Original Research Paper

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Radiodiagnosis

COMPARATIVE EVALUATION OF BREAST LESION BY ELASTOGRAPHY AND MRI WITH ITS HISTO - PATHOLOGICAL CORRELATION

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ABSTRACT **Methods:** A prospective study of 33 patients were carried in the Department of Radio-diagnosis, GMCH, KOTA [RAJASTHAN].

Patients from all the age groups including women only with BIRADS III/IV/V were included. Already diagnosed cases/cases on treatment/recurrence/BIRADS-I/II/VI were excluded.

Results: Of 33 cases examined, we had 14 cases of ductal carcinoma, 6 cases of fibro-adenoma, 3 cases of phylloides tumor, 3 cases of abscess, 1 case each of lobular carcinoma, papillary carcinoma, mucinous adenocarcinoma, mastitis, mastitis with abscess, granulomatous mastitis and complex cyst.

Conclusion: Differentiation between BI-RADS III, IV and V by sono-elastography had 88% sensitivity and 86% specificity and MRI had 83% sensitivity and 73% specificity.

Discussion: Elastography is extremely helpful in accurate estimation of breast benign vs malignant pathology differentiation and helps in avoid many unnecessary procedure. The elasticity score is an important parameter for lesion characterization. Combination of morphologic and dynamic MRI studies is very important for breast lesion evaluation.

KEYWORDS : Breast Ultrasound, Breast Elastography, Breast Mri.

INTRODUCTION –

Breast pathologies is a major health problem that warranted efforts to be paid in order to increase the diagnostic capability of the routinely used diagnostic aids. Breast lesions were first classified as malignant or benign categories .

The most prevalent malignant lesions were further subdivided into three subgroups including: ductal carcinoma in situ (DCIS), invasive ductal carcinoma of nonscirrhous type, and invasive ductal carcinoma of scirrhous type . Similarly, the most prevalent benign lesions were divided into three subgroups, including intraductal papilloma, fibroadenoma, and aberrations of normal development and involution (ANDI) [1] .

In developing countries like India it is often observed that breast cancer patients tend to present at a later stage due to shyness of the patient and reluctant attitude of families towards female. Thus in present Indian scenario spreading the awareness is as important as treating the patient.

Early diagnosis and prompt treatment has always been the key to reduce the mortality and morbidity from the breast cancer. Tremendous work has been done to make non invasive and earliest possible diagnosis of breast cancer by vast array of continuously advancing breast imaging modalities.

MATERIALS AND METHODS

This is a prospective study conducted in **Department of Radiodiagnosis Government medical college kota , Rajasthan.**

Patients –

In our prospective study we included 33 patients The patients ranged in age from 18 to 70 years, with a mean age of 44 years. Each patient undergone ultrasound breast with elastography & color Doppler . In every patient with category BI- RADS 3 or more on Ultrasound, we performed contrast enhanced MRI breast. Results were correlated with Histopathology in every single patient.

Duration of study – 1 year from July 30 2016 to July 29 2017.

Exclusion criteria –

- Patients with BI-RADS 1, BI-RADS 2 and BI- RADS 6.
- Patients on chemotherapy.
- Patients with recent biopsy from the lesion.
- Pregnant females.

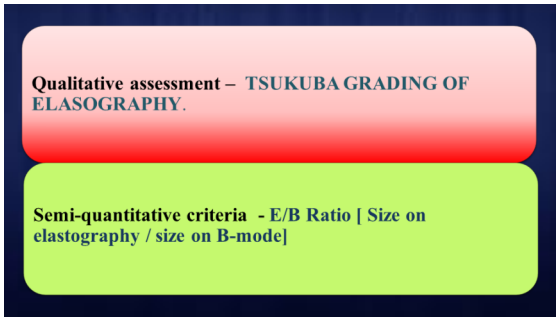
EQUIPMENTS –

ULTRASOUND – ALPINION E – CUBE 15

MRI – 1.5 T Phillips ACHIEVA

IMAGING ANALYSIS -

Elastography –



MR Mammography – Each MR – Mammography was done with dedicated 16 channel breast coil with patient in prone position.

MR – protocol-

- T2 – weighted sagittal fat suppressed
- T1 – weighted sagittal non – fat - suppressed 3D FSPGR
- T1 - weighted fat suppressed sagittal 3D FSPGR before and following
- Post contrast (DYNAMIC CONTRAST IMAGING)
- 2-mm slice thickness, no gap
- Subtraction
- Maximum intensity projection
- Computer aided detection
- Diffusion weighted imaging (DWI)
- Lesion identification and characterization -
- Index lesion identification done on T2 SPAIR and subtraction.
- In case of multiple lesions most suspicious lesion is studied.
- For kinetic analysis ROI is placed on most enhancing area of

lesion. DCE upto 6th dynamic.

- For first 2 mins wash in rate was classified as Rapid, medium and slow .
- Rapid > 80 % of peak SI achieved with in first two minutes , 50 - 80% intermediate and slow <50 %.
- Enhancing lesions are categorized under one of the three types of delayed enhancement patterns

a. Type I is a pattern of progressive enhancement, with a continuous increase in signal intensity on each successive contrast- enhanced image.
b. Type II – Type II is a plateau pattern, in which an initial increase in signal intensity is followed by a flattening of the enhancementcur ve.
c. Type III – a washout enhancement pattern, involves an initial increase and subsequent decrease in signal intensity.

- More than 10% decrease in peak SI was considered wash out.
- DWI done in precontrast scan . ADC mapping with b value 0,1000
- We classified every lesion as per appropriate BIRADS lexicon .

Table - 1 Major and minor suspicious feature of breast malignancy.

LESS SUSPICIOUS FEATURES	MAJOR SUSPICIOUS FEATURES
Round / irregular shape	Spiculated margins
Hetrogeneous internal enhancement.	Rim enhancememnt without smooth margins
Irregular margins	Non mass – segmental / clumped
Low to intermediate T2 density.	Low ADC (<1x10-3 mm2/s) without benign morphology
Type II or III kinetics	
Non mass – linear / regional / heterogenous	

Statistical Analysis –
Sensitivity, specificity, positive and negative predictive value for each parameter is calculated.

RESULTS

In our study we included 33 patients in each patient USG with elastography, breast MRI was done and followed by histopathology. Most common age group for benign lesions was 30 – 40 yrs and for malignant lesions was 40 – 50 yrs.

Table 2. Distribution of lesions according to age group.

AGE GROUP	BENIGN	MALIGNANT
0 – 10 YRS	0	0
11 – 20 YRS	3	0
21 -30 YRS	1	2
31 – 40 YRS	6	2
41 – 50 YRS	3	6
51 – 60 YRS	2	4
61 – 70 YRS	0	4
TOTAL	15	18

On histopathology 15 cases found benign while 18 cases were malignant. Fibroadenoma was the most common benign lesion and most common malignant lesion was ductal carcinoma.

Table 3: Analysis Of Benign Lesions According To Their Histopathological Correlation

HPE Diagnosis		Number	Percentage
Benign	Abscess	3	20
	Fibroadenoma	6	40
	granulomatous mastitis	1	6.6
	Mastitis	1	6.6
	mastitis with abscess	1	6.6
	Benign phylloides	2	13.2
	Cyst	1	6.6
	Total	**15**	**100.0**
Malignant	ductal carcinoma	14	77.7
	lobular ca	1	5.5
	mucinous adenocarcinoma	1	5.5
	phylloides tumor	1	5.5
	Papillary carcinoma	1	5.5
	Total	**18**	**100.0**

Table 4 - Distribution of the lesions according to their elasticity score.

Elastography Elasticity score				
		FNAC _Diagnosis		Total
		Benign	Malignant	
Elastography Elasticity score	2	3	0	3
	3	7	2	9
	4	4	2	6
	5	1	14	15
Total		**15**	**18**	**33**

We divided distribution of E/B Ratio [Size on Elastography / size on B-mode] in lesions in three patterns Less than 1, 1 to 1.5 and more than 1.5 . Less than 1 is seen in 5 Benign lesion, 1 to 1.5 is seen in 9 benign and 7 malignant lesion and more than 1 is seen in 1 benign and 10 malignant lesion.

Table 5 - Distribution of the lesions according to their E/B ratio.

Elastography_E/B Ratio [Size on elastography/size on B mode]				
		FNAC_Diagnosis		Total
		Benign	Malignant	
Elastography_E/B Ratio [Size on elastography/ size on B mode]	<1	5	0	5
	>1	2	2	4
	>2	0	1	1
	1	2	2	4
	1.10	3	0	3
	1.2	2	1	3
	1.4	0	1	1
	1.5	0	1	1
	1.6	0	3	3
	1.65	0	1	1
	1.7	0	2	2
	1.8	0	2	2
	2	0	2	2
	2.2	1	0	1
Total		**15**	**18**	**33**

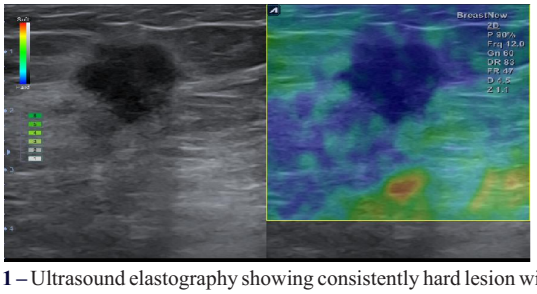


Fig 1 – Ultrasound elastography showing consistently hard lesion with elasticity score of 5 and E/B ratio > 1.5, corresponding gray scale showing spiculated margins.

We had total 33 cases out of which 30 was masses and 3 were non mass like enhancements.

According to BI- RADS lexicon we divided margin of the lesion in smooth, lobulated, irregular and spiculated.

8 out of 15 benign lesions showed smooth or lobulated margins. None of the benign lesion showed spiculated margin. 2 of the malignant lesion showed lobulated margins.

Table 6 : Distribution of lesions according to margins.

MRI margins FNAC Diagnosis Cross-tabulation				
		FNAC_Diagnosis		Total
		Benign	Malignant	
MRI MARGIN	-	1	1	2
	Irregular	4	1	5
	lobulated	2	2	4

	Smooth	8	4	12
	spiculated	0	10	10
Total		**15**	**18**	**33**

Delayed enhancement pattern on dynamic scan was divided in type I (progressive), type II (plateau) and type III (washout) type of kinetics. Most common type of curve in benign lesions was type I. Most common type of curve in malignant lesions is type II (9 cases), type III (7 cases) and type I (1 case).

Table7 :Distribution of mass lesions type of delayed enhancement curve in lesion on dynamic contrast studies.

	TYPE I	TYPE II	TYPEIII
BENIGN	5	6	0
MALIGNANT	1	9	7

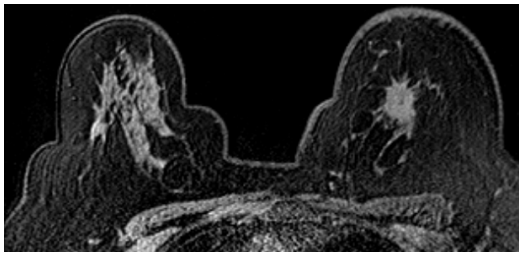


Figure 2 - On dynamic contrast enhanced MR solid enhancing mass lesion with spiculated margins.

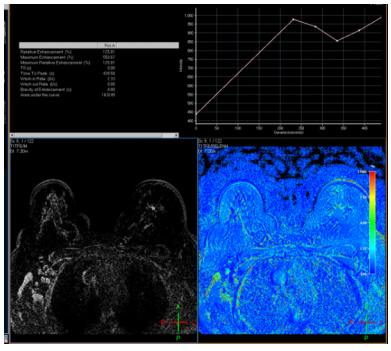


Fig 3 – On kinetic analysis, rapid wash - in and rapid wash – out enhancement type III curve is seen.

DISCUSSION

The current indications for breast MRI include determination of the stage and extent of disease in a patient with newly diagnosed breast cancer, evaluation of a patient with an unknown primary tumor, evaluation of a patient with positive surgical margins after breast conservation surgery, monitoring of a patient undergoing neoadjuvant chemotherapy, evaluation of breast implant integrity, screening for breast cancer in a woman at very high risk for the disease, to evaluate accessory breast (axillary), and use as a problem – solving tool for a woman with equivocal mammographic findings.

In a study of 74 lesions, Harms and colleagues [2] showed significant overlap between malignant and benign lesions such as fibroadenomas, sclerosing adenosis, and proliferative fibrocystic changes, Harms and colleagues suggest that analyzing a lesion's morphologic characteristic may help to improve the specificity of MRI. Similar to its use in mammography and ultrasound, border characteristics such as well defined or spiculated may be a useful adjunct to enhancement features.

In a study of 192 patients, Nunes and colleagues [3] exclusively analyzed architectural distortion features to devlop a tree shaped interpretation model to distinguish benign from malignant lesions. Masses with irregular borders and rim enhancement were associated with carcinoma, while masses with lobulated borders and internal septations were associated with fibroadenoma.

In concordance with these studies we found that irregular shape was more common in malignant masses (88%). Irregular margins were seen commonly in malignant lesions though not specific. In our study spiculated margins were specific for malignancy (100% specific) but seen only in 55% cases.

Oval shape was very specific for benignity in our study.

In our study also most common shape of malignant lesion was irregular (88% malignant masses were irregular in shape) as seen in multiple previous studies.

Kaiser and colleagues [4] found that malignancies showed a sudden increase in signal intensity of 100% within the first 2min. gradual, mild contrast uptake was seen in benign tissue.

A series performed by Stack and coworkers [5] had similar findings, with malignant lesion showing a steep increase during the first 60s, followed by a more smaller, more gradual increase over 4 to 8 min. Benign tissue only showed a gradual increase in signal intensity at a lower rate, while fibroadenomas demonstrated a marked increase in signal intensity over a 8 min period. Boetes and colleagues [6] achieved a sensitivity and specificity of 95% and 86%, respectively.

In our study we divided early enhancement (the initial rise of the enhanced curves) of mass into (2 minutes after agent injection), "slow", "medium", and "rapid". An initial peak signal intensity within 90 seconds >90% is defined as rapid enhancement, which is highly suggestive of malignancy.

Orel and coworkers [7] evaluated both the morphologic and enhancement characteristics of suspicious breast lesions. They used a fat-saturated spoiled gradient echo sequence to acquire high – resolution images along with temporal information. Their data confirmed some of the previous studies that signal intensities and enhancement characteristics overlapped between benign and malignant lesions, particularly fibroadenomas. Although carcinomas had a tendency toward more rapid enhancement and washout, there was still a significant overlap with enhancement patterns of fibroadenomas. In her morphologic analysis of lesions, Orel discovered architectural features were helpful in differentiating between benign and malignant lesions. Carcinomas exhibited irregular borders and rim enhancement, while fibroadenomas often had lobulated borders, with nonenhancing internal septations.

The ACR recommended to classify the imaging features as standard ACR BIRADS lexicon. Which includes morphological features , enhancement patterns and additional findings.

Fischer and coworkers[8,9] suggested that not only the early postcontrast period, but also the intermediate and late postcontrast phase yields diagnostically useful information : Lesions with persistent signal intensity increase (type 1a, 1b) were more likely to be benign, whereas lesions with signal intensity plateau (type 2) or with a washout (type 3) tended to be malignant.

In our study the signal intensity 2 minutes after contrast injection was defined as "delayed phase", which are divided into "persistent" (type I), "plateau" (type II), and "washout" (type III). Persistent (type 1) a pattern of progressive enhancement, with continuous increase in signal intensity; plateau (type 2) – the signal intensity reached peak 2 minute after contrast injection, followed by a flattening during the delayed phase; washout (type 3) – an initial increase and subsequent decrease in signal intensity 2 minutes after contrast injection.

In our study most malignant lesions showed rapid initial enhancement pattern (72%) but (20%) benign lesions also demonstrated rapid initial enhancement pattern, suggested that this is not the specific parameter for malignancy.

Type III curve was 100% specific for malignancy in our study but only with sensitivity of 38%. Most malignant lesions displayed type II delayed curve (50%). Also, (40%) benign masses displayed type 2 delayed curves.

Type I curve was seen in most benign lesions (33%) in ou r study and specific (83%) for them.

Pattern of internal enhancement can give information about nature of lesions in some cases. The absence of a visible lesion on contrast-enhanced MR images that corresponds to a palpable or mamographically visible abnormality is highly predictive of benign finding. However, the absence of observed enhancement at breast MR imaging does not exclude in situ or invasive cancer. Many invasive

cancers that show no enhancement are small or have a small invasive[10]. Lack of enhancement has a high negative predictive value (NPV) for malignancy (88-96%) [3, 10]. We didn't have any non - enhancing lesion in our study.

Non enhancing internal septations are considered to be diagnostic for fibroadenoma[5] . 40% to 60% of enhancing fibroadenoma contain non-enhancing internal septations, which, if seen, are diagnostic for benign fibroadenoma to >95% certainty[10] . But multiple recent studies show that they are not exclusive for malignancy.

A study by schnall et al revealed that 47% of malignant lesions were shown to have nonenhancing internal septa[11] . If a mass is lobulated and shows no enhancement or only minimal enhancement, it is likely benign (NPV 100%)[3] . If a mass is lobulated and shows moderate to marked enhancement (NPV 67%), further evaluation may be warrented [3]. Correlation between the enhancing portion of the lesion and its T2 – weighted signal intensity is helpful . T2-weighted signal hyperintensity in the same portion of the lesion that appears enhanced on T1 weighted images is highly suggestive of benignity, although not all masses with high signal intensity on T2-weighted images are benign.

In our study we had 3 lesions with non-enhancing septations and all 3 were benign on histopathology.

Rim enhancement is most predictive of malignancy, usually seen with an invasive carcinoma; however, rim enhancement can be a cause of false-positive findings, sometimes associated with benign inflamed cysts and fat necrosis. The appearance of a inflammatory cyst is usually not a diagnostic dilemma when the rim is thin and regular and the cyst does not enhance. T2 weighted images usually confirm the presence of a cyst[12] .

Most of the malignant lesion in our study showed heterogenous internal enhancement. Except for abscesses and fat necrosis, rim enhancement was seen only in malignant lesions in our study. None of the solid, benign lesion showed rim enhancement.

The presence of secondary morphologic features increase suspicion of carcinoma. These features include skin and nipple changes, chest wall and pectoral invasion, and lymphadenopathy. Architectural distortion can be present, extending beyond the limits of malignancy.

Extension to the skin or fibrosis associated with the tumor can also cause dimpling and retraction. Skin thickening is seen in both benign and malignant masses but more commonly in malignant masses. Unilateral and enhancing skin thickening is suggestive of malignancy and seen 7 in our cases, 6 were malignant and 1 was benign (mastitis).

In a study by Malich et al., the existence of uni- and perifocal edema was found in 41% of malignant cases and only in 12% of benign lesions[13].

In our study perilesional edema is seen in 8 lesions, 4 malignant and 4 benign.

A hook sign symbolizes a hook like speculated dendrite coming from the lesion's center, leading to the pectoral muscle, determined on T2-weighted images. In 3 of our cases hook sign was present and all were malignant.

As well as infiltrating into adjacent glandular and adipose tissue, breast cancer can incite a scirrhous reaction in surrounding tissue. This results in architectural distortion that may or may not be due to direct tumor involvement.

In 11 of our cases we had architectural distortion and 10 of them were malignant.

On breast MRI we detected 1 malignancy with chest wall invasion and 5 with pectoral invasion which were initially missed on ultrasound, upstaging the lesion.

Non mass like enhancement is a challenging finding in breast MR imaging interpretation. Liberman et al. reported that the feature with highest positive predictive value for malignancy was clumped internal enhancement in lesions showing non-mass like enhancement.

Ultrasound & Elastography -

In Itoh et al.[1] study, they believed that an elasticity score of 1, which shows even strain in the entire hypoechoic lesion at B – mode US, indicates that lesions have almost the same compressibility as the surrounding breast tissue.

In our study, no malignant lesions had a score of 1, this result suggests that invasive diagnostic procedures, such as histologic examination, may be omitted for patients who have lesions with a score of 1.

Of the malignant lesions, 88% had ES of 5 and 4, whereas 66% of benign lesions had ES of 2 and 3.

In our study no malignant lesions show elastography score 1, 66% of benign lesions showed elastography score 2 and 3 and 88% of malignant lesions present elastography score 4 and 5.

In Itoh et al.[1] study, an elasticity score of 3, which indicates strain at the periphery of the hypoechoic lesion, was mainly found in benign lesions, including intraductal papillomas. The importance of strain at the periphery is unclear at present and requires further investigation. We recommend that all lesions with elasticity scores of 3 or higher be examined by means of aspiration cytology or needle biopsy because two (13%) of the 15 lesions with a score of 3 were malignant.

In our study 2 (22%) out of 9 cases that show elastography score 3 were malignant and 2 (33.33%) out of 6 elastography score 4 were malignant.

In our study sensitivity and specificity of elastography was 88% and 86% for malignant lesion which is near to the previously mentioned results.

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