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Original Research Article

Comparison of Diagnostic Effectiveness of Ultrasound Elastography and Color Doppler in Breast Mass Lesion Presuming Histopathology as Gold Standard

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Abstract

Background: Breast cancer originates from breast tissue, most commonly from the inner lining of milk ducts or the lobules that supply the ducts with milk. Breast ultrasonography (US) is widely used as a diagnostic tool in evaluating mammographically detected masses, palpable lumps, nipple discharge and in guiding biopsy. The purpose of our study is to confirm the utility of elastography and color Doppler with B-mode ultrasound to differentiate benign from malignant breast masses.

Aims: To assess & compare the diagnostic effectiveness of B-mode ultrasound, color Doppler and US elastography in evaluation of breast masses assuming histopathological examination as gold standard.

Materials and Methods: The observational study group consisted of 150 patients suspicious breast masses referred from Surgery Department for mammography, ultrasound and elastography.

Results: In the study patients were between 18-60 years of age. Benign lesions were common in the 21-30 years and malignant lesions in the 41-50 age group. The commonest benign lesion encountered in the study was fibroadenoma (38) followed by fibrocystic disease (27). Majority of malignant lesions was invasive ductal carcinomas. Benign masses were predominantly well defined hypoechoic, round or oval in shape, regular margins, having pseudo capsule or smooth margins, homogenous solid mass or anechoic cystic mass with regular margins showing posterior acoustic enhancement. Breast carcinoma were predominantly hypoechoic, ill-defined mass with irregular margins, heterogeneous echotexture and showed posterior acoustic shadowing. On color Doppler USG high proportion of malignant lesions showed increased vascularity as compared to benign lesions, with malignant lesions showing predominantly grade 2, however Doppler alone gave high false positive values. On US elastography malignant lesions showed more toward blue pattern indicating hardness of lesions while benign lesions showed more of red pattern indicating soft lesions thus predicting chances of malignancy.US elastography proved to be more accurate than Doppler and B– mode USG in categorizing the majority of disease entities. Sensitivity, specificity, PPV, NPV and accuracy of US elastography is 85.4%, 91%, 83.6%, 92%, and 89% respectively, which were definitely higher than B mode ultrasound and Doppler.

Conclusion: US elastography is a safe and effective method for evaluation of breast lesion. In maximum number of cases the synchronized evaluation and characterization of breast lesion

by US elastography will help in overall assessment of breast lesions. By use of US elastography, highest level of sensitivity, specificity and accuracy was achieved.

Keywords: Breast masses, Ultrasound, Ultrasound Elastography, Malignant Breast Lesions

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Background

Breast ultrasonography (US) is widely used as a diagnostic tool in evaluating mammographically detected masses, palpable lumps, nipple discharge and in guiding biopsy. The Breast Imaging Reporting and Data System (BIRADS) with US provide standardized terminology to describe US mass features, assessments, and recommendations.

Generally, breast cancer tissue is harder than the adjacent normal breast tissue. This property serves as the basis for some examinations, such as palpation, that are currently being used in the clinical assessment of breast abnormalities, as well as for Elastography.

The principle of elastography is that tissue compression produces strain (displacement) within the tissue and that the strain is smaller in harder tissue than in softer tissue. Therefore, by measuring the tissue strain induced by compression, we can estimate tissue hardness, which may be useful in diagnosing likelihood of breast cancer. So malignant mass typically appears dark and have high contrast with background breast tissue during deformation while benign masses typically appear lighter and have lower contrast with background breast tissue during deformation.

The appearance of masses on strain images and lesion size discrepancies between B-mode and strain images may be promising tools for distinguishing benign from malignant lesions

Ultrasound Elastography

This technique combines ultrasound technology with the basic physical principles of elastography. US elastography is non-invasive and assesses tissue deformability by providing information on the elasticity.

The basic principles of elastography

Elastography is based on the assumption that cell density is increased in most solid tumors and that this condition changes the tissue elasticity. Krouskop *et al*. reported different coefficients of elasticity in normal and neoplastic breast and prostate tissues.

Elastography methods:

1. Strain imaging by compression or Real time elastography (RTE),
2. Acoustic radiation force impulse (ARFI)[1]
3. Real-time shear velocity (RSV) or Shear wave elastography (SWE)

Reproducibility of breast Elastography and technique

Points for maintaining the reproducibility of breast Elastography examination techniques.

(1) **Establishment of region of interest (ROI)**

The Elastography currently used in clinical practice shows the distribution of relative strain. It is necessary to include a sufficient area of surrounding normal gland in the ROI to correctly determine the difference in hardness of the lesion compared with the surrounding area.

(2) **Techniques for obtaining Elastography images**

The techniques of examination consist of the following two elements.

A. Degree of initial compression (the initial intensity of compression by a probe applied to the breast)
B. Amplitude and movement speed of a probe

The appropriate vertical amplitude when moving a probe is between 1 and 2 mm.

Elastography criteria's

Real time elastography (RTE)

Stiff nodules appear larger at elastography than at US resulting in a dimensional difference. This phenomenon has been attributed to a desmoplastic reaction occurring in many breast tumors. The dimensional difference can be expressed as the ratio between the diameters of the lesion on the elastogram as compared to the US image; a ratio of ≥1 is suggestive of malignancy.

The scoring system suggested by Itoh *et al*[2] assigns a score from 1 to 5: score 1 indicates deformability of the entire lesion; score 2, deformability of most of the lesion with some small stiff areas; score 3, deformability of the peripheral portion of the lesion with stiff tissue in the center; score 4, the entire lesion is stiff; score 5, the entire lesion and surrounding tissue are stiff. If a lesion is classified between 1 and 3 it is considered benign; if classified 4 or 5 it is considered to be malignant. An aliasing artefact that appears as a blue-green-red (BGR) pattern can be seen in a simple cyst.

Strain ratio (LFR: lesion to fat ratio)[3-6]

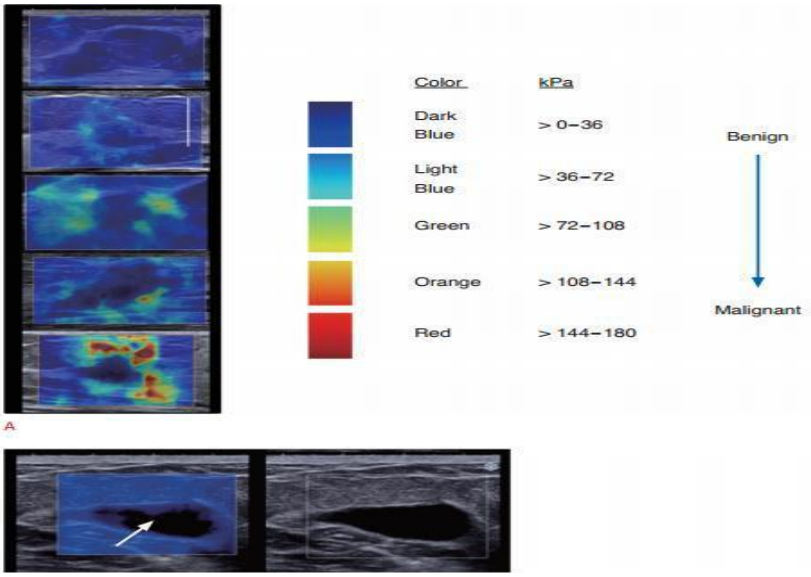
This diagnostic approach was advocated by Ueno *et al*.[3] (Ueno E 2007) as a semi-quantitative method of evaluating stiffness. It is the ratio of the strain in a mass to the strain in subcutaneous fat, and it is a semi-quantitative method for evaluating how much stiffer a mass is compared with fat.

ARFI criteria[7-9]

Interpretation of images obtained at ARFI ―strain imaging uses criteria similar to those of RTE, evaluating size and stiffness of the lesions. Malignant tumors show a larger diameter at elastography as compared to US and they are encoded in darker shades of gray.

Real-time shear velocity (RSV) criteria[10]

Using SWE, transversely oriented shear waves are generated by acoustic radiation force, and these waves propagate faster in hard tissue than soft tissue. A color-coded image displaying the shear wave velocity (m/sec) or elasticity (kilopascals, kPa) for each pixel in the region of interest (ROI) is acquired. Generally, a color scale ranging from 0 (dark blue, soft) to +180 Pa (red, hard) is used for breast lesions.



The positive predictive value for malignancy increases with increasing elasticity, from 0.4% for dark blue to 81.8% for red colors.

BREAST MASSES [11]

Benign lesions

Fibroadenoma [12,13]

Fibroadenoma is a benign tumor, composed of stromal and epithelial elements. Fibroadenoma is the second most common solid tumor in the breast after carcinoma, which is well-circumscribed, round to ovoid, or macrolobulated mass with generally uniform hypo echogenicity on USG.

Fibrocystic disease (FCD)

By ultrasound, cysts exist in up to one third of women 35 to 50 years of age, with most of these being nonpalpable. In women older than 60 years of age, cysts are uncommon (5%).

Cysts

On USG, must be round or oval with an anechoic interior, have sharp anterior and posterior margins and demonstrate posterior acoustic enhancement. Lesions with internal echoes or septations and posterior acoustic enhancement represent complicated cysts that contain proteinaceous fluid or debris from prior internal haemorrhage or infection.

Duct Ectasia

Duct ectasia is a nonspecific dilatation of the major subareolar ducts. Ultrasound shows tubular anechoic structures or ducts filled with debris.

Galactocoele[14]

A galactocele (milk filled cyst) commonly appear on ultrasound as multicystic or mixed cystic solid lesions with distal acoustic enhancement.

Infection and breast abscess

Subareolar duct ectasia and obstruction of major ducts may lead to proliferation of bacteria and subsequent abscess. Sonographic features of breast abscess were hypoechoic, ill-defined masses with some internal echoes, thick walls and internal septations.

Malignant breast masses [15-18]

Non-invasive carcinoma

Non-invasive neoplasms are broadly divided into two major types: LCIS and DCIS. LCIS is recognized by its conformity to the outline of the normal lobule, with expanded and filled acini. DCIS is a more heterogeneous lesion morphologically.

Invasive Breast Cancers

Invasive ductal cancer, or infiltrating ductal carcinoma, is the most common presentation of breast cancer, accounting for 50 to 70% of invasive breast cancers.

Invasive lobular carcinoma accounts for l0% to 15% of breast cancer.

Infiltrating Ductal Carcinoma

Tubular carcinomas are usually seen on sonography as hypoechoic masses with ill-defined margins and posterior acoustic shadowing. Mucinous carcinoma commonly presents as a mass with microlobulation on sonography. The presence of both cystic and solid components and the presence of distal enhancement are important sonographic features that might suggest the diagnosis.

Infiltrating Lobular Carcinoma:

On ultrasonography, these hypoechoic tumors are irregularly shaped, have ill-defined margins, sometimes with echogenic corolla, demonstrate posterior acoustic shadowing and cause distortion of the surrounding tissues.

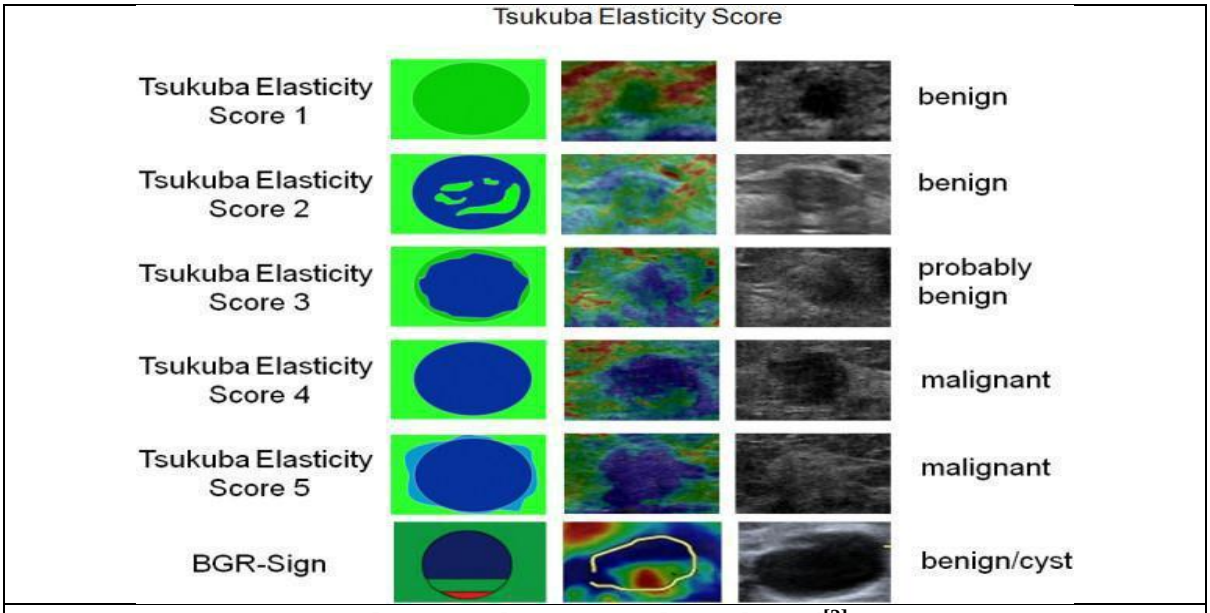
Material and Methods

Source of Data

Our study was carried out on 150 patients visiting the OPD/IPD referred from Surgery Department, J. L. N. Medical College & Associated Group of Hospitals, Ajmer, from 1st August 2017 to 31st December 2018.

Study Type: A hospital based validational type of observational study.

Method: Ultrasound scan was performed on machine SAMSUNG HS70A with high-frequency using CA1-7A probe (1-7MHZ) and LA3-16A (3-16MHZ) linear array transducers



Elastography scoring (by Itoh *et al*[2])

Inclusion criteria

- Patients suspected to have breast masses who underwent mammography, ultrasound and elastography.

Exclusion criteria

- Not operated or non-availability of the FNAC /histopathological examination report.
- Uncooperative or unstable patients.

Results

Table 1: Distribution of cases into benign and malignant lesion as per histopathology

Histopathology	No. of cases
Benign	102
Malignant	48
Total	150

Table 2: Distribution of breast lesions as per histopathology

S. No.	Lesion	Number	Percentage
1	Fibroadenoma	38	25.33
2	Fibrocystic disease	27	18
3	Breast abscess	13	8.66
4	Breast cyst	13	8.66
5	Duct ectasia	7	4.66
6	Hematoma	4	2.66
7	Breast carcinoma	48	32
	Total	**150**	

Table 3: Age distribution of lesions

Sl. No.	Lesion	<20	21-30	31-40	41-50	>50	Total
1	Fibroadenoma	5	22	6	5	--	38
2	FCD	--	5	10	9	3	27
3	Breast abscess	1	6	2	4	--	13
4	Breast cyst	--	7	4	2	--	13
5	Duct ectasia	--	--	5	2	--	7
6	Hematoma	--	--	2	2	--	4
7	Breast carcinoma	--	--	14	21	13	48

Table 4: Signs and Symptoms

Sl. No.	Signs and symptoms	Number of cases	Percentage
1	Nipple discharge	52	34.66
2	Pain	79	52.66
3	Nipple retraction	30	20

Table 5: Location of Lesion on B-Mode USG

S.No.	Quadrant	No. of lesions	Percentage
1	Superolateral	66	44
2	Superomedial	27	18
3	Inferolateral	16	10.66
4	Inferomedial	8	5.33
5	Diffuse	33	22
	Total	150	100

Table 6: Shape of individual lesion on B-Mode USG

S.No.	Lesion	Round	Oval	Lobulated	Irregular	Total
1	Fibroadenoma	20	9	9	--	38
2	Fibrocystic disease	16	7	--	4	27
3	Breast abscess	--	10	1	2	13
4	Breast cyst	11	2	--	--	13
5	Duct ectasia	--	2	--	5	7
6	Hematoma	3	1	--	--	4
7	Breast carcinoma	9	7	7	25	48

	Total	59	38	17	36	150

Table 7: Margins of lesions on B-Mode USG

Sl. No.	Lesion	Well Circumscribed	Poorly Circumscribed	Micro Lobulated	Spiculated	Total
1	Fibroadenoma	30	8	--	--	38
2	Fibrocystic disease	20	7	--	--	27
3	Breast abscess	3	10	--	--	13
4	Breast cyst	13	--	--	--	13
5	Duct ectasia	--	6	--	1	7
6	Hematoma	4	--	--	--	4
7	Breast carcinoma	9	12	7	20	48
	Total	79	43	7	21	150

Table 8: Echo pattern of various lesions on B –Mode USG

Sl. No.	Lesion	Hyper-echoic	Hypo-echoic	Mixed	Anechoic
1	Fibroadenoma	1	30	7	--
2	Fibrocystic disease	20	--	1	6
3	Breast abscess	--	10	3	--
4	Breast cyst	--	--	--	18
5	Duct ectasia	2	--	5	--
6	Hematoma	4	--	--	--
7	Breast carcinoma	2	27	19	--
	Total	29	67	35	24

Table 9: Presence of calcification and lymphadenopathy

Sl. No.	Lesion	Presence of lymphadenopathy	Presence of calcification
1	Fibroadenoma	0(0%)	2(7%)
2	Fibrocystic disease	0(0%)	0(0%)
3	Breast abscess	5(38.4%)	1(7.69%)
4	Breast cyst	0(0%)	0(0%)
5	Duct ectasia	0(0%)	1(14.2%)
6	Hematoma	0(0%)	0(0%)
7	Breast carcinoma	32(66.6%)	25(52.0%)

Table 10: Color Doppler grading of lesion

Sl. No.	Lesion	Doppler Grading		
		0	1	2
1	Fibroadenoma	0	17	21
2	Fibrocystic disease	26	0	1
3	Breast abscess	1	6	6
4	Breast cyst	13	0	0
5	Duct ectasia	4	0	3
6	Hematoma	4	0	0
7	Breast carcinoma	0	18	30
	Total	48	41	61

Table 11: Differentiation of lesions according to elasticity scoring

Sl. No.	Lesions	Elastography score					
		1	2	3	4	5	BGR
1	Fibro adenoma	9	15	9	5	--	--
2	Fibrocystic disease	4	20	3	--	--	--
3	Breast abscess	--	8	5	--	--	--
4	Breast cyst	--	--	--	--	--	13
5	Duct ectasia	--	2	3	2	--	--
6	Hematoma	--	--	3	1	--	--
7	Breast carcinoma	--	--	7	30	11	--
	Total	13	45	30	38	11	13

Table 12: Strain ratio of lesions

Sl. No.	Lesions	Strain Ratio	
		<2	>2
1	Fibro adenoma	30	8
2	Fibrocystic disease	25	2
3	Breast abscess	11	2
4	Breast cyst	--	--
5	Duct ectasia	5	2
6	Hematoma	1	3
7	Breast carcinoma	2	46
	Total	74	63

Table 13: Concordance Rate between USG diagnosis and final HPE diagnosis

B-Mode USG	Cases on B-mode USG	Final histopathological diagnosis								
		Fibro adenoma	FCD	Abscess	Breast cyst	Duct ectasia	Hematoma	Breast carcinoma	Concordant Rate	Percentage (%)
Fibroadenoma	38	30	0	0	0	0	0	8	30/38	78.9
Fibrocystic disease	18	0	18	0	0	0	0	0	18/27	66.6
Breast Abscess	10	0	0	10	0	0	0	0	10/13	76.9
Breast cyst	13	0	0	0	13	0	0	0	13/13	100
Duct ectasia	2	0	0	0	0	2	0	0	2/5	40
Hematoma	4	0	0	0	0	0	4	0	4/4	100
Breast Carcinoma	65	8	9	3	0	5	0	40	40/48	83.3
Total	150	38	27	13	13	7	4	48	117/150	78

Table 14: Comparison of various modalities in differentiation of benign and malignant lesions

S. No.	Modality	Benign	Malignant
1	B –mode ultrasound	85	65
2	Color Doppler	89	61
3	US elastography	71	49
4	Final histopathological diagnosis	102	48

Table 15: Results comparison for malignancy detection

Imaging Modality	Sensitivity	Specificity	PPV	NPV	Accuracy
B-mode ultrasound	81.20%	74.76%	60%	89%	76.80%
Color Doppler	62.50%	69.60%	49.10%	79.70%	67.33%
US elastography	85.40%	91%	83.60%	92%	89%

Representative cases

Figure 1a: Showing well defined heterogeneous hypoechoic lesion in left breast in a 20-year-old female. **Figure 1b:** On Elastography lesion is showing Tsukuba elasticity score 2 with predominantly green pattern with strain ratio of 1.71. Histopathology revealed the lesion as fibroadenoma.

Figure 2a: Showing well defined anechoic lesion in right breast in a 30 year old female. **Figure 2b:** On Elastography lesion is showing BGR pattern suggestive of breast cyst with strain ratio 0.98. Histopathology revealed the lesion as simple breast cyst.

Figure 3a: Showing irregular heteroechoic lesion in left breast in a 35 year old female.
Figure 3b: On Elastography lesion is showing Tsukuba elasticity score 4 with predominantly blue pattern with strain ratio of 3.83. Histopathology revealed the lesion as invasive ductal carcinoma.

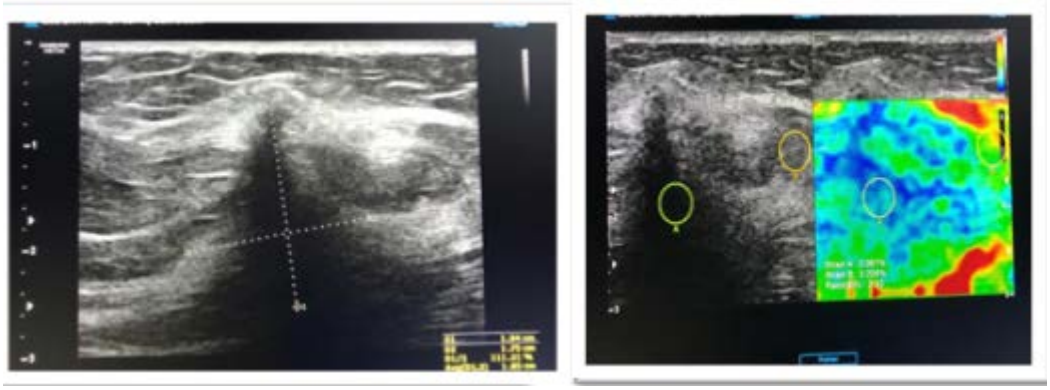


Figure 4a: Showing heterogeneous hypoechoic lesion in left breast in a 50 year old female.
Figure 4b: On Elastography lesion is showing Tsukuba elasticity score 4 with predominantly blue pattern with strain ratio of 3.43. Histopathology revealed the lesion as invasive ductal carcinoma.

Discussion

Our study was conducted on patients referred to Department of Radio diagnosis, J.L.N. Medical College and Attached Hospitals, Ajmer. The patients were within the age group of 18 years and 60 years.

In our study fibroadenoma accounted for maximum number of benign cases i.e. 38. Palpable lump is the most common presenting symptom, following by mastalgia.

Table 16: Final result of breast B-mode ultrasound

	Sensitivity	Specificity	PPV	NPV	Accuracy
B-Mode USG	81.2%	74.7%	60%	89%	76.8%

Fibroadenoma

According to the study of Hangensen *et al* in 1973, fibroadenoma is the most common tumor below 30 years of age. Present study had similar observations, 27 out of 38 cases were below 30 years of age.

In the present study, out of 38 fibroadenoma, 30(78.9%) were hypoechoic and 1 (2.6%) were of hyperechoic. Out of 38 fibroadenomas 30 (78.9%) had regular margins and 8(21%) had irregular margin, 25 (65.7%) showed posterior acoustic enhancement.

Fibrocystic disease

Stavros AT *et al* [19] studied 750 breast lesions and fibrocystic disease accounted for 131(21%) of all lesions. In this study we came across 27 cases of duct fibrocystic

disease. In present study mean age is between 30-40 years. 20 cases (74.0%) had well circumscribed margins, and most of the patients showed posterior acoustic enhancement.

Breast Cyst

Stavros AT *et al* [19] has reported 21% incidence in his study of 750 breast lesions. Breast cysts are the leading cause of breast lump in women between 35-55 years. In our study, breast cysts are accounted for 13(8.66%) of lesions. Maximum number of cases was between 21-30 years, 7 (53.8%).

Breast Abscess

In the present study out of 13 cases of breast abscess, 8 were lactating mothers and 2 was post-traumatic.10 cases were hypoechoic and 3 were mixed variety, with irregular and ill-defined margins, internal echoes and showed posterior acoustic enhancement.

Mammary Duct Ectasia

In this study we came across 7 cases of duct ectasia. 5 patient is presented with discharge and while 2 patient presented with discharge and pain, and 3 cases with nipple retraction.

Breast hematoma

In this study we came across 4 cases of breast hematoma, which was least common benign lesion encountered in our study. In present study mean age is between 30-50 years. These are round to oval and well circumscribed in appearance.

Breast Carcinoma

Stavros AT *et al* [19] in a study of 750 breast lesion reported incidence of malignant lesion to be 17%, out of these 81.6% were infiltrating ductal carcinoma whereas Ciattos *et al* reported 83.4% lesions as infiltrating ductal carcinoma of all malignant lesions. In the present study we came across 48 malignant lesion, in which 40 (83.3%) were infiltrating ductal carcinomas.

Table 17: Color Doppler USG

Imaging Modality	Sensitivity	Specificity	PPV	NPV	Accuracy
Color Doppler	62.5%	69.6%	49.1%	79.7%	67.33%

In our study highest vascularity shown by solid lesions breast carcinoma followed by fibroadenomas. 30 of breast carcinomas and 21 (37.5%) of fibroadenomas showed Doppler grading 2. Breast cysts and Fibrocystic disease were well characterized by use of Doppler, with absence of vascularity.

Table 18: Elastography result

Imaging Modality	Sensitivity	Specificity	PPV	NPV	Accuracy
US Elastography	85.4	91	83.6	92	89

In our study, we found that the specificity, accuracy, and positive predict value for the US Elastography were higher than those of B-mode USG.

17 of 102 benign lesions were misdiagnosed by US elastography. That rate was much lower than those for B-mode USG and color doppler, which would decrease unnecessary biopsies considerably.

Shiina *et al* [20], which can detect the strain of the tissue accurately in real time. It can compare the strain of two notable areas by analysing the different color maps to obtain the strain index or ratio (SR) (i.e., the breast tissue-to-tumor strain ratio).

We took the cut off as 2 for differentiating benign and malignant lesions. SR <2 suggests benign nature of lesion while >2 suggests malignancy. In our study 46 out of

48 (95.8%) malignant lesions showed SR >2, so 95.8% detection rate of malignancy by using strain ratio method. While 72 out of 102(70.5%), benign lesions, showed SR<2.

Conclusion

US elastography is a safe and effective method for evaluation of breast lesion. Our results suggest that US elastography in conjunction with B-mode USG is a reliable method for the confirmation of benign breast lesions and the differentiation of malignant lesions. The findings indicate that US elastography is beneficial in the identification of typical benign features of BIRADS category II & III lesions and in the differentiation of category IV malignancies, which pose most diagnostic problems from a clinical perspective. In this case, US elastography reduced the rate of false-positive finding.

In conclusion, the combined use of US elastography and color Doppler US increased diagnostic performance in distinguishing benign from malignant breast masses. Thus, ultrasound elastography is safe, relatively inexpensive, widely available, and free of radiation hazards, non-invasive essential modality for evaluation of breast lesions and should be one of the first investigation for evaluating a breast lesion before proceeding to aggressive invasive procedures.

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