

Double-Phase ^{99m}Tc -Sestamibi Scintimammography and Trans-Scan in Diagnosing Breast Cancer

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The goal of our study was to assess the value of both scintimammography with ^{99m}Tc -sestamibi (SMM) and trans-scan (T-scan) in detecting breast cancer. **Methods:** A total of 121 women were evaluated by palpation, mammography, SMM and T-scan. SMM was performed in the prone, breast dependent position. Immediate and delayed views (double-phase) were obtained. T-scan is a new breast imaging method that maps noninvasively the distribution of tissue electrical impedance and capacitance. **Results:** SMM had 88.9% sensitivity, 88.4% specificity and 88.4% accuracy in detecting breast cancer. SMM had 100% sensitivity in detecting breast tumors >1 cm and only 66% sensitivity in detecting tumors <1 cm. T-scan had 72.2% sensitivity and 67% specificity in detecting breast cancer. It detected one more breast cancer than SMM, at the expense of 27 additional false-positive results. **Conclusion:** Double-phase SMM was sensitive and specific in detecting breast cancer. This method may reduce the rate of negative breast biopsies in tumors >1 cm. T-scan was only moderately accurate in detecting breast cancer. Its addition to SMM did not improve significantly the rate of breast cancer detection. However, because of its complete noninvasiveness, large-scale applicability and low cost, T-scan deserves further refining.

Key Words: ^{99m}Tc -sestamibi scintimammography; breast cancer; trans-scan

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Breast cancer is the second most common cancer after lung cancer, and 1 in 30 women will die of the disease (1). Excepting physical examination, mammography is the most widely used method for breast cancer detection. Small tumors, a few millimeters in size, or occult carcinomas associated with microcalcifications can be detected by mammography. However, mammography lacks specificity, and 75% of mammographic suspicious lesions are benign. Moreover, this method is not reliable in detecting tumors in dense breasts, with a false-negative rate of 25%–45% (2).

New imaging methods have been developed to reduce the

rate of false-negative breast biopsies without reducing the sensitivity of cancer detection. ^{201}Tl -scintimammography (3), MRI (4) and ^{99m}Tc -sestamibi scintimammography (SMM) (5–7) were found to be accurate in detecting breast cancer. It was found that SMM may reduce by 55% unnecessary biopsies in nonpalpable breast lesions (8). Also, SMM was sensitive (97%) in detecting lesions >1 cm and much less sensitive (50%) in detecting lesions <1 cm (9).

Trans-scan (T-scan) is a new breast-imaging method that maps noninvasively and in real time the local distribution of tissue electrical impedance at various frequencies, using a very low intensity electrical current applied through an electrode distant from the breast. Previous studies, using a prototype device called a Mammoscan (Transcan Research and Development Co. Ltd., Migdal Hoemek, Israel) (10), have shown the value of the method for early detection of breast cancer. In this study, a new generation device, the T-scan 2000 (Transcan Research and Development Co. Ltd.), was used.

The purpose of this study was to assess SMM and T-scan in evaluating patients with suspicious breast lesions and to compare these methods.

MATERIALS AND METHODS

Patients

A total of 121 women with breast lesions detected by physical examination or mammography were entered in this prospective study. Patients were evaluated in a breast clinic by an experienced surgeon and by an experienced radiologist during a 2-y period. All patients underwent SMM and T-scan. Seventy-nine palpable and 42 nonpalpable lesions were identified. All patients underwent excision biopsy or mastectomy within 1 mo of evaluation. In patients with nonpalpable lesions, needle localization was performed before biopsy. The mean age of the patients was 53 y (range 42–70 y).

Palpatory lesions suspected of malignancy were: irregular hard masses, nipple discharge with an underlying mass, masses with fixation to the pectoral muscle or to overlying skin or edema of overlying skin (*peau d'orange*).

^{99m}Tc -Sestamibi Scintimammography

Patients were injected with 20–25 mCi (740–925 MBq) ^{99m}Tc -sestamibi, according to body weight. The injection was given

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intravenously as a bolus in the arm on the opposite side of the known breast lesion to avoid false-positive uptake in the axillary lymph nodes. For patients with bilateral breast lesions, the radionuclide was given in a pedal vein. After the injection, the patients were positioned in the prone, breast dependent position as described by Khalkhali et al. (11).

Scintimammography was performed using a gamma camera with a parallel-hole, high-resolution collimator. The study consisted of two lateral breast images and an anterior view. Imaging started immediately after injection, and delayed views were obtained 90–120 min later. Between early and delayed phase imaging, patients rested in a quiet waiting room. One breast at a time was imaged, gathering left and right lateral views for a preset time of 10 min. The breast was positioned as close as possible to the camera. A third planar view was obtained in the anterior projection with the patient supine and the arms elevated above the head, including the tail of the breast.

Visual interpretation of tracer uptake was performed by two experienced nuclear medicine physicians, who were blinded to each other's results and to the clinical, mammographic and pathological findings. The intensity of focal tracer uptake, when present, was graded on a visual scale comparable to the corresponding region on the opposite breast. We found after performing more than 400 SMM studies that the double-phase SMM is more specific and has similar sensitivity to early-phase SMM. We used this technique during this study. The duration of double-phase SMM was 1.5–2 h, compared to 10–20 min for early-phase SMM. However, the increased specificity of double-phase SMM, compared to early-phase SMM, justified the longer duration of the study. Double-phase SMM scans were considered suspicious of malignancy when there was focal tracer uptake, which persisted on delayed images (Fig. 1). Scans were considered negative when there was no focal tracer uptake or when the focal uptake disappeared on delayed images.

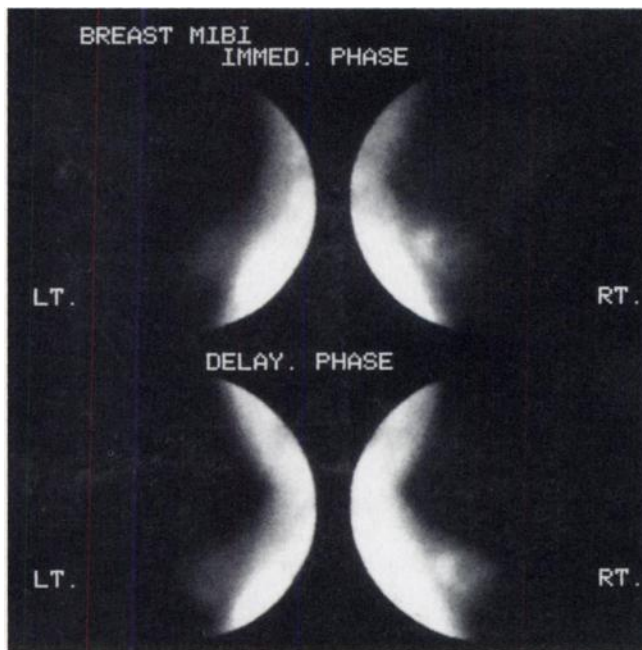


FIGURE 1. Breast scintimammography with ^{99m}Tc -sestamibi demonstrates 1.5-cm carcinoma of right breast. There is immediate focal tracer uptake (top right) that persists on delayed image (bottom right). Common scale is shown on right side.

Conventional Mammography

Mammography was performed in the craniocaudal and mediolateral projections. All mammograms were interpreted by the same experienced radiologist, with knowledge of patient history, physical examination and results of previous mammograms. Mammographic findings considered to represent a high risk of malignancy were mass lesions with irregular margins or clusters of microcalcifications. Mammographic lesions considered to have a low risk of malignancy were architectural distortions, duct dilatation or breast asymmetry.

T-Scan

The T-scan 2000 device has a small handheld probe similar to that used in ultrasonography and maps each breast into 9 sectors, 1 centered on the nipple and 8 surrounding it. The corresponding capacitance and conductivity images are simultaneously shown side by side for the 3×3 frontal image of each breast and for the individual sectors, using a gray scale set by an automatic algorithm. Patients are scanned in the supine position with the ipsilateral shoulder elevated by a pillow. The probe is firmly applied to the breast using a conductance gel.

An abnormal finding suspicious of malignancy was a discernible bright spot in addition to the two nipples, without a corresponding spot on the contralateral breast (Fig. 2). Contact artifacts were bright spots at the periphery of a sector or focal brightness symmetrical in both breasts due to proximity of cartilage, bone or pectoral muscle or associated with the inframammary ridge (Fig. 3).

RESULTS

Breast carcinoma was found in 18 of 121 patients (14.9%).

^{99m}Tc -Sestamibi Scintimammography

The results of SMM are detailed in Table 1. SMM detected 16 of 18 breast tumors (88.9%). Compared to the pathological results, SMM had an overall sensitivity of 88.9%, specificity of 88.3% and accuracy of 88.4% in detecting breast cancer. It had a 100% sensitivity for palpable lesions and a 75% sensitivity for nonpalpable lesions. SMM had a 100% sensitivity in detecting breast cancers >1 cm in diameter. However, the sensitivity dropped to 66% in detecting breast cancers <1 cm.

There was 100% agreement between the two observers regarding early-phase SMM interpretations. When analyzing the results of double-phase SMM, one observer recorded persistent focal tracer uptake on the delayed images in 1 case of fibroadenoma and in 1 patient with sclerosing adenosis. Actually, in these cases, tracer uptake diminished on delayed images but did not disappear. The second observer correctly interpreted these scans as negative. The results of double-phase SMM of all malignant breast tumors were interpreted similarly by the two observers, resulting in an overall agreement of 98%. However, we decided to present the data of the observer with the greater number of false-positive results.

There were 91 true-negative results, comprising cases of normal fibro-fatty tissue, fibrocystic disease, fibroadenomas and sclerosing adenosis. There were 12 false-positive cases, including 10 fibroadenomas and 2 cases of sclerosing

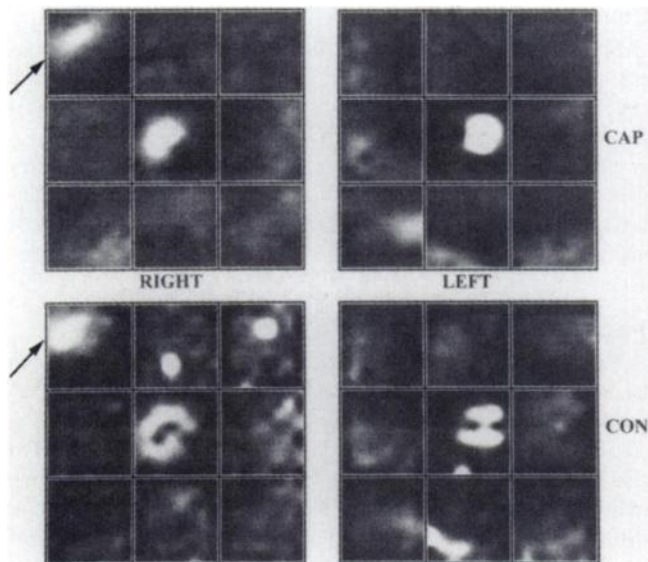


FIGURE 2. T-scan in patient with 2-cm carcinoma of upper lateral quadrant of right breast. Capacitance (CAP) and conductance (CON) images depict well-delimited asymmetrical bright spot in upper lateral sector of the right breast (arrows).

adenosis. All these lesions were >1.8 cm diameter. There were 16 breast cancers (10 palpable and 6 nonpalpable) detected by SMM, comprising 10 infiltrating duct carcinomas (IDC) (7 palpable and 3 nonpalpable), 3 nonpalpable duct carcinomas in situ (DCIS) and 3 palpable infiltrating lobular carcinomas (ILC). Only 4 of the 10 IDC were <1 cm, and 3 of these tumors were nonpalpable. SMM did not detect a nonpalpable 0.9-cm IDC or a nonpalpable 0.7-cm ILC.

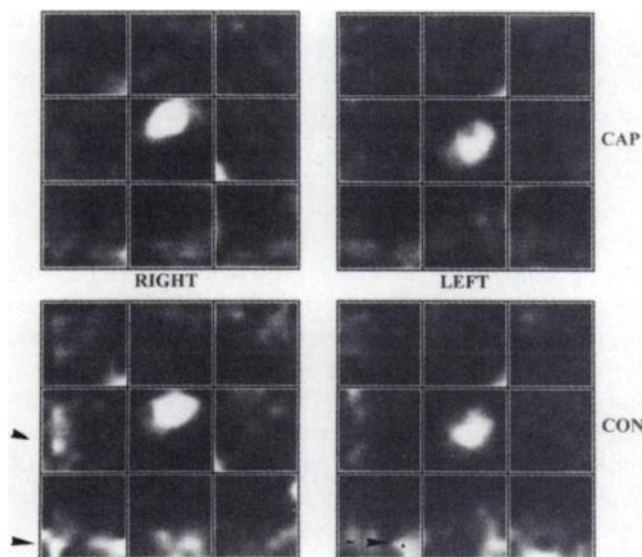


FIGURE 3. T-scan in healthy patient. Capacitance (CAP) and conductance (CON) images are considered normal. There are no asymmetric or well-delimited bright spots. Symmetric bright spots in central sectors represent the nipples. Bright spots at periphery of sectors are poorly delimited and are considered artifacts (arrowheads).

T-Scan

The results of T-scan are shown in Table 2. The overall sensitivity, specificity and accuracy of T-scan in diagnosing breast cancer was 72.2%, 67% and 67.8%, respectively. For palpable and nonpalpable lesions, there was an 80% and 63% sensitivity, respectively. T-scan had a low positive predictive value of 27.7%.

T-scan detected 13 of 18 breast tumors (Fig. 2). It did not detect 2 nonpalpable (0.7–0.9 cm) IDC, a palpable 1.5-cm IDC, a nonpalpable 0.7-cm ILC and a DCIS. There were 69 true-negative results. In 34 patients, T-scan was false-positive, and the pathological evaluation demonstrated normal fibro-fatty tissue, fibrocystic disease, fibroadenomas or sclerosing adenosis. Hypercellularity was found in most of these lesions.

The comparison between SMM and T-scan is shown in Table 3. SMM had a higher specificity than T-scan (88.3% versus 67%). Twenty-seven breast lesions were found to be true-negative by SMM and were falsely interpreted to be malignant by T-scan. These cases included 4 fibroadenomas (2–2.7 cm), 2 sclerosing adenosis lesions (1.7–2.2 cm), 8 cases of fibrocystic disease with marked hypercellularity and 13 fibroadenomas (1.5–2.4 cm) with hypercellularity. Five fibroadenomas (1.5–2.2 cm) were correctly interpreted by T-scan but were misinterpreted as malignant by SMM. Two of these lesions were hypercellular.

Also, the sensitivity of SMM was higher than that of T-scan (88.9% versus 72.2%). A nonpalpable 0.9-cm IDC was identified by T-scan and not by SMM, and another nonpalpable 0.7-cm ILC was missed by both tests. However, T-scan missed 4 of 16 (25%) tumors detected by SMM. These cases included 2 nonpalpable IDC (0.7–0.9 cm), a palpable 1.5-cm IDC and a DCIS.

DISCUSSION

SMM has been reported to be accurate in detecting breast cancer (5–7), with a reported sensitivity of 83%–93.7% and a specificity of 83%–100% (5,6,11–13). This test is not intended to replace physical examination or mammography, but it may reduce by up to 55% the rate of unnecessary breast biopsies in nonpalpable breast lesions (14). Mammography has a low specificity with a positive predictive value of 10%–35% for nonpalpable malignancy (14). Radionuclides such as ^{201}Tl (8), SMM, $^{99\text{m}}\text{Tc}$ -DMSA (15) and MRI (4) have been evaluated in breast cancer detection. These methods were found to be useful in the evaluation of breast lesions, but they were invasive, exposing patients to irradiation, additional expenses or both.

In our series, SMM had an 88.9% sensitivity, 88.3% specificity and 88.4% accuracy in detecting breast cancer. SMM had 100% sensitivity in detecting tumors >1 cm and 66% sensitivity in detecting smaller tumors.

Our results are comparable to those reported by Palmedo et al. (5), Villanueva-Meyer et al. (6), Khalkhali et al. (11), Taillefer et al. (12) and Kao et al. (13). These authors reported a sensitivity of 83%–93.7% and a specificity of

TABLE 1
Pathological and Double-Phase ^{99m}Tc-Sestamibi Scintimammography Findings

Results	No. of patients	Pathological diagnosis	No. of tumors (mean diameter in cm)		
			<1 cm	>1 and <1.5 cm	>1.5 cm
T-N (n = 91)	16	Normal			
	47	Fibrocystic disease			
	24	Fibroadenoma			24 (2.3)
	4	Sclerosing adenosis		2 (1.3)	2 (1.9)
T-P (n = 16)	10	Infiltrating ductal carcinoma	4 (0.9)	4 (1.2)	2 (2.2)
	3	Ductal carcinoma in situ*	na		
	3	Infiltrating lobular carcinoma			3 (2.4)
F-P (n = 12)	10	Fibroadenoma			10 (2.6)
	2	Sclerosing adenosis			2 (1.9)
F-N (n = 2)	1	Infiltrating ductal carcinoma	1 (0.9)		
	1	Infiltrating lobular carcinoma	1 (0.7)		

*These lesions do not represent a mass, and therefore their dimensions are not presented.

T-N = true-negative; T-P = true-positive; na = not assessed; F-P = false-positive; F-N = false-negative.

83%–100% in detecting breast cancer. The variation in sensitivity may result from different proportions of small tumors in these studies. The variation in specificity may result from different preponderance of hypercellular benign lesions or from inflammatory lesions, which can show significant radiotracer uptake and result in false-positive scintigrams (11).

The reason for performing early-phase (10 min) and delayed-phase (90–120 min) imaging was to differentiate better between benign and malignant lesions. We presumed that the tracer uptake of malignant tumors would be persistent on delayed phase in contrast to the uptake of benign lesions, which would fade away on delayed images. The results regarding double-phase SMM are contradictory. Lu et al. (16) found that delayed-phase imaging was not beneficial for

detecting breast cancer. However, data acquisition was performed in the sitting or standing positions and a higher background activity may have obscured small tumors. Abrus et al. (17), using a breast prone position, found that late-phase images were optimal in detecting breast tumors.

We used a new device, the T-scan 2000, and combined it with SMM, physical examination and conventional mammography to increase the accuracy of detecting breast cancer. All 121 patients were evaluated by each of these methods, and there was an overall sensitivity of 72.2% and specificity of 67% in detecting breast cancer. Seventy-nine of these tumors were palpable, and 42 were nonpalpable. Five carcinomas (0.7–1.5 cm) were not detected by T-scan. False-positive results were found in 37 cases, and a few of these may be technical artifacts, due to incomplete contact

TABLE 2
Pathological and T-Scan Findings

Results	No. of patients	Pathological diagnosis	No. of tumors (mean diameter in cm)		
			<1 cm	>1 and <1.5 cm	>1.5 cm
T-N (n = 69)	18	Normal			
	39	Fibrocystic disease			
	10	Fibroadenoma			10 (2.2)
	2	Sclerosing adenosis			2 (1.8)
T-P (n = 13)	8	Infiltrating ductal carcinoma	3 (0.8)	3 (1.3)	2 (1.9)
	2	Ductal carcinoma in situ*	na		
	3	Infiltrating lobular carcinoma			3 (2.3)
F-P (n = 34)	24	Fibroadenoma			24 (2.4)
	8	Fibrocystic disease	na		
	4	Sclerosing adenosis			4 (2.2)
F-N (n = 5)	3	Infiltrating ductal carcinoma	2 (0.8)	1 (1.5)	
	1	Infiltrating lobular carcinoma	1 (0.7)		
	1	Ductal carcinoma in situ*	na		

*These lesions do not represent a mass, and therefore their dimensions are not presented.

T-N = true-negative; T-P = true-positive; na = not assessed; F-P = false-positive; F-N = false-negative.

TABLE 3
Comparison of T-Scan and Double-Phase ^{99m}Tc-Sestamibi Scintimammography (SMM)

T-scan*	Double-phase SMM*				Total
	T-N	T-P	F-P	F-N	
T-N	64	0	5	0	69
T-P	0	12	0	1	13
F-P	27	0	7	0	34
F-N	0	4	0	1	5
Total	91	16	12	2	121

*The results of T-scan and SMM were compared to pathological findings.

T-N = true-negative; T-P = true-positive; F-P = false-positive; F-N = false-negative.

between the probe and the breast or from the presence of underlying cartilage, bone or pectoral muscle.

T-scan is based on different impedance characteristics of normal breast and tumor tissue (18). The impedance and its frequency dependence are related to tissue structure. When the structure is heterogeneous, as it may be in tumors, the impedance values are high because of the resulting network of capacitors and resistors. These elements are represented by cells of different sizes and orientations.

SMM had an 88.3% specificity in breast cancer detection compared to 67% for T-scan. However, there were 5 cases that were falsely interpreted as malignant by SMM and were correctly identified as benign by T-scan. These discrepancies may result from different tissue characteristics evaluated by these tests. Also, the sensitivity of SMM (88.9%) was higher than that of T-scan (72.2%). T-scan detected only one additional breast tumor than SMM, at the expense of 27 false-positive results. The accuracy of T-scan (67.8%) was significantly lower than that of SMM (89.4%), and the addition of T-scan to SMM did not increase the accuracy of the latter test. However, this method is in its initial stages of development, and refinement of the method may increase its accuracy. This test is rather simple, is completely noninvasive and is inexpensive when compared to the expense of performing a significant number of tests. The device is portable and has large-scale applicability. We are now evaluating an improved device for accuracy in breast cancer detection.

CONCLUSION

Double-phase SMM has a high sensitivity and specificity in detecting breast cancer. This procedure may reduce the number of negative biopsies of breast lesions >1 cm. T-scan is a new breast-imaging modality that has moderate sensitivity and specificity in detecting breast cancer but does not yield additional benefit when associated with SMM. This test is noninvasive and needs to be refined further.

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