

# Mammography Correlated with Histopathology in the Diagnosis of Mass Lesions of the Breast in a Tertiary Teaching Hospital: An Analytical Study

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## Abstract

**Introduction:** Tumors of the breast are characterized by uncontrolled growth of cells in the mammary epithelial tissue. The most frequent type of tumor occurring in females is breast tumors worldwide. Mammography computer-aided digital technique has helped in the diagnosis of early benign and malignant lesions of breast since the beginning of the 21<sup>st</sup> century. However, false positives are a major concern in breast tumor screening. They are not evaluated as a prognostic factor for tumor detection.

**Aim:** To evaluate the association of false positive results of mammography confirmed with fine needle aspiration cytology (FNAC), histopathological (HPE) features and repeat mammography over a period of 4 years.

**Study Design:** This is a retrospective comparative analytical study.

**Study Period:** June 2012-May 2016 (4 years).

**Materials and Methods:** Results of 2196 patients who underwent mammography in a tertiary teaching hospital, Kerala were included in the study. Demographic details of the sample were obtained from the medical records of the patients. False positive results were identified based on negative FNAC and HPE findings. Subsequent mammography results of patients of such false positive patients were done to find the incidence of tumor risk.

**Results:** The total number of women patients attending the daily OPDs of the hospital was 6, 70,440 for 4 years. The prevalence of women reporting breast related complaints and undergoing mammography was 0.32%. There was a positive family history of malignant tumors of breast in 14 of the 54 patients (25.92%) confirmed with malignant tumors in this study. Among the 2196 mammography procedures, 1479 were reported as normal (67.34%). Benign lesions of the breast such as cysts, hematoma, localized abscesses, galactocele, and fibroadenosis were reported in 389 women (17.71%). 274 women had shown benign tumors of breast reported following mammography (12.47%) such as fibroma, neurofibroma, fibroadenoma, and simple adenoma. The remaining 54 mammography results were showing features of a malignant tumor on mammography were subjected to dynamic contrast enhanced magnetic resonance imaging (DCEMRI), and diffusion-weighted images (DWI) of the breast.

**Conclusion:** Mammography screening proves to be an excellent tool in the diagnosis of diseases of the breast. There is a definite relation between the presence of a false positive test and the risk of cancer detection in subsequent screening participations. The association was much clear in false positives involving a cytology examination or biopsy, and in women with a family history of breast cancer.

**Key words:** Breast screening, Biopsy, False positive and risk factors, Fine needle aspiration cytology, Tumors of the breast

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## INTRODUCTION

After mammography was introduced as a screening tool in the diagnosis of tumors of the breast the mortality from cancer breast has dropped drastically since 1990.<sup>1</sup> However, the limitation of mammography lies in patients with dense breasts where lesions identification is limited by surrounded

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fibroglandular tissue<sup>2</sup> and post-operative patients with excisions of tumors from breasts. Digital subtraction mammography and contrast enhanced mammography have an important role differentiating the benign from malignant tumors.<sup>3,4</sup> Positive mammography patients are subjected to fine needle aspiration cytology (FNAC) and/or biopsy histopathological (HPE) for confirmation and necessary treatment is adopted. However, the false positive result becomes a major concern wherein the FNAC and HPE turn out to be negative. It leads to psychological and behavioral consequences in the false positive mammography women.<sup>5,6</sup> It leads to further repeat biopsies or excision biopsies.<sup>7</sup> The incidence of false positive results in Europe is 20 to 30% and in USA 49%.<sup>8-10</sup> Benign breast lesions are a known risk factor for subsequent breast cancer<sup>11,12</sup> and women with benign breast surgery have lower sensitivity at screening.<sup>13</sup> There are not many studies which report the association between false positive results and detection of breast cancer in subsequent screenings.<sup>14</sup> In this context, this study is conducted to evaluate the association of false positive results of mammography confirmed with FNAC, HPE features and repeats mammography over a period of 4 years.

## MATERIALS AND METHODS

Results of 2196 patients who underwent mammography in a tertiary teaching hospital, Kerala were included in the study. Demographic details of the sample were obtained from the medical records of the patients. Women showing positive radiological signs of mammography for malignant tumors were further subjected to dynamic contrast enhanced magnetic resonance imaging (DCEMRI), and diffusion-weighted images (DWI) of the breast. False positive results were identified based on negative fine needle aspiration (FNAC) and HPE findings. Repeat mammography and repeat FNAC and/or excision biopsy was done in the patients to find the incidence of tumor risk. Institutional Ethical Clearance was obtained, and consent was not necessary because the study was a retrospective one.

### Inclusion Criteria

(1) Women aged above 45 years and below 70 years were included,<sup>2</sup> women with complaints of lump in the breast, discharge from the nipples and tenderness in the breast were included,<sup>3</sup> patients with positive mammography signs and negative FNAC and/or HPE were included.

### Exclusion Criteria

(1) Women aged below 45 and above 70 years were excluded,<sup>2</sup> women with positive mammography and positive FNAC and/or HPE were excluded. Demographic details

of the sample were obtained from the medical records of the patients. Repeat mammography results of patients of such false positive patients were done to find the incidence of tumor risk. If the tumor was excluded after additional evaluation, women were routinely invited to participate in the screening program for 2 years regular follow-up. All the data were analyzed using standard statistical methods.

## RESULTS

Results of 2196 patients who underwent mammography in a tertiary teaching hospital, Kerala were included in the study over a period of 4 years. The total number of women patients attending the daily outpatient departments of the hospital was 6, 70, 440 for 4 years. The prevalence of women reporting breast related complaints and undergoing mammography was 0.32%. There was a positive family history of malignant tumors of breast in 14 of the 54 patients (25.92%) confirmed with malignant tumors in this study. Among the 2196 mammography procedures, 1479 were reported as normal (67.34%). Benign lesions of the breast such as cysts, hematoma, localized abscesses, lactocele, and fibroadenosis were reported in 389 women (17.71%). 274 women had shown benign tumors of breast reported following mammography (12.47%) such as fibroma, neurofibroma, fibroadenoma, and simple adenoma. The remaining 54 mammography results were showing features of malignant tumor on mammography were subjected to dynamic contrast enhanced MRI (DCEMRI), and DWI of the breast. 48 of the 54 patients with MRI diagnosis of malignant tumors were confirmed by FNAC, and the remaining 6 were proved negative for FNAC and HPE. These patients were termed as false positive cases and advised regular follow-up for 2 years. During this period 3 of them were subjected to FNAC at 3 monthly intervals. They were negative for malignant cells on FNAC on all three attempts. Hence, 2 patients were subjected to excision biopsy and HPE. Both the cases were proved negative for malignancy reported by two independent pathologists. One patient was lost for further follow-up. The remaining 3 patients underwent excision biopsy, and the tumor mass was negative for HPE. 2136/2196 patients were premenopausal (6.19%) and 1960 were postmenopausal (93.80%) (Table 1).

Women belonging to low socioeconomic group were 1065 (48.49%), middle socioeconomic group was 691 (31.46%), and upper socioeconomic group was 470 (21.40%), (Table 2).

The benign conditions of the breast reported on mammography were 397 (17.71%), and their break up is shown in Table 3.

The benign tumors of the breast reported on mammography were 274 (12.47%), and their break up is shown in Table 4.

Among the 54 patients with positive mammography 48 patients showed positive to malignancy both by FNAC and HPE. The false positive cases were 6 in number (Table 5).

**Table 1: The menstrual status of women in the study (n=2196)**

Age in years	Premenopausal - 136	Postmenopausal - 2060	Total
45-49	136	634	770
50-54	000	518	518
55-59	000	468	468
60-65	000	343	343
66-70	000	097	097

**Table 2: The socioeconomic group of women in the study (n= 2196)**

Age in years	Low socio group - 1065	Middle socio group - 691	Upper socio group - 470	Total
45-49	464	158	148	770
50-54	239	202	077	518
55-59	161	179	128	468
60-65	168	113	062	343
66-70	033	039	025	097

**Table 3: The benign lesions in the study group (n=397)**

Age in years	Abscess	Galactocele	Fibroadenosis	Diabetes fibrous mastopathy	Cysts	Pseudoangiomatous stromal hyperplasia	Radial scar and complex sclerosing lesion	Total
45-49	55	42	26	12	31	06	04	176
50-54	46	00	00	44	28	07	02	127
55-59	22	00	00	21	13	05	03	064
60-65	04	00	00	06	04	02	02	018
66-70	01	00	00	03	05	02	01	012

**Table 4: The benign tumors in the study group (n=270)**

Age in years	Fibroadenoma	Granular cell tumor	Hamartoma	Nipple adenoma	Adenoma	Lipoma	Total
45-49	15	08	16	11	17	07	74
50-54	14	05	07	14	12	02	54
55-59	04	06	08	11	14	03	46
60-65	03	14	00	15	14	03	49
66-70	01	13	00	18	10	09	51

**Table 5: The types of malignant tumors encountered in the study (n=48)**

Age in years	Invasive ductal carcinoma (NST) - 27 (56.25%)	Invasive lobular carcinoma - 05 - (10.41%)	Pure tubular carcinoma - 03 (6.25%)	Medullary carcinoma - 06 (12.5%)	Mucinous carcinoma - 04 (8.33%)	Invasive micro papillary carcinoma - 03 (6.25%)
45-49	05	02	01	02	01	00
50-54	11	01	00	00	01	01
55-59	04	01	01	01	01	01
60-65	05	01	01	02	01	00
66-70	02	00	00	01	00	01

## DISCUSSION

According to International Agency for Research on Cancer (IARC), the global cancer burden has increased and is now second leading cause of death due to cancer worldwide.<sup>15</sup> Early diagnosis with improved diagnostic tools required to differentiate benign from malignant lesions to reduce the mortality and morbidity and also avoid painful biopsy. This would help those women who do not have distant metastases; hence their long-term survival period is prolonged after the diagnosis.<sup>16</sup> Screening of all the quadrants of breast and axilla is possible with current imaging devices.<sup>17</sup> Diagnosis of breast tumors is difficult in younger women when compared to older women because of their dense structure of breast.<sup>18</sup> In addition, there are dilemmas between findings of ultrasound and mammography signs and techniques. In mammograms, fat is radiolucent and appears dark, but fibroglandular tissues are radiodense and appear white.<sup>19</sup> Few studies have shown that a tumor becomes detectable on a mammogram only after 40 cell doublings from the growth of the first tumor cell in breast cancer.<sup>20</sup> Thus, a possibility of false positive or false negative reporting is present requiring more efficient correlation mechanism better prediction of malignant tumors. The prevalence of women reporting

breast related complaints and undergoing mammography was 0.32% in this study of 2196 cases. It amounts to 3.2 cases/1000 screening mammograms. This finding is similar a study by X. Castells *et al.*<sup>21</sup> It was observed women with a false positive involving cytology or biopsy had a higher risk of cancer detection than those with a false positive involving only an additional imaging procedure. This risk remained significantly higher 4 years or more after the false positive test. Similarly, the cancer detection risk increases substantially if the women had a first-degree familial history of breast cancer. The increased cancer detection risk in women with a false positive test observed in this study is in agreement with the results of X. Castells *et al.*<sup>21</sup> Similar opinions were quoted in studies by Euler-Chelpin *et al.*<sup>15</sup> and McCann *et al.*<sup>22</sup> However, some authors reported false negative mammography tests in women undergoing additional evaluation after a positive mammographic test.<sup>23,24</sup> Absence of malignancy in a false positive mammography does not rule out existence of a benign breast lesion.<sup>25</sup> Hence, few authors have kept in mind the impact of the previous benign lesions while undertaking mammography for breast cancer. In this study, the false positives involving a cytology examination or biopsy had an increased cancer detection risk compared with additional imaging procedures. In patients with increased breast density are associated with more number of false positive mammography reports as well as increased breast cancer risk.<sup>26</sup> Women with a false positive result should be encouraged to return for further screening as they have an increased cancer detection risk, and a decreased re-attendance probability.<sup>27</sup> Berg *et al.*, have reported a sensitivity, specificity, and accuracy of 83%, 34%, and 67.8% for ultrasound investigations. In the same study, they have reported sensitivity, specificity, and accuracy of 67.8%, 75%, and 70.2% for mammography investigations. The combined ultrasound, mammography, and clinical examination have yielded sensitivity and accuracy of 93% and 70.9%.<sup>28</sup> In this study, the sensitivity, specificity, and accuracy related to benign conditions and tumors were 100%. Similarly, the sensitivity, specificity, and accuracy for malignant tumors were 88.88%.

## CONCLUSIONS

Mammography screening proves to be an excellent tool in the diagnosis of diseases of the breast. There is a definite relation between the presence of a false positive test and the risk of cancer detection in subsequent screening participations. The association was much clear in false positives involving a cytology examination or biopsy, and in women with a family history of breast cancer.

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