

# Technetium-99m-MIBI Scintimammography by Planar and SPECT Imaging in the Diagnosis of Breast Carcinoma and Axillary Lymph Node Involvement

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## Abstract.

We compared SPECT and planar Tc-99m MIBI scintimammography (SMM) in the detection of primary breast cancer and metastatic axillary lymph node involvement, and the scintigraphic results with the histopathological/cytological findings. Three hundred and three consecutive patients with 308 suspicious or indeterminate lesions on mammography were entered in this study. After intravenous injection of 740 MBq of Tc-99m MIBI, anterior supine, right and left lateral planar images were acquired in prone position at 10 minutes post injection using a dual-head gamma camera equipped with low-energy, high resolution, parallel-hole collimators. After this a SPECT study (60 projections, 64x64 matrix, 30 sec/frame, 360 degrees arc) was obtained in supine position in the same patient. Filter Hanning, order 5, cut off 2.3 were applied for reconstruction with filtered backprojection. Eighty-five malignant (nine histological types) and 223 benign breast lesions were confirmed by histopathology/cytology. Planar imaging missed 15 malignant lesions while SPECT missed only 7. Twenty-one benign lesions showed focal uptake of Tc-99m MIBI on planar imaging while only 19 on SPECT. The overall sensitivity in the detection of breast cancer was 92% (78/85) for SPECT and 82% (70/85) for planar imaging ( $P=NS$ ); While overall specificity was 91% (204/223) for SPECT and 91% (202/223) for planar scans ( $P=NS$ ). Metastatic axillary lymph node involvement was seen in 35 patients; per-axilla overall sensitivity was 66% (23/35) for SPECT and 54% (19/35) for planar images ( $P=NS$ ). overall specificity was 76% (38/50) and 86% (43/50), for planar and SPECT

studies respectively ( $P=NS$ ). Our results confirm the high diagnostic accuracy of Tc-99m MIBI scintimammography in the diagnosis of breast cancer, and show SPECT to be slightly more sensitive than planar imaging, especially in detecting malignant breast lesions. We found sensitivity of both imaging modalities to be quite low in the detection of metastatic axillary lymph node involvement. SPECT provides additional information to planar SMM with respect to localization of Tc-99m MIBI uptake and tumor extent and improves diagnostic certainty. We recommend more wide-spread use of SPECT in combination with planar SMM.

**Keywords:** Tc-99m MIBI, Scintimammography, SPECT, Breast cancer, Axillary lymph node metastasis

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## Introduction

Breast cancer is the leading cause of cancer-related death in women throughout developed countries (1, 2). Since patients with breast cancer detected at an early stage have a better survival rate (3), much work has been done to improve the early breast cancer detection.

Besides the physical examination, the most widely tool for diagnosis of primary breast cancer is x-ray mammography, which has been widely used in screening for breast cancer (4). However, mammography can also yield false-negative results in some cases (5); e.g., it is less reliable for detecting lesions in dense fibroglandular breasts (6). In addition, it cannot always accurately differentiate between benign and malignant lesions (7, 8, 9) and it is characterized by a low specificity and a low positive predictive value (10). Ultrasonography and magnetic resonance imaging can slightly improve the sensitivity of mammography in some conditions. But both the techniques have low specificity (11-13).

Tc-99m Scintimammography (SMM) has been reported to have high sensitivity as well as specificity for the detection of breast carcinoma in selected patient population (14-18). These studies have mostly been conducted with high-resolution cameras using the planar imaging technique.

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There are very few reports in literature on the use of SPECT imaging for the diagnosis of breast cancer (2,11,19-25). The value of SMM using SPECT has not yet been fully established.

The aim of this study was to compare SPECT and planar Tc-99m MIBI imaging in the detection of primary breast cancer and axillary lymph node involvement, and to compare the scintigraphic results with the histopathological/cytological results.

## Materials and methods

### Patients

Three hundred and three consecutive patients (300 females and 3 males) with an age range of 17 - 82 years (mean age=46 years) with 308 suspicious or indeterminate lesions on x-ray mammography were entered in this study. All patients had previously undergone clinical examination, mammography and ultrasonography. One hundred seven lesions were palpable and 201 were nonpalpable. Two hundred and fifty-three patients had the histopathologic confirmation by excisional or core needle biopsy, lumpectomy or mastectomy within 3 wk of SMM. In 55 patients, the fine-needle aspiration cytology results were used as the final diagnosis. In breast cancer patients, the final histopathological confirmation of axillary lymph node involvement was obtained after the lymph nodes excision at axillary lymph node dissection (ALND).

### Tc-99m MIBI scintimammography protocol

Studies of all patients were performed using a dual-head gamma camera (Apex Helix SPX, Elscint, Israel) equipped with low-energy, high-resolution, parallel-hole collimators.

Planar imaging began 5-10 min after the injection of 740 MBq of Tc-99m MIBI in the arm contralateral to the breast with the suspicious abnormality or in a pedal vein. Radiolabelling and quality control procedures with respect to the tracer were carried out according to the manufacturer's instructions. Images were obtained with a 256 x 256 matrix for the acquisition time of 10 min in both the lateral and anterior views. Lateral views were obtained in the prone position on a special table with the breasts freely pendent while the anterior planar view was acquired in the supine position with the arms raised above the head and with the chest, both breasts and the axillae included in the field of view.

SPECT imaging was initiated at 20-30 min postinjection with a 64 x 64 matrix, 1800 rotation per head, 30 angular step-and-shoot technique and an acquisition time of 30 sec per frame. Filter Hanning (order 5, cut off 2.3) was applied for reconstruction with filtered backprojection to produce transaxial slices. Coronal and sagittal views were then obtained.

### Data analysis

Tc-99m MIBI uptake in planar and SPECT images of both breasts and axillae was visually evaluated separately. The

scintigrams were classified as normal or abnormal. The focal tracer accumulation in the breast and the axilla was a criterion for the abnormal scan.

The first-step analysis consisted of the separate evaluation of planar and SPECT imaging. The second-step analysis involved the interpretation of planar images combined with SPECT ones. The results of both diagnostic approaches - the separate (planar and SPECT) and the combined reading (planar plus SPECT) - were compared and correlated with the final histopathological/cytological diagnoses.

### Statistical analysis

Tc-99m MIBI planar and SPECT images showing abnormal increased focal radiotracer uptake were classified as true positive when the final diagnosis was malignancy. Similarly the studies were categorised as true negative or false negative when the images did not reveal any focal abnormalities depending on the final histological diagnosis of malignancy or not. In all cases histopathology and/or cytology were taken as gold standard for final diagnosis. Sensitivity, specificity, positive and negative predictive value and accuracy of different approaches for the detection of both primary breast cancer and axillary lymph node metastasis were calculated. Statistical evaluation was performed using a chi-square test. A "P" value of < 0.05 was considered statistically significant.

## Results

In 81 patients 85 malignant lesions (nine histological types) were confirmed by histopathology (Table 1). Seventy-seven patients had unilateral disease while 4 had bilateral disease. Breast cancers (without 8 malignant lymphomas) were in the following pTNM stages: 2 carcinoma in situ, 39 pT1 (11 pT1b, 28 pT1c), 29 pT2, 4 pT3 and 4 pT4. The mean size of malignant lesions was 24 mm (range 6-52 mm)

Histology	Lesions (n)
Infiltrating ductal carcinoma	49
Infiltrating lobular carcinoma	13
Mixed ductal and lobular carcinoma	4
Mixed infiltrating ductal carcinoma and ductal carcinoma in situ	2
Ductal carcinoma in situ	2
Malignant lymphoma	8
Medullary carcinoma	5
Mucinous carcinoma	1
Papillary carcinoma	1
<b>Total</b>	<b>85</b>

**Table 1** Distribution of histopathological findings in malignant breast lesions (N=85)

in greatest diameter. The smallest tumor was a mixed infiltrating ductal carcinoma and ductal carcinoma in situ (diameter 6 mm). The remaining patients had 223 benign lesions (Table 2).

Histology/Cytology	Lesions (N)
Fibroadenoma	78
Fibrocystic disease	53
Intraductal papiloma	7
Atypical lobular hyperplasia	7
Ductal hyperplasia	4
Local inflammation	7
Florid adenosis	5
Dysplasia	7
Benign cytological finding	55
<b>Total</b>	<b>223</b>

**Table 2** Distribution of histopathological/cytological findings of benign breast lesions (N=223)

	Planar imaging	SPECT	Planar imaging + SPECT
True positive	70	78	78
True negative	202	204	202
False positive	21	19	21
False negative	15	7	7

**Table 3** Results of scintimammography (Number of breast lesions = 308).

	Planar imaging	SPECT	P	Planar imaging + SPECT
Sensitivity	82% (70/85)	92% (78/85)	NS	92% (78/85)
Specificity	91% (202/223)	91% (204/223)	NS	91% (202/223)
PPV*	77% (70/91)	80% (78/97)	NS	79% (78/99)
NPV†	93% (202/217)	97% (204/211)	NS	97% (202/209)
Accuracy	88% (272/308)	92% (282/308)	NS	91% (280/308)

\* positive predictive value, † negative predictive value

**Table 4** Statistical analysis of the results of planar and SPECT imaging and combined planar and SPECT evaluation (breast lesions; n=308).

Planar scintigraphy was able to locate correctly 70 and SPECT 78 of the malignant lesions. Planar imaging missed 15 malignant lesions while SPECT only seven. Figure 1 shows a true-positive SPECT finding in a patient with non-palpable breast carcinoma that was negative on planar imaging. Twenty one benign lesions showed uptake of Tc-99mMIBI on planar images while only 19 showed uptake on SPECT. Overall sensitivity in the detection of malignant breast lesion was 82% for planar imaging and 92% for SPECT, and overall specificity was 91% for both these modalities. The difference in sensitivity was not statistically significant (Tables 3 and 4).

Tables 3 and 4 also summarize the results of the combined planar and SPECT interpretation. Overall sensitivity in the detection of malignant breast lesion was 92% and specificity 91%.

Metastatic axillary lymph node involvement was seen in 35

patients: the results of the planar and SPECT imaging, and combined interpretation of both modalities are summarized in Tables 5 and 6. Overall sensitivity in the detection of axillary lymph node metastasis was 54% for planar imaging and 66% for SPECT; overall specificity was 89% for planar imaging and 76% for SPECT. The differences were not statistically significant. For combined interpretation of both planar and SPECT imaging, the overall sensitivity and specificity was 66% and 72% respectively.

## Discussion

Scintimammography using SPECT was found to be generally more sensitive in detecting primary breast lesions than planar imaging (92% vs 82%). However on statistical analyses, the difference in sensitivity of both imaging modalities was not statistically significant.

	Planar imaging	SPECT	Planar imaging + SPECT
True positive	19	23	23
True negative	43	38	36
False positive	7	12	14
False negative	16	12	12

**Table 5** Scintimammographic results (axillary lymph node involvement; n=85).

	Planar imaging	SPECT	P	Planar imaging + SPECT
Sensitivity	54% (19/35)	66% (23/35)	NS	66% (23/35)
Specificity	89% (43/50)	76% (38/50)	NS	72% (36/50)
PPC*	73% (19/26)	66% (23/35)	NS	62% (23/37)
NPC†	73% (43/59)	76% (38/50)	NS	75% (36/48)
Accuracy	73% (62/85)	72% (61/85)	NS	69% (59/85)

\*positive predictive value, † negative predictive value

**Table 6** Statistical analysis of the results of planar and SPECT imaging and combined planar and SPECT imaging (axillary lymph node involvement; N=85).

Planar imaging missed 15 malignant lesions while SPECT failed to identify only seven. SPECT changed 8 false negative findings into true positive. The size of 8 undetected lesions by planar imaging ranged between 10 and 25 mm in greatest diameter. Planar imaging did not delineate any uptake of MIBI in 4 of these 8 cases with malignant lesions (2 infiltrating ductal carcinoma, 1 medullary carcinoma and 1 malignant lymphoma). In 3 patients with infiltrating ductal carcinoma, diffuse uptake of MIBI was classified as normal in planar imaging. In one patient, planar imaging was unable to detect the malignant lesion (infiltrating lobular carcinoma of size 23 mm) which was localized close to the chest wall; absence of the focal MIBI uptake was probably caused by superimposition of background activity. Four of the 8 false positive images were localized in internal lower quadrants of the breast. All these 8 patients had clear focal uptake of MIBI on the SPECT images enabling the visualization in different slice orientations.

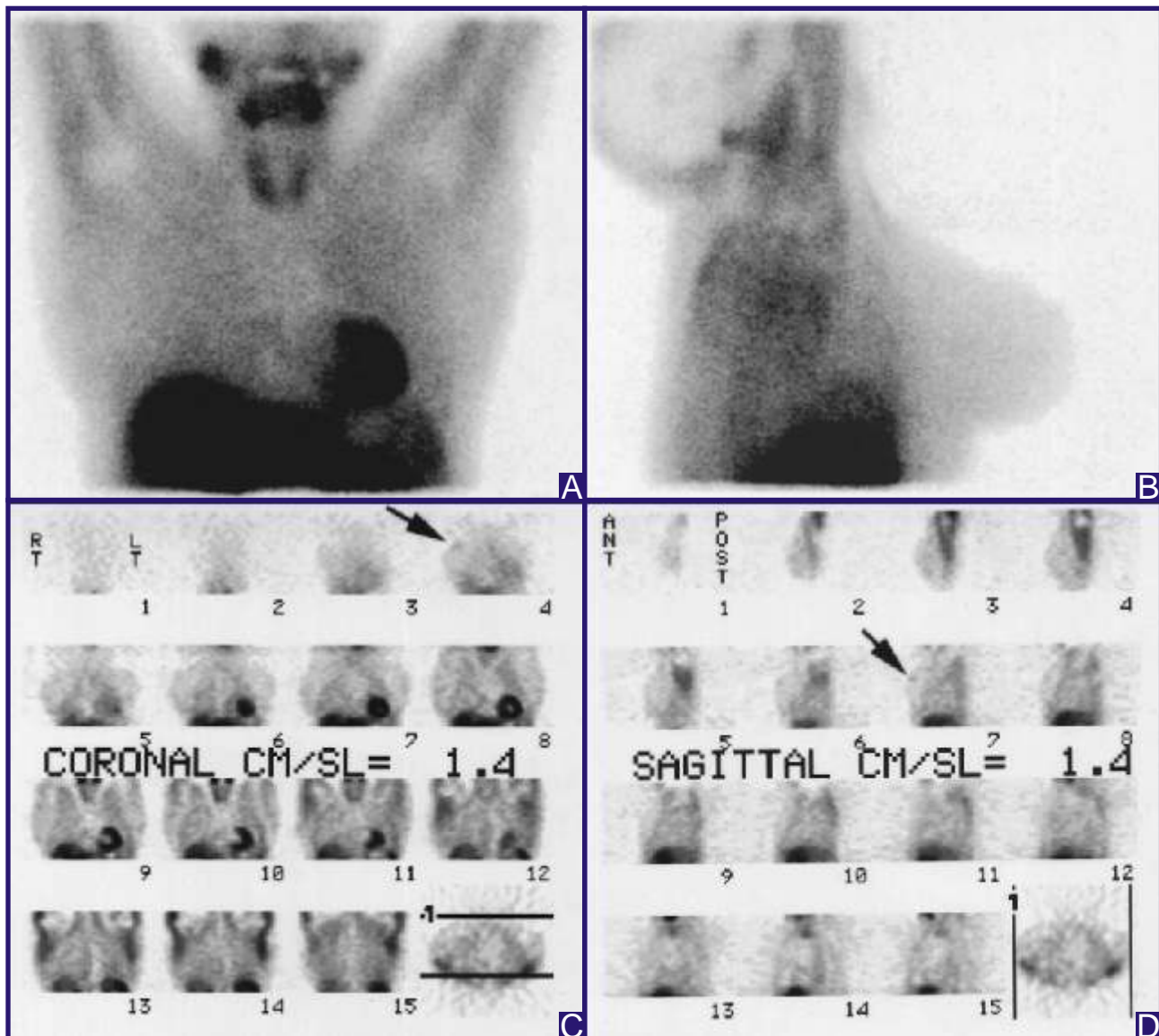
Twenty-one benign breast lesions showed the focal uptake of MIBI on planar imaging while only 19 showed uptake on SPECT. However, specificity of SPECT was the same as that of planar SMM in detecting primary breast lesions. Similar specificity of SPECT and planar imaging has been reported by Palmedo et al. (2) and Aziz et al. (22).

A few other studies compared planar and SPECT Tc-99m MIBI imaging for the detection of primary breast cancer with conflicting results. Some authors found that SPECT could not improve the diagnostic accuracy of planar scintimammography (2, 21) while data of others suggested SPECT imaging being more sensitive (11, 19, 20, 22, 23, 25).

In the present study we found SPECT to be useful in determining the extent of tumors and in localizing them precisely in some patients. We also observed that the interpretation of SPECT scans was easier in some cases in

comparison to planar images alone. According to Tiling et al SPECT was useful only in cases of indeterminate and positive planar scintimammography. But according to the authors, if planar SMM was negative, the routine use of SPECT was questionable (19). In our study, however, a relatively large number of lesions (8 of 85) would have been missed without performing SPECT. Further, a study by Aziz et al suggested that SPECT would be useful in ruling out malignancy if there is no uptake seen in the breast on planar images (22). Another study by Spanu et al recommend SPECT for its use more extensively in the management of breast cancer patients (11). Our experience further supports wider use of SPECT in conjunction with planar scintimammography, since the combination of the two modalities improves the diagnostic yield, particularly of tumours localized deep inside the breast tissue and especially in the internal quadrants.

Axillary lymph node metastases were detected in 19 out of 35 patients using planar SMM and in 23 of 35 patients with SPECT (sensitivity 66% for SPECT and only 54% for planar imaging). False-positive interpretations occurred in 7 patients with planar SMM and in 12 patients using SPECT (specificity 86% for planar imaging and 76% for SPECT). Differences between sensitivity and specificity of planar imaging and SPECT were not statistically significant. Results of Schillaci et al. (20, 25) have shown SPECT to be more sensitive than planar imaging, especially in detecting axillary lymph node involvement. Spanu et al have reported an overall sensitivity of SPECT and planar imaging in the detection of axillary lymph node metastasis to be 93% and 52.3%, respectively (11). They also have demonstrated that SPECT has a particularly important role in the detection of metastasis in axilla with involvement of 3 non-palpable lymph nodes. In our study SPECT demonstrated better resolution of abnormalities. But overall the sensitivity of SPECT and planar studies were quite low in detecting



**Figure 1** Patient with a proven non-palpable 11 mm infiltrating ductal carcinoma in the upper external quadrant of the right breast. Planar scintimammography does not show any site of abnormal Tc-99m MIBI uptake in both anterior (A) and right lateral prone (B) views. SPECT imaging shows a focal area of increased uptake corresponding to the carcinoma in both coronal (C) and sagittal (D) slices (arrows).

axillary lymph node metastases.

In conclusion, our results demonstrated the sensitivity of SPECT to be slightly higher than that of planar imaging, especially in detecting malignant breast lesions. SPECT provides information additional to planar imaging as to the localization of the MIBI uptake and tumor extension and improves diagnostic certainty. On the basis of our experience, we recommend wider use of SPECT imaging in conjunction with planar studies in the diagnosis of breast cancer.

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