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Dr. Pratiksha Yadav
Dr. D. Y. Patil Medical College
and Research Centre,
Maharashtra, India

**Dr. Variar Saroja
Padmanabhan**
Dr. D. Y. Patil Medical College
and Research Centre,
Maharashtra, India

Utility of whole breast ultrasound and digital tomosynthesis as an adjunct with mammography in dense breast to detect breast lesions

Dr. Pratiksha Yadav and Dr. Variar Saroja Padmanabhan

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Abstract

Mammography has been widely adopted as the primary screening tool in breast cancer detection and assessment. Screening in dense breast makes it difficult to detect lesions on screening and lowers its sensitivity to detect small lesions. Sensitivity and specificity improves with use of digital breast tomosynthesis and whole breast ultrasound in detecting lesions and also in differentiating benign and malignant breast lesions. Breast ultrasound and DBT have shown equivocal significance in detecting breast lesion on screening in the present study.

The aim of the study was to evaluate utility of whole breast ultrasound and digital tomosynthesis as an adjunct with mammography in dense breast to detect breast lesions.

Keywords: Dense breast, mammography, digital breast tomosynthesis, breast cancer

Introduction

Breast cancer is the most common cancer to occur in women. It accounts for 21% of all cancers in women worldwide. The projected incidence of breast cancer is suggested to increase in the following years. An initiative to reduce breast cancer can be achieved by health awareness and breast cancer screening [1].

Radiological imaging forms an important part in cancer detection. The most important role of mammography in an unselected, asymptomatic woman is to detect any breast lesion at an earlier stage and to differentiate it from any potential malignant lesion. Detecting cancer using mammography when they are at a smaller size and earlier stage has been shown to reduce or delay mortality from breast cancer [2-6].

Digital breast tomosynthesis creates thin-slice reconstructions of the breast from low-dose digital mammographic images acquired at multiple angles which improves lesion visibility by reducing over-lapping tissue. Thereby have the potential to increase breast cancer detection and to reduce false-positive findings.

Limitation noted in this technique is a slight increase in radiation exposure which is acceptable in favour of accurate lesion assessment [2]. Ultrasound is a safe method of screening lesions not detected in mammography but is highly subjective and less sensitive.

Detection and characterization of breast disease with assessment of its local extend is better evaluated on magnetic resonance imaging (MRI). The breast MRI has shown increased sensitivity and low-to-moderate specificity ranging from 37% to 97% in various studies. Comparative studies conducted have revealed that MRI has the same specificity as that of mammography and specificity higher than that of breast ultrasound.³ Time consumption for the test and the expense for the test are the limitations faced on the part of cases coming for screening. Mammographic density is considered a risk factor for breast cancer and is important in screening [2].

My aim hence was to detect lesions on digital breast tomosynthesis and ultrasound that were not detected in dense breast on mammography while screening.

In my study 164 women with dense breast from an unselected population were screened with mammography followed by digital breast tomosynthesis and ultrasound. In lesion showing characteristics of malignancy biopsy correlation was carried out.

Corresponding Author:
**Dr. Variar Saroja
Padmanabhan**
Dr. D. Y. Patil Medical College
and Research Centre,
Maharashtra, India

Global burden of breast cancer

Across the globe, breast cancer is the most common cancer in women. As per the GLOBOCAN database, breast cancer is the most commonly diagnosed cancer amongst women with global burden anticipated to cross 2 million by the year 2030, with increasing proportions from developing countries [7].

The burden of breast cancer in India

Breast cancer is the major cause of morbidity and mortality among women residing in major cities in India, whereas in rural areas it still holds a second position [1]. GLOBOCAN 2012 states that India with other few countries collectively contribute to one third of the breast cancer across the globe. Increased incidence and mortality in India is due to illiteracy, lack of awareness, financial limits in rural areas of India [1, 11].

Aim and objectives

The aim of this study was to study the utility of whole breast ultrasound and digital tomosynthesis as an adjunct with mammography in dense breast to detect breast lesions. We categorized the findings on all the three modalities according to ACR BIRADS classification. The utility of digital breast tomosynthesis and whole breast ultrasound as an adjunct to mammography in detecting lesions in dense breast was studied. Histopathological correlation where carried out wherever applicable.

Patients and Methods

An observational study was conducted in a tertiary care hospital over the period of 2 years from October 2017 to September 2019.

Patient selection

Female participants above the age of 40 years coming for breast screening were included, however women presenting with palpable lump, having operative history of carcinoma breast or radiation for breast carcinoma were excluded. Of the women undergoing screening 164 women satisfying the exclusion and inclusion criteria were considered in the study.

Mammography screening of breast was done on MAMMOMAT inspiration Mammography screening of breast was done on MAMMOMAT inspiration in standard mediolateral-oblique (MLO) and craniocaudal (CC) projections. Digital Breast tomosynthesis (DBT) images were acquired by the swivel arm of the MAMMOMAT Inspiration with an angular range of +25° to -25° where 25 views are obtained. Exposure was taken at every 2°. Image acquisition was performed with a pulsed, short exposures during continuous motion of the x-ray tube. Image reconstruction was performed immediately after image acquisition with slice thickness 1 mm. For mammography and digital breast tomosynthesis the participant is asked to stand with the feet facing towards the unit. CC and MLO projection taken with

proper positioning. Nipple in profile and pectoral nipple distance (PND) within 1 cm prompts an ideal positioning for CC projection. Ideal positioning of MLO projection should have lower end of pectoralis muscle at the level of PNL or below, PND less than 1 cm and nipple in profile. Screening study of dense breast will be done using high frequency linear transducer of HITACHI ALOKA ARIETTA S 60 colour Doppler ultrasound machine.

Observations and Results

The present study “Utility of whole breast ultrasound and digital tomosynthesis an adjunct with mammography in dense breast to detect breast lesions” was carried out in 200 participants, of which 36 were lost to follow up. Hence 164 women satisfying the inclusion and exclusion criteria were considered in the study. Digital breast tomosynthesis and ultrasound were also carried out. Mammographic findings amongst the participants were categorised as asymmetric density in 46 participants (28%), architectural distortion in 7 (4.3%), cystic lesion and calcifications in 41 (25%) and 43 (26.2%) participants respectively.

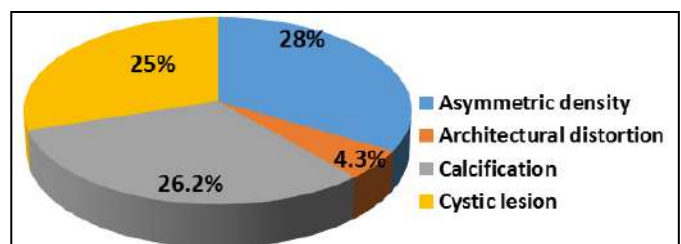


Fig 1: Schematic presentation of mammographic findings in study participants

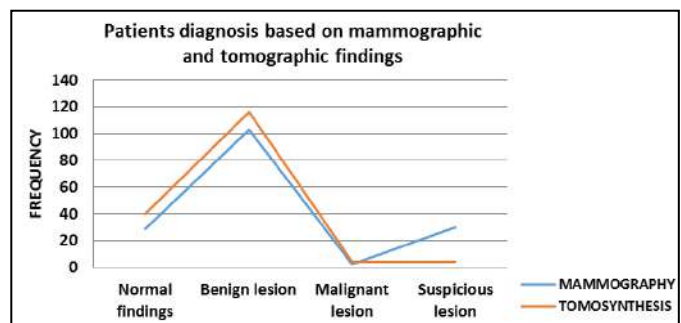


Fig 2: Schematic representation of patient diagnosis on mammographic and tomographic findings

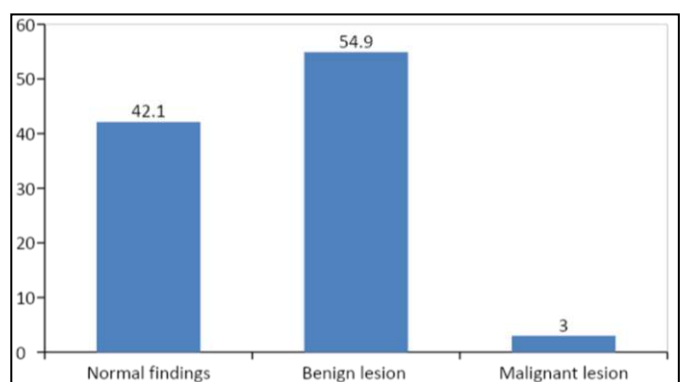


Fig 3: Patients diagnosis based on Ultrasonography findings (N=164)

In our present study, 54.9% were benign lesion, 42.1% were normal and malignancy was detected in 3%.

Table 1: Patients final diagnosis based on collective findings (N=164)

Diagnosis	Frequency	Percentage
Normal findings	37	22.6
Benign lesion	124	75.6
Malignant lesion	3	1.8

Collective diagnosis showed benign lesions in 75.6%, malignancy in 1.8% and normal findings in dense breast in 22.6%.

Table 2: Comparison of findings between ultrasonography and final diagnosis in differentiating malignant and benign lesions

Diagnosis by ultrasonography	Final diagnosis		Total
	Malignant	Benign	
Malignant	3	2	5
Benign	0	90	90
Total	3	92	95

Table 3: Comparison of findings between tomography and final diagnosis in differentiating malignant and benign lesions

Diagnosis by tomography	Final diagnosis		Total
	Malignant	Benign	
Malignant	3	1	4
Benign	0	116	116
Total	3	117	120

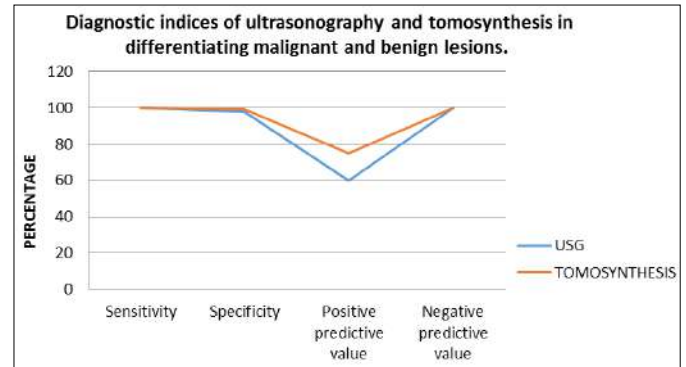


Fig 4: Schematic presentation of diagnostic indices of ultrasound and tomosynthesis in differentiating malignant and benign lesions

Table 4: Agreement of findings between ultrasonography and final diagnosis (N=164)

Diagnosis by Ultrasonography	Final diagnosis			Total	Kappa value: 57.7% p value: 0.001*
	Benign n (%)	Malignant n (%)	Normal n (%)		
Benign	90 (72.6)	0	0	90 (54.9)	
Malignant	2 (1.6)	3 (100)	0	5 (3)	
Normal	32 (25.8)	0	37 (100)	69 (42.1)	
Total	124 (100)	3 (100)	37 (100)	164 (100)	

Note: p value based on Kappa statistics, * statistically significant ($p < 0.05$)

Table 5: Agreement of findings between tomography and final diagnosis (N=160)

Diagnosis by ultrasonography	Final diagnosis			Total	Kappa value: 93.7% p value: 0.001*
	Benign n (%)	Malignant n (%)	Normal n (%)		
Benign	116 (96.7)	0	0	116 (72.5)	
Malignant	1 (0.8)	3 (100)	0	4 (2.5)	
Normal	3 (2.5)	0	37 (100)	40 (25)	
Total	120 (100)	3 (100)	37 (100)	160 (100)	

Note: p value based on Kappa statistics, * statistically significant ($p < 0.05$)

Table 6: Agreement of findings between mammography and final diagnosis (N=134)

Diagnosis by mammo-graphy	Final diagnosis			Total	Kappa value: 74.7% p value: 0.001*
	Benign n (%)	Malignant n (%)	Normal n (%)		
Benign	94 (95.9)	1 (33.3)	8 (24.2)	103 (76.9)	
Malignant	0	2 (66.7)	0	2 (1.5)	
Normal	4 (4.1)	0	25 (75.8)	29 (21.6)	
Total	98 (100)	3 (100)	33 (100)	134 (100)	

Note: p value based on Kappa statistics, * statistically significant ($p < 0.05$)

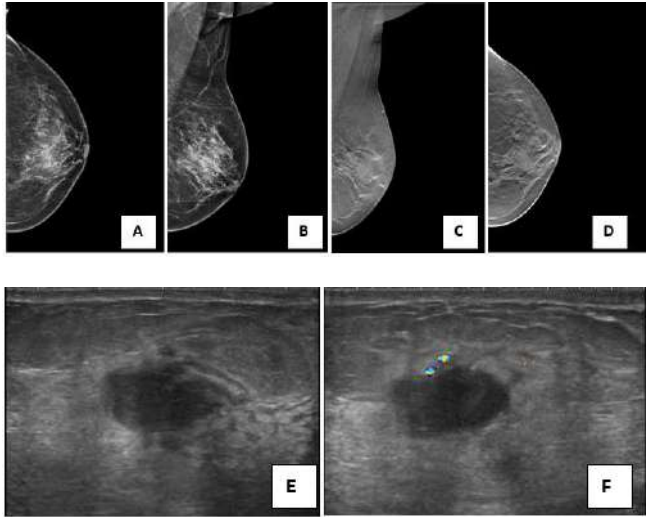
Table 7: Agreement of findings between mammography and tomography (N=164)

Diagnosis by Mammography	Tomography			Suspicious n (%)	Total	Kappa value: 55.6% p value: 0.001*
	Benign n (%)	Malignant n (%)	Normal n (%)			
Benign	94 (81)	1 (25)	8 (20)	0	103 (62.8)	
Malignant	0	2 (50)	0	0	2 (1.2)	
Normal	2 (1.7)	0	27 (67.5)	0	29 (17.7)	
Suspicious	20 (17.2)	1 (25)	5 (12.5)	4 (100)	30 (18.3)	
Total	116 (100)	4 (100)	40 (100)	4 (100)	164 (100)	

Note: p value based on Kappa statistics, * statistically significant ($p < 0.05$)

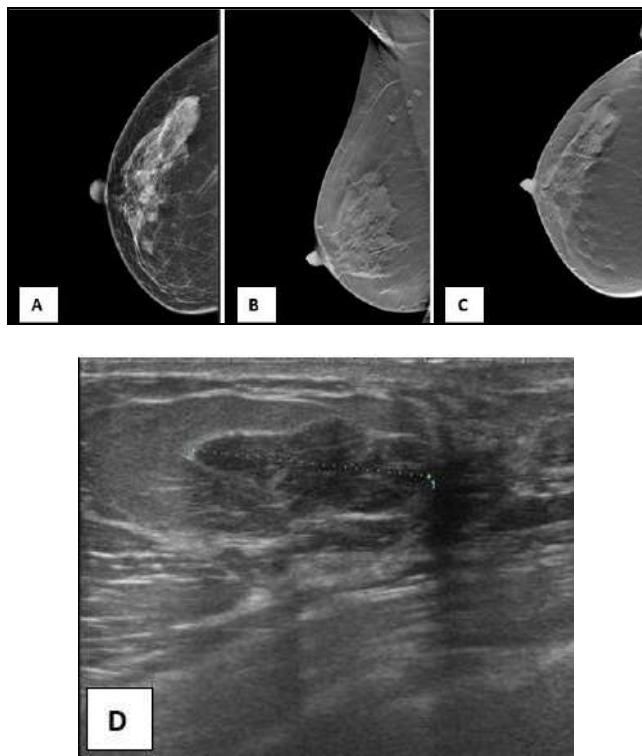
Illustrative cases

Case No 1



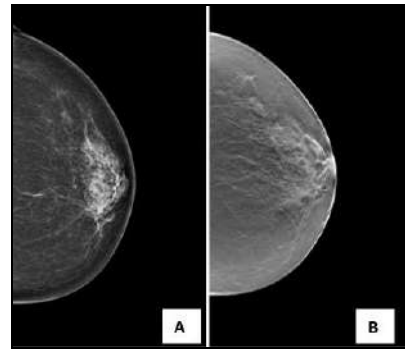
(A), (B) Asymmetric density noted in the middle 1/3rd of left breast on CC and MLO projection of mammography.(C,D) MLO and CC projection on tomosynthesis show an ill-defined mass of equal density and obscured margins at 12'o clock position. Architectural distortion and trabecular thickening was noted in the adjacent parenchyma. (E) USG revealed an ill-defined irregular Hypoechoic mass with minimal vascularity on Color Doppler. The lesion was reported as ACR BIRADS 4C category which on histopathology was proved to be malignant.

Case No 2



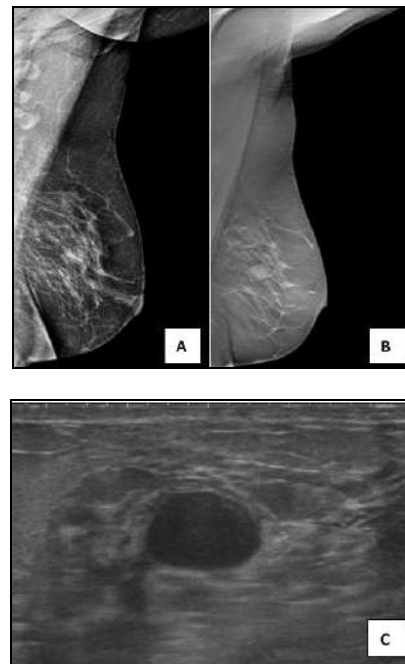
(A) Asymmetric density in the upper outer quadrant of right breast. (B, C) On tomosynthesis, it appears as asymmetric breast parenchyma with capsule suggestive of hamartoma. (D) USG revealed an oval heterogeneously hypoechoic mass with capsule suggestive of hamartoma.

Case No 3



(A) Mammography CC projection of left breast demonstrate asymmetric density. (B)On Tomosynthesis, it appears to be overlapping breast parenchymal tissue, no mass was detected.

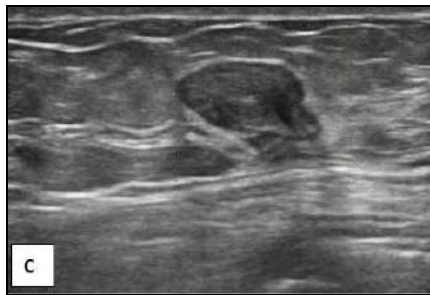
Case No 4



(A) MLO projection of left breast on mammography show dense breast with suspicious is Odense mass in upper inner quadrant (B) on tomosynthesis the lesion appeared as well circumscribed mass with benign characteristics and was diagnosed as fibroadenoma on Ultrasound (C).

Case No 5

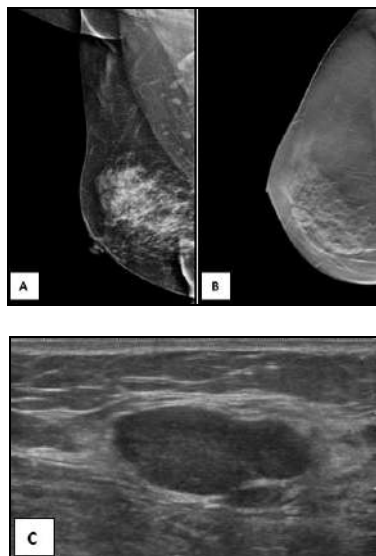




(A) MLO projection of right breast reveal dense breast which could obscure lesions. (B) On tomosynthesis an is Odense mass with indistinct margins posteriorly was noted in the posterior 1/3rd of breast parenchyma. (C) On USG the lesion appeared heterogeneously hypoechoic with no internal vascularity on Color Doppler.

The lesion was reported as 4A low suspicion of malignancy. However on histopathology the lesion turned out to be fibroadenoma.

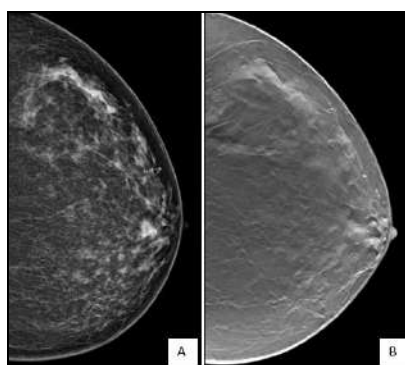
Case No 6



(A) MLO projection of right breast on mammography show dense breast which may obscure lesions. (B) On tomosynthesis the lesion appeared well defined mass with circumscribed margins and peripheral hypodense halo (C) On USG the lesion appeared heterogeneously hypoechoic with no internal vascularity on color Doppler.

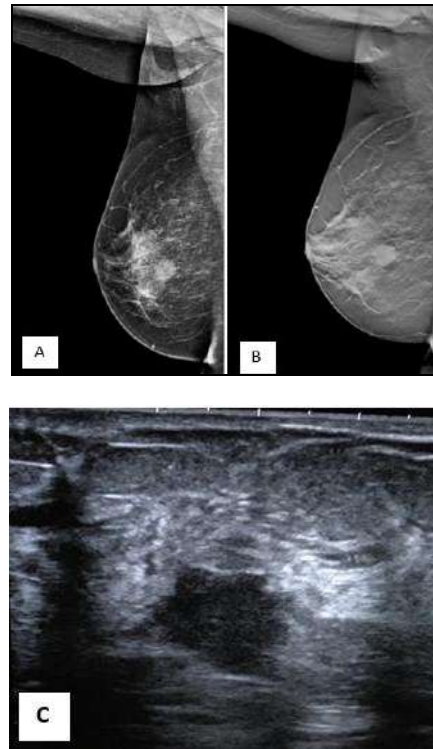
Findings were consistent with benign etiology – fibroadenoma.

Case No 7



(A) CC projection of left breast on mammography demonstrates a small density in the retroareolar region. (B) CC projection f left breast on tomosynthesis revealed that the density was due to overlapping breast parenchyma. This case represents a false positive case on mammography.

Case no 8



(A) MLO projection of the right breast show an ill-defined high density mass with indistinct margins. (B) MLO projection on tomosynthesis show a high density mass with obscured margins at lower inner quadrant. (C) USG revealed an irregular mass with spiculated margin and minimal vascularity on Color Doppler.

The lesion was reported as ACR BIRADS 5 category on ultrasound which on histopathology was proved to be an Invasive Ductal Carcinoma.

Discussion

The incidence of breast cancer is rising steadily and is the leading cause of mortality in women worldwide after lung carcinoma.

In the present study, of the women undergoing routine screening, 164 women satisfying the inclusion and exclusion criteria had dense breast of which 140 (85.4%) had type C heterogeneously dense breast while the remaining 24(14.6%) had type D very dense breast.

Age distribution of study participants revealed majority of the dense breast in the age group of 40 to 45 years with frequency being 74 (45.1%), followed by frequency of 64 (39%) in the age group of 46-59 years and 26 women (15.9%) above the age of 60 years. Similar findings were reported by Checka C M *et al.* where out of 7007 screening mammograms, 3234 (46%) had heterogeneous dense breast and 645 (9%) had extremely dense breast, with majority in the age group of 40-49 years [23].

The women having dense breast in present study were subjected to tomosynthesis and ultrasound to rule out the presence of any lesion in their early stages. Based on the

ACR BIRADS 5th edition for mammography the lesions were categorized as benign lesion in 103 participants (62.8%), lesions with suspicious characteristics in 30 participants (18.3%) and lesions with malignant features in 2 participants (1.2%). Negative mammogram was obtained in 29 participants (17.1%).

Diagnostic indices of mammography in differentiating malignant and benign showed sensitivity of 66.6%. On Digital Breast Tomosynthesis the diagnostic indices in differentiating malignant and benign lesions were sensitivity of 100%, a specificity of 99.1%, PPV of 75% and NPV of 100%. In the present study Diagnostic indices of ultrasound in differentiating malignant and benign lesion revealed a sensitivity of 100%, a specificity of 97.8%, and positive predictive value of 60% and negative predictive value of 100%.

Similar findings were reported by Tan KP *et al.* stating that in women with dense breast USG was more sensitive than mammography by 40%. However, the specificity of mammography was found to be superior to ultrasound. Ultrasound had greater PPV and NPV as compared to mammography^[25].

Phi XA *et al.* in a research article reported that Digital Breast Tomosynthesis has a superior sensitivity and specificity than mammography in diagnostic setting in dense breast where as an increase in cancer detection rate was noted in combining Digital Breast Tomosynthesis and Mammography in dense breast^[3, 8]. Similar findings were reported by Bernardi D *et al.* in their study over 9672 screening participants^[26].

Of the benign lesions observed on mammography, Digital Breast Tomosynthesis and ultrasound 43 turned out to be fibroadenoma, 30 were cysts, 2 were hamartoma, 1 showed duct dilatation and calcification in 26 patients. Amongst the calcification majority were found to be vascular calcification. Calcification were better appreciated on mammography and tomosynthesis than on ultrasound.

Of the 5 malignant lesion collectively diagnosed on mammography, Digital Breast Tomosynthesis and ultrasound 3 were confirmed to be malignant on histopathological evaluation. The remaining two lesions were proven to be of benign etiology on HPE.

In this study the lesions missed on mammography due to dense breasts were subsequently detected on tomography and ultrasound with statistical significance. This proves that DBT and ultrasound help in detecting breast pathology in dense breast on screening study. This has not been much reported in literature. Breast ultrasound and DBT have shown equivocal significance in detecting breast lesions on screening in the present study.

Early detection with screening techniques such as mammography, digital breast tomosynthesis and ultrasound play a key role in the early detection of breast lesions and thus reduction of mortality. DBT and ultrasound is used as an adjunct to mammography to further evaluate in women with dense breasts. Advantages of the ultrasound are lack of radiation exposure. The possible way to reduce mortality is its early detection and prompts treatment.

In this study the lesions missed on mammography due to dense breasts were subsequently detected on tomography and ultrasound with statistical significance. This proves that DBT and ultrasound help in detecting breast pathology in dense breast on screening study. This has not been much reported in literature. Breast ultrasound and DBT have

shown equivocal significance in detecting breast lesions on screening in the present study.

Previous studies conducted by Tagliafico AS *et al.* in year 2012-2015 and 2015 -2017 stated that ultrasound breast better detected cancer than tomosynthesis in mammo graphically negative dense breast, However, ultrasound was found to have more false positives in comparison to tomosynthesis^[20, 27].

Summary and Conclusions

Present study entitled “The aim of this study was to study the utility of whole breast ultrasound and digital tomosynthesis as an adjunct with mammography in dense breast to detect breast lesions” was carried out at the Department of Radio diagnosis, in Western India between the time periods July 2017- September 2019. In our study mammography showed a lower sensitivity (66.1%) in detecting breast lesions. Digital breast tomosynthesis and ultrasound revealed greater sensitivity and specificity in differentiating malignant and benign lesions. All the three modalities showed diagnostic indices that are statistically significant and hence help in detecting lesions during screening test. Of the 5 malignant lesion collectively diagnosed on mammography, DBT and ultrasound 3 were confirmed to be malignant on histopathological evaluation. The remaining two lesions were proved to have benign etiology on HPE. In this study the lesions missed on mammography due to dense breasts were subsequently detected on tomography and ultrasound with statistical significance. This proves that DBT and ultrasound help in detecting breast pathology on screening study. Breast ultrasound and DBT have shown equivocal significance in detecting breast lesion on screening in the present study.

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