somatostatin receptor densities who might benefit from treatment with a somatostatin analog. It is necessary to obtain early (0.5-hr) as well as late (24-hr) scintigrams. Early scintigraphy is important because, at that time, no increased uptake is seen in patients without breast tumors, but it is always seen in the breast tumor patients. Late scintigraphy is most important for selecting patients who might benefit from treatment with somatostatin analogs. Because bilaterally increased uptake is seen in some patients with unilateral disease, scintigraphy is probably of limited value to stage uni/bilateral disease.

REFERENCES

1. Krenning EP, Bakker WH, Breeman et al. Somatostatin receptor scintigraphy with (^{111}In-DTPA-d-Phe)- and (^{123}I-Thy)-pentetreotide: the Rotterdam experience with more than 1000 patients. *Eur J Nucl Med* 1993;20:716-731.
2. Lamberts SWJ, Krenning EP, Reubi J-C. The role of somatostatin and its analogs in the diagnosis and treatment of tumors. *Endocrinol Rev* 1991;12:450-482.
3. Lamberts SWJ, Reubi J-C. Krenning EP. Somatostatin receptor imaging in the diagnosis and treatment of neuroendocrine tumors. *J Steroid Biochem Molec Biol* 1992;43:185-188.
4. Reubi JC, Waser B, Foekens JA, et al. Somatostatin receptor incidence and distribution in breast cancer using receptor autoradiography: relationship to EGF receptors. *Int J Cancer* 1990;46:416-420.
5. Reubi JC, Laissue J, Krenning E, Lamberts SWJ. Somatostatin receptors in human cancer: incidence, characteristics, functional correlates and clinical implications. *J Steroid Biochem Molec Biol* 1992;43:27-35.
6. Reubi JC, Waser B, van Hagen M, et al. In vitro and in vivo detection of somatostatin receptors in human malignant lymphomas. *Int J Cancer* 1992;50:895-900.
7. Nesland, JM, Holm R, Johannessen JV, Gould VE. Neuroendocrine differentiation in breast lesions. *Path Res Pract* 1988;183:214-221.
8. Papotti M, Macri L, Bussolati G, Reubi JC. Correlative study on neuroendocrine differentiation and presence of somatostatin receptors in breast carcinomas. *Int J Cancer* 1989;43:365-369.
9. van Eijck CHJ, Krenning EP, Bootsma A, et al. Somatostatin-receptor scintigraphy in primary breast cancer. *Lancet* 1994;343:640-643.
10. Foekens JA, Portengen H, van Putten WLJ, et al. Prognostic value of receptors for insulin-like growth factor 1, somatostatin and epidermal growth factor in human breast cancer. *Cancer Res* 1989;49:7002-7009.
11. Bajc M, Palmer J, Ohlsson T, Edenbrandt L. Distribution and dosimetry of ^{111}In DTPA-D-Phe-Octreotide in man assessed by whole-body scintigraphy. *Acta Radiol* 1994;35:53-57.
12. Bajc M, Ingvar C, Persson B, et al. Dynamic octreotide scintigraphy in neuroendocrine tumours. *Acta Radiol* 1995;36:474-477.
13. Weber C, Merriam L, Koschitzky T, et al. Inhibition growth of human breast carcinomas in vivo by somatostatin analogue SMS 201-995: treatment of nude mouse xenografts. *Surgery* 1989;106:416-422.
14. Sepeshazy K, Milovanovic S, Lapis K, et al. Growth inhibition of estrogen independent MXT mouse mammary carcinomas in mice treated with an agonist or antagonist of LH-RH, an analogue of somatostatin, or a combination. *Breast Cancer Res Treat* 1992;21:181-192.

Technetium-99m-MIBI Scintimammography for Suspicious Breast Lesions

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The aim of this study was to evaluate the diagnostic accuracy of scintimammography with ^{99m}Tc-MIBI in patients with suspected primary breast cancer as monitored by SPECT or planar imaging. **Methods:** Patients with a suspect lesion detected by palpation or mammography were entered in the study. Excisional biopsy was performed on all patients and a mammography was performed within three weeks prior to scintigraphy. All patients received intravenously 740 MBq ^{99m}Tc-MIBI in the arm, contralateral to the suspicious breast, and were subsequently examined in a prone position. At 5–10 min postinjection, planar images were obtained in both the lateral and anterior views with an acquisition time of 10 min. After planar imaging, SPECT imaging was performed using a two-head high-resolution gamma camera. **Results:** In the total patient group of 54 patients, 40 lesions were palpable and 14 were nonpalpable but were detected by mammography. Breast cancer was confirmed in 24 of the patients and 20 of the palpable masses were found to be carcinomas. The tumor size ranged from 6 to 90 mm in diameter. In scintigraphic studies, the overall sensitivity was 88% for planar imaging and 83% for SPECT. Specificity was 83% and 80%, respectively. Sensitivity for palpable lesions was 100%. The smallest detectable tumor measured was 9 mm in diameter and could only be visualized in the planar scintigram. **Conclusion:** Scintigraphy with ^{99m}Tc-MIBI is extremely sensitive for the detection of primary breast cancer in patients with a palpable mass. SPECT, however, did not improve the diagnostic accuracy over planar scintimammography.

Key Words: breast cancer; scintimammography; technetium-99m-MIBI

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Breast cancer is the leading cause of cancer-related death in women throughout developed countries (*1*). Statistically, one of nine women will suffer from breast cancer during her life. Patients who have cancer and have it detected at an early stage will have a better survival rate (*2*).

Besides the physical examination, the most widely tool for primary breast cancer is mammography, which has high diagnostic value in detecting breast lesions (*3*). In older women with an involution of the breast, small lesions, a few millimeters in size, can be detected. Additionally, occult carcinomas can be detected by monitoring microcalcifications in the tumor (*4*). Nevertheless, mammography has a low positive predictive value for breast cancer (*5,6*). Thus, breast cancer can be confirmed in only about one-third of the patients undergoing excisional biopsy. Sensitivity of mammography in patients with dense breasts can be low (*7–9*), and in patients with fibrocystic changes of the breast, mammographical diagnosis of cancer can be difficult. In some of these cases, it is not possible to diagnose breast cancer solely by the means of mammography (*7*).

Although ^{201}Tl-chloride is useful to diagnose breast cancer in patients with a suspicious breast mass (*10,11*), in comparison to ^{99m}Tc, the gamma emission characteristics of ^{201}Tl are less favorable and patient's absorbed doses are higher. Therefore, a ^{99m}Tc-labeled tracer would be advantageous. Recently, it has been observed that ^{99m}Tc-MIBI accumulates in various kinds of tumors (*12–22*). For suspect tumors of the breast, some studies demonstrated that scintigraphy with ^{99m}Tc-MIBI differentiated benign from malignant lesions (*23–25*). In current studies, the sensitivity of ^{99m}Tc-MIBI to detect primary breast cancer in patients with a palpable breast mass ranged from 84% to 100%; the specificity ranged from 72% to 100% (*24–29*). For breast tumors smaller than 10 mm and for the detection of axillary lymph node metastases, ^{99m}Tc-MIBI scintigraphy seems to be less sensitive (*27*). All of the forementioned studies used planar imaging techniques.

The aim of this study was to evaluate the diagnostic accuracy of ^{99m}Tc-MIBI in both primary breast cancer and lymph node metastases using SPECT detection in comparison to planar imaging.

MATERIALS AND METHODS

A total of 54 women with suspicious lesions detected by physical examination or mammography were entered in the prospective study. Excisional biopsy was performed within 3 wk after ^{99m}Tc-MIBI scintigraphy. Patients who had fine-needle biopsy for cytological examination within 7 days prior to scintimammography were excluded from the study. The mean age of the patients was 55 yr (range of 22–81 yr).

Radiolabeling and quality control procedures for MIBI were performed according to the manufacturer's instruction. Each patient received an intravenous injection in the arm on the contralateral side of the breast lesion. Before and after the ^{99m}Tc-MIBI injection a "cold" injection, with saline solution, ensured that no extravasation was possible. When both breasts had lesions, the injection was given in a dorsalis pedis vein.

For all study patients, planar tumor imaging and SPECT imaging were performed. Planar imaging began 5–10 min after the injection of 740 MBq ^{99m}Tc-MIBI. Planar images were obtained with a 256 × 256 matrix for an acquisition time of 10 min in both the lateral and anterior views. At 20–30 min postinjection, SPECT was initiated using a two-head high-resolution gamma camera with a 64 × 64 matrix, a 180° rotation, a 6° step-and-shoot technique and an acquisition time of 30 sec per frame.

During the imaging procedure, a patient was examined in the prone position on a special table with the breasts freely pendent. For the lateral view in planar imaging, a layer of lead was interposed between the breasts to avoid artifacts from the contralateral side. Planar and SPECT images were interpreted separately and blindly by two well-trained nuclear medicine physicians. The scintigrams were classified as normal or abnormal. Focal tracer accumulation in the breast was the criterion for an abnormal scintigram. Interobserver variability was low and the scintigraphic classifications of the two physicians were identical except in one case. In that instance, a third nuclear medicine physician decided the scintigram classification.

RESULTS

In 24 patients, an adenocarcinoma could be confirmed by histopathology (Table 1). Scintigraphy with ^{99m}Tc-MIBI was able to correctly locate 21 of the cancers in these patients. Overall sensitivity in the detection of primary breast cancer was 88% for planar imaging and 83% for SPECT, and the overall specificity was 83% and 80%, respectively (Table 2). In the total patient group, there were 40 palpable and 14 nonpalpable lesions. With ^{99m}Tc-MIBI, the sensitivity was 100% for palpable breast masses and 25% for nonpalpable lesions; the specificity was 80% and 90%, respectively. Three tumors generated false-negative results and had a maximal diameter of 10, 8 and 6 mm. In these three patients, the planar and SPECT images were completely normal. The smallest tumor detected was 9 mm (Fig. 1) and could not be visualized by SPECT (Table 3). In one patient with false-negative scans, mammography was normal and MRI revealed a lesion 4 mm in diameter that did not fulfill the criteria for malignancy. False-positive results were found in five patients, two of whom had fibroadenomas (focal uptake of low intensity), two had local inflammation and one had an inflammed axillary lymph node. Planar imaging as well as SPECT generated false-positive results in these five patients. In addition to these concordant cases, SPECT generated one more false-positive scintigram in a patient with fibrocystic disease (Table 5). Fibrocystic disease of the breast was found in 35 patients, 17 of whom showed a proliferative type of fibrocystic alteration. No patient with fibrocystic tissue demonstrated focal accumulation on planar images.

TABLE 1
Malignant Tumors

Patient no.	Pathology	Exam (cm)	Scintimammography: Planar Breast/Axilla	Scintimammography: SPECT Breast/Axilla
1	pT1b N0, 0.6 cm	rt nonpal	n/n	n/n
2	pT1b N0, 0.8 cm	rt nonpal	n/n	n/n
3	pT1b N0, 0.9 cm	lt nonpal	p/n	n/n
4	pT1b N0, 1 cm	rt nonpal	n/n	n/n
5	pT1c N0, 1.2 cm	rt, 1×1	p/n	p/n
6	pT1c N0, 1.5 cm	lt, 1.5×1.5	p/n	p/n
7	pT1c N0, 1.5 cm	rt, 1.5×2	p/n	p/n
8	pT1c N0, 1.9 cm	lt, 1.5×2	p/n	p/n
9	pT1c N1, 1.8+1.5 cm	lt, 3×3	p/n	p/n
10	pT2 N0, 3 cm	rt, 2×2	p/n	p/n
11	pT2 N0, 3.5 cm	lt, 3×4	p/n	p/p
12	pT2 N0, 3 cm	lt, 2×2	p/n	p/n
13	pT2 N0, 4 cm	rt, 3×5	p/n	p/n
14	pT2 N1, 3.4 cm	rt, 2×3	p/p	p/p
15	pT2 N1a, 4 cm	lt, 6×5	p/n	p/n
16	pT4 N0, 6 cm	rt, 7×9	p/n	p/n
17	pT4 N1, 5 cm	lt, 5×5	p/p	p/p
18	pT4 N1b, 4.5 cm	rt, 5×5	p/p	p/p
19	pT4 N1b, 5 cm	rt, 5×6	p/p	p/p
20	pT4 N1b, 5 cm	lt, 5×7	p/p	p/p
21	pT4 N1b, 6 cm	rt, 7×7	p/p	p/p
22	pT4b N2, 5 cm	rt, 5×4	p/p	p/p
23	pT4b N2, 5 cm	lt, 5×6	p/p	p/p
24	r+1 pT4 N1a, 4+5 cm	rt, 3×3	p/p	p/p
		lt 4×5	p/p	p/p

rt = right breast; lt = left breast; nonpal = nonpalpable; p = positive scintigram; n = negative scintigram.

In the three patients with mammographically dense breasts (grade 4) and an equivocal mammogram, scintimammography demonstrated focal uptake corresponding to a carcinoma (Table 1; Patients 14, 20). From 38 lesions assessed as "probably malignant" by mammography, scintimammography had a true-negative scan in 15 patients (Table 6).

In 11 patients with axillary lymph node metastases (Table 1), planar and SPECT imaging demonstrated a positive scintigram in 9 patients. Supposing that the focal axillary accumulation corresponds to lymph node metastases, this would result in a sensitivity of 82% for the detection of axillary lymph node metastases (Table 4). All patients with no histological evidence of axillary lymph node metastases had negative planar images. Two patients had false-positive axillary SPECT images. Taking into account only those patients with positive breast scintigrams, planar and SPECT imaging had, respectively, a specificity of 100% and 94% for lymph node metastases. In four patients, SPECT depicted two areas of focal tracer accumulation, which correlated histopathologically to lymph node metastases, whereas planar images presented only a single focus of increased activity (Fig. 2).

In three patients, SPECT of the neck and chest revealed multiple, disseminated metastases. Scintigraphy with ^{99m}Tc-

TABLE 2
Benign Lesions

Patient no.	Pathology	Exam (cm)	Scintimammography Planar Breast/Axilla	SPECT Breast/Axilla
1	FA 0.7 cm, fi.ti.	rt nonpal	n/n	n/n
2	FA 1.2 cm, fi.ti.	rt nonpal	n/n	n/n
3	FA 1.3 cm	lt, 1×1	n/n	n/n
4	FA 1.5 cm	lt, 1.5×1.5	n/n	n/n
5	FA 1.5 cm	rt, 1×1.5	p/n	p/n
6	FA 2.7 cm, fi.ti.	rt, 2×3	p/n	p/n
7	FA 3.5 cm, fi.ti.	rt, 1.5×2	n/n	n/p
8	FA 1.1 cm	lt, 1×1	n/n	n/n
9	FA 1.5 cm	rt, 1.5	n/n	n/n
10	FA 2×3 cm, fi.ti.	lt+rt, 2×3	n/n	n/n
11	Fibrocystic tissue	rt, 1.5×2	n/n	n/n
12	Fibrocystic tissue	lt, 1.5×2	n/n	n/n
13	Fibrocystic tissue	lt, 4×4	n/n	n/n
14	Fibrocystic tissue	rt, nonpal	n/n	n/n
15	Fibrocystic tissue	lt, 1.5×2	n/n	n/n
16	Fibrocystic tissue	rt, nonpal	n/n	p/n
17	Fibrocystic tissue	lt, nonpal	n/n	n/n
18	Fibrocystic tissue	lt, nonpal	n/n	n/n
19	Fibrocystic tissue	lt, nonpal	n/n	n/n
20	Fibrocystic tissue	lt, 1×1.5	n/n	n/n
21	Fibrocystic tissue	lt, 1×1.5	n/n	n/n
22	Fibrocystic tissue	lt, 1×1.5	n/n	n/n
23	Fibrocystic tissue	rt, 1.5×2	n/n	n/n
24	Fibrocystic tissue	lt, nonpal	n/n	n/n
25	Fibrocystic tissue	rt, 1.5×2	n/n	n/n
26	Fibrocystic tissue	lt, nonpal	n/n	n/n
27	Inflam. LN	rt, nonpal	n/p	n/p
28	Inflammatory cyst	lt, 3×4	n/n	n/n
29	Local inflammation	r 2×3	p/n	p/n
30	Local inflammation	lt, 3×2	p/n	p/n

fi.ti. = fibrocystic tissue of the breast; FA = fibroadenoma; rt = right breast; lt = left breast; nonpal = nonpalpable; p = positive scintigram; n = negative scintigram; LN = lymph node; inflam. = inflamed.

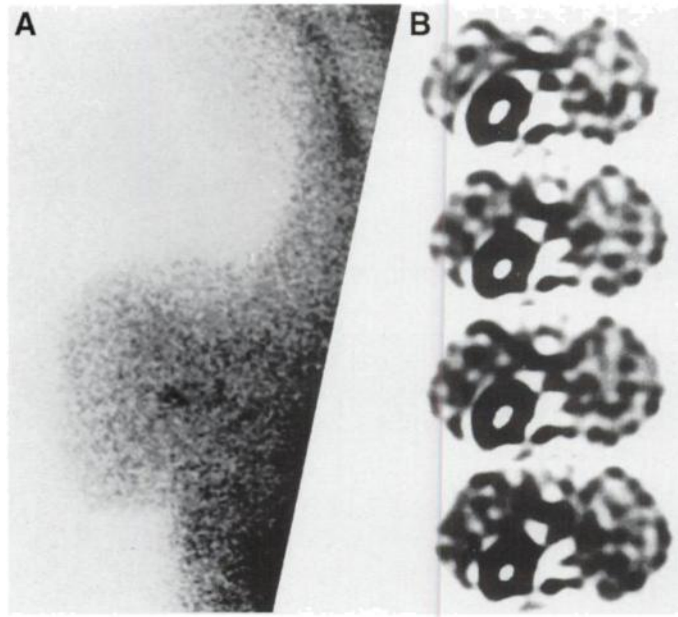

FIGURE 1. Planar scintigram with ^{99m}Tc-MIBI from left lateral view (A) and SPECT transverse slices (B). This patient had an adenocarcinoma of the left breast measuring 8 × 9 mm. Planar scintigraphy (A) showed focal tracer uptake in the center of the left breast and correlated with a lesion found by MRI in an unrelated study. This, the smallest detectable tumor found in the current study, could not be detected by SPECT imaging (B). The patient was imaged in prone position.

MIBI confirmed pulmonary metastases in one patient and a spine-infiltrating metastasis of a thoracic vertebra in another patient. The metastasis of the vertebra caused a paraplegia of the patient and was proven histopathologically during surgery of the spine. Both imaging techniques correctly diagnosed a metastasis of the orbita in another patient. All three patients had undergone mastectomy because of breast cancer 1–2 yr previous and were examined for suspicious lesions in the remaining breast.

DISCUSSION

In our study, SPECT could not increase the diagnostic accuracy of ^{99m}Tc-MIBI for the detection of primary breast cancer (although it was useful to ensure diagnosis in one patient with a noninvasive intraductal adenocarcinoma with low focal tracer uptake). In some patients, however, SPECT was useful in determining the extent of the tumor and in precisely localizing the lesion. Khalkhali et al. (*25,26*) proposed planar imaging techniques as the optimal procedure because of the absence of landmarks for tumor localization during SPECT. Our experience, however, is that interpretation of SPECT images is sometimes easier in comparison to planar images alone. In some patients, for example, localization of a hot spot in planar images is difficult because heart activity renders it impossible to correlate tracer accumulation of the lateral view image to that found in the anterior view image. In patients with high tracer uptake, three-dimensional images, which can be generated by SPECT, provide favorable tumor localization. One possible explanation for the better diagnostic accuracy of planar imaging in comparison to SPECT could be that the breasts can be examined close to the camera due to their peripheral localization. Another point is that SPECT is less effective if count statistics are low and if an organ with high activity, such as the heart, is situated in the reconstruction volume.

The smallest detectable tumor in our study had a maximal diameter of 9 mm. Our results are similar to those reported by other investigators who were able to detect tumors of 10 mm by planar imaging (*28,29*). The three tumors that had false-negative results were 10, 8 and 6 mm and, thus, are near or below the lower practical limit of detection. We observed a higher sensitivity of scintimammography in palpable breast masses than in nonpalpable nodules of the breast. Waxman et al. reported (*27*) a sensitivity of only 50% in the detection of primary breast cancer in six patients with nonpalpable nodules. Sensitivity of scintimammography seems to depend on tumor size, but further studies on patients with small, nonpalpable tumors are necessary. One potential reason for the false-negative scintigrams in three of our patients could be the low grade differentiation of these three carcinomas.

In our study, the sensitivity for the detection of primary

TABLE 3
Primary Breast Cancer Detected Using Technetium-99m-MIBI with Planar or SPECT Imaging*

	Tumor size by histopathology <1 cm	1.0–1.5 cm	>1.5 cm
Total number of cancer	3	4	18
Positive planar results	1	3	18
Positive SPECT results	0	3	18

*Detections were related to the tumor size.

TABLE 4
Detection of Axillary Lymph Node Metastases (LNM) by Technetium-99m-MIBI with Planar or SPECT Imaging

	LNM-positive		
	<3 LNM	>3 LNM	LNM-negative
Total number	2	9	13
Positive planar results	0	9	0
Positive SPECT results	0	9	1

breast cancer was 88%, specificity was 83%, the positive predictive value was 81% and the negative predictive value 89%. Kao et al. (*24*) found a similar sensitivity of 84% but reported a specificity of 100%. In the Kao et al. study (*24*), the six patients with benign breast tumors had fibrocystic disease. In the present study, there was no patient with fibrocystic changes in breast tissue who had a positive ^{99m}Tc-MIBI scintigram. Thus, the lower specificity in our group results from patients with fibroadenoma and inflammatory processes. Other authors also have reported that fibroadenomas can show significant uptake, thereby resulting in false-positive scintigrams and lower specificity (*25,26,28*). The two patients in our study with fibroadenomas and false-positive scintigrams had juvenile fibroadenoma, which is characterized by a high mitotic activity and may have caused the significant ^{99m}Tc-MIBI uptake. In two other study patients, chronified, local inflammation of the breast demonstrated positive scans. Histopathology showed high cellular concentration in these areas. This might provide another explanation for the focal tracer uptake in addition to a potential increased perfusion. Khalkhali et al. (*25*) reported a sensitivity of 94% for scintimammography with ^{99m}Tc-MIBI. Our results agree with those of Waxman et al. (*27*), in that ^{99m}Tc-MIBI scintigraphy had a sensitivity of 100% in detecting palpable breast masses. Scopinaro et al. (*30*) reported that only patients with lymph node metastases had positive breast scintigrams (*30*). The imaging technique used in that study, however, consisted only of anterior view images, and the count acquisition (10^6 counts) was not adequate for diagnostic accuracy. With a field of view including half of the liver, one million counts refer to an acquisition time of approximately 1–2 min. Additionally, heart activity renders it sometimes impossible to diagnose breast cancer in the anterior view, which demonstrates the necessity to perform lateral or SPECT images. Furthermore, the patients were examined in the supine, not prone, position, which may be another reason for the poor diagnostic results.

Kao et al. (*24*) investigated 32 patients with breast cancer and observed a 70 × 40 × 30-mm carcinoma that had no significant tracer accumulation. They concluded that sensitivity does not depend on lesion size. In our study, we did not find a tumor larger than 10 mm without significant ^{99m}Tc-MIBI uptake. In a patient, however, with a 40 × 35-mm noninvasive intraductal adenocarcinoma, focal uptake was of low intensity compared to other true-positive scintigrams. This is similar to a finding presented by Khalkhali et al. (*25*) who also observed low tracer uptake for a tumor with noninvasive components. Scopinaro et al. (*30*) correlated ^{99m}Tc-MIBI uptake with the amount of microvessels as a marker of angiogenesis. They found a high correlation between tracer uptake and breast cancer invasiveness, which may possibly explain the low uptake of noninvasive, intraductal carcinomas. One mechanism of ^{99m}Tc-MIBI cellular uptake could be blood flow-dependent extraction. This would explain that inflammatory processes can result in false-positive scans as seen in three of our patients (two patients with a local inflammation, one with inflammatory disease of the axillary lymph nodes). Another possible mechanism for MIBI uptake is intracellular transport by a membrane protein and accumulation in active mitochondria (*31*).

TABLE 5
Positive Scintigrams of Planar and SPECT Imaging in Benign Breast Lesions

	Fibroadenoma	Fibrocystic tissue		Inflammation
		Proliferative	Other	
Total number	10	8	8	4
Size range	0.7–3.5 cm	1–4 cm	0.9–2.5 cm	1–4 cm
Planar	2	0	0	3
SPECT	2	1	0	3

TABLE 6
Comparison of Mammographic and Scintimammographic Findings

	Mammography	
	Indeterminate	Probably malignant
Total number	16	38
True-positive SMM	3	18
True-negative SMM	10	15

SMM = scintimammography

For the detection of axillary lymph node metastases, sensitivity with ^{99m}Tc-MIBI scintigraphy was identical for planar and SPECT imaging. In four patients, however, SPECT demonstrated better resolution in areas of focal tracer accumulation. SPECT's specificity was lower compared to planar imaging because of two patients who had false-positive axillary scintigrams. One problem is nonspecific axillary uptake probably due to muscular accumulation and paravascular infiltration despite tracer injection in the contralateral arm. Furthermore, it is not clear yet if positive uptake in the respected axillary region is indicative of metastatic disease or if it is the result of inflammatory nodes. Further studies must prove if positive axillary uptake can change a patient's therapeutic regimen. Axillary revision as a standard procedure could only be replaced by an imaging technique able to detect micrometastases.

CONCLUSION

SPECT cannot improve the diagnostic accuracy of planar scintimammography. We found that scintimammography with ^{99m}Tc-MIBI was extremely sensitive in differentiating malignant from benign palpable breast lesions. In patients with suspicious lesions that cannot be evaluated mammographically because of dense breast tissue, scintimammography should be performed.

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REFERENCES

1. Kelsey JL, Gammon MD. The epidemiology of breast cancer. *Cancer* 1991;41:146–165.
2. Habbema JDF, van Oortmarssen GV, van Putten DJ, Lubbe JT, van der Maas PJ. Age-specific reduction in breast cancer mortality by screen: an analysis of the results of Health Insurance Plan of greater New York study. *J Natl Cancer Inst* 1986;77:317–320.
3. Hall FM. Screening mammography-potential problems on the horizon. *N Engl J Med* 1986;314:53–55.
4. Pollei SR, Mettler FA, Bartow SA, Moradian G, Moskowitz M. Occult breast cancer: prevalence and radiographic detectability. *Radiology* 1987;163:459–462.
5. Hermann G, Janus C, Schwartz IS, Krivisky B, Bier S, Rabinowitz JG. Nonpalpable lesions: accuracy of prebiopsy mammographic diagnosis. *Radiology* 1987;165:323–326.

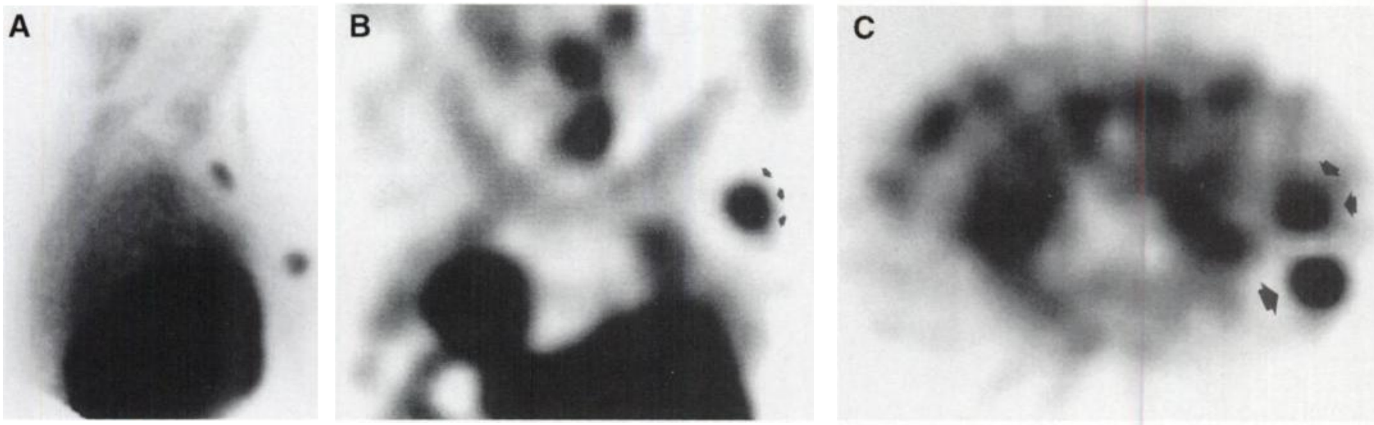

FIGURE 2. Planar scintigram with ^{99m}Tc-MIBI from right lateral view (A) and SPECT with (B) coronal and (C) transverse slices. Patient 1 with adenocarcinoma of the right breast and axillary lymph node metastases (arrows). Two focal axillary accumulations in the transverse slice (arrows) could not be resolved by planar imaging. The patient was imaged in the prone position.

6. Kopans DB. Positive predictive value of mammography. *AJR* 1992;158:521–526.
7. Mann BD, Giuliano AE, Bassett LW, et al. Delayed diagnosis of breast cancer as a result of normal mammograms. *Arch Surg* 1983;118:23–25.
8. Kalisher L. Factors influencing false negative rates in mammography. *Radiology* 1979;133:297–301.
9. Kopans DB. Conventional wisdom: observation, experience, anecdote and science in breast imaging. *AJR* 1994;162:299–303.
10. Lee V, Sax EJ, McAneny DB, et al. A complementary role for ^{201}Tl scintigraphy with mammography in the diagnosis of breast cancer. *J Nucl Med* 1993;34:2095–2100.
11. Waxman AD, Ramanna L, Memsic LD, et al. Thallium scintigraphy in the evaluation of mass abnormalities of the breast. *J Nucl Med* 1993;34:18–23.
12. Aktolun C, Bayhan H, Kir M. Clinical experience with ^{99m}Tc-MIBI imaging in patients with malignant tumors: preliminary results and comparison with ^{201}Tl. *Clin Nucl Med* 1992;17:171–176.
13. Aktolun C, Bayhan H, Pabuccu Y, Bilgic H, Acar H, Koylu R. Assessment of tumor necrosis and detection of mediastinal lymph node metastasis in bronchial carcinoma with ^{99m}Tc-sestamibi imaging: comparison with CT scan. *Eur J Nucl Med* 1994;21:973–979.
14. Caner B, Kitapci M, Aras T, Erbengi G, Ugur O, Bekdik C. Increased accumulation of sestamibi technetium in osteosarcoma and its metastatic lymph nodes. *J Nucl Med* 1991;32:1977–1978.
15. Briele B, Hotze A, Kropp J, et al. A comparison of ^{201}Tl and ^{99m}Tc-MIBI in the follow-up of the differentiated thyroid carcinomas. *Nuklearmedizin* 1991;30:115–124.
16. Caner B, Kitapci M, Erbengi G, Gogus T, Bekdik C. Increased accumulation of ^{99m}Tc-MIBI in undifferentiated mesenchymal tumor and its metastatic lung lesions. *Clin Nucl Med* 1992;17:144–145.
17. Scott AM, Kostakoglu L, O'Brien JP, Straus DJ, Abdel-Dayem HM, Larson SM. Comparison of ^{99m}Tc-MIBI and ^{201}Tl-Cl uptake in primary thyroid lymphoma. *J Nucl Med* 1992;33:1396–1398.
18. Caner B, Kitapci M, Unlu M, et al. Technetium-99m-MIBI uptake in benign and malignant bone lesions: a comparative study with ^{99m}Tc MDP. *J Nucl Med* 1992;33:319–324.
19. Biersack HJ, Briele B, Hotze AL, et al. The role of nuclear medicine in oncology. *Ann Nucl Med* 1992;6:131–136.
20. O'Tuama LA, Treves ST, Larar JN, et al. Thallium-201 versus ^{99m}Tc-MIBI SPECT in evaluation of childhood brain tumors: a within-subject comparison. *J Nucl Med* 1993;34:1045–1051.
21. Hassan IM, Sahweil A, Constantinides C, et al. Uptake and kinetics of ^{99m}Tc-sestamibi in benign and malignant lesions in the lungs. *Clin Nucl Med* 1989;14:333–340.
22. Müller SP, Paas M, Reiners C. ROC analysis of tumor identification using ^{201}Tl-Cl and ^{99m}Tc-sestamibi. *Nuklearmedizin* 1994;33:15–23.
23. Campeau RJ, Kronemer KA, Sutherland CM. Concordant uptake of ^{99m}Tc-sestamibi and ^{201}Tl in unsuspected breast tumor. *Clin Nucl Med* 1992;17:936–937.
24. Kao CH, Wang SJ, Liu TJ. The use of technetium-99m-methoxyisobutylisonitrile breast scintigraphy to evaluate palpable breast masses. *Eur J Nucl Med* 1994;21:432–436.
25. Khalkhali I, Ismael M, Diggles L. Review of imaging techniques for the diagnosis of breast cancer: a new role of prone scintimammography using technetium-99m-sestamibi. *Eur J Nucl Med* 1994;21:357–362.
26. Khalkhali I, Mena I, Jouanne E, et al. Prone scintimammography in patients with suspicion of breast cancer. *J Am Coll Surg* 1994;178:491–497.
27. Waxman A, Nagaraj N, Ashok G, et al. Sensitivity and specificity of ^{99m}Tc-MIBI in the evaluation of primary carcinoma of the breast: comparison of palpable and nonpalpable lesions with mammography [Abstract]. *J Nucl Med* 1994;35:78.
28. Lastoria S, Varrella P, Mainolfi C, et al. Technetium-99m-sestamibi scintigraphy in the diagnosis of primary breast cancer [Abstract]. *J Nucl Med* 1994;35:79.
29. Khalkhali I, Cutrone J, Mena I, et al. Clinical and pathologic follow-up of 100 patients with breast lesions studied with scintimammography [Abstract]. *J Nucl Med* 1994;35:80.
30. Scopinaro F, Schillaci O, Scarpini M, et al. Technetium-99m-MIBI as an indicator of breast cancer invasiveness. *Eur J Nucl Med* 1994;21:984–987.
31. Chiu ML, Kronauge JF, Piwnica-Worms D. Effect of mitochondrial and plasma membrane potentials on accumulation of hexakis 2-methoxyisobutylisonitrile technetium in cultured mouse fibroblasts. *J Nucl Med* 1990;31:1646–1653.