## Original Article

# Role of $^{99m}$Tc-MIBI Scintimammography and X-ray mammography in the diagnosis of locoregional recurrence of breast cancer

Sharjeel Usmani, Khalid Niaz, Maseeh-Uz-Zaman, Shahid Kamal, Kashif Niyaz, Javed Mehboob, Adnan Hashmi, Salman Habib, Hina Hashmi

Nuclear Medicine Department, Karachi Institute of Radiotherapy and Nuclear Medicine, Karachi.

## Abstract

**Objective:** To evaluate the utility of Tc- MIBI scintimammography in the loco-regional recurrence of breast cancer and its comparison with mammography.

**Methods:** The study population comprised of 33 subjects (mean age, 44.9 ± 14.1 years); evaluated for suspected loco-regional recurrence of breast cancer on clinical examination. All subjects received a 740-1000 MBq bolus IV injection of 99mTc-MIBI preferably in pedal vein. At 5-10 min and 60-90 min post injection planar images were obtained in prone lateral and supine anterior position using double head gamma camera. MIBI uptake was scored as follows: 1: as normal uptake (compared with contralateral side); 2: focal low intense uptake (equivocal); 3: focal high intense uptake (positive). Mammography was performed by two standard views of cranio-caudal and mediolateral oblique in 26 patients. All patients had either excision biopsy or fine needle aspiration cytology (FNAC) for tissue diagnosis.

**Results:** Out of 33 patients, 21 had confirmed as recurrence on hiostopathology/cytology. Scintimammography was found true positive in 18 and true negative in 11 patients. The sensitivity, specificity, positive predictive value, negative predictive value and accuracy were 85.7%, 91.7%, 94.7%, 78.6% and 87.8% respectively. In comparison, mammography was true positive in 9 and true negative in 6 patients with sensitivity of 52.9%, specificity, 66.7%, PPV 75%, NPV 42.9% and accuracy 57.7%.

**Conclusion:** Scintimammography has better diagnostic accuracy than mammography in the detection of loco-regional recurrence of breast cancer (JPMA 57:172;2007).

## Introduction

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

Actual cancer incidence data has never been available for any population in Pakistan except for Cancer Registry in Karachi[3] and some sporadic data reported by few radiotherapy centers and multi-institutional basis.[4] In Pakistani females, breast cancer is the commonest cancer observed representing more than one third of female cancers and about one fourth of all malignancies. The age-standardized rate (ASR) is the highest in Asia, except the Jews in Israel.[5]

Patients who have been treated for breast cancer may develop recurrence of primary cancer. In a large Italian cohort study local recurrence rate was 1-2% per year.[6] Most recurrences appear within first two or three years after treatment, but breast cancer can occur many years later.[7] The rate of loco-regional recurrence at 10 years is 12% with mastectomy and 20% with breast-conserving surgery.[8]

Recent studies found that one third of recurrence were manifested by history, one third detected by physical examination and one sixth by mammogram.[7] After breast conserving treatment, there are significant changes in the sensitivity and specificity of mammography and physical examination. In 25-50% cases recurrence is often missed on mammography.[9] Dershaw[10] describe that mammography can be expected to detect 30-40% of breast cancer recurrence. Traditionally X-ray mammography was used to assess the post surgical breast, but post surgery and radiotherapy changes to the breast reduce the accuracy. Interpretation of X-ray mammography relies on anatomical features of breast cancer and thus its positive predictive value may be as low as 15-30%.[11]

It is therefore important to find a sensitive and accurate diagnostic method for detecting early loco-regional breast cancer recurrence. Tc-99m MIBI, is a potential tumour imaging agent, which can be used for visualization of different tumors such as breast[12], parathyroid[13], thyroid and bone tumours.[14,15] The exact mechanism of MIBI uptake by tumour 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. Malignant tumors show increased transmembrane potentials due to the increased metabolic requirements, which induce, increased accumulation of MIBI in tumours.[16] The principle aim is to study the role of Tc-99m MIBI scintimammography in evaluation of loco-regional recurrence of breast cancer in comparison with mammography.

## Patients and Methods

A total of 33 diagnosed breast cancer patients (mean age, 44.9 14.1 years; median age 40 years; age range, 22-77 years) were studied, 15 patients had undergone lumpectomy and 18 had mastectomy. Patients were selected for this study if there was a clinical suspicion of loco-regional recurrence of breast cancer.

In 26 individuals mammography (XMM) was performed using a standard two-view protocol of craniocaudal and mediolateral oblique projections was performed with 26 to 28 KeV X-rays with automatic exposure control (Metal Tronica). A senior radiologist having knowledge of the patient's history, clinical presentation and previous mammogram, interpreted the images. The results are reported using three point system of positive for cancer, negative and equivocal.

All patients had scintimammography (SMM) 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. At 5-10 min and 60-90 min post injection planar images were obtained in prone lateral and supine anterior position. MIBI uptake was scored as follows: 1) as normal uptake (compared with contralateral side); 2) focal low intense uptake (equivocal); 3: focal high intense uptake. Two experienced nuclear physicians, who were blind to the clinical information of the patient, analyzed the scintimammograms. Only focal uptake was interpreted as positive.

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

The sensitivity, specificity, positive predictive value, negative predictive value and accuracy of scintimammography, mammography were calculated.

## Results

Out of 33 patients 21 had evidence of recurrence on hiostopathology/cytology. Scintimammography was positive in 19 out of 33 patients. It was equivocal in two patients and in remaining 12 patients scan was negative for abnormal tracer uptake. Mammography was done in twenty six patients (79%), it was positive in 12 patients, equivocal in 4 and negative in remaining 10 patients (Table 1).

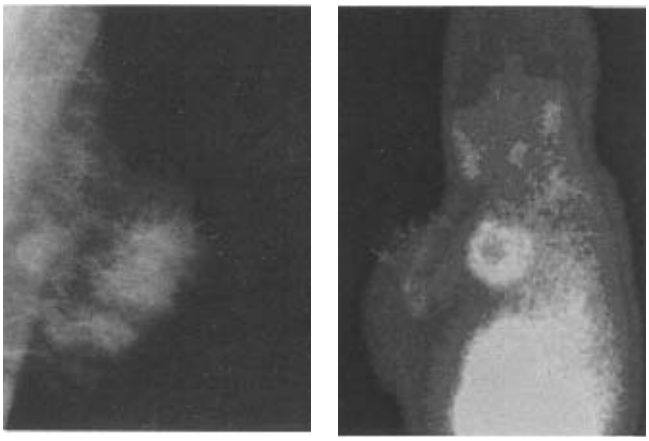
The overall sensitivity of planar Tc-99m MIBI scintimammography in detecting recurrent breast cancer was 85.7%, the specificity 91.7%, positive predictive value 94.7%, negative predictive value 78.6%, and the accuracy was 87.8%.

The overall sensitivity, specificity, PPV, NPV and accuracy of mammography were found to be 52.9%, 66.7%, 75%, 42.9% and 57.7%.

## Discussion

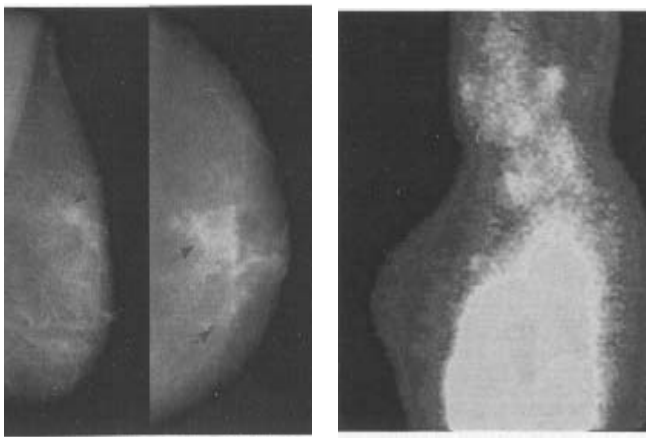
In this study, sensitivity of scintimamography is in close proximity to those reported by Buscombe et al1[17], which was 85%. Regarding 3 false negative scans in this study; in one patient abnormal tracer uptake was superimposed by left ventricular myocardial uptake while in remaining lesions were smaller in size <2cm. Scintimammography has low sensitivity for detecting small cancers, usually in the range 1±1.5 cm and smaller.[18]

The specificity of scintimammography in this study was high. A false positive result was noted in one patient on planar images, while cytology revealed local inflammation, similar results had been reported by Cwikla et al.[19] Local inflammation, fibroadenomas and fibrocystic changes represent the major source of false positive images on scintimammography.[18]



(a) (b)

Figure 1. A 65 year old woman with a 9 month history of left side breast cancer treated by lumpectomy only. She presented with a lump in left upper outer quadrant & left axilla. (a) Medio-lateral obligue view of left breast mammography is highly suspicious for recurrence. (b) Scintimammography shows focal increased tracer uptake in left breast and axilla. Atypical cells were found on FNAC.



(a) (b)

Figure 2: A 38 year old woman with 12 month history of left sided breast cancer treated by lumpectomy & chemotherapy. She presented with a lump in left upper outer quadrant. (a) Mammography was highly suspicious for breast cancer. (b) Scintimammography revealed no abnormality. Scar tissue was found at biopsy.

In our study, the sensitivity, specifically, PPV and NPV of mammography was low as compared to scintimamography. This may be because mammography is less sensitive in the treated breast than in the untreated breast

**Table 1. Scintimammography and Mammography findings.**

| | TP | FN | TN | FP | Total |
|---|---|---|---|---|---|
| Scintimammography | 18 | 3 | 11 | 1 | 33 |
| Mammography | 9 | 8 | 6 | 3 | 26 |

TP= true positive; FN= false negative; TN= true negative; FP= false positive.

**Table 2. Results of Scintimammography and Mammography.**

| | Sensitivity | Specificity | PPV | NPV | Accuracy |
|---|---|---|---|---|---|
| Scintimammography | 85.7 % | 91.7% | 94.7% | 78.6% | 87.8% |
| Mammography | 52.9% | 66.7% | 75% | 42.9% | 57.7% |

PPV= Positive predictive value; NPV= Negative predictive value

due to surgery and radiation induced changes in the parenchymal pattern[20] (Figure 2). The reported sensitivity and specificity of mammography for detecting local recurrence of breast cancer following surgery and radiation therapy thus vary and range from 38-74% and 17-60% respectively.[21] Similarly Hassell et al[22] described that the mammography has sensitivity and specificity of 38% and 60% respectively in the detection of local recurrence of breast cancer. Post surgical findings may mimic or mask local tumour recurrence. For better accuracy, baseline mammogram after primary treatment should be present, any new findings from the baseline examination, such as a developing density, mass or calcifications should be evaluated and correlated with thorough clinical history, including information regarding the type of surgical intervention, and pathologic correlation which are needed for adequate assessment. Accuracy of the mammography is related to the quality of reporting and leads to high number of equivocal reports, causing uncertainity for the patients and doctors. However, with scintimammography only, the presence and absence of radiotracer gives positive or negative results.[23] Therefore, scintimammography is a more accurate and sensitive diagnostic method for detecting early loco-regional breast cancer recurrence than mammography and has primary role in detecting recurrent breast cancer.[24]

Scintimammography is a simple noninvasive and reliable diagnostic tool for the diagnosis of loco-regional breast cancer recurrence. Compared with mammography, scintimammography has a better diagnostic accuracy in the detection of loco-regional breast cancer recurrence. Scintimammography can be used with conviction for discrimination of post surgical and post radiation changes and scar tissue tumour from recurrence.

## References


1. Landis SH, Murray T, Bolden S. Cancer statistics, 1998. CA Cancer J Clin 1998; 48:6-29.
2. American Cancer Society. Breast Cancer Facts & Figures 2003. Atlanta , GA: American Cancer Society Inc 2003; pp. 5008-3.
3. Bhurgri Y. Cancer registration in Pakistan. Asia Pacific 1 Cancer Prev, IARC (Supple) 2001; 2:51-4.
4. Aziz Z, Sana S, Saeed S, Akram M. Institution Based Tumor Registry from Punjab: Five Year Data Based Analysis. J Pak Med Assoc 2003; 53:179-83.
5. Bhurgri Y, Bhurgri A, Sheema H. Cancer incidence in Karachi: first results from Karachi cancer registry. Int J Cancer 2000; 85:325-9.
6. Veronesi U, Marubini, Del Vecchio M. Local recurrence and distant metastases after conservative cancer treatment: Partly independent events. J Natl Cancer Ist 1995;87:19-27
7. K Herman, J. W Rodger. Ongoing Care of Patients After Primary Treatment for Their Cancer. CA Cancer J Clin 2003; 53:172-196
8. Fisher B, Anderson S, Bryant J. Twenty year follow-up of a randomized trial comparing total mastectomy, lumpectomy, and lumpectomy plus irradiation for the treatment of invasive breast cancer. N Engl J Med 2002; 347:1233-41.
9. Orel SG, Fowble BL, Solin LJ, Schultz DJ, Conant EF, Troupin RH. Breast cancer recurrence after lumpectomy and radiation therapy for early stage disease: prognostic significance of detection method. Radiology 1993; 188:189-94.
10. Dershaw DD, McCormick B, Osborne MP. Detection of local recurrence after conservative thearapy for breast carcinoma. Cancer 1990; 70:493-6.
11. Kopans DB. Positive predictive value of mammography. Am J Roentgenol 1992; 158: 521-6.
12. Khalkhali I, Villanueva-Meyer J, Edell SL. Diagnostic accuracy of 99mTc-sestamibi breast imaging: multicentretrial results. J Nucl Med 2000; 41:1973-9.
13. Aktolun C, Bayhan H, Kyr M. Clinical experience with Tc-99m MIBI imaging in patients with malignant tumors: preliminary results and comparison with Tl-201. Clin Nucl Med 1992; 17:171-6.
14. Foldes I, Levay A, Stotz G. Comparative scanning of thyroid nodules with technetium-99m pertechnetate and technetium-99m methoxyisobutylisonitrile. Eur J Nucl Med 1993; 20:330-33.
15. Caner B, Kitapcy M, Aras T, Erbengi G, Bekdik C. Increased accumulation of hexakis (2-methoxyisobutylisonitrile) technetium in osteosarcoma and its metastatic lymph nodes. J Nucl Med 1991; 32:1977-8.
16. Romero L, Khalkhali I, Varqas HI. The Role of Nuclear Medicine in Breast Cancer Detection: A Focus on Technetium-99 Sestamibi. Current Oncology Reports 2003; 5:58-62.
17. Cwikla J.B, Buscombe J.R, Parbhoo S.P, Holloway B, Davidson S.P, Mcdermot Nt et al. Use of 99mTc-MIBI in the assessment of patients with suspected recurrent breast cancer. Nucl Med Comm1998; 19:649-55.
18. Khalkhal I et al. Functional breast imaging using the single photon technique. Nucl Med Commun 2002; 23:609-11.
19. Cwikla JB, Kolasinska A, Buscombe JR, Hilson AJ. Tc-99m MIBI in suspected recurrent breast cancer. Cancer Biother Radiopharm 2000; 15:367-72.
20. Giess C. S. Local Tumor Recurrence following Breast-Conservation Therapy: Correlation of Histopathologic Findings with Detection Method and Mammographic Findings. Radiology 1999; 212:829-35.
21. Temple L. K F, Wang E.E.L. Preventive health care update: Follow up of breast cancer. CMAJ 1999; 16:1001-8.
22. Hassell PR, Olivotto IA, Mueller HA, Kingston GW, Basco VE. Early breast cancer: detection of recurrence after conservative surgery and radiation therapy. Radiology 1990; 176:731-5.
23. Kolasinska AD, Buscombe JR, Cwikla JB, Holloway B, Parbhoo SP, Davidson T et al. The role of scintimammography and mammography in recurrent breast cancer. Evaluation of their accuracy using ROC curves. Nucl Med Rev Cent East Eur 2001;4:77-82.
24. Kolasinska AD, Cwikla JB, Buscombe JR, Parbhoo SP, Davidson T, Holloway B, et al. Scintimammography in recurrent breast cancer: A primary or secondary role? Nucl Med Comm 2000; 21:389-95.