New York Science Journal

Websites:
http://www.sciencepub.net/newyork
http://www.sciencepub.net

Emails:
newyorksci@gmail.com
editor@sciencepub.net

MARSLAND PRESS
Multidisciplinary Academic Journal Publisher

The Role of Ultrasound in Screening of Dense Breast

Prof. Magda Shaaban Yakoot[1], Dr. Abdalla Hussein Ahmed[1], Dr. Gehan Hassan Gamal[2], Hanan Shawky Mohammed Al Sorady[1]

[1]Radiodiagnosis Department, Faculty of Medicine for Girls, Al-Azhar University, Egypt
[2] Radiodiagnosis Department, Faculty of Medicine, October 6 University, Egypt

Abstract: Background: Despite recent improvements in mammography equipment and technique, the radiographically dense breast remains difficult to image. The problems in imaging the dense breast account for a large percentage of the cases of mammographically "missed" carcinomas. Other imaging modalities-such as ultrasonography, transillumination, thermography, computed tomography, magnetic resonance imaging, and radionuclide imaging-have been investigated for use in breast cancer detection. **Objectives:** The aim of this study was to assess the reliability of the sonographic Breast Imaging Reporting and Data System (BIRADS) classification in differentiating benign from malignant breast masses. **Patients and Methods:** This is prospective study involved 50 asymptomatic females their age range from 40 to 70 years. These females are carefully selected from a lot number of females who subjected to screening mammography. These 50 females with mammographically dense breast undergo additional screening by ultrasonography. To assess the role of ultrasound in screening of female with mamoghraphiclly dense breast at radiology department of Al- zahraa university hospital. The present study started at January 2019 till August 2019. **Results:** Lesions that are classified as BIRADS II all were benign and not subjected to histopathology, while lesions classified as BIRADS III, IV were subjected to histopathology. Among all lesion classified as BIRADS III 94.5% were benign and only 5.5% were malignant, finally lesions classified as BIRADS IV show 100 % malignant. Of the 21 lesion subjected to histopathology 17 were benign and 4 were malignant. Of the benign lesion all are fibro adenoma. Of the malignant lesion 3 lesions were invasive ductal carcinoma and one lesion was invasive lobular carcinoma. The results of the present study demonstrate the clear association between ACR BTIRADS classification and the pathology results. **Conclusion:** Every woman in the state of Connecticut who undergoes mammography and demonstrates breast density >50% must be informed of the following: ''If your mammogram demonstrates that you have dense breast tissue, which could hide small abnormalities, you might benefit from supplementary screening tests, which can include abreast ultrasound screening or a breast MRI examination, or both, depending on your individual risk factors.

[Magda Shaaban Yakoot, Abdalla Hussein Ahmed, Gehan Hassan Gamal, Hanan Shawky Mohammed Al Sorady. **The Role of Ultrasound in Screening of Dense Breast.** *N Y Sci J* 2019;12(12):41-48]. ISSN 1554-0200 (print); ISSN 2375-723X (online). http://www.sciencepub.net/newyork. 6. doi:10.7537/marsnys121219.06.

Keywords: Ultrasound, Dense Breast

1. Introduction

Despite recent improvements in mammography equipment and technique, the radiographically dense breast remains difficult to image. The problems in imaging the dense breast account for a large percentage of the cases of mammographically "missed" carcinomas. Other imaging modalities-such as ultrasonography, transillumination, thermography, computed tomography, magnetic resonance imaging, and radionuclide imaging-have been investigated for use in breast cancer detection ***(Crystal et al., 2003).***

Mammography is the only screening modality that has been proved to reduce breast cancer mortality. However, its ability to depict small non-calcified carcinomas varies greatly with breast tissue composition. While mammography detects up to 98% of carcinomas in fatty breasts, sensitivity declines significantly with increasing breast density and may be as low as 30%–48% in extremely dense breasts ***(Nelson et al., 2009).***

Ultrasound is a promising adjunctive screening modality, because it is widely available, relatively inexpensive, and well tolerated by patients. In addition, suspicious breast lesions can be readily biopsied under ultrasound guidance ***(Crystal et al., 2003).***

Multiple studies demonstrate that supplemental screening breast US generates an incremental cancer detection rate of 2.3–4.6 cancers per 1000 women screened ***(Kaplan et al., 2001).***

However, screening breast US is limited by low specificity and low positive predictive values (PPVs) compared with those of screening mammography. Because there is no direct proved mortality benefit

from screening breast US, it is also controversial ***(Kopans et al., 2004).***

Women with dense breast tissue have up to a six fold greater risk of interval cancer and an overall worse prognosis for subsequent cancers detected clinically. In addition, the risk of developing cancer is four to six times higher in women with dense breast tissue compared with the risk in women without dense breast tissue ***(Harvey and Bovbjerg, 2004).***

Aim of the Work

The role of ultrasound in screening of dense breast in Al-zahraa university hospital. This study aims to evaluate the role of ultrasound in screening of dense breast and detection of any breast lesion and classification according breast imaging, reporting and data system [BI-RADS] and pathology diagnosis after biopsy as the reference study.

2. Patients and Methods

This is prospective study involved 50 asymptomatic females their age range from 40 to 70 years. These females are carefully selected from a lot number of females who subjected to screening mammography. These 50 females with mammographically dense breast undergo additional screening by ultrasonography. To assess the role of ultrasound in screening of female with mamoghraphiclly dense breast at radiology department of Al- zahraa university hospital. The present study started at January 2019 till August 2019.

Inclusion criteria:

All patients included in this study had the following criteria:

- Females
- Age (40--70) years old

Exclusion criteria:

- Age below 40 years old.
- Pregnant.
- Males.

Patient assessment:

Assessment composed of;

- Full history and clinical data; proper and full history from the patient taken including age, age of last child, date of last period and it is regularity (if still menstruating), complaint, positive family history, past history of (presence of hormonal replacement etc)
- Explanation of the procedure to the patient and her consent,
- Ask the patient to exposed the examined area including both breast and axilla.

Actual exam: two examination were done.

A-Mammography; was done for:

- Evaluation of breast density and grading according to ACR-BIRADS (A, B, C and D) and only female with ACR_C and D included at this study and subjected to additional screening ultrasound.
- Detection of micro calcification, architectural distortion and asymmetry in breast density.
- Mammography was done at digital mammography model FFDM at mammography unit at radiology department of alzahraa university in the following step.

Craniocudal view (CC)

Key Steps in Positioning CC View

- The patient stands with the feet slightly apart with weight equally distributed., The breast is mobilized upwards and is also pulled outwards away from the body as much as possible, so that The arm on the side to be examined is by the Side, The contra lateral arm is raised holding the machine for support. The patient's head was away from the side being examined. The breast is lifted and the image receptor is positioned at the level of the infra mammary crease. The nipple should be centered. Both the medial and lateral halves of the breast should be in the collimated area and we usually start by the right breast.

B- Ultrasound

The US equipment we used was Phillips health care affinitin70 G. The breast examination performed by high resolution ultrasound transducers (5– 12 MHz). The room was darkened sufficiently to eliminate screen reflections and to create optimal conditions to perceive image details. The machine and the operator are on the right of the patient. The patient is placed in a supine position with arms raised over the head for examination of medial half of the breast. The lateral half of the breast is examined while in slight oblique position.

Scanning Technique

The transducer should always be perpendicular to the skin surface. Compression is useful to avoid refraction and scattering from normal anatomical structures. Both breasts were systematically examined by right one firstly with overlapping scans in clockwise pattern. Then retro areolar region was separately scanning with angled views to ensure the complete coverage of all breast tissue. The breast scanned to determined the parenchymal echo texture and identification of any diffuse or focal abnormality. A color Doppler examination used to supplement the gray scale evaluation of either diffuse or focal abnormality of the breast. Axilla bilaterally are examined simultaneously with ipsilateral breast. After examination of both breast and axilla and identification of the lesion we interpretate image as follow.

Statistical analysis:

Data were analyzed using Statistical Program for Social Science (SPSS) version 15.0. Quantitative data were expressed as mean± standard deviation (SD). Qualitative data were expressed as frequency and percentage. Independent-samples t-test of

significance: was used when comparing between two means. Chi-square test: was used when comparing between non-parametric data. A one-way analysis of variance (ANOVA): when comparing between more than two means. Probability (P-value): P-value < 0.05 was considered significant, P-value < 0.001 was considered as highly significant, P-value > 0.05 was considered insignificant.

3. Results

This table shows the description of age in studied patients. The mean age in studied patients was 45.9 ± 5.1 years with minimum age of 40 years and maximum age of 57 years. There were 29 patients (58%) ≤ 45 years and 21 patients > 45 years (Table 1).

Table (1): Description of age in studied patients.

Variables		**Studied patients**	
Age (years) (N = 50)	**Mean ±SD**	45.9 ± 5.1	
	Min - Max	40 – 57	
Age groups (N = 50)	**≤ 45 years**	29	58%
	> 45 years	21	42%

This table shows the description of predisposing factors in studied patients. There were 8 patients (16%) had positive family history, 5 patients (10%) had hormonal risk factor while there were 37 patients (74%) had no predisposing risk factors (Table 2).

Table (2): Description of predisposing factors in studied patients.

Variables		**Studied patients (N = 50)**	
Predisposing factors	**No PF**	37	74%
	Positive FH	8	16%
	Hormonal factor	5	10%

This table shows no statistical significant difference **(p-value > 0.05)** between age of patients as regard U/S results (Table 3).

Table (3): Comparison between age of patients as regard U/S results.

Variables		**U/S results**			**P-value**
		Normal (n = 35)	**Benign (n = 12)**	**Suspicious (n = 3)**	
Age (years)	**Mean**	46.7	43.6	44.0	0.125
	±SD	4.9	4.7	6.08	NS

NS: p-value > 0.05 is considered non-significant.

This table shows the description of BIRADs in studied patients. There were 35 patients (70%) BIRADs I, 2 patients (4%) BIRADs II, 10 patients (20%) BIRADs III and 3 patients (6%) BIRADs IV (Table 4).

Table (4): Description of BIRADs in studied patients.

Variables		**Studied patients (N = 50)**	
BIRADs	**I**	35	70%
	II	2	4%
	III	10	20%
	IV	3	6%

This table shows the description of recommendations in studied patients. Biopsy was recommended in 3 patients (6%), follow up every 6 months was recommended in 12 patients (24%) and routine screening every year was recommended in 35 patients (70%) (Table 5).

Table (5): Description of recommendations in studied patients.

Variables		Studied patients (N = 50)	
Recommendations	Biopsy	3	6%
	Follow up every 6 month	12	24%
	Routine screening every year	35	70%

This table shows the description of histopathology in studied lesions. There were 17 lesions (81%) were benign, 4 lesions (19%) were malignant. All benign lesions (81%) were fibro adenoma, 3 malignant lesions (14.2%) were invasive ductal carcinoma and 1 malignant lesion (4.8%) was invasive lobular carcinoma (Table 6).

Table (6): Description of histopathology results in studied lesions.

Variables		Studied lesions (N = 21)	
Histopathology	Benign lesion	17	81%
	Malignant lesion	4	19%
Benign lesions	Fibro adenoma	17	81%
Malignant lesions	Invasive ductal carcinoma	3	14.2%
	Invasive lobular carcinoma	1	4.8%

This table shows the Diagnostic performance of U/S in relation to Histopathology results. Total studied patients were 21 patients. There were 3 patients (14.3%) true positive, 17 patients (81%) true negative, 0 patient (0%) false positive and 1 patients (4.7%) false negative. Thus U/S had the sensitivity of 75%, specificity of 100%, PPV of 100%, NPV of 94.4% and accuracy of 95.2% (Table 7).

Table (7): Diagnostic performance of U/S in relation to Histopathology results.

(n = 21)	True positive		True negative		False positive		False negative	
U/S	3	14.3%	17	81%	0	0%	1	4.7%
	Sensitivity		Specificity		PPV		NPV	Accuracy
U/S	75%		100%		100%		94.4%	95.2%

This table shows no statistical significant relation **(p-value > 0.05)** between U.S results and age of patients (Table 8).

Table (8): Relation between U.S results and age of patients.

Variables		U/S results		P-value
		Benign (n = 18)	Suspicious (n = 3)	
Age (years)	Mean	44.5	44.0	0.863
	±SD	4.9	6.08	NS

NS: p-value > 0.05 is considered non-significant.

This table shows no statistical significant relation **(p-value > 0.05)** between U.S results and risk factors of patients (Table 9).

Table (9): Relation between U.S results and risk factors of patients.

Variables		U/S results				P-value
		Benign (n = 18)		Suspicious (n = 3)		
Risk factors	No risk factors	8	44.4%	0	0%	0.097 NS
	Positive Family history	6	33.3%	3	100%	
	Hormonal factor	4	22.2%	0	0%	

NS: p-value > 0.05 is considered non-significant.

This table shows no statistical significant relation **(p-value > 0.05)** between U.S results and ACR of patients (Table 10).

Table (10): Relation between U.S results and ACR of patients.

Variables		U/S results				P-value
		Benign (n = 18)		Suspicious (n = 3)		
ACR	C	6	33.3%	0	0%	0.237
	D	12	66.7%	3	100%	NS

NS: p-value > 0.05 is considered non-significant.

This table (Table 11) shows the description of lesion morphology in studied patients. As regard shape, there were 5 lesions (20%) rounded, 18 lesions (72%) oval, and 3 lesions (12%) irregular. As regard margin, there were 21 lesions (84%) circumscribed, 4 lesions (16.3%) not circumscribed. As regard orientation, there were 3 lesions (8%) not parallel and 22 lesions (73.3%) parallel. As regard echogenicity, there were 6 lesions (24%) anechoic, 17 lesions (68%) hypo echoic and 2 lesions (8%) iso-echoic. As regard PAF, there were18 lesions (72%) no PAF, 5 lesions (20%) enhanced, 1 lesion (4%) shadowing and 1 lesions (4%) combined pattern. As regard calcification, there were 21 lesions (84%) had no calcification and 2 lesion (8%) had macro calcification and 2 lesions (8%) had micro calcification. As regard vasculature, there were 24 lesions (96%) had no vasculature and 1 lesions (6%) had vasculature. As regard composition, there were 6 cystic lesions (24%), 19 solid lesions (74%) (Table 11).

Table (11): Description of lesion morphology in studied patients.

Variables		Studied lesions (N = 25)	
Shape	Rounded	5	20%
	Oval	18	72%
	Irregular	3	12%
Margin	Circumscribed	21	84%
	Not circumscribed	4	16%
Orientation	Not parallel	2	8%
	Parallel	23	92%
Echogenicity	Anechoic	6	24%
	Hypo echoic	17	68%
	Iso-echoic	2	8%
PAF	No PAF	18	72%
	Enhanced	5	20%
	Shadowing	1	4%
	Combined pattern	1	4%
Surrounding tissue	No effect	24	96%
	Architecture distortion	1	4%
Calcification	No	21	84%
	Macro	2	8%
Vasculature	No	24	96%
	Present	1	4%
Composition	Cystic	6	24%
	Solid	19	74%

4. Discussion

Mammography is the only screening modality that has been proved to reduce breast cancer mortality. However, its ability to depict small non-calcified carcinomas varies greatly with breast tissue composition. While mammography detects up to 98% of carcinomas in fatty breasts, sensitivity declines significantly with increasing breast density and may

be as low as 30%–48% in extremely dense breasts ***(Nelson et al., 2009).*** Ultrasound is a promising adjunctive screening modality, because it is widely available, relatively inexpensive, and well tolerated by patients. In addition, suspicious breast lesions can be readily biopsied under ultrasound guidance ***(Crystal et al., 2003).***

Multiple studies demonstrate that supplemental screening breast US generates an incremental cancer detection rate of 2.3–4.6 cancers per 1000 women screened ***(Kaplan et al., 2001).*** The American College of Radiology (ACR) has developed a system of sonographic descriptors for breast masses the Breast Imaging Reporting and Data System – Ultrasound (BI-RADS – US) as a means to promote the clinical efficacy of breast US and standardize reporting terminology and clinical management ***(Weigert and Steenbergen, 2015).***

The lexicon introduced by the BI-RADS system includes sonographic descriptors referring to lesion shape, orientation, margins, boundary, echo pattern, posterior acoustic features and surrounding tissue. On the basis of these descriptors, each lesion is assigned a level of suspicion, which is associated with a recommendation for management ***(Miyamoto et al., 2014).*** The aim of this study was to assess the reliability of the sonographic Breast Imaging Reporting and Data System (BIRADS) classification in differentiating benign from malignant breast masses ***(Destaunis et al., 2013).***

BI-RADS establishes reporting standards for breast ultrasound. Just as in mammography, all features need to be considered in evaluating a lesion. Mammographic findings should be combined with ultrasound findings to provide the most accurate diagnosis. The worst characteristic of a lesion drives the decision-making process. Moreover, as in mammography, auditing of results should routinely be carried out to improve interpretation accuracy ***(Mendelson et al., 2013).***

In our study of the screening ultrasound performed the mean age in studied patients was 44.08 ± 6.5 years with minimum age of 40 years and maximum age of 57 years. There were 29 patients (58%) ≤ 45 years and 21 patients > 45 years. Of 21 patients > 45 years nearly 4/21 patient had suspicious lesion, so the risk of malignancy increase with age. The current study had the same results of ***Kamińska et al. (2015***) in which breast cancer is most frequently found in women around menopause. It is significantly less frequently found in women below 45 years of age. The analysis of morbidity coefficients for the Polish population has indicated a linear increase in the group of women aged between 40 and 59 years, then it reaches a plateau with a slight decreasing tendency in women aged 70 and older. Another study also confirm our results conducted by ***(Weigert, 2012)*** in which Age reported for 18 of the cases of malignancy ranged from to 42–78 years of age with an average of 54.5 years.

In our study there were 8 patients (16%) had positive family history (6/8) had breast lesion (4/6) have benign lesion and (2/6) hade malignant lesion so the risk of breast cancer increase with age The current study had the same results of ***Kamińska et al. (2015***) in which there is Another intrinsic factor conditioning the occurrence of breast cancer is the familial susceptibility to this type of neoplasm. The most important are genes BRCA1and BRCA2 (breast cancer susceptibility 1 and 2) fulfilling the function of tumor suppressor genes in a cell. The correlation of epidemiologic and population studies has allowed for the estimation of the number of familial breast cases. They constitute about 10% of all newly diagnosed neoplasms. Identification of mutations in BRCA1 or BRCA2 genes is associated with an increased risk of occurrence of breast in 65%, depending on the mutation type.

In our study 5 patients (10%) had hormonal risk factor. (3/5) patient had breast lesion. 2/3 benign, (1/3) suspicious so the risk of breast cancer increase by hormonal factor. The current study had the same results of ***Lindegren et al. (2017)*** in which a total of 19.6 million person-years and 11,517 incident breast cancers had accumulated in 1,797,932 women between the ages of 15 and 49 years. Before the first switch to another hormonal contraceptive, 14.0 million person-years and 9101 incident breast cancers had accumulated As compared with women who had never used hormonal contraceptives, the relative risk of breast cancer among all current or recent users of any hormonal contraception was 1.20. The risk of breast cancer increased with the duration of use, from 1.09 (95% CI, 0.96 to 1.23) with less than 1 year of use to 1.38 (95% CI, 1.26 to 1.51) after more than 10 years of use (P = 0.002). As compared with women who had never used hormonal contraception, an increased risk of breast cancer was observed among woman who had previously used hormonal contraception for long periods of time (i.e., ≥5 years).

In our study of the screening ultrasound performed 74% was classified as BI-RADS 1 or 2 and 20% was classified as BI-RADS 3, and 6% was classified as BIRADS IV. The current study had the same results of ***(Hooley, 2012)*** in which of the screening breast US examinations, in 701 (75.0%), results were classified as Breast Imaging Reporting and Data System (BI-RADS) category 1 or 2; in 187 (20.0%), results were classified as BI-RADS category 3; and in 47 (5.0%), results were classified as BI-RADS category 4. Sensitivity, specificity, PPV, NPV and accuracy are important determining factors for

diagnostic tests. In our study, the sensitivity, specificity, positive predictive value, negative predictive value and accuracy of 85.7%, 75%, 100%, 100% and 94.4 %, respectively. These are compared to other similar studies conducted by ***Giuliano (2013)*** in which The sensitivity and specificity of US were 97.67% and 99.70%, respectively, in mammographically dense breasts. The positive predictive value of US was 80.77%.

In our study there is 10 patients (20%) of 18 lesion had solid breast lesion and histopathology confirm that 17 (94%) lesion was already fibro adenoma this indicate that the fibro adenoma most common benign breast lesion The current study had the same results of ***Madjar and Mendelson (2010)*** in which The most common benign breast tumors are fibro adenomas. In our study the result of histopathology of suspicious lesion (BIRADS IV) was invasive ductal carcinoma in 75% of all malignant breast lesion while invasive lobular carcinoma represent 25% of the all malignant lesion The current study had the same results of (***Giuliano, 2013)*** in which Invasive breast cancer accounted for 81% (42 out of 52) solid breast masses detected by US, of which 93% (39 out of 42) were invasive ductal carcinomas, and 7% were invasive lobular carcinoma.

Sonographic criteria for benign lesion include oval or round shape, circumscribed margin, parallel orientation presence of macro calcification and no effect on the surrounding tissue. In our study (83.4 %) of all lesion had round or oval shape, (84% had circumscribed margin), (83.2 %) had parallel orientation, (5.5 %) had macro calcification and (79%) had no effect on the surrounding tissue this result compared to result conducted by ***Ghebrehiwet et al. (2007)*** in which the features most predictive of benign tissue diagnosis were oval or round shape (94% of masses with this feature were benign), circumscribed margin (91% o of masses with this feature were benign), and width to –AP dimension ratio greater than 1.4 (89% of masses with this feature were benign.

Sonographically suspicious criteria for malignancy include irregular shape, not circumscribed margin, not parallel orientation (Taller-than-wide shape). In our study (16% of all lesion had irregular shape), (16.4 % had not margin), (16.4 % had not parallel orientation). 1 lesion (5.5% had shadowing) and (11 % causing archetexural distortion) this result compared to result conducted by ***Ghebrehiwet et al. (2007)*** in which the features most predictive of malignant tissue diagnosis were speculated or micro lobulated margin (67% of masses with this features were malignant, irregular shape (61% were malignaqnt, ill defined margin (50% were malignant) and width to –AP diameter ratio 1.4 or less (40% were malignant).

Conclusion

Every woman in the state of Connecticut who undergoes mammography and demonstrates breast density >50% must be informed of the following: ‘‘If your mammogram demonstrates that you have dense breast tissue, which could hide small abnormalities, you might benefit from supplementary screening tests, which can include abreast ultrasound screening or a breast MRI examination, or both, depending on your individual risk factors.

ACR-BIRADS can be considered an appropriate classification in the assessment of breast lesion, in order to avoid unnecessary fine needle aspirations and to assist in making decision about when it should be performed. This classification improves communication and reduces confusion among physicians and patients. Our experience demonstrated that the BI-RADS classification is highly reproducible, since it is based on B-mode characteristics of the lesion and application of Doppler study, especially when performed by experienced radiologists, acquainted with its use.

References

1. Crystal P, Strano SD, Shcharynski S, Koretz MJ (2003): Using sonography to screen women with mammographically dense breasts, AJR Am. J. Roentgenol. 181(1): 177–182.
2. Destaunis SV, Sickles EA, Mendelson EB (2013): BIRADS Update and challenge (an interactive session). In Refresher Course the 99th Annual Meeting of the Radiological Society of North America, RSNA. Chicago.
3. Ghebrehiwet M, Paulos E, Andeberhan T (2007): The role of combined ultrasonography and mammography in the diagnosis of breast cancer in Eritrean women with paplable abnormalities of the breast. Journal of the Eritrean Medical Association; 2(1).
4. Giuliano V, Giuliano C (2013): Improved breast cancer detection in asymptomatic women using 3D-automatedbreast ultrasound in mammographically dense breasts. Clin Imaging. 2013;37:480-6. [PMID: 23116728]. doi:10.1016/j.clinimag. 2012.09.01
5. Harvey JA, Bovbjerg VE (2004): Quantitative assessment of mammographic breast density: relationship with breast cancer risk. Radiology; 230(1):29–41.
6. Hooley RJ, Greenberg KL, Stackhouse RM, et al (2012): Screening US in patients with mammographically dense breasts: initial

experience with Connecticut Public Act 09-41. Radiology; 265:59–69.
7. Kamińska M, Ciszewski T, Łopacka-Szatan K, Miotła P, Starosławska E (2015): Breast cancer risk factors. Przeglad menopauzalny= Menopause review.; 14(3):196.
8. Kaplan SS (2001): Clinical utility of bilateral whole breast US in the evaluation of women with dense breast tissue. Radiology; 221(3): 641–649.
9. Kopans DB (2004): Sonography should not be used for breast cancer screening until its efficacy has been proven scientifically. AJR Am J Roentgenol; 182(2):489–491.
10. Lindegren L, Stuart A, Herbst A, Källén K (2017): Improved neonatal outcome after active management of prolonged pregnancies beyond 41+ 2 weeks in nulliparous, but not among multiparous women. Acta obstetricia et gynecologica Scandinavica; 96(12):1467-74.
11. Madjar H, Becker S, Doubeck T et al (2010): Impact of breast ultrasound screening in gynecological practice. Ultraschall in Med 2010; 31: 289–295.
12. Mendelson EB, Bohm-Velez M, Berg WA, et al. ACR BI-RADS ultrasound. In: ACR BI-RADS Atlas, Breast Imaging Reporting and Data System. 2013; 108(4):djv367.
13. Miyamoto Y, Ito T, Takada E, et al. (2014): Efficacy of sonazoid (perflubutane) for contrast-enhanced ultrasound in the differentiation of focal breast lesions: phase 3 multicenter clinical trial. AJR Am J Roentgenol.; 202:W400–W407.
14. Nelson HD, Tyne K, Naik A, Bougatsos C, Chan BK, Humphrey L (2009): Screening for breast cancer: an update for the U.S. Preventive Services Task Force, Ann. Intern. Med. 151(10): 727–737.
15. Weigert J, Steenbergen S (2012): The Connecticut experiment: the role of ultrasound in the screening of women with dense breasts. Breast J; 18:517–52.

12/14/2019