

## Dense breast as a risk factor in breast malignancy

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### Abstract:

**Background:** One of the strongest risk factors for breast cancer is high breast density, relatively little fat in the breast and more connective and glandular tissue.

**Objectives:** this study aims to measure risk of increase breast density in correlation of CA breast & compare our results with results in other population, to compare the performance of ultrasonography and mammography in measuring breast density according to BIRADS system

**Materials & methods:** The study included 45 females .Measuring risk of increase breast density in correlation of CA breast & comparing the performance of ultrasonography and mammography in measuring breast density according to BIRADS system.

**Results :** there is strong influence of breast density as a risk factor of breast CA, according to mammography, it had been significantly found that mammographic density was the more prevalent among CA patients it found in According to mammography, also use of RI as significant and important way for estimation of density as use of 0.6 as a cutoff point, as 91% of dense breast had RI more than 0.6.

**Conclusions :** increase breast density is associated with possible increase risk of CA breast and use of ultrasound, mammogram and RI play a role in estimating breast density.

**Keywords:** Breast Density, Mammography, Doppler Ultrasound, Resistive Index.

*Fac Med Baghdad*  
*2014 Vol.56, No.4*  
*Received: May, 2014*  
*Accepted Nov., 2014*

### Introduction:

The concept of breast density is based on the radiological appearance of breast parenchyma and denser breast have a higher proportion of epithelial and connective tissue in relation to fat, while non-dense breasts are richer in fat. Breast density decreases after menopause and with increase body mass index (BMI). It has been related to hormonal factors such as menopausal status and use of hormone replacement therapy (HRT) [1].

Mammographically detected density is a risk factor for breast and is attributed to alterations in compositions of breast tissue [2]. Previous studies [3-7], which indicate that retro areolar tissue region can provide most discriminative texture features for differentiating women at high risk for cancer from women at low risk [8].

A breast which is composed almost completely of glandular tissue during pregnancy, but which sometimes presents isodense to fatty tissue, would be correspondingly classified as ACR4; a breast with about 50% fibrous echogenic glandular body would on the other hand be classified as ACR2 [9]. In the United States, the Breast Imaging Reporting and Data System (BI-RADS) was developed to standardize mammography reporting terminology and the assessment and recommendation categories [10].

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The four-category system (almost entirely fat; scattered fibroglandular densities; heterogeneously dense, may lower the sensitivity of mammography; extremely dense, which could obscure a lesion on mammography) is based on quantitative assessment, although the categories are not defined by the percentage of density [11-12].

### Materials and methods:

This study is cross sectional study collected during the period covered one and half years from June 2011 to December 2012 in the National Center for Early Detection of Breast Tumor in Baghdad Medical City Teaching Complex.

The study included 45 females with an age ranging between 31-64 years. The RI (resistive index) for an additional ten females was taken as a control in order to compare it with the results for the 45 females. The eligibility criteria included any patient with suspicious mass or previously diagnosed as breast CA (BIRADS V or VI). 420 patients were examined during the period of data collection & only 50 patients included in the study whom identified as BIRADS V&VI. Only 45 patients out of 50 were histologically proven to have breast CA. A specially designed protocol was used to assist in the process of data collection. Most of those patients were complaining from pain aggravated by menstruation (for those of reproductive ages) and other suffered from multiple nodules. The ultrasonographic examinations were systematically performed by a specialist

radiologist using an electronically focused near-field probs with bandwidth of 5-11 MHz (Siemens ACUSON X300). No special preparation was needed. The whole breasts were scanned. Pectoralis muscle had to be seen on all images to be sure that the entire breast was examined.

The ultrasonographic examination was done for contra lateral breast of cases with proved breast CA of other breast, the density of contra lateral breast is measured by measuring fibro glandular tissue as fatty, scattered glandular tissue, heterogeneous texture & homogenous texture & the density was classified subjectively as normal or dense according to age. Also on ultrasonographic examination of contra lateral breast, measuring RI of breast tissue is done for determining tissue with high RI & comparing the results with breast density as a risk factor of CA breast

The study also included small control group as random group without any specific criteria for selection & measuring RI for them to find mean RI above which it was considered high and below it considered normal.

Mammograms of contra lateral breast were obtained with dedicated screen film mammography units (comet AG CH-3097 Liebefeld-Bern, Switzerland) for 45 patients. The main technical features are constant potential high frequency generator, KV 22-35/MAs 40-60, automatic and manual KV, MAs, Mo filter, and circular gantry with isocentric / automatic / motorized movements. We used automatic exposure factors. Collimation was used to decrease scattered radiation and compression to reduce movement and reduce thickness asymmetry of the breast parts.

Those forty five patients were examined with digital mammography (MAVIG GmbH, General Electronics Medical System S.C.S. Societe); Cranio-caudal and oblique views of contra lateral breast were obtained for all patients. The density of the breast was decided in accordance to the ACR BI-RADS categorized (0-25%, 25-50%, 50-75% & 75-100%) and defined as low or high density in correlation with age of patient .

### Results:

There were 45 patients recruited in this study all with breast carcinoma. The mean age patients was (49.3 ± 8.2) years. According to mammography, it had been significantly found that mammographic density was (0 - 25%) in 9 (20%) of patients, (25 - 50%) in 11 (24.4%) of patients, ( 50-75%) was the more prevalent among CA patients it found in 22 patients (48.9%) and only three patients (6.7%) with density of (75-100%), P.value < 0.05,

As it is shown in table 1, Heterogeneous density was the more prevalent, it was found in 24 (53.3%) of the patients. Homogenous density was the least finding; present in only

3 (6.7%) of the patients, P<0.05, patients with CA breast were significantly more likely to have dense breast, it was found in 34 (75.6%) of the patients (P=0.001).

The correlation between mammographic density and RI, is shown in table 2, it had been significantly (P< 0.05) concluded that mammographic density had directly correlated to RI values when 0.6 point used as cut off point, 38 patients with RI more than 0.6 versus 7 with less than or equal 0.6. 34 patients had dense mammography versus 11 did not, of them 31 (91.2%) had RI more than 0.6, versus 3 (8.8%) RI ≤ 0.6, while of those 11 patients who didn't had dense mammography 7 (63.6%), had RI of > 0.6 versus 4 did not, (P.value = 0.022).

**Table 1: Distribution of Ultrasound density among patients.**

| Ultrasound density             | Number of patients | Percent |
|--------------------------------|--------------------|---------|
| Fatty                          | 9                  | 20.0    |
| Scattered                      | 9                  | 20.0    |
| Heterogeneous                  | 24                 | 53.3    |
| Homogenous                     | 3                  | 6.7     |
| Total                          | 45                 | 100.0   |
| P.value = 0.0001 (significant) |                    |         |

**Table 2: Correlation between Breast density and RI among patients with CA breast.**

|                               |           | RI         |             | Total        |
|-------------------------------|-----------|------------|-------------|--------------|
|                               |           | ≤ 0.6      | >0.6        |              |
| Density                       | Dense     | 3<br>8.8%  | 31<br>91.2% | 34<br>100.0% |
|                               | Not dense | 4<br>36.4% | 7<br>63.6%  | 11<br>100.0% |
| Total                         |           | 7<br>15.6% | 38<br>84.4% | 45<br>100.0% |
| P.value = 0.022 (significant) |           |            |             |              |

### Discussion:

They found that women with a high breast density (≥ 75%) had a nearly 5-fold increased risk for breast cancer compared with women with a low density (< 10%). The risk remained high for a period of 8 years, both at screening and between screens. Extensive mammographic density is present in 25% of women with breast cancer [13]. There are 2 possible mechanisms for the effect of increased density on breast cancer risk: extensive mammographic density might make it more difficult to detect breast cancer, and this masking effect might delay diagnosis, or there might be a biologic connection between dense breast tissue and breast cancer

[13]. This study showed a strong influence of breast density as a risk factor of breast CA, as it showed that women with high mammographic breast density have 3.1 fold increased risk of developing breast CA compared with fatty breast. Although additional exams such as ultrasound or magnetic resonance imaging are time consuming and costly, as they must be performed by trained radiologists, it is clear that they can improve detection rates of cancer substantially in women with dense breasts. Probably the greatest challenge to mammographic density is that it is a two dimensional method, and there are still no automatic methods that have been found to work as well or better than the computer-assisted methods. Thus once a robust automatic volumetric method for mammographic density has been developed, and estimates are immediately provided to clinicians, then mammographic density may become much more widely used both in mammographic screening programs as well as in clinical practice. Until then, this is mostly a measure for epidemiologists [14]. For the threshold-based method, 28 of 32 US test cases and for the proportion-based density classifier, 27 of 32 US test cases were found to be in agreement with the radiologist "ground standard" mammographic interpretations, resulting in overall accuracies of 87.5% and 84.4%, respectively. The experiment result showed that the proposed methods could be a reference opinion and offer concordant and reliable quantification of breast density for the radiologist [15]. In this work we assessed breast density by digital mammography and ultrasound and then compared between the two methods. As a result both methods were good in assessing the breast density with approximate results of both methods and very slight difference between two methods. This difference between our results and others may be due to that ultrasound slightly over estimate density or mammogram slightly under estimate density. The Doppler technique probably plays a role as an adjuvant to the gray scale in the evaluation of suspicious nodules. It is important to note that this method is not a diagnostic study [16]. In this work we used RI as another way for prediction of breast density and we found this way as significant and important way for estimation of density as use of 0.6 as a cutoff point, as 91% of dense breast had RI more than 0.6 with P value of 0.022 (significant correlation).

### Conclusions

Mean age of CA breast in our study was 49.3 years Increase breast density is associated with possible increase risk of CA breast .The influence of dense breast in our study is more than the influence of family history in relation to increase CA risk Increase breast density is more in patient with positive family history of CA breast. Both

ultrasound & mammogram play a role in estimating breast density. The use of RI as another way for estimating breast density & increase risk of CA with breast parenchyma of high RI (more than 0.6)

### Author contributions:

Study conception: Study design Dr. Saabh Ismail Khalil  
Acquisition of data analysis: Saabh Ismail Khalil, Dr. Enam Azez Khalel  
Interpretation of data: Dr. Enam Azez Khalel  
Dr. Tharwat Idres Sulaiman : Drafting of manuscript, Critical revision

### References:

1. Olsson A, Sarter H, Borgquist S, Zackrisson S & Manjer J. Breast density and mode of detection in relation to breast cancer specific survival. *BMC Cancer*. 2014;14:229.
2. Spyros S, Vassiliki T, Panagiota R, et al. Versican but not decorin accumulation is related to malignancy in mammographically detected high density and malignant-appearing microcalcifications in non-palpable breast carcinomas. *BMC Cancer*. 2011;11:314.
3. Huo Z, Giger ML, Wolverson DE, Zhong W, Cumming S, Olopade OI. Computerized analysis of mammographic parenchymal patterns for breast cancer risk assessment: feature selection. *Med Phys*. 2000; 27,4-12.
4. Huo Z, Giger ML, Olopade OI, et al. Computerized analysis of digitized mammograms of BRCA1 and BRCA2 gene mutation carriers. *Radiology*. 2002; 225,519-526.
5. Li H, Giger ML, Olopade OI, Margolis A, Lan L, Chinander MR. Computerized texture analysis of mammographic parenchymal patterns of digitized mammograms. *Acad Radiol*. 2005;12,863-873.
6. Li H, Giger ML, Huo Z, et al. Computerized analysis of mammographic parenchymal patterns for assessing breast cancer risk: effect of ROI size and location. *Med Phys*. 2004;31:549-555.
7. Li H, Giger ML, Olopade OI, Lan L. Fractal analysis of mammographic parenchymal patterns in breast cancer risk assessment. *Acad Radiol*. 2007;14:513-521.
8. Despina Kontos, Lynda C. Ikejimba, BS, Predrag R. Bakic, Andrea B. Troxel, et al. Analysis of Parenchymal Texture with Digital Breast Tomosynthesis: Comparison with Digital Mammography and Implications for Cancer Risk Assessment. *Radiology*. 2011; 261, 80-91.
9. Thomas M. Kolb, Jacob Lichy, and Jeffrey H. Newhouse Comparison of the Performance of Screening Mammography, Physical Examination, and Breast US and Evaluation of Factors that Influence. *Radiology*. 2002; 225, 165-175.

10. Kevin M. Kelly, Judy Dean, W. Scott Comulada, and Sung-Jae Lee. *Breast imaging reporting and data system (BI-RADS)* Reston, American College of Radiology, 1993 ;270:338–343.
  11. Berg WA, Campassi C, Langenberg P, Sexton MJ. *Breast Imaging Reporting and Data System: Inter- and intraobserver variability in feature analysis and final assessment.* *AJR Am J Roentgenol*,2000; 174:1769-1777.
  12. Kerlikowski K, Grady D, Barclay J, et al. *Variability and accuracy in mammographic interpretation using the American College of Radiology Breast Imaging Reporting and Data System.* *J Natl Cancer Inst.*1998; 90:1801-1809.
  13. *N Engl J Med, High Breast Density Is a Major Risk Factor for Breast Cancer.* *Medscape Medical News.* 2007;356:227-236, 297-299.
  14. Kavanagh AM, Byrnes GB, Nickson C, Cawson JN, Giles GG, Hopper JL, et al. *Using mammographic density to improve breast cancer screening outcomes.* *Cancer Epidemiol Biomarkers Prev*,2008; 17: 2818-24.
  15. Chen JH, Huang CS, Chien KC, Takada E, Moon WK, Wu JH, et al. *Breast density analysis for whole breast ultrasound images* ,Department of Radiology, China Medical University Hospital, Taichung, 40402, Taiwan *Med Phys.*2009; 36(11):4933-4943.
- Blohmer JU, Oellinger H, Schmidt C, et al. Comparison of various imaging methods with particular evaluation of color Doppler sonography for planning surgery for breast tumors.* *Arch Gynecol Obstet.*1999;262:159-71.