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Radiology Section

Combined Evaluation of Breast Carcinoma with Digital Mammography and Sonomammography-A Prospective Study

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ABSTRACT

Introduction: The incidence of breast cancer is rising in developing countries with an annual increase of 3.1% in India. Early diagnosis, work up and intervention is saving many lives.

Aim: To study and compare the mammographic and sonomammographic characteristics of breast carcinoma. Also, to evaluate the additional benefit of combining ultrasound with mammography by categorising them on the BIRADS system.

Materials and Methods: This prospective study was conducted over a period of one and a half year with a study population of 30 patients in the Radiodiagnosis Department of Dayanand Medical College and Hospital, Ludhiana, India. All the cases underwent X-ray mammography and ultrasound (using high frequency linear probe, 5-12MHz). Elastography was also done in all patients. All malignant breast lesions were characterised on both modalities and comparison of characteristics was done. BIRADS score was given on each modality separately as well as by combining the findings of both modalities in all the patients.

Results: Our results show that findings of mammography and sonomammography correlated well. Mammography was better in detecting architectural distortion and microcalcifications while sonomammography provided additional benefit by determining exact mass size, duct dilatation and hardness of malignant mass. When the results of both modalities were interpreted together, it was found to improve the diagnostic accuracy.

Conclusion: We concluded that mammography and ultrasound are complementary to each other in malignant breast lesions and increase the confidence of diagnosis. Every radiologist should give a combined BIRADS score to grade breast masses irrespective of the age of patient and density of breast tissue, so as to avoid delay in diagnosis and treatment.

Keywords: Elastography, Malignant, Microcalcifications, Microlobulated, Spiculated

INTRODUCTION

Breast cancer has become the most common female cancer in urban India with an annual incidence of approximately 1,44,000 new cases [1]. Since, breast cancer is a progressive disease, evolving through stages of cellular dedifferentiation and growth, the time at which breast cancer is detected is crucial. The earlier it is detected, the higher is the chance of survival. The combination of imaging, clinical examination and needle biopsy known as triple assessment, is the expected standard for breast diagnosis [2]. The primary method used for breast cancer screening is mammography, which uses low dose X-rays to image the breasts. Mammography is the most widely used screening tool for breast cancer that reduces cancer related deaths through early detection [3]. However, now a days there is a trend of using multimodality approach by adding screening ultrasound to mammography. It has been found that addition of screening ultrasound annually in high risk women detected more cases of breast carcinoma with an addition of 4.2 cases per 1000 women [4,5]. Ultrasound is a safe adjunct screening tool especially in mammographically dense breasts. It is widely available, inexpensive, requires no contrast injection, does not use ionizing radiation, and is well tolerated by patients. We in the present study evaluated and analysed the results of combining digital mammography and sonomammography in cases of breast carcinoma.

Anatomy of Breast: The breast is a tubulo acinar type of modified apocrine sweat gland. It consists of three types of tissue: the skin, subcutaneous adipose tissue and the functional glandular tissue. Centrally, there is the nipple areolar

complex. Collecting ducts open onto the tip of the nipple. Breast parenchyma consists of 15-25 lobes. Each lobe contains a branching ductal system draining about 20-40 lobules. Basic unit of milk production is Terminal Duct Lobular Unit (TDLU) which drains into collecting ducts leading to the nipple areolar complex [6].

The number of lobules per lobe depends upon the age, parity, hormonal and lactational status of female. At the end of reproductive life there is an increase in the amount of adipose tissue and, although the main duct system is preserved, there is considerable loss of lobular units. These changes in breast composition are manifested by changes in the breast density on mammography.

The breast composition is assigned four categories in the fifth edition of the BI-RADS lexicon [7]. These are:

a) The breasts are almost entirely fatty. Mammography is highly sensitive in this setting.

b) There are scattered areas of fibroglandular density.

c) The breasts are heterogeneously dense, which may obscure small masses.

d) The breasts are extremely dense, which lowers the sensitivity of mammography.

Normal mammographic anatomy: The mammographic appearance of the normal breast depends on the amount of the main components: the fat tissue appears radiolucent and the stroma and the gland appear radiopaque. The skin appears as a thin, continuous, radiopaque rim of homogeneous density, of about 1 mm well distinguishable from the radiolucency of the underlying subcutaneous fat tissue.

The areola usually has a thickness of 3-5 mm with a central opacity of cylindrical shape corresponding to the nipple.

Posteriorly, there is the retroareolar region, a triangular shaped area which is of particular interest because it may hide focal anomalies such as breast tumours. Deep to the skin, a thick radiolucent band of subcutaneous fat is seen which shows echogenic linear strands corresponding to crests of Duret and Cooper's ligaments.

The retromammary fat separates the breast gland from pre-pectoral fascia.
In fatty breasts, the blood vessels appear as linear opacities with tramline calcifications especially in elderly and diabetic women.

Sonographic anatomy: The breast can be divided into three zones, from superficial to deep. The most superficial zone is the premammary zone or subcutaneous zone, which lies between the skin and the anterior mammary fascia. Deep to the anterior mammary fascia, lies breast parenchyma. Glandular tissue in the form of lobules, most of the TDLU's, lobar ducts and fibrous stromal elements constitute breast parenchyma. Posterior most is the retromammary zone which contains fat, blood vessels and lymphatics. This zone is not much appreciated on ultrasound. Echogenicity of various structures in breast parenchyma on ultrasound varies from midlevel gray to intensely hyperechoic.

MATERIALS AND METHODS

This prospective longitudinal study was conducted over a period of one and a half year from August 2015 to January 2017. The institutional ethical committee accorded ethical clearance to this study. Informed consent and detailed clinical history was taken from each patient.

This study was conducted on female patients of all age groups with or without positive family history who were clinically suspected to have breast carcinoma and were referred from indoor/outdoor patient department to the Department of Radiodiagnosis at Dayanand Medical College, Ludhiana, India. All patients of any age group with pathologically proven breast carcinoma were included in the study.

All the male patients and patients with large ulcerated breast masses where digital mammography was technically not possible were excluded from the study.

A total of 30 patients were included in the study. Relevant detailed history was elicited from all patients. Before starting mammography, the procedure was explained to the patients in their vernacular language to allay the fear and anxiety and written informed consent was taken. Digital mammography was followed by sonomammography in every patient.

All features of both the investigations were recorded in the proforma as follows:

Digital mammography: Cranio-Caudal (CC) and Mediolateral Oblique (MLO) views were done in all patients. Various mammographic features considered were-

- Parenchymal pattern: Extremely dense, heterogenously dense, scattered fibroglandular and fatty.
- Evidence of asymmetry
- Architectural distortion
- Mass Lesion: Location, outline (well defined or ill-defined), margins (circumscribed, micro or macro-lobulated, indistinct , spiculated), density (high, low, intermediate, fatty), calcification (amorphous, pleomorphic, granular or fine branching)
- Overlying skin (normal, thickened)
- Nipple (retracted or non-retracted)

Sonomammography: Various features considered were-

- Shape of mass: oval, round, irregular
- Margins: circumscribed, microlobulated, indistinct, angular, spiculated
- Orientation: parallel, non-parallel
- Posterior acoustic features: enhancement, shadowing, none
- Lesion boundary: abrupt interface, echogenic halo

- Echopattern: hyperechoic, hypoechoic, isoechoic, complex
- Microcalcificatons: present, absent
- Elastography: mean score

Independent as well as combined BIRADS score was given in all patients on both modalities as-

- Grade 4a/4b/4c-Suspicious abnormality with confidence of <2%/2-94 %/> 95% respectively.
- Grade 5- Highly suggestive of malignancy

Interpretations

All sonomammographies were performed by single radiologist with an experience of 10 years in ultrasound. Every digital mammography was interpreted by two radiologists independently with an experience of 10 and more than 10 years in reporting. Most of the reports matched and interobserver variations were reinterpreted and final reports were issued with consensus of a third radiologist.

Technique of imaging the Breast

Mammography in all patients included in this study was carried out on M/S Wipro GE Healthcare Pvt. Ltd. machine-Alpha RT Model in the Department of Radiodiagnosis and Imaging, Dayanand Medical College and Hospital, Ludhiana, India, which was followed by sonomammography on Philips IU22 ultrasound machine using linear probe (5-12MHz) and convex probe (2-5MHz). Elastography was done using advanced elastography software already installed in the equipment and mean elasticity scores and strain ratios were calculated.

STATISTICAL ANALYSIS

The data was recorded in a proforma and analysed using descriptive statistics.

RESULTS

A total of 30 patients with pathologically proven breast carcinoma were included in the study and their mammographic and sonomammographic findings were analysed and compared. BIRADS grade was given on each modality separately and was compared with the combined BIRADS grade. The mean age of women was 55.6 years with standard deviation of about 8.8. About 80% of the cases were <60 years of age. Only five patients (16.7%) had a positive family history of breast carcinoma in their first-degree relatives. A palpable mass was the commonest complaint in 86.7% cases while 6.7% patients presented with pain. Only one patient who came for routine screening was found to have breast carcinoma. Most of the patients (70%) had a solitary lesion while nine cases (30%) had more than one lesion on mammography. In majority of the cases primary lesions were seen in upper outer quadrant of left breast (33.3%). Six cases had lesions involving more than one quadrant (20%). Microlobulated (53.6%) and spiculated (34.1%) margins were most commonly observed. Associated features that support the possibility of malignancy included skin and trabecular thickening in 70% cases, nipple retraction in 20% cases, asymmetry in 10% cases and architectural distortion in maximum number of cases (56.7%) [Table/Fig-1]. 20 patients were labeled BIRADS Grade 5 on mammography.

Most of the malignant lesions (83.3%) were irregular in shape on sonomammography. Although, taller than wider is a characteristic of malignant lesions, 56.7% cases in this study had parallel orientation. Posterior acoustic shadowing and micro calcifications were seen in 50% cases each [Table/Fig-2]. In all 21 patients were labeled BIRADS Grade 5 on sonomammography.

Mammographic Characters of Lesions (n=30)		Present n (%)	Absent n (%)
Margins	Spiculated	14 (34.1%)	-
	Microlobulated	22 (53.6%)	
	Circumscribed	4 (9.7%)	
Microcalcification		22 (73.3%)	8 (26.7%)
Skin Thickening		21 (70%)	9 (30%)
Nipple Retraction		6 (20%)	24 (80%)
Architectural distortion		17 (56.7%)	13 (43.3%)
Asymmetry		3 (10%)	27 (90%)

[Table/Fig-1]: Characterisation of malignant breast lesions on digital mammography.

Sonomammographic Characters of Lesions (n=30)		Frequency (n)	Percentage (%)
Shape of Mass	Irregular	25	83.3
	Oval	4	13.3
	Round	1	3.3
Size of Mass	<1 cm	2	6.7
	1-2 cm	19	63.3
	2-3 cm	4	13.3
	3-4 cm	2	6.7
	>4 cm	3	10
Orientation	Non-parallel	13	43.3
	parallel	17	56.7
Posterior Acoustic Features	Shadowing	15	50
	Combined	3	10
	None	12	40
Micro-calcifications	Present	15	50
	Absent	15	50
Ductal dilatation	Present	7	23.33
	Absent	23	76.66

[Table/Fig-2]: Characterisation of malignant breast lesions on sonomammography.

BIRADS Grades	Mammography n (%)	Sonomammography n (%)	Elastography (Mean elasticity score) of lesions with BIRADS grading on ultrasound			Combined BIRADS Grade on three modalities
			Grade 3 n (%)	Grade 4 n (%)	Grade 5 n (%)	
4b	3 (10)	1 (3.3)	1 (3.3)	00	00	1 (3.3)
4c	7 (23.3)	8 (26.7)	00	5 (16.6)	3 (9.9)	5 (16.6)
5	20 (66.7)	21 (70)	00	14 (46.6)	7 (23.3)	24 (80.0)

[Table/Fig-3]: BIRADS grading of lesions on different modalities. (n=30).

On ultrasound elastography, maximum number of lesions had mean elasticity score of 4 (63.2%). The mean value of strain ratio was found to be 5.06 with a minimum of 3.5 and maximum value of 7.1.

Findings of mammography and sonomammography correlated well. Architectural distortion (an important predictor of malignancy) and microcalcification were better appreciated on mammography. Sonography helped in detecting exact mass size, ductal dilatation and lymphadenopathy. Elastography provided additional benefit as a predictor of malignancy. A combined BIRADS Grade was found to be more accurate than grading the lesions on each modality individually [Table/Fig-3].

DISCUSSION

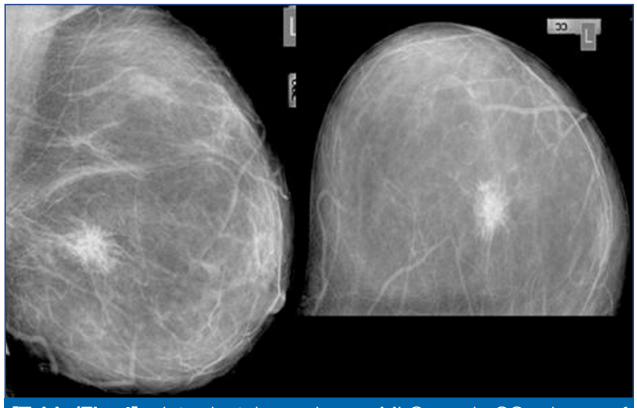
Breast cancer is the commonest cause of cancer mortality in females. Evolving ultrasound technology and improved understanding of imaging patterns of early disease has led to increased detection rate and treatment success of early stage disease. A study of 30 patients of pathologically proven breast carcinoma was conducted in our department and the results suggested that mammography and sonomammography are complementary to each other in the diagnosis of breast carcinoma and are not substitute to one another. Correlation of the findings of both the modalities helps to increase the radiologist's confidence in diagnosing breast carcinoma.

In our study carcinomas were seen above 40 years (100%) and the youngest patient was 42 years old. It has been observed in the past that most of breast carcinomas are seen above age of 45 years [8].

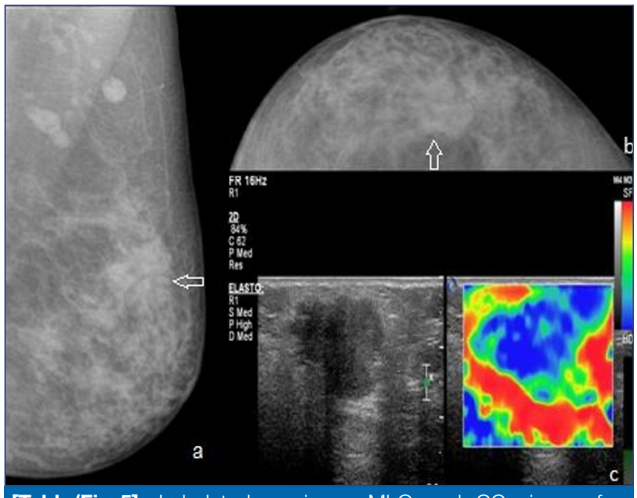
Most of the patients presented with a palpable mass and only one patient was detected on routine screening. The role of mammography in patients with palpable breast lumps is to rule out malignancy. It helps in earlier intervention for a malignant lesion along with screening for additional lesions in the ipsilateral and contralateral breast. It is also useful in assessing the extent of malignancy [9]. It has been reported that most breast cancers appear as palpable masses, usually found by the patients [10]. However, in younger females especially less than 40 years, glandular nodularity may be mistaken for masses on palpation.

Mammography is primary method of detection and diagnosis of breast disease with sensitivity of 85%-95% [11]. The specific mammographic features like high soft tissue density, irregular margins, multiple lobulations and spiculations with or without microcalcifications point towards the diagnosis [12,13] [Table/Fig-4].

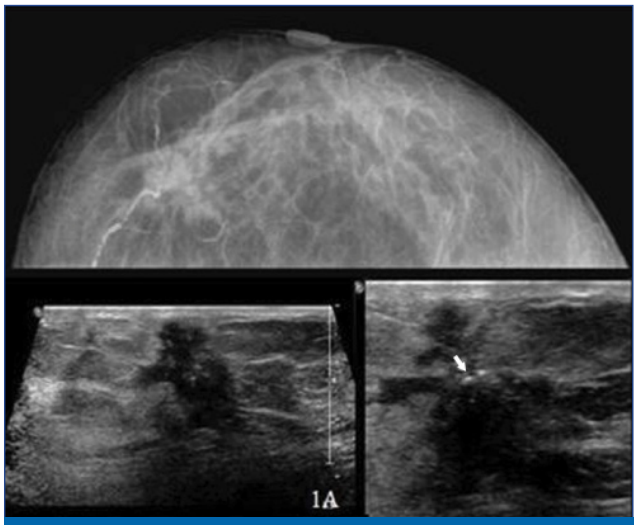
The major radiographic signs of carcinoma, tumour mass and clustered calcifications were found in most patients. Most of the malignant lesions had spiculated or microlobulated margins (87.7%), similar to description by Sickles EA [14]. In our study, microlobulated margins were seen in a larger number of lesions (22) as compared to spiculated margins



[Table/Fig-4]: Intraductal carcinoma-MLO and CC views of predominantly fatty breasts reveal a small, high density, irregular mass with microlobulated margins.



[Table/Fig-5]: Lobulated carcinoma-MLO and CC views of a heterogenous parenchyma show an ill defined, microlobulated, non palpable mass: a,b) Sonomammography; c) shows a microlobulated high density mass with Grade 5 elastography score hardness.



[Table/Fig-6]: Intraductal carcinoma- CC view shows a high density, spiculated mass with microcalcifications and architectural distortion in the upper outer quadrant. Also note benign vascular calcification overlapping the lesion. Sonomammography reveals a spiculated, markedly hypoechoic mass with microcalcifications (white arrow), posterior acoustic shadowing and hyperechoic halo.

which makes microlobulations, an important predictor of malignancy [Table/Fig-5].

It has been opined earlier that cancers with extensive intraductal component with or without a mass were more likely to show microcalcification compared to those without an intraductal component (73% versus 27%) [15].

Microcalcifications are more common in carcinoma insitu and early infiltrative carcinoma. In our study, microcalcifications were detected in 19 patients on digital mammography and 13 of them appeared as echogenic spots on ultrasound. Ultrasound had sensitivity and specificity of 68.4% and 100 % respectively to detect microcalcifications [Table/Fig-6].

The sensitivity of ultrasound for detecting microcalcifications has been reported to be 81.8% with a specificity of 94.5% [16]. Most common patterns were granular and fine branching seen in invasive ductal carcinoma. one patient with mesenchymal tumour and another with invasive ductal carcinoma had coarse calcifications.

All the malignant lesions in our study had high density (89%). None of the lesions had low density on mammography. Density of a mass is related to expected attenuation of equal volume of fibro glandular tissue. These findings are in accordance with previous studies which opined that high breast mass density is significantly associated with malignancy [17].

Asymmetry and architectural distortion is commonly observed with malignant lesions [18]. On mammography, architectural distortion may appear as spicules radiating from a central mass. In response to local infiltration into the surrounding tissue, the architectural distortion may have a star-shaped pattern [19]. In our study, architectural distortion was seen in 56.7% cases and was found to be highly suggestive of malignancy.

It has been found that asymmetric breast tissue, architectural distortion, and focal asymmetric densities are frequently encountered at mammography. These findings are significant, if associated with a palpable mass [20]. Focal asymmetry was present in 10% of the cases in our study.

The associated features of malignancy appreciated were skin thickening and nipple retraction seen in 30 and 20% cases respectively. The most common parenchymal pattern in our study was scattered fibroglandular seen in 23 cases followed by fatty (in five cases) and heterogenously dense (in two cases). In cases with heterogenously dense pattern, the masses were quite large in size at the time of presentation, so it did not pose any diagnostic difficulty.

Mammography is also helpful in determining the number and location of lesions. Majority of the patients presented with a single palpable mass but on mammography, nine cases had more than one lesion. While seven of these nine patients had well-circumscribed second lesion, two patients had second suspicious looking spiculated lesions, one in same breast and in the other case in contralateral breast which were interpreted as BIRADS 4c.

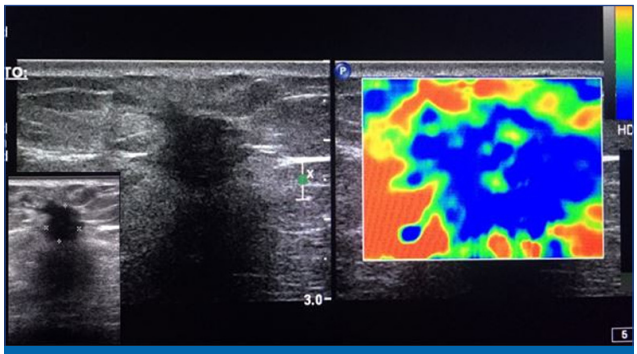
Locations of cancers closely paralleled those from previously published large consecutive series composed primarily of palpable lesions [21].

An absolute majority (43.3%) of tumours arose from the upper outer quadrant of the breast, with about 13.3% each coming from the upper inner and lower outer quadrants and 10% from lower inner quadrant. 20% of the lesions involved more than 1 quadrant.

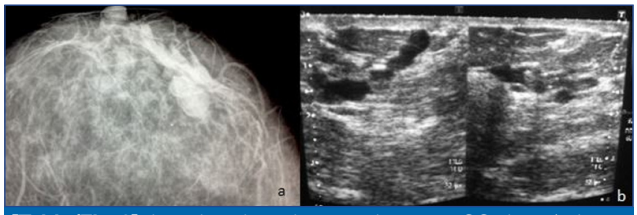
Hence, in women with palpable breast mass it is important to screen both breasts for non palpable cancer by mammography and sonomammography. It is reported that preoperative ultrasound screening of both breasts in a known patient of breast carcinoma detects up to 88% of synchronous contralateral malignant lesions, out of which 43% are occult on a mammography [22].

It has been observed that irregular shape, contour, extensive hypoechogenicity, surrounding halo and distortion of surrounding tissue were associated with highest predictive valve for malignancy [23] [Table/Fig-7].

It has been stated that a larger AP dimension is primarily a feature of small malignant nodules (with volume less than 1 mL). Benign lesions respect normal tissue boundaries and grow parallel to tissue planes. Thus, they are wider than taller, however malignant lesions invade tissue planes and are lobulated and grow taller than wider. The taller than wide shape in small, but not large, cancers



[Table/Fig-7]: Sonomammography of the same patient shows a microlobulated, markedly hypoechoic mass with posterior acoustic shadowing, hyperechoic halo and Grade 5 score on elastography.



[Table/Fig-8]: Intraductal carcinoma- pipe type: CC view a) shows a tubular lobulated opacity with microcalcifications along the lateral aspect of breast leading to nipple. Ultrasound; b) shows a dilated duct with intraductal mass showing calcifications.

reflects the shape of the underlying lobule in which it arose. Most cancers are thought to arise at the level of the Terminal Duct Lobular Unit (TDLU), at the junction of the extralobular terminal duct with the lobule. The DCIS then grows proximally in the terminal duct toward the large ducts and peripherally into the lobule, cancerising intralobular ductules. A larger number of lesions in our study had a parallel orientation i.e., wider than tall in contradiction to the above mentioned studies. This can be attributed to a smaller sample size or the larger size of lesions at the time of diagnosis.

About 76.6% lesions were hypoechoic on sonography. The hypoechoic echo pattern has a lower positive predictive value than irregular shape and non circumscribed margins, but the reliability of this feature increases if it is associated with the other suggestive findings.

According to other authors shape, margins, and echo pattern were significant factors for differential diagnosis on sonography [24].

In the literature, three patterns of ductal carcinoma have been described on ultrasound understanding its spread along pre-existing framework of ducts. These are-Cumulus type: ovoid or hypoechoic mass; Coral type: irregular or angular shape with ductal dilatation; and Pipe type: hypoechoic nodular mass with dilated duct leading to the retroareolar region [25]. In the present study, cumulus and coral were the most common patterns and presented as palpable lumps. Only two cases of pipe type were detected [Table/Fig-8].

Presence of an echogenic halo showed a very high predictive malignant value (86.4%). All the lesions in the present study demonstrated an echogenic halo. Low grade breast tumours show classical features of malignant masses in the form of spiculated margins and posterior acoustic shadowing on ultrasound but high grade tumours can paradoxically mimic benign masses as they may exhibit well defined margins and posterior acoustic enhancement [26]. As in our study, a relatively larger number of lesions had microlobulated margins rather that spiculated margins and lesser number of lesions had posterior acoustic shadowing, this may indicate higher grade of malignancy.

Another element of malignancy is hardness of malignant tissue as compared to normal parenchyma. Itoh A et al., first used ultrasound elastography to characterise breast lesions and proposed the 5-point scoring system. They reported the mean ± standard deviation of 4.2±0.9 of elasticity score for malignant lesions [27]. Higher sensitivity of elastography over standard ultrasound with a specificity of 91.5% has been reported [28]. In this study, elastography values of malignant lesions were correlating with the previous studies with a mean elasticity score of 4 and 5 in maximum number of patients and mean strain ratio of 5.06 with minimum value of 3.5 and maximum value of 7.1. All lesions with elasticity score of 5 were graded BIRADS 5.

It was found that combined evaluation of malignant masses with mammography and sonomammography improved the diagnostic accuracy. Combined role of two modalities has been described to be superior in differentiating benign from malignant lesions by many authors earlier [29,30].

Mammography allowed screening of ipsilateral as well as contralateral breast for non palpable masses, detection of microcalcifications and architectural distortion which are important predictors of malignancy. Ultrasound was of utmost importance in characterising the masses detected at mammography, in determining the multicentricity or multifocality of lesions and other associated features of malignancy like ductal dilatation and lymphnodes especially supraclavicular and internal mammary group, which are inaccessible on mammography alone. Elastography helped to confidently diagnose malignant lesions with higher mean elasticity scores and increased strain ratios. The role of imaging in a palpable breast lump is to differentiate benign from malignant lesions and if found malignant, to proceed for early intervention, screen rest of breast tissue for satellite lesions and assess locoregional lymphadenopathy. Most of the literature focuses on the sensitivity, specificity, negative and positive predictive values of mammography and sonomammography independently or in combination to differentiate malignant breast lesions from benign ones.

Present study evaluated only malignant masses and graded them by mammography, sonomammography and elastography separately as well in combination on BIRADS grading system. Thus, role of combining these modalities to differentiate suspicious lesions (BIRADS 4) from those highly suggestive of malignancy (BIRADS 5) was studied. It was observed that combined evaluation increased the diagnostic accuracy.

It is well highlighted in the past that BIRADS criteria are not sufficient for differentiating malignant from benign lesions. Subcategories 4a, 4b, and 4c are useful in predicting the likelihood of malignancy and are more difficult for smaller lesions [31].

We could not find any reference literature which graded a suspicious lesion on BIRADS system and differentiated Grade 4 from Grade 5 lesions using multimodality approach. It is of utmost importance to a clinician because if a lesion is BIRADS Grade 5 on imaging, he/she can straightway plan for staging and treatment depending upon the histological grade of malignancy.

LIMITATION

The major limitations of our study were that results were obtained in exclusively palpable tumours. Our only patient, who came for routine screening, had a small classical malignant spiculated lesion. More data is required including lesions limited to ducts only or with subcentimeter dimensions. Other limitations of this study were smaller sample size and non consideration of nodal, lymphovascular and distant metastasis.

CONCLUSION

Digital mammography, sonomammography and elastography are complementary to each other in evaluation of breast carcinoma and are not substitute for each other. They have their individual advantages in evaluating various signs of malignancy and combined together increase the diagnostic accuracy and add to the confidence of radiologist. This approach is of utmost importance to diagnose early and smaller lesions and is a step towards lowering breast cancer related mortality.

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