

## ORIGINAL ARTICLE

# Diagnostic association of mammographic suspicious breast lesions with cytology and histopathology: a tertiary cancer center experience from India

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### Abstract

**Background:** Breast cancer is recognized as the commonest cancer in females worldwide. Triple assessment is a very useful diagnostic tool to evaluate patients with breast lumps and to detect patients with breast cancers with high accuracy. This is a study to see the correlation of suspicious breast lesions on mammography with cytology and histopathology.

**Methods:** Suspected women with breast cancer attending the oncology department underwent complete evaluation in form of clinical history and examination. Selected women after clinical examination underwent a mammography. All lesions with BIRADS categorization of 2 and above underwent FNAC and biopsy for histological diagnosis. Pathological reports were collected and data was entered in computer and analysed.

**Results:** Over a period of 1 year, 100 patients with symptomatic breast lesion were included in this study and cancer diagnosis was confirmed based on radiological and pathological tests. The mean age of patients was 51.67 years (range of 35-74 yrs). Among all patients, 66% were postmenopausal and 44% were premenopausal. Most common finding was mass lesions (54%) followed by mass with micro-calcifications (19%). Out of the 100 biopsies done, 59% were benign lesion and 41% were malignant. The most common benign pathological diagnosis was fibrocystic disease and fibroadenoma. Patients with BIRADS 4 and 5 on mammography were found to have malignant lesions after cytology and histopathology in 85% of cases. Further analysis indicated that the Positive Predictive Value (PPV) for BIRADS 5 is 100%.

**Conclusions:** The use of BIRADS categorization does improve the quality of risk assessment information and it is useful in predicting the chance of malignancy and also in avoiding unnecessary biopsy. Our analysis of biopsy modalities illustrated that core needle biopsy is preferred to excision biopsy for optimal diagnosis and management of radiographically detected lesions.

**Keywords:** Breast lesions; Mammography; Cytology; Histopathology

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## **Introduction**

Malignant neoplasms remain a leading cause of death worldwide [1]. Breast cancer is recognized as the commonest cancer in females, and the second commonest malignant tumor, after lung cancer, in overall figures worldwide [2]. Breast cancer is the most common type of cancer among women with the highest fatality rates [3]. Globally over the last several decades, the incidence of breast cancer has increased and the greatest increase has been seen in Asian countries where breast cancer incidence peaks among women in their forties whereas in the United States and Europe, it peaks among women in their sixties [4-6].

India with its multilingual, and multiethnic society has reported breast cancer as the commonest cancer in urban Indian females, and the second commonest in the rural Indian women (ICMR, 2016). As per the ICMR-HBCR data, breast cancer is the commonest cancer among women in urban registries of Delhi, Chandigarh, Mumbai, Chennai, Guwahati, and Trivandrum where it constitutes 20 - 30% of all cancers in female [7].

Almost all Indian women often do not present for medical care early enough due to various reasons such as illiteracy, lack of awareness financial constraints, lack of an organized screening program and paucity of diagnostic aids. It is hardly surprising that the majority of breast cancer patients in India are still treated at locally advanced and metastatic stages [8]. Detection of it in earlier stages is made possible by a triple assessment which includes clinical examination, radiological imaging and tissue pathology. Triple assessment is a very useful diagnostic tool to evaluate patients with breast lumps and to detect patients with breast cancers with an overall accuracy of 99.3% [9].

The role of mammography in reducing breast cancer mortality has been demonstrated in

multiple randomized clinical trials. Meta-analysis of all the randomized clinical trials [RCT's] testing the efficacy of screening mammography to date, demonstrated a significant reduction in breast cancer mortality of 20–35% in women of age group 50–69 years [10,11]. The American College of Radiology developed the Breast Imaging Reporting And Data System (BIRADS) categorization of mammograms in 1993 which is useful in estimating the risk of malignancy, thereby guiding management decisions.

FNAC, together with core needle biopsy, is the initial pathological investigative method of choice (Ahmed et al., 2007). This approach obviates standard excision biopsy when all three components of the triple test are conclusively negative or positive [12].

Since there are limited published Indian data evaluating the correlation of mammographic and histopathological findings of breast lesion, this is a hospital based study from south India to see the correlation of mammographic suspicious breast lesions with cytology and histopathology.

## **Material and methods**

This present study was conducted between June 2014 and June 2015. Suspected women with breast cancer attending the Surgery and Oncology Out Patient Department (OPD) in the hospital underwent detailed history taking and clinical examination in pre-designed proforma. Selected women after clinical examination underwent a digital mammogram.

In our study, 100 females above the age of 35 years, attending the surgical OPD with signs and symptoms of breast disorders, were enrolled for this study. Previously diagnosed women of carcinoma of the breast, pregnant women with carcinoma breast were excluded from this study,

The standard digital mammography was obtained using standard cranio-caudal and medio-lateral views and additional projections were included as and when required for better delineation of the site of lesion. All mammograms were reported using the Breast Imaging-Reporting and Data System (BIRADS), trademarked and published by the American College of Radiology (ACR).

The indication for biopsy was based on clinical suspicion, risk profile and desire of the patient, clearly demonstrating that mammography was only one aspect in the consideration for biopsy. All lesions with BIRADS categorization of 2 and above underwent biopsy for histological diagnosis. Techniques such as Fine needle aspiration cytology (FNAC), Trucut biopsy/Core needle biopsy, Open biopsy (incision or excision), and Image guided biopsy (Ultrasound or Mammography guided) were used to obtain a tissue sample for cytological and histological diagnosis. Pathological reports were collected and data was computed and analyzed. Results were analyzed using SAS 9.2. The study protocol was approved by the institutional ethics committee.

**Results and analysis**

Over a period of 1 year, 100 patients with symptomatic breast lesion were included in this study and further radiological and pathological tests were done for disease confirmation. The mean age of female patients in the study was 51.67 years with a range of 35 to 74 years.

In this study, 66% women were postmenopausal. Among them 41 % women were found to be positive for breast malignancy. Five women were nulliparous. One out of 20 women was diagnosed breast cancer with history of contraceptive pills intake or hormone replacement therapy whereas 6 % women were found to have breast cancer that has family history of breast cancer.

Right and left breast pathologies were almost equal in the study group. Among the symptoms, self-detected breast lump was the commonest symptom (54%) and 37% tumor were located in upper outer quadrant of the breast. Among the axillary lymph node involvement, 34 patients were presented with central group involvement. Details of clinico-pathological profile were depicted in Table I.

**Table I:** Clinico-pathological profile of study subjects

	Percentage
<b>Age group(years)</b>	
31-40	11%
41-50	37%
51-60	32%
61-70	17%
71-80	3%
<b>Marital status</b>	
Unmarried	5%
Married	95%
<b>Menopause status</b>	
Postmenopausal	66%
Premenopausal	44%
<b>Breast Involvement</b>	
Right Breast	49%
Left Breast	51%
<b>Major Symptoms</b>	
Lump in Breast	57%
Mastalgia	38%
Nipple discharge	5%
<b>On examination</b>	
Skin involvement present	12%
Lump mobility present	14%
Chest wall fixity of lump seen	3%
Nipple Areola complex involvement	13%
Axillary Lymph Node involvement	34%

Out of 100 women who underwent mammography, only one had normal finding. Mammographic findings of patients are listed in Table II. Most common finding was mass lesions (54%) followed by mass with micro-calcifications (19%), cysts (10%), architectural distortion (7%), asymmetrical density (5%), and micro-calcifications alone (4%). Most lesions which turned out to be cancer, presented with mass with micro-calcification on mammographic study. More than 65% lesions were categorized as BIRADS 3 (37%) and BIRADS 4 (31%).

**Table II** Breakdown of mammographic findings

	Finding	Percentage
1	Mass	54%
2	Micro calcifications	4%
3	Mass with micro calcifications	19%
4	Asymmetrical density	5%
5	Architectural distortion	7%
6	Cyst	10%
7	Normal	1%

BIRADS categorizations with respect to various histopathologies were shown in Table III. The most common benign pathological diagnosis was fibrocystic disease and fibroadenoma. Fibrocystic changes were represented in 55% (11 out of 20) and 40% (8 out of 20) of lesion biopsied in BIRADS category 2 and 3 respectively whereas fibroadenoma was represented in 33.33% (5 out of 15) and 60% (9 out of 15) of patients in category 2 and 3 respectively. The most common malignant histologic diagnosis was infiltrating ductal carcinomas (36.36%). More than 85% of patients who were categorized as BIRADS 4 and 5 on mammography were found to have malignant lesions after cytology and histopathology. Further analysis indicated that

the Positive Predictive Value (PPV) for BIRADS 5 is 100%.

The utilization rates of different biopsy techniques were also examined with respect to BIRADS. Trucut biopsy was the most common technique representing 52% of all biopsies. Image guide FNAC/biopsy was obtained in 18% of patients mostly in BIRADS category 2 and 3 lesions. For lesions of BIRADS 5, trucut or excision biopsy was the preferred modality. Out of the 99 biopsies done, 58.58% were benign lesion and 41.41% were malignant.

**Discussion:**

Our results indicate that BIRADS categorization remains a useful tool to stratify risk of malignancy in a female population with increased breast density such as ours. The overall cancer incidence in our study population was 41.41%, which is comparable to figures from other reported series, which range from 20% to 53% [13,14].

Breast malignancy was seen to peak in women at the age of 41-50 years, a decade earlier compared to their western counterparts, in this study and this were also reported by Aggarwal et al. [8] and Murthy et al. [15]. Mean age in patients of breast cancer was 46.2 years with a range of 28-72 years [16] and Age at presentation of 100 patients of breast cancer was 51.4 ± 10.86 years [17].

In our study, patients who were diagnosed with breast cancer, family history were present in 4% of the patients. Numerous studies have reported a low rate of familial pattern of breast cancer in Indian patients. In a study by Shankar et al. on 532 histopathology proven breast cancer patients, family history was present in 8% of the patients [18].

**Table III:** BIRADS categorization with respect to various histopathologies

Pathology	BIRADS					Total (%)
	1	2	3	4	5	
Fibrocystic disease	0	11	8	1	0	20.20%
Fibroadenoma	0	5	9	1	0	15.15%
Ductectasia/papilloma	0	0	3	0	0	3.03%
Benign Cyst	0	3	4	0	0	7.07%
Atypical ductal/lobular hyperplasia	0	1	3	0	0	4.04%
Abscess	0	1	2	1	0	4.04%
Benign phylloides	0	0	2	3	0	5.05%
Intraductal Carcinoma*	0	1	5	21	9	36.36%
Ductal Carcinoma in situ*	0	0	1	2	0	3.03%
Intra-lobular carcinoma*	0	0	0	2	0	2.02%
<b>Total</b>	0	22	37	31	9	---

Our study revealed that malignancy was more common in post-menopausal women (65.6%) and the risk of breast cancer was more for women who attained menopause after 50 years of age similar to a study by Meshram et al.,2009 [19]. In a study by Shankar et al, [20] among 532 breast cancer patients, 395 patients (74.3%) were postmenopausal and 137 patients (25.7%) were postmenopausal.

Women in our study mainly sought medical attention for a breast lump (57%) and mastalgia (38%). The lumps were clinically detected to be more in upper outer quadrant which is explained by the fact that the upper outer quadrant of the breast contains a greater volume of tissue than do the other quadrants. Axillary nodal metastasis was present in 34% of the breast cancer patients in the study cohort. This was contrary to a study in New Delhi which showed that 80% of the patients treated for breast cancer over a period of 1 decade had metastatic disease in the axillary lymph nodes [18].

As a screening and diagnostic tool, mammography offers a high sensitivity, low specificity technique for identifying breast

lesions [19,20]. The mammographic image of a lesion is generally non pathognomonic, and benign and malignant conditions can present with overlapping mammographic findings. The correlation between the BIRADS category and malignant outcomes has been shown by research as well [21,22]. The BIRADS rating refers to the mammographic impression only, and the complete clinical picture is used to make the decision to biopsy.

One patient in BIRADS 1 was not subjected to biopsy as they had no clinically palpable lumps and had normal mammographic findings. Placing a breast lesion in BIRADS 2 indicates a benign finding. Among the 22 women of the study cohort categorized as BIRADS 2, one was detected to have breast cancer. This patient underwent open biopsy due to a clinically suspicious lump. This discrepancy between mammographic and pathological finding may be due to decreased sensitivity of mammograms in patients with dense breasts.

BIRADS 3 with the maximum number of cases (36.7%) in our study sample. One set of prior studies show that the BIRADS 3 lesions has a PPV approximately between 3-5% [23,24], whereas the other set of studies from Sickles,

1991 and Rosen et al., 2002 reported 10.6% (17 from 161 biopsies) and 28.7% (51 from 178 biopsies), respectively. BIRADS category 3, the 'probably benign' finding, is reserved for findings where the risk of malignancy is low (<2%) and short-interval follow-up is preferred over biopsy in almost all cases. The American College of Radiology also recognizes that data concerning the efficacy of short-term follow-up are still evolving and that the approach to management of lesions in this category is largely intuitive at present [25].

The criteria for biopsy that can contribute to the biopsy of category 2 lesions and increase the rate of biopsy of category 3 lesions include suspicious mammographic findings, patient's risk factors, patient anxiety, patient preference, facility policy, and the proportion of second opinion referrals. We biopsied all the lesions categorized as BIRADS 2-5 for the purpose of the study. Eliminating biopsy for categories 1, 2 and 3 would reduce the number of biopsies performed by 60% but then nine invasive cancers and one DCIS patient would have been given routine follow-up. Future investigations into the overall rates of biopsy of category 3 lesions and more information about false negative rates associated with short-term follow-up of these lesions will help settle the question.

The BIRADS Category 4 classification is associated with a higher risk of malignancy ("suspicious lesion") and a biopsy should be considered. The BIRADS category 4 further divided into subcategories 4A, 4B, and 4C in 2003, with an increasing risk of malignancy. Not many studies till date, has provided the positive predictive value (PPV) of category 4 lesions and those of its sub-categories 4A, 4B and 4C. In our study, 31 women had their mammograms categorized to have BIRADS 4 lesions but the sub categorization was difficult on the part of the radiologist.

According to the BIRADS format, category 3 and category 4 lesions represent the boundary between imaging follow-up and biopsy. Hence stratifying findings into categories 3 and 4 has significant management and economic consequences. The PPV for category 5 lesions in this and other studies [21, 26] illustrate that radiologists are able to very accurately predict the status of a highly suspicious lesion. Studies revealed a PPV ranging from 81-97% in BIRADS 5 [13, 21, 23, 24]. All 9 patients with lesions in BIRADS 5 category turned out to be malignancy on histopathology, giving a PPV of 100%.

BI-RADS categorization may help us to select between percutaneous or open surgical methods for biopsy of breast lesions. Trucut biopsy (core needle biopsy) was the most common modality used in this study. Lee et al. [27] demonstrated that stereotactic 14G automated core biopsy obviated the need for open surgery in 81% of lesions.

### **Conclusions**

Mammography is one of the most important diagnostic tools in the diagnosis of breast diseases. The use of BIRADS categorization does improve the quality of risk assessment information and it is useful in predicting the chance of malignancy and also in avoiding unnecessary biopsy.

On histological analysis, benign lesions were more common, and among malignant lesions, invasive cancers were recorded at a higher rate. Our analysis of biopsy modalities illustrated that core needle biopsy is preferred to excision biopsy for optimal diagnosis and management of radiographically detected lesions as it has the benefits of less morbidity, improved cosmesis and a better overall experience by avoiding an unnecessary surgical procedure. In spite of mammographically-dense breasts, BI-RADS categorization is still a useful predictor of malignancy in our Indian population.

**Conflicts of Interest:** None.

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