. In this study, a person's age can rang from 30 to 75. The graphical representation of the previous table is shown in the graph below. A palpable breast lump was the most frequent presenting complaint (n = 39). Five patients arrived with discharge from their nipples but no palpable tumour

IMAGING FINDINGS

ULTRASONOGRAPHY:

Radial and anti-radial orientation total breast ultrasonography was performed on all subjects. Sonography revealed a tumor, calcifications, thickening of the skin, and nodes in the axilla. Sonographic results were used to designate BI-RADS groups. The most frequent ultrasonographic finding in this investigation was focal mass. There were calcifications in 18 individuals. In 11 cases, axillary lymph nodes were seen.

Table 4: Frequency distribution as per shape of the index lesion onsonomammography

Shape	In Benign masses	In Malignant Masses	Total
Irregular	7 (33.33)	13 (56.52)	20 (45.45)
Oval	14 (66.67)	8 (34.78)	22 (50.00)
Round	0	2 (8.70)	2 (4.5)

We can see from the above table that the most typical form of benign lesions was oval (n=14). Malignant masses most frequently had an irregular form (n=13). Seven benign lesions have a strange form. Eight cancerous tumors had an oval shape.

In this case, the Chi-square test was employed to examine the relationship between the shape of the lesions and the USG diagnosis. Shape and USG diagnosis are independent in this case because the p-value is not significant. In the whole study, 50% of individuals had mass lesions that were oval in shape, and 45.45% had mass lesions that were irregular in shape.

Table 5: Frequency distribution as per margins of the index lesion onsonomammography

Margins	In Benign Masses	In Malignant masses	Total (All masses)
Angular	1 (4.76)	4 (17.39)	5 (11.36)
Irregular	4 (19.05)	1 (4.35)	5 (11.36)
Microlobulated	5 (23.81)	5 (21.74)	10 (22.73)
Smooth	11 (52.38)	0	11 (25.00)
Spiculation	0	13 (56.52)	13 (29.55)

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In our analysis, the majority of patients (n=13, n=11) had smooth or spiculated margins around their index mass lesions, respectively. Ten masses, five of which were benign and five of which were malignant, all had microlobulated borders. Four cancerous tumors had margins with angles. The edges of one benign lesion were angular. Uneven margins were visible in four benign lesions. Uneven margins could be seen in one malignant tumor. Only malignant lesions had spiculated borders; the majority of benign lesions had smooth margins.

Pseudocapsule was discovered in the current investigation in 20% of all masses and 42.86% of all benign lesions. A pseudocapsule was not visible in any malignant lesion.

In 66.67% of benign masses and 8.7% of malignant masses, posterior acoustic amplification was seen. Of all malignant tumors, posterior acoustic shadowing was observed in 26.09% of cases.

When comparison to those with enhanced posterior echogenicity, the odds of having cancer are 75.40 (CI: 3.153, 1802.60) times higher for those with reduced posterior echogenicity.

The posterior acoustic shadow of no benign tumor was visible.

In the current study, 97.73% of the masses in both benign and malignant lesions were hypoechoic. Fibrocystic disease was the only benign lesion that was anechoic. There were no hyperechoic benign and malignant tumors. In this case, the p value is not significant, and the chi-square test is unaffected by echogenicity or the type of lesion.

Color Doppler Ultrasonography was used to assess all 44 index lesions to look for color uptake. 22 of 23 (95.65%) malignant lesions and 18 of 21 (85.71%) benign tumors showed color uptake. Three benign lesions and one cancerous lesion had no color uptake. The chi square test was used to determine the relationship between vascularization and the kind of lesions. Since the p-value in this case is not significant, vascularization and type of lesions are independent in this case.

Table 10: Distribution of pattern of vascularity in Index Lesion

Pattern of vascularity	Benign	Malignant	Total	p-value
Central	9 (42.86)	4 (17.39)	13 (29.55)	0.002499
Penetrating	3 (14.29)	16 (69.57)	19 (43.18)	
Peripheral	6 (28.57)	2 (8.70)	8 (18.18)	

Penetrating vascularization (43.18%) was the most frequent pattern. In 69.57% of malignant lesions and 14.29% of benign lesions, a penetrating vascular pattern was seen. 42.86% of benign lesions exhibited a central vascular pattern. 8.70% of malignant lesions and 28.57% of benign lesions displayed a peripheral vascular pattern.

The pattern of vascularization and type of lesions are dependant, according to the Chi-square test. The odds ratio is calculated to determine how strongly two things are related.

For participants with piercing patterns of visualization compared to subjects with central patterns of visualization, the chance of being malignant is 12 (CI: 2.18, 66.031) times greater.

When compared to people with penetrating pattern of visualization, peripheral pattern of visualization had a 0.0625 (CI: 0.008, 0.4712) times lower chance of being malignant.

Out of 45 subjects, six did not have a calculable resistivity index, and one of the benign lesions with RI greater than 0.99 was an intra-ductal papilloma. Mann-Whitney test was used to compare the median resistive index of benign and malignant masses.

In the current investigation, suspicious calcifications

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were found in 69.56% of malignant lesions and 9.52% of benign lesions. Both the fibroadenoma and the intraductal papilloma were benign lesions, however only one of them had worrisome calcification.

The study found that category 3 (45.45%) and category 5 (36.36%) were the two most prevalent BI-RADS categories. In eight patients (18.18%), category 4 was present. Malignant lesions mostly fell into categories 4 and 5. The majority of benign lesions belonged to categories 3 and 4.

On pre-contrast and post-contrast enhanced MRI, one patient had no index mass lesion; only skin thickening was visible. In 11 patients' pre-contrast and 11 patients' post-contrast sequences, axillary lymphadenopathy was seen. On T2WI, the majority of the malignant tumors (73.91%) were hypointense, followed by hyperintense (21.73%). The chi-square test's p-value in this case is significant. Type of lesions and signal strength on T2WI are related.

In our investigation, the irregular (n=13, 56.52%) and oval (n=8, 34.78%) shapes of the malignant index lesions were the most prevalent. Two of the cancerous tumors were rounded. Two benign tumors had a circular shape, and six benign lesions had irregular shapes. Oval lesions were the most prevalent shape (n=13,61.90%).

In our study, the highest number of patients (n=20) with BI-RADS category 5 on MRI were all diagnosed with malignant lesions, followed by BI-RADS category 4 (n=2). The majority of the benign lesions (n=11) were BI-RADS category 2 categorized. Eight patients were placed in category 3, while five patients were placed in category 4. The BI-RADS score and type of lesions are dependent, according to the chi-square test.

Histopathologic findings:

The most frequent breast lesion, observed in 46.66% of patients, was carcinoma. Out of 23 malignant tumors, 11 patients had metastatic deposits in their axillary lymph nodes. Of the 44 cases, benign lesions were found in 21 of them. The benign lesion most frequently observed in 9 (20%) patients was a fibroadenoma. It was determined that each of the three papillary breast tumors was an intra-ductal papilloma.

Invasive ductal carcinomas made up the majority of the tumors discovered in our study (78.26%). One instance each of medullary cancer, DCIS, and lymphoma (4.34 %) was observed.

For ultrasound, the following statistics apply: 86.95% sensitivity, 81.81% specificity, 85.71% negative predictive value, 83.33% positive predictive value, and 84.44% classification rate.

The MRI approach has a 91.11% classification rate, a sensitivity of 95.65%, a specificity of 86.36%, a negative predictive value of 95%, and a positive predictive value of 88%. Positive predictive rate has a more significant role in clinical research like cancer studies. In this situation, MRI has a higher positive predictive rate; as a result, it is superior to ultrasound.

4. Discussion –

The leading cause of illness and mortality in women is breast cancer. For patients who are symptomatic as well as for screening in circumstances of mass population or for high-risk patients, numerous imaging strategies have developed. Mammography is frequently used to diagnose breast cancer, frequently in conjunction with breast USG, and the diagnosis is confirmed by FNAC and/or biopsy. Additionally, it has been established that 5% to 15% of breast tumors detected by mammography are occult. These variables cause the main cancer to be under staged or the disease to be diagnosed later. In addition, mammography may not detect the multifocal and multicentric illness. (Orel et al., 1994)

For the diagnosis and staging of breast cancer, contrast-enhanced MRI is being used more and more. When determining the size of the tumor and the local extent of primary breast cancers, MRI is superior to mammography. (Boetes et al., 2015, Mumtaz et al., 1997) Breast MRI has a sensitivity of above 90% for finding invasive malignancies. (Wiener et al., 2005, Fischer et al., 1999). Specificity ranges between 39% and 95%, but contrast enhancement on MRI is also detected in many benign diseases.6,9,56. (Boetes et al., 2015, Fischer et al., 1999, Huang et al., 2004).

In this observational study, 45 patients who were candidates for breast surgery were assessed to determine the effectiveness of USG and MRI in clinically and ultrasonographically suspected breast masses to distinguish benign from malignant lesions and to assess the extent of primary breast carcinoma and its effects on surgical management. Each and every patient had a contrast-enhanced MRI. In this study,

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histopathology served as the gold standard. All patients underwent surgery.

Our study's findings were comparable to those in the studies under evaluation (Berg et al.,58 Mumtaz et al., (Mumtaz et al., 1997) & Liberman et al., 72(Liberman et al., 2003). A palpable breast lump was detected in the majority of the individuals (Harms et al., 1993). Five patients had mastalgia, serosanguinous nipple discharge, and nonspecific lumpiness in the breast but no palpable lumps. Some patients complained about multiple things.

Malignant lesions in the current study exhibited comparable shapes on MRI and ultrasound; 13 of them were asymmetrical, 8 were oval, and 2 were round. On ultrasound, 7 benign tumors had an irregular shape, and 14 were oval in shape. On MRI, the shapes were 6 irregular, 13 oval.

According to Stavros et al., (Stavros et al., 1995) the ellipsoid form is associated with benign lesions with a sensitivity of 97.6% and a specificity of 51.2%. Skaane et al., (Skaane & Engedal, 1998) showed that 28.9% of intra-ductal carcinomas and 85.6% of fibroadenomas had a round or oval shape. Rahbar et al., (Rahbar et al., 1999) showed that 61% of malignant lesions had an irregular form and that 94% of benign lesions had a round or oval shape.

By Stavros et al., (Stavros et al., 1995) a few sparse, well-defined lobulations (macrolobulation) were regarded as a benign feature, but numerous little lobulations (microlobulation) of 1-2 mm were seen as a malignant trait. They discovered that microlobulation had a sensitivity, specificity, and accuracy for association with malignancy of 75.2%, 83.8%, and 82.4%, respectively. Microlobulation was found in 10.6% of fibroadenomas and 27.3% of carcinomas, according to Skaane et al. Chala et al (Chala et al., 2006) reported microlobulation in 5.6% ofbenign and 15.4% of malignant lesions with positive predictive value of 44.4% for malignancy. Spiculation consists of alternating hypoechoic and hyperechoic straight lines which radiate perpendicularly from the surface of the solid nodule,

With a positive predictive value of 3.5% for malignancy, Chala et al. (Chala et al., 2006) observed frequency of 78.5% in benign masses and 9.6% in malignant masses. Rahbar et al. (Rahbar et al., 1999) reported a 91% benign mass frequency and a 9% malignant mass frequency. On both USG and MRI, the majority of benign tumors displayed smooth borders comparable to those examined in the literature. On MRI and USG, no malignant lesions and 52.38% of benign lesions had circumscribed or smooth edges.

A pseudocapsule has a high sensitivity of 95% and specificity of 76% for predicting a benign lesion.14. According to Chala et al., (Chala et al., 2006) the frequency of malignancy was 44.6% in benign masses and 0.0% in malignant tumors. In the current investigation, no malignant lesions and 42.86 (n=9)% of benign lesions had pseudocapsules. In this investigation, pseudocapsule was present in all benign masses (fibroadenomas), and its absence was regarded as a non-specific finding. The posterior acoustic enhancement and shadowing were characterized as posterior acoustic characteristics or posterior echogenicity. (Rahbar et al., 1999). Contrarily, non-specific findings included posterior acoustic amplification or a lack of distal sound beam modulation.

Rahbar et al. (Rahbar et al., 1999) reported that benign tumors attenuate by 75% and malignant masses by 25% more frequently. According to Stavros et al., (Stavros et al., 1995) the sensitivity for attenuation is 48.8%, and the specificity for connection with malignancy is 94.7%. Shadowing and enhancement were both observed in the current investigation, with shadowing occurring in 26.09% (n=6) of malignant lesions and none of the benign lesions, while enhancement occurred in 8.7% (n=2) of malignant lesions and 66.67% (n=14) of benign lesions. One had a cystic component, and the other was medullary carcinoma of the two malignant lesions with posterior acoustic enhancement. Echogenicity has received less attention for the differentiation of solid masses, in part because the parameter lacks a consistent definition and is the most operator-dependent. (Stavros et al., 1995)

Microcalcification was seen in 9.6% of benign masses and 48% of malignant masses, according to Chala et al. According to Moon et al., ultrasound has a sensitivity, specificity, and positive predictive value of 82%, 83%, and 76% for detecting microcalcification, respectively. In the current investigation, suspicious calcifications were found in 69.56% of malignant lesions and 9.52% of benign lesions. Both the fibroadenoma and the intraductal papilloma were benign lesions, however only one of them had worrisome calcification.

In our study, the resistance index was greater than 0.99 in more than 50% of the malignant tumors. 72.73% of the individuals had a resistance index of less than 0.99 for benign masses.

On T2WI, the majority of the malignant tumors (73.91%) were hypointense, followed by hyperintense (21.73%). On T2WI, the majority of the benign lesions (76.19%) were hyperintense.

On T2W images, one benign and one malignant lesion displayed mixed signal. Only 2 of the 21 benign lesions had hypointense signal on T1W imaging, while 12 of the 21 had it.

Low T2 signal strength was determined by Nunes et al. to be a marker of benignity when connected to lobulated, non-septate enhancing masses. They discovered that when the model was limited to lobulated, non-septate enhancing masses, only 81% (25 of 31) of all cases resulted in the prediction of benignity, as opposed to 100% (three of three) in all other situations.

Evaluation of pectoralis major muscle in patients with posterior breast tumours

One patient in our study had a lump at the back of the breast, and a clinical examination revealed a possible fixation to the chest wall. On USG, there was a lack of interface where the bulk met the pectoralis major muscle. On MRI, the mass had invaded the muscle with aberrant muscular augmentation, and muscle involvement was discovered on histological investigation.

Four participants in our study who had a positive family history of breast cancer got a USG and an MRI each. One of these was a post-operative case of Ca breast that had been checked for NME or no lesions in the contralateral breast. On histology, the other two patients had fibrocystic illness.

Comparison of imaging modalities

Accurate assessment of tumor size, multifocal disease, involvement of the nipple or pectoralis muscle, and axillary node metastases define the best course of treatment for patients with breast cancer. According to reports, MRI performs somewhat better than ultrasonography at finding index lesions. On MRI and ultrasonography, all 44 index tumors could be found, but one lesion assumed to be a category 3 lesion on USG was not a lesion and was determined to be fat necrosis on MRI and histology. Involvement of the pectoralis muscle was suspected on USG but confirmed on MRI and histology.

In our investigation, ultrasonography had an 86.95% sensitivity for the detection of index lesions compared to an MRI sensitivity of 95.65%. Numerous investigations have found that breast MRI is more sensitive than sonography.

The sensitivity of the current study was somewhat higher than Chao et al.17 but lower than that reported by numerous studies14,18,28. For both IDC and ILC, Berg et al. 30 found that US had higher sensitivity than mammography, detecting 104 of 110 (94%) instances and 25 of 29 (86%), respectively.

The current single-center investigation was conducted on a rather limited sample size. The statistical power of the results would increase with a larger sample size. This study only looked at breast mass and did not assess how well it could diagnose more widespread inflammatory/infectious disorders like mastitis. Multicentric research including bigger patient populations are required to assess the viability and to further enhance the specificity and accuracy of MRM diagnosis.

5. Conclusion -

Breast cancer is the leading cause of death and morbidity in women. Early detection of breast lesions is essential to determining a good prognosis. Ultrasound mammography is the most widely accepted and well-established technique for finding breast lesions. When used in conjunction with current techniques like DWI, ADC values, and MRS, such as breast lesions, DCE-MRM now offers a more accurate and rapid diagnosis. The objective of the current work was to determine the morphology of breast masses using MRI, Ultrasonography, and other techniques.

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