Use of ^{99m}Tc-Furifosmin Scintigraphy—Planar and SPECT—to Evaluate Suggestive Palpable and Nonpalpable Breast Lesions

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Our objective was to evaluate the role of ^{99m}Tc-furifosmin scintigraphy—planar and SPECT—in discriminating benign from malignant breast disease. **Methods:** The trial was prospective, open, and diagnostic. We recruited 30 consecutive patients with 14 palpable and 16 nonpalpable breast lesions. After receiving informed consent, we injected 555–640 MBq ^{99m}Tc-furifosmin intravenously in the arm contralateral to the breast lesion. Planar imaging and SPECT were performed. All patients underwent excision of the tumor within 2 wk. Using histology as the gold standard, we calculated sensitivity, specificity, and positive and negative predictive values for ^{99m}Tc-furifosmin in planar and SPECT technique. **Results:** For 18 malignant and 12 benign breast lesions, a sensitivity of 50% for planar imaging and 72% for SPECT was seen. Specificity and positive and negative predictive values were 83%, 82%, and 53%, respectively, for planar imaging and 50%, 68%, and 55%, respectively, for SPECT. For the 14 palpable tumors (10 malignant, 4 benign), which averaged 17 ± 10 mm in size (size range, 4–45 mm), a sensitivity of 60% for planar imaging and 80% for SPECT was achieved. Sixteen lesions were not palpable (median size, 9 ± 3 mm [size range, 4–13 mm]). In this subgroup, ^{99m}Tc-furifosmin scintigraphy yielded a sensitivity of 37% for planar and 62% for SPECT technique ($P > 0.05$). **Conclusion:** ^{99m}Tc-furifosmin scintigraphy is not a potent competitor to established scintigraphic procedures. In comparing this tracer with ^{99m}Tc-sestamibi and ^{99m}Tc-tetrofosmin, we cannot recommend ^{99m}Tc-furifosmin for the diagnosis of breast cancer.

Key Words: ^{99m}Tc-furifosmin; breast cancer; scintimammography

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Early diagnosis of breast cancer is the ultimate goal in achieving favorable cure rates. Because the incidence of breast cancer is high and slightly rising (*1*), different diagnostic approaches have been tested for usefulness in the clinical setting. Mammography is the screening standard of choice, but sensitivity and specificity rates vary in different patient groups. In young female patients with dense breasts, mammography yields lower sensitivity rates, missing up to one third of cancer patients (*2*). In these patients, sonography, ^{99m}Tc-sestamibi scintigraphy, or, lately, ^{99m}Tc-tetrofosmin scintigraphy have been used to better diagnose malignant disease (*3,4*).

Furifosmin (*trans*-(1,2-bis(dihydro-2,2,5,5-tetramethyl-3(2H)-furano-4-methyleneamino)ethane)bis(Tris(3-methoxy-1-propyl)-phosphine)-technetium-(III)-99m) is a new diagnostic agent (*5*). It was proposed as a good tracer for oncologic imaging, similar in effectiveness to ^{99m}Tc-tetrofosmin, ^{99m}Tc-sestamibi, and ^{201}Tl-chloride, although with different myocardial kinetics (*6*). Many investigators agree that the technetium in technetium-labeled tracers causes only limited radiation exposure and that sestamibi and tetrofosmin scintigraphy are highly valuable in the diagnosis of breast cancer (*7*). Nevertheless, any new agent that may eventually improve diagnosis in patients with malignant disease should be tested. Thus, we initiated a trial investigating furifosmin scintigraphy in the diagnosis of breast cancer.

MATERIALS AND METHODS

A prospective, open trial began in 1998 in the Department of Nuclear Medicine and the Department of Obstetrics and Gynecology of our institution to evaluate ^{99m}Tc-furifosmin scintigraphy in the diagnosis of breast cancer, using the tracer to discriminate benign from malignant breast disease. Initially, we planned to enroll 100 patients. At 4 mo, an interim analysis of data from 30 patients showed ^{99m}Tc-furifosmin scintigraphy to have low diagnostic power, and the study was immediately stopped. The patients had been recruited consecutively from the outpatient unit. At recruitment, all had already undergone mammography and clinical examination and had been referred to our department for further diagnosis of an undetermined breast lesion. After obtaining informed consent, we performed ^{99m}Tc-furifosmin scintimammography within 2 wk before each patient's surgery.

Scintigraphy

^{99m}Tc-furifosmin (Mallinckrodt Diagnostika, Hennef, Germany), 555–640 MBq, was injected into the cubital vein contralateral to the affected breast. After 3–5 min, planar images of the breast and both axilla were obtained. The patients were placed supine and parallel to a double-head γ camera (Toshiba, Tokyo, Japan) equipped with a low-energy ultra-high-resolution parallel-hole collimator. Patient positioning was then adapted to obtain a lateral oblique view of the affected breast and axilla with the upper

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limb positioned cranially. Images were acquired in 3 min using a 128 × 128 matrix and a 40-cm field of view without zoom. After planar imaging, SPECT was performed with a triple-head γ camera (Picker Inc., Cleveland, OH) equipped with a low-energy ultra-high-resolution parallel-hole collimator. SPECT was performed with the patients lying prone and raising their arms. Images were elliptic and were obtained in step-and-shoot mode, in 3° steps, in a 120° orbit, and at 20 s per frame.

Images were interpreted on film. Findings were considered negative when the radioisotope was bilaterally and symmetrically distributed throughout the breast and matched the background soft tissue in intensity. Findings were considered positive when focally increased tracer uptake was identified by 2 independent, experienced investigators.

Analysis of Data

Imaging findings were compared with histopathologic findings and classified as true-positive, true-negative, false-positive, or false-negative for malignancy. We calculated the sensitivity, specificity, and positive and negative predictive values of ^{99m}Tc-furifosmin in the planar and SPECT techniques. For comparisons, we used the χ^2 test or Student t test when appropriate. Values of P less than 0.05 indicated statistical significance. Interobserver variability was low, and the classifications of the 2 independent examiners were identical except in 1 patient, about whom disagreement was resolved by consensus.

Most patients had already undergone conventional mammography and sonography when they first presented to our department. After 2 independent members of our staff interpreted the results of these examinations as positive or negative, we also calculated their sensitivity, specificity, and positive and negative predictive values.

RESULTS

Thirty patients (median age [±SD], 53 ± 11 y) were included. Eighteen had malignant breast lesions, of which 10 were palpable (mean size, 17.7 ± 11 mm; size range, 4–45 mm). Planar technique detected 6 of these 10 palpable malignancies, and SPECT detected 8, yielding sensitivities of 60% and 80%, respectively. Eight malignant tumors were not palpable (mean size, 9.9 ± 3 mm; size range, 5–13 mm). Furifosmin revealed 3 of these 8 in planar imaging and 5 in SPECT, resulting in sensitivities of 37% and 62%, respectively, for nonpalpable breast cancer (Table 1).

Twelve patients had benign breast tumors (Table 2). Four of these tumors were palpable (mean size, 12–15 mm) and represented fibroadenomas. Planar findings for 3 patients were true-negative, whereas SPECT findings were true-negative for only 2 of these 3. Of 8 benign, nonpalpable breast lesions, the findings of furifosmin planar imaging were correctly true-negative for 7. The findings of SPECT were correctly true-negative for only 4, with the other 4 misinterpreted as positive (i.e., false-positive).

Overall, sensitivity, specificity, and positive and negative predictive values were 50%, 83%, 82%, and 53%, respectively, for planar imaging and 72%, 50%, 68%, and 55%, respectively, for furifosmin SPECT. Planar imaging and SPECT revealed 5 lesions in contralateral breasts in which no lesion had been suspected. In all these patients, further diagnostic steps were considered unnecessary, except for clinical and mammographic follow-up. Interpreting these 5 lesions as false-positive furifosmin SPECT findings yields an overall specificity and positive predictive value of 71%

TABLE 1
Characteristics of Patients with Malignant Breast Disease

Patient no.	Age (y)	Tumor size (mm)	Histopathology	Grade	Hormonal receptor	Planar view	SPECT
1	52	9	Infiltrating ductal, apocrine	2	++	FN	FN
2	74	12	Infiltrating ductal, NOS, DCIS	3	−	FN	FN
3	47	19	Infiltrating ductal, NOS	3	−	FN	FN
4	49	10	Infiltrating ductal, NOS, multifocal	3	++	FN	FN
5	67	12	Infiltrating ductal, NOS	3	+	FN	FN
6	54	8	DCIS	3	++	FN	TP
7	64	8	Infiltrating ductal, NOS	2	+++	FN	TP
8	66	13	Infiltrating ductal, NOS, multifocal	3	++	FN	TP
9	42	12	Infiltrating ductal	2	−	FN	TP
10	57	5	DCIS	1	+++	TP	TP
11	56	45	Infiltrating lobular and ductal, NOS	3	+	TP	TP
12	51	14	Infiltrating ductal	3	−	TP	TP
13	57	6	Infiltrating ductal, NOS, DCIS, multifocal	3	−	TP	TP
14	50	4	Infiltrating ductal, DCIS	3	+	TP	TP
15	64	23	Infiltrating lobular and ductal	2	++	TP	TP
16	54	13	Infiltrating lobular	2	++	TP	TP
17	68	20	Carcinoma medullare	3	−	TP	TP
18	75	23	Infiltrating ductal, NOS	3	++	TP	TP

FN = false-negative; NOS = not otherwise specified; DCIS = ductal carcinoma in situ; TP = true-positive.

TABLE 2
Characteristics of Patients with Benign Breast Disease

Patient no.	Age (y)	Tumor size (mm)	Histopathology	Planar view	SPECT
1	53	13	Fibroadenoma	TN	TN
2	57	—	Micropapilloma	TN	TN
3	39	—	Fibrocystic mastopathy	TN	TN
4	36	9	Fibroadenoma	TN	TN
5	31	12	Fibroadenoma	TN	TN
6	53	—	Fibrocystic mastopathy	TN	TN
7	38	5	Fibroadenoma	TN	FP
8	73	4	Lymphadenitis	TN	FP
9	48	—	Mastitis	TN	FP
10	47	12	Fibroadenoma	FP	FP
11	40	15	Fibroadenoma	FP	FP
12	46	—	Fibrocystic mastopathy	FP	FP

TN = true-negative; FP = false-positive.

and 69%, respectively, for planar images and 35% and 54%, respectively, for SPECT.

The axilla of 15 patients were dissected. Twenty of 249 resected axillary lymph nodes were metastatically involved. Two patients had 4 nodes positive for malignancy, whereas 8 patients had fewer than 2 positive nodes. Furifosmin did not reveal any positive nodes.

DISCUSSION

We tested furifosmin scintigraphy prospectively in 30 outpatients. Although tracer uptake in cell lines has suggested clinical usefulness (*8,9*), clinical reports on small numbers of patients have shown no benefit over other technetium-labeled tracers in patients with breast or ovarian cancer (*5,10*). Our study was intended to investigate a larger group of patients to obtain sounder statistical values but was stopped because of low sensitivity and specificity rates. Our results thus agree well with earlier reports (*5,10*).

To our knowledge, only a few studies have investigated furifosmin scintigraphy in cancer patients. In 1 study, no tracer uptake was seen in 10 of 10 breast cancer patients (furifosmin accumulated in inflammatory breast tissue), nor could recurrent ovarian cancer be detected (8 patients) (*5*). In thyroid cancer, furifosmin yielded a 30%–40% sensitivity compared with FDG PET, which was more than 90% sensitive (*10*).

CONCLUSION

Furifosmin scintigraphy was not helpful in the diagnostic evaluation of breast cancer patients, nor could it effectively rule out a patient's having only benign disease. We could not define any patient subgroup that would benefit from furifosmin scintigraphy. A randomized, prospective study comparing furifosmin and sestamibi scintigraphy does not seem justified.

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