# Functional Breast Imaging With Tc-99m Mibi For Detection Of Primary Breast Lesion And Axillary Lymph Node Metastases

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## ABSTRACT

Breast cancer is the most common cancer among women and the second leading cause of death in women after lung cancer. The principle aim is to study the utility of Tc- MIBI scintimammography in evaluation of breast cancer and lymph node metastases.

### Materials and Methods

A total of 36 patients both with breast lumps or/and axillary masses suspected breast cancer on clinical examination and/or at conventional imaging procedures (CIP's) were included in this study. The mean age was 47.13 years, median age 47 and age range 22-77 years. All patients received a 740-1000 MBq bolus IV injection of $^{99m}$Tc-MIBI preferably in a pedal vein. At 5-10 min post injection planar images were obtained in prone lateral and supine anterior position using dual head gamma camera. MIBI uptake was scored as follows: 1 for normal uptake (compared with contralateral side), 2 for focal low intense uptake (equivocal), 3 for focal high intense uptake (positive). All patients had histopathology for tissue diagnosis.

### Results

There were 36 patients who presented with breast lesions (30 palpable, 6 non-palpable) and 8 patients with axillary lump. Scan was found true positive in 24 patients and was true negative in 7 patients with breast lesion. In case of axillary lump, it was true positive in 4 and true negative in 2 patients. Planar scintimammography showed sensitivity of 86%, specificity 88%, PPV 96%, NPV 64% and accuracy of 86% ($p< 0.01$). However sensitivity, specificity, PPV, NPV and accuracy for axially metastasis were 86%, 67%, 80%, 67% and 75% respectively. (P-value <0.01).

### Conclusion

It is concluded from the study that SMM has good diagnostic accuracy in the detection of breast cancer specially in palpable lesion and lymph node metastases

### Key Words

*Carcinoma breast, Scintimammography, 99mTc MIBI.*

## Introduction

Breast cancer is the most common malignant tumor among women and the second leading cause of death in women after lung cancer [(1)]. Approximately 178000 new cases are detected yearly in the USA, and in the European Union the number is more than 135000 [(2)]. Approximately 1 out of 9 women will develop breast cancer during her lifetime [(3)].

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Breast imaging is valuable in the investigation of symptomatic breast disease [(4)]. There have been numerous major advances in breast imaging over the past 25–35 years, which permit not only the more accurate diagnosis of benign breast disease but also, more importantly, the earlier diagnosis and more effective preoperative staging of breast cancer[(1)]. At present the most commonly used imaging modalities to detect primary breast cancers are mammography, breast ultrasonography, MRI and scintimammography.

Mammography is the primary screening technique for breast cancer It has become the

method of choice for screening women over 50 years of age [6,7]. Mammography can detect cancer earlier than physical examination. It has the ability to locate the area of the tumor but unable to separate normal gland tissue from the tumor. It is more effective when gland tissue diminished with increasing age. It has an overall of 25% false positive rate [8], it lacks specificity, being only 35-54% which leads to unnecessary biopsies[8]. In most women the medial upper triangle, peripheral areas next to the chest wall, and the inframammary sulcus of the breast cannot be visualized with mammography. Mammography has an overall 20% false negative rate in women under age 60 and up to 40% in women under age 50 due to breast density [8].

Ultrasound is used predominantly to differentiate between cystic and solid masses. This technique reduces the number of unnecessary biopsies. However, it has poor resolution in comparison to mammography. The role of ultrasound may expand with such developments as color Doppler [9]. Ultrasound is considered safe for women of any age [10]. When ultrasound is used in conjunction with mammography, breast cancer can be diagnosed with sensitivity and specificity of 92 and 98 percent, respectively [10]. Ultrasound can miss solid lesions, especially in fatty breasts.

MRI of the breast is emerging as a valuable adjunct to mammography and sonography for specific clinical indications. MRI of the breast has been shown to be quite effective at pinpointing (as small as 2-3 mm) lesions [11]. It identifies a clinically or mammographically occult primary tumor in the patient presenting with axillary breast cancer. A major limitation of breast MRI is its relatively low specificity and cost effectiveness[12]. The specificity of MRI in demonstrating breast cancers has been reported as low as 30-40 percent and may lead to unnecessary biopsies of false positive lesions [13].

Several techniques have been proposed to improve the specificity of conventional imaging procedure, these include, single photon scintimammography and positron emission tomomography. Numerous single photon radiopharmaceuticals have been evaluated for Scintimammography [14]. The use of 99mTc MIBI is currently the mainstay [15,16]. The exact mechanism of MIBI uptake by tumor is not very clear. It is reported that MIBI is accumulated within mitochondria (90% of tracer activity) and cytoplasm of cells on the basis of transmembrane electrical potentials [17]. Malignant tumors show increased transmembrane potentials due to the increased metabolic requirements, which induce, increased accumulation of MIBI in tumors [18]. The aim of the study was to investigate the role of Tc-99m MIBI scintimmamography in evaluation of breast cancer and axillary lymph node metastasis.

## Materials And Methods

A total of 36 consecutive patients with breast lumps or/and axillary masses from September 2004 to August 2006 with suspected breast cancer on clinical examination and/or at conventional imaging procedures (CIP's) were included in this study. The mean age was 47.13 years median 47 and rage of 22-77 years.

## Scintimammography (SMM)

All patients had scintimammography using TOSHIBA GCA 7200A/PI (Double head camera) with low-energy high resolution parallel hole collimator. The energy peak was centered at 140keV with a 20% window. All patients received a 740-1000 MBq bolus IV injection of 99mTc-MIBI preferably in a pedal vein. At 5-10 minutes post injection planar images were obtained in prone lateral and supine anterior position. The detector was positioned below and as close as possible with the involved breast/chest wall and axilla included in the field of view. A lead shield was positioned in midline to minimize the counts originating from the contralateral breast.(Fig. 1)

## Histopathology and Cytology

All patients with suspicious breast cancer had either fine needle aspiration cytology (FNAC) or core biopsy or definite wide local excision to confirm final diagnosis. If there was suspicion of axillary lymph node disease either clinically or by any imaging modality, then lymph node sampling was also performed. All the surgical procedures were performed by competent surgeons and assessed by experienced pathologists.

## Statistical Analysis

The sensitivity, specificity, positive predictive value, negative predictive value and accuracy of scintimammography, were calculated. Chi-square test was also applied to compare the level of significance between the imaging modalities used in the study with histopathological results. A statistically significant difference was considered when p values are <0.05.

## Results

Out of 36 patients, 28 had evidence of cancer on hiostopathology/cytology. Planar scintimammography was true positive in 24 and false negative in 4 patients. [Table 1]. In case of axillary lump, it was true positive in 4 and true negative in 2 patients. In breast lesion planar scintimammography showed sensitivity 86%, specificity 88%, PPV 96%, NPV 64% and accuracy 86% (p< 0.01). However sensitivity, specificity, PPV, NPV and accuracy for axillary metastasis were 86%, 67%, 80%, 67% and 75% respectively. (P-value <0.01). (Fig. 2)

## Discussion

In this study planar scintimammography resulted in a sensitivity of 86 %. The results were true positive in 24 cases (24/25) 96% and false negative in 4 patients (36%). These results were

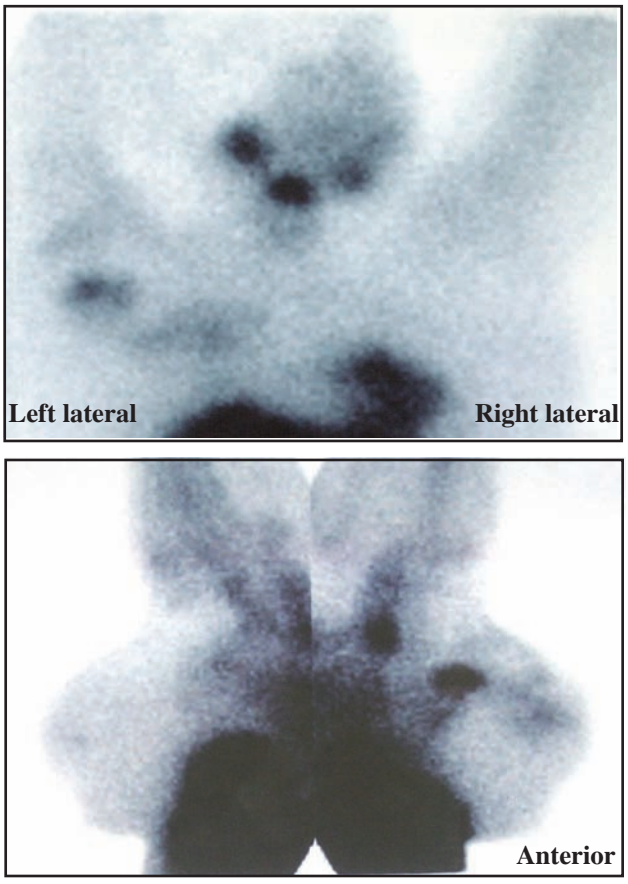


**Fig. 1: A 65 year old woman presented with a lump in right upper outer quadrant & right axilla. Scintimammography shows focal increased tracer uptake in right breast and axilla. Atypical cells were found on FNAC.**

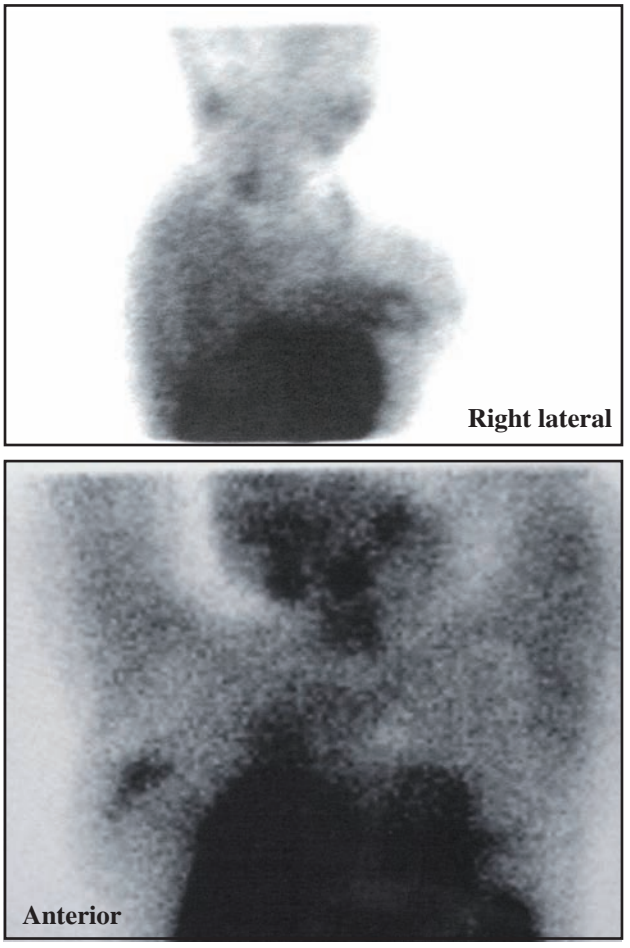


**Fig. 2: A 35 year old women presented with a swelling in the right breast. XMM was inconclusive due to dense breast. SMM show focal area of increase tracer uptake in right breast. While biopsy revealed invasive ductal carcinoma.**

| | TP | FP | TN | FN | Sensitivity | Specificity | PPV | NPV | Accuracy |
|---|---|---|---|---|---|---|---|---|---|
| Breast | 24 | 1 | 7 | 4 | 86 | 88 | 96 | 64 | 86 |
| Axilla | 4 | 1 | 2 | 1 | 80 | 67 | 80 | 67 | 75 |
| PPV= Positive predictive value; NPV= Negative predictive value (p<0.05) | | | | | | | | | |

**Table 1: Scintimammography findings.**

similar to those reported by khalkhali et al[16]. In this study, false negative can be attributed to a non localization of the tumor near the heart in one patient and the remaining two lesions were undetected due to smaller size. Schillaci O et al.[19] has also reported the fact that lesions of about 1 cm and less are difficult to detect by the standard gamma camera. Other probable causes that may contribute to a negative scintigram are related to blood flow, mitochondrial transmembrane electronegativity which being inversely related to necrosis and fibrosis and over expression of multi drug resistant gene [20,21].

The specificity of scintimammography in this study is 88%. The planar SMM was true negative in 7 patients. A false positive result was noted in one patient on planar images, while cytology revealed local inflammation. These are comparable to results reported by Palmedo H et al [22]. Local inflammation, fibroadenomas and fibrocystic changes represent the major source of false positive images on scintimammography[23].

In our study, a total 8 patients were evaluated for axillary lymph node metastasis. All the above eight patients had palpable nodes which appeared enlarged at US but with typical signs of malignancy in four cases, and benign in 4 cases. The 99mTc MIBI was true positive in all 4 (80%) patients with proven lymph node metastases at histology or cytology, (range lymph node size, 1-5 cm clinically). The sensitivity is good and comparable to that of Taillefer, et al [28]. The axillary lymph node chains are the major regional drainage sites for breast. Presently, in patients with proven breast cancer or suspected breast lesions, axillary lymph node status is determined either clinically or pathologically. The clinical evaluation of lymph node status, however, is frequently inaccurate. Physical examination in general is less than 50% effective in detecting axillary lymph nodes harboring breast cancer metastasis [24]. Axillary lymph node involvement is also an important prognostic factor in patients with breast cancer and excellent result of SMM was reported in different trials [25,26,27]. It shows a sensitivity of 65-95% and specificity of and 85-100% [28].

Tc-99m MIBI has high sensitivity in detecting breast cancer and improves the specificity of mammography for breast lesions [29]. Because of high negative predictive value of SMM using MIBI it also help to decrease the biopsy per cancer ratio in mammographic abnormalities [22]. The scintimammography has been proposed for the detection of the multicentric breast cancer. The sensitivity of mammography is low in patients aged 40-49 years (with more dense breast tissue) in comparison to older women. Tc-99m MIBI scintimammography is independent of the breast density or structural distortion and the sensitivity for detection of breast cancer is not affected by the density of breast tissue [30].

The negative and positive predictive values of scintimammography are high with palpable breast lesion. This procedure could be performed immediately after mammography, instead of waiting 6-12 months [31]. However the sensitivity of non palpable lesion is low 72% [15] Scintimammography is not affected by the density or the type of breast tissue, so it can demonstrate the presence of one or more focus of increases uptake [32]. Although scintimammography cannot be used as a screening tool for breast cancer, however it is useful in evaluation of high risk patients with normal mammogram and ultrasound[33]. Scintimammography can also be performed for the detection of breast cancer among males.

## Conclusion

Scintimammography is a simple noninvasive, low cost and reliable diagnostic tool in breast cancer. Scintimammography has high diagnostic accuracy in the detection of breast cancer and axillary lymph node metastses and appear more useful for detecting invasive breast tumors presenting as masses greater than 1 cm. Scintimammography has a greater accuracy in younger patients with dense breast.

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