Inconclusive Triple Diagnosis in Breast Cancer Imaging: Is There a Place for Scintimammography?

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Scintimammography (SM) can be used as a complementary test to mammography in patients with suspected breast cancers. This study was undertaken to evaluate the impact of SM on the management of patients with a doubtful or discordant triple diagnosis—that is, mammography, ultrasound, and fine-needle aspiration cytology. The clinical question was variable: initial diagnosis of cancer, suspicion of recurrence, doubtful tumor extension, or search for a primary tumor. **Methods:** We performed a retrospective study of 118 procedures in 104 patients with a suggestion of breast cancer, either at initial presentation or after treatment (relapse), with an inconclusive triple diagnosis. Planar and tomographic imaging was performed after injection of ^{99m}Tc-labeled methoxyisobutylisonitrile (^{99m}Tc-MIBI). Results were compared with histopathologic analysis (surgery or core biopsy) in 82 cases and with clinical and imaging follow-up in 36 cases. **Results:** Breast cancer was proven in 69 cases. SM-SPECT had a sensitivity of 88.4% and a specificity of 67%. Eleven cancers were detected by SPECT, although planar images were negative. SM-SPECT was more sensitive in patients scanned at initial presentation (95%) than in those with suspected recurrence (81%). SM-SPECT correctly evaluated multicentricity or bilaterality in 8 of 11 patients and resulted in an increased tumor size in 8 patients. Overall, SM-SPECT modified the patient management in 58 of 118 cases (49%): SM made the diagnosis of cancer in 30 cases with doubtful or discordant triple diagnosis and ruled out malignancy in 28 cases. **Conclusion:** SM-SPECT is a useful complementary tool for the diagnosis and evaluation of disease extent in patients with an inconclusive triple diagnosis including fine-needle aspiration. The procedure altered the patient management in 49% of the population. These results must be confirmed in a prospective trial.
Key Words: scintimammography; SPECT; breast cancer; triple diagnosis

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Scintimammography (SM) has been found to be useful in diagnosing breast cancer, especially in women with dense or fibrous breasts (1–3). The procedure is also useful for the detection of locoregional relapse, because the tracer uptake is not or only marginally influenced by architecture distortion or prosthetic implants, which reduce the accuracy of morphologic procedures such as mammography or ultrasound (4–7). SM has therefore emerged as a second-line complementary diagnostic tool when mammography or ultrasound is not decisive (7–10). The routine breast imaging work-up is not limited to mammography. In our institutions, 3 procedures are routinely performed, along with palpation: mammography, ultrasound, and, fine-needle aspiration (FNA) of abnormalities suggestive of cancer. Additional methods such as SM or MRI are ordered when this "triple procedure" (or triple diagnosis [TD]) is either inconclusive or contradictory (e.g., highly suggestive imaging with benign cytology) or when the tumor extension cannot be assessed. There is evidence in the literature that supports the use of SM to look for tumor relapse (4–7) and to evaluate the tumor extension—in particular, the multifocal or multicentric nature of the disease (11). On the basis of these results, clinicians tend to order SM for patients with a doubtful TD, regardless of the current clinical problem (initial diagnosis, search for recurrence, or other). The majority of published studies on the use of SM in assessing breast cancer are based on a single clinical problem: Is SM useful in women with dense breasts or what is the place of SM in women with a clinical suspicion of recurrence? We thought it would be interesting to consider the impact of the procedure as it is used in a daily practice—that is, as a second-line imaging technique ordered only when the first-line procedures do not allow reaching a definite diagnosis or opinion on the extent of the disease. Thus, the inclusion criterion was not related to the clinical question but rather to the complexity of the case. We wanted to review the per-

formance of SM in such a difficult population and its impact on clinical management.

MATERIALS AND METHODS

The medical files of 104 patients were retrospectively reviewed. The mean age was 57 y (range, 34–87 y), with 63 patients being <60 y old. One hundred eighteen SMs were performed: 12 patients were scanned twice and 1 patient was scanned 3 times. Before SM, every patient (and at each evaluation in cases with multiple SMs) underwent a complete work-up, including palpation, x-ray mammography, ultrasound, and FNA.

Mammograms were performed on dedicated mammography machines: a DMR mammography unit (GE Healthcare) or a Lorad-M IV Unit (Lorad Medical Systems-Hologic). Mammography was performed with both mediolateral oblique and craniocaudal views in every case, with an additional lateromedial oblique view when necessary.

Ultrasound was performed using the direct contact method with real-time equipment (Corevision Pro SSA-350A; Toshiba) and a broadband linear probe (6–12 MHz). Ultrasound-guided FNA biopsy was performed freehand with a Cameco syringe holder connected to a 10-mL syringe and a 22-gauge needle. Conclusions of TD were based on the American College of Radiology (ACR) classification (class 1, negative; class 2, benign findings; class 3, probably benign findings; class 4, suspicious abnormality; class 5, highly suggestive of malignancy) (12). MRI was available in only 30 of 118 cases and, therefore, was not included in this analysis.

SM was ordered either because the TD procedure was inconclusive or contradictory or to evaluate tumor extent. According to the ACR classification, TD results were class 3 or 4 in 54% of cases, class 5 in 22%, and class 2 in 24%. In class 5 cases, SM was ordered to evaluate multifocality or multicentricity. In class 2 cases, 65% had a previous history of surgery and 35% had polycystic dense or very dense breasts, which led the clinician to order SM.

For the analysis, the cases were grouped according to the clinical question: initial diagnosis of malignancy (group 1, $n = 37$), suspicion of tumor recurrence (group 2, $n = 48$), assessment of multicentricity (group 3, $n = 26$), and search for a primary tumor in patients with axillary lymph nodes (group 4, $n = 7$). In group 1, the ACR classification was class 2 in 10 patients, class 3 in 17 patients, class 4 in 10 patients; in group 2, class 2 in 18 patients, class 3 in 18 patients, and class 4 in 12 patients; in group 3, class 5 in all 26 patients; and in group 4, class 4 in all 7 patients.

Care was taken to perform SM at least 2 wk after a large-core biopsy to avoid false-positive results caused by inflammatory changes. The mean interval between SM and TD was 19 d.

SM

^{99m}Tc-Labeled methoxyisobutylisonitrile (^{99m}Tc-MIBI) was injected through a catheterized vein of the contralateral forearm or of the foot if bilateral disease was suspected. Ten minutes after injection of 740 MBq (20 mCi) of ^{99m}Tc-MIBI, a tomographic acquisition was first performed on a triple-head system (Multispect; Siemens) using a high-resolution, low-energy collimator (64 angles of 20 s, 128×128 matrix). Patients were placed in the supine position with arms raised above the head. Data were reconstructed using an iterative algorithm (ordered-subsets expectation maximization).

Planar images were subsequently obtained with the patient lying in the prone position on a dedicated cushion so that the breasts were hanging freely. Lateral views of both breasts were obtained (10 min/view, 256×256 matrix).

SPECT and planar images were interpreted visually by 2 observers who reached a consensus when necessary. When a focus of increased ^{99m}Tc-MIBI uptake was noted on one or both modalities, the case was classified as positive for tumor. A hot spot in the axillar region was also regarded as positive for tumor. No quantitative indices were used in the study.

Gold Standard

Histopathologic validation was available in 82 of 118 cases: microbiopsy in 19 cases and surgery in 63 cases. In the remaining 36 cases, the clinical and imaging follow-up of minimum 12 mo was used as the gold standard.

Data Analysis

Sensitivity, specificity, positive and negative predictive values, and accuracy of SM to detect breast cancer were calculated for the whole study population as well as for the 4 subgroups. Differences in sensitivity, specificity, and accuracy between planar imaging and SPECT were evaluated using the McNemar χ^2 test. $P < 0.05$ was considered significant.

We analyzed the impact of SM on patient management. SM was found to modify the therapeutic strategies when (a) SM made the diagnosis of cancer when the conventional work-up was inconclusive or discordant, (b) SM detected unknown additional lesions (bilaterality, multicentricity), and (c) SM excluded cancer in cases with doubtful TD.

RESULTS

The presence of cancer was proven in 69 of 118 cases (58%): invasive ductal ($n = 26$) or lobular ($n = 17$) carcinoma, comedocarcinoma ($n = 3$), in situ ductal carcinoma ($n = 4$), multifocal in situ lobular carcinoma ($n = 1$), poorly differentiated carcinoma ($n = 2$), mixed invasive and in situ ductal carcinoma ($n = 5$), mixed invasive ductal and lobular carcinoma ($n = 4$), mixed invasive ductal and in situ lobular carcinoma ($n = 2$), mixed invasive ductal and tubular carcinoma ($n = 2$), and mixed invasive ductal and comedocarcinoma ($n = 3$).

Forty-nine cases (42%) were classified as benign disease, proven by large-core biopsy ($n = 13$) or based on the clinical and imaging follow-up: fibrodysplasia ($n = 33$, 7 proven by biopsy), fibroadenoma ($n = 4$, all 4 proven by biopsy), postsurgical or postradiotherapy fibrosis ($n = 12$, 2 proven by biopsy).

The diagnostic performance of SM is detailed in Table 1. The sensitivity and specificity of SM were 88.4% and 67%, respectively. Eleven cancer lesions were detected by SPECT only: 2 were infracentimetric lesions and 9 were supracentimetric lesions. Comparison between planar imaging and SPECT results are detailed in Tables 2 and 3. For the whole study population, SPECT was significantly more sensitive than planar imaging ($P < 0.05$). Planar imaging was found to be more specific than SPECT but the differ-

TABLE 1
Diagnostic Performance of SM

Group	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
Overall ($n = 118$)	88.4	67	79	80.5	80
1: Initial diagnosis ($n = 37$)	95	70.5	79	92.3	83.7
2: Suspicion of recurrence ($n = 48$)	81	65.6	54	87.5	71
3: Assessment of multifocality ($n = 26$)	73	100	100	83	88
4: Detection of unknown primary ($n = 7$)	75	na	na	na	na

PPV = positive predictive value; NPV = negative predictive value; na = not applicable.

ence did not reach statistical significance. However, when cancers were classified according to tumor size (Table 3), the sensitivity of SPECT was statistically superior to planar imaging for T1c lesions only ($P < 0.05$).

In group 1 ($n = 37$), 20 cancers were diagnosed. SM was true-positive in 19 of 20 cases and false-negative for 1 case of infiltrative lobular carcinoma (17 mm). SM was false-positive in 5 cases: fibroadenoma was diagnosed in 3 cases and there was no sign of disease evolution at follow-up in the other 2 cases.

In group 2 ($n = 48$), scanned because of suspected recurrence, SM was performed 3–240 mo after initial treatment. Tumor relapse was present in 16 cases. SM was true-positive in 13 of 16 and FN in 3 of 16 cases (9-, 3-, and 6-mm infiltrative carcinomas). In the last case (6-mm carcinoma), the microbiopsy was negative and the tumor was found at analysis of the surgical specimen. SM was interpreted incorrectly as positive in 11 cases without recurrence. In all cases, ^{99m}Tc-MIBI uptake was weak and in 7 cases was seen only on the SPECT images. One case corresponded to fat necrosis with inflammation against a foreign body, detected 3 mo after initial surgery. In the other cases, no evidence of disease was seen at follow-up. The mean time interval between initial treatment and SM was shorter in the false-positive cases (17 mo; range, 3–29 mo) than that in the rest of the group (84 mo for true-positive cases, 36 mo for true-negative cases, and 88 mo for false-negative cases).

In group 3 ($n = 26$), SM was ordered to assess multicentricity (mainly for in situ or lobular carcinoma), multifocality, or bilaterality. SM indeed accurately diagnosed multicentric lesions in 2 patients and confirmed multicentricity already suspected by TD in 2 patients. SM detected contralateral tumors (Fig. 1) in 2 patients in whom TD showed only unilateral tumor. TD showed bilateral tumors in 1 patient, confirmed by SM. One patient had bilateral tumors seen with TD, and 1 tumor was multicentric: SM correctly showed both lesions and correctly assessed the multicentricity of the right one. In 8 additional patients, the size of the tumor was found to be larger on SM compared with TD: all were surgical (mastectomy) and the histopathologic analysis confirmed that the tumor size was underestimated by TD. In 3 cases, SM missed additional lesions: one 3-mm, one 4-mm, and one in situ carcinoma, respectively.

In group 4 ($n = 7$), SM detected a primary breast tumor in 3 patients with metastatic axillary lymph nodes (infiltrative lobular carcinoma in all cases). SPECT detected all 3 tumors, although planar imaging was false-negative in one case. In all cases, TD failed to detect the primary breast tumor. SM was false-negative for a multifocal mixed carcinoma (6- and 7-mm size). No primary tumor was diagnosed in the remaining 3 cases.

Lobular carcinomas ($n = 21$) were separately reviewed. Overall, there were 17 cases with infiltrative lobular carci-

TABLE 2
Comparison Between Planar Imaging and SM-SPECT in Whole Series ($n = 118$)

Parameter	Planar imaging	SM-SPECT
Sensitivity (%)	72.4	88.4*
Specificity (%)	79.5	67†
Negative predictive value (%)	67	80.5
Positive predictive value (%)	83.3	79
Accuracy (%)	75.4	80†

*$P < 0.05$, McNemar test.
†P = not significant, McNemar test.

TABLE 3
Comparison of Sensitivity for Cancer Detection ($n = 69$) Between Planar Imaging and SPECT According to Tumor Size

Lesion	n	Planar imaging	SPECT
T1a	0	—	—
T1b	19	11/19 (58)	14/19 (74)
T1c	23	15/23 (65)	21/23 (91)*
≥T2	27	24/27 (89)	26/27 (96)

*$P < 0.05$, McNemar test.
T1a, ≤5 mm; T1b, >0.5 ≤1 cm; T1c, >1 ≤2 cm; T2, >2 ≤5 cm.
Values in parentheses are percentages.
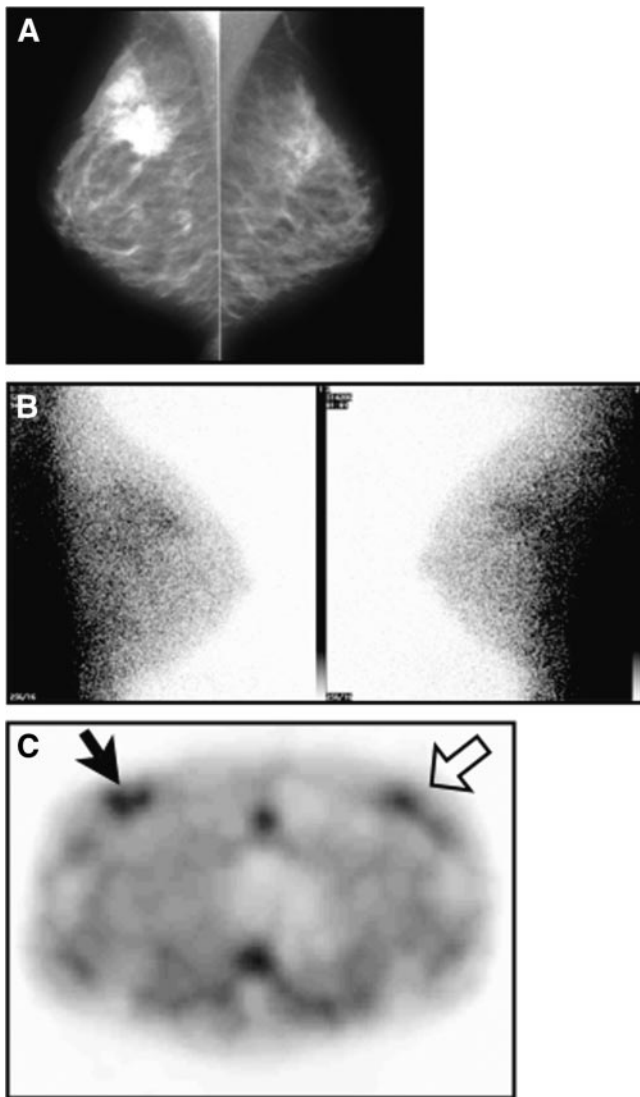
FIGURE 1. (A) X-ray mammogram, profile views. Polycystic dysplasia of both breasts. (Left) Suspicious lesion in supraareolar region of right breast, corresponding to ductal carcinoma on FNA. (Right) Left breast is dense, especially in superoexternal part of gland. Multiple cysts are seen with ultrasound but no suggestive lesion was evident. (B) SM (planar lateral views) shows bilateral uptake (left, right breast; right, left breast). (C) Axial SPECT views show bilateral lesions (arrows). SPECT allowed precise localization of tumors and oriented large-core biopsy of left breast lesion (open arrow, invasive ductal carcinoma).

noma and 4 with mixed infiltrative ductal and lobular carcinoma. SM was true-positive in 18 of 21 cases (86% sensitivity); 4 of 18 tumors were detected only by SPECT. False-negative cases were 4-, 3-, and 17-mm carcinomas. In this subpopulation, TD was inconclusive in 16 of 21 cases (76%).

SM was found to influence the patient management in 49% of cases (58/118). SM diagnosed a cancer in 10 cases with a discordant conventional work-up—that is, doubtful

imaging and negative FNA. Despite a negative FNA, 3 invasive ductal, 3 in situ ductal, and 4 invasive lobular carcinomas were found in the surgical specimen. Without SM, all patients would have been scheduled for imaging follow-up. SM was found to be decisive in making the diagnosis of cancer in 20 patients with ACR class 3–4 and contradictory FNA results. In 5 of them, SM detected unsuspected contralateral cancer in 2 and multicentricity in 3. Detailed management information of the 30 patients is given in Table 4.

In 35 cases, SM was true-negative but microbiopsy was still performed in 7 cases. SM results were thus found to be decisive in 28 of 35 cases.

DISCUSSION

Our results support the use of SM with tomography (SM-SPECT) in patients with inconclusive TD, either at the initial stage of their clinical history or when a locoregional tumor relapse is suspected. With our inclusion criteria, SM-SPECT was found to alter patient management in 49% of cases.

For this study, we pooled patients from several clinical categories: initial diagnosis, suspicion of recurrence, assessment of multifocality or bilaterality, and metastatic lymph nodes with no primary tumor identified. In all cases, clinicians in charge could not reach a conclusion on the basis of the usual diagnostic methods—that is, physical examination, mammography, ultrasound, and FNA.

Several studies have reported the use of SM as an adjunct to mammography alone for the diagnosis of breast cancer (8–10,13,14) and showed it to be useful—in particular, for assessing dense breasts (1,2,15). A multicentric study confirmed that the sensitivity of SM was not reduced when dense breasts were imaged, to the contrary of mammography (2). In dense breasts, ultrasound was found to be more sensitive than SM (92% vs. 83%, respectively) but at the cost of decreased specificity (38% vs. 88%) (3).

A previously published study has demonstrated that adding SM to TD resulted in increased sensitivity to detect breast cancer: 95.6% for TD versus 100% for TD plus SM for addressing palpable lesions and 89.1% versus 97.2% for nonpalpable lesions (16). Although less sensitive than TD (85.5% vs. 92.7%, respectively), SM was also found to increase the sensitivity (up to 98.7%) when added to TD in a study by Danielsson et al. (17), suggesting that SM is particularly useful when TD is inconclusive. However, this statement was not confirmed by Leidenius et al., who found that SM was poorly sensitive (63%) in patients with doubtful TD (18). This is in contradiction with our results: We observed 88.4% sensitivity in a population whose patients are referred for SM because of inconclusive TD. The sensitivity is 95% in women imaged at initial diagnosis (group 1)—although at the cost of 70.5% specificity—but the overall accuracy remains high (83%) in this group. Our results

TABLE 4

TABLE 4
Impact of Positive SM on Management of 30 Patients with Doubtful or Contradictory TD

Patient no.	TD results		Decision based on positive SM result
	ACR class	FNA	
1	IV	Benign	Microbiopsy of RSEQ: in situ ductal carcinoma
2	IV	Benign	Microbiopsy of RIMQ: in situ ductal carcinoma
3	III	Benign	Microbiopsy of RSIQ: invasive ductal carcinoma
4	III	Benign	Surgery of LSMQ: lobular carcinoma
5	III	Benign	Surgery of LSEQ: lobular carcinoma
6	V (L)	Invasive ductal carcinoma (L)	Microbiopsy of RSMQ: lobular carcinoma
	II (R)		
7	IV	Benign	Surgery of LSEQ: lobular carcinoma
8	V (R)	Invasive ductal carcinoma (R)	Microbiopsy of LSEQ: invasive ductal carcinoma
	III (L)		
9	Previous R mastectomy	Positive axillary lymph node, negative at scar level	SM positive at scar level, leading to repeated FNA: invasive ductal carcinoma
10	IV	Benign	Microbiopsy of LSMQ: in situ ductal carcinoma
11	IV	Cellular atypia, inconclusive	Microbiopsy of LSQ: invasive ductal carcinoma
12	III	Inconclusive	Surgery: lobular carcinoma of RIEQ
13	IV	Doubtful	Microbiopsy of LSEQ: invasive ductal carcinoma
14	III	Cellular atypia, inconclusive	Microbiopsy of LSEQ: lobular and invasive ductal carcinoma
15	IV	Doubtful, epitheliosis?	Microbiopsy of RIEQ: invasive ductal carcinoma
16	III	Doubtful, hyperplasia	Microbiopsy of LSEQ: invasive ductal carcinoma
17	III	Doubtful, hyperplasia	2 foci, leading to surgery: multicentric invasive ductal carcinoma
18	IV	No material	Surgery of RSEQ: lobular carcinoma
19	V	Invasive ductal carcinoma	2 positive foci: microbiopsy showing multicentric carcinoma (invasive ductal and in situ ductal)
20	IV	Doubtful	Microbiopsy of RSQ: invasive ductal carcinoma
21	IV	Doubtful, cellular atypia	Microbiopsy of LSEQ: invasive ductal carcinoma
22	IV	Doubtful, cellular atypia	Microbiopsy of LSEQ: invasive ductal carcinoma
23	IV	Doubtful, hyperplasia	Surgery of LIIQ: comedocarcinoma
24	V	Invasive ductal carcinoma	2 foci showing multicentricity, confirmed by surgery (invasive and in situ ductal carcinoma)
25	IV	No material	Microbiopsy of LSEQ: lobular carcinoma
26	IV	Doubtful	Surgery of LIEQ: lobular carcinoma
27	III	Doubtful	Surgery of LSEQ: comedocarcinoma
28	III	Doubtful	Microbiopsy of RSEQ: invasive ductal carcinoma
29	III	Doubtful	Surgery of retroareolar region: invasive ductal carcinoma
30	IV	Doubtful, hyperplasia	Microbiopsy of RSEQ: invasive ductal carcinoma

RSEQ = R superoexternal quadrant; LSEQ = L superoexternal quadrant; LIEQ = L inferoexternal quadrant; LIIQ = L inferointernal quadrant; LSQ = L superior quadrant; RSQ = R superior quadrant; RSMQ = R superomedial quadrant; RSIQ = R superointernal quadrant; RSEQ = R superoexternal quadrant; RIMQ = R inferomedial quadrant; LSMQ = L superomedial quadrant; RIEQ = R inferoexternal quadrant.

fully support the hypothesis that SM is very useful to solve clinical problems when TD is doubtful or discordant. The poor results reported by Leidenius may have been caused by the fact that they used planar SM only. We systematically used planar imaging and SPECT acquisition and iterative reconstruction, which is known to increase the sensitivity of SM (*19*). We found a sensitivity of 88.4% for diagnosing cancer, comparable with that reported by other groups using SPECT (*20,21*). In our study, 11 cancers were detected only by SPECT (Fig. 2). With planar SM only, we would have diagnosed or assessed tumor extension correctly in only 50

of 69 cases (72%). Therefore, we believe that SPECT is mandatory in clinical practice: It represents a significant increase in sensitivity and is not difficult to perform in the supine position.

Our specificity (67%) is slightly inferior to that usually reported (69%–87%) in multicentric studies (*8,22,23*). Although our results are not fully comparable because our population is a mixture of different clinical conditions (as opposed to multicentric trials focusing on initial diagnosis only), this lower specificity can be explained by the criteria used to classify an image as positive: even a faint [99m]Tc-
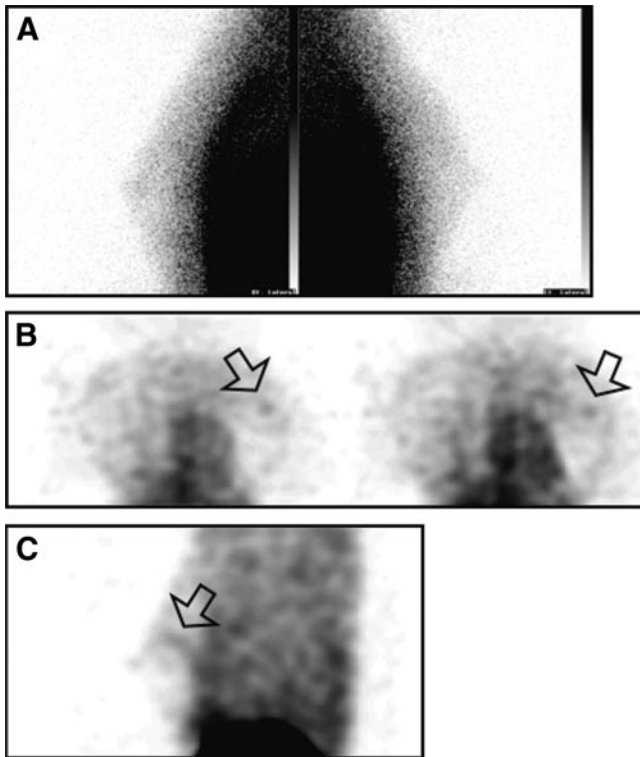
FIGURE 2. Patient with suggestion of recurrence: comedo-carcinoma surgery 2 y earlier, multicystic dysplasia, more pronounced in superoexternal part of left breast. (A) SM (planar lateral views) shows no frank abnormalities. (B and C) Coronal (B) and sagittal (C) SPECT images show moderate but focal uptake in left breast (arrow). Core biopsy confirmed presence of tumor recurrence (in situ ductal carcinoma).

MIBI uptake was considered as positive for malignancy and we did not use any scoring system. This method is supported by other groups with similar results in terms of specificity (10,23). Faint diffuse ^{99m}Tc-MIBI uptakes were shown to correspond to lobular or in situ carcinoma, so we believe that they cannot be systematically classified as benign or nonspecific. Interestingly, 11 of 16 false-positive cases were seen in the group scanned for suspected recurrence—thus, after initial treatment. Moreover, the time interval between initial treatment and SM happened to be the lowest in the false-positive cases (17 mo on average, compared with 36–88 mo in other patients of group 2). Previous surgery and radiotherapy may lead to fibrotic changes with a certain degree of inflammation and, thus, increased ^{99m}Tc-MIBI uptake, especially early after treatment. But, compared with published series on SM in suspected recurrent breast cancer, our results show a lower sensitivity and specificity (81% and 65.6%, respectively). Spanu et al. reported a sensitivity of 96.8% and a specificity of 77.7% with SPECT acquisition (4). In their study, 19 of 20 patients scanned for suspected locoregional recurrences were found to have a relapse, corresponding to a 95% prevalence, which is markedly higher than the one observed in our study

(33%). There is certainly an issue of patient selection. The same issue stands for the study of Bongers et al. (5), who reported a high sensitivity and only 4 false-positive findings in a series of 54 patients. In their study, patients were all symptomatic (redness, swelling, pain, or palpable mass) and, thus, the pretest probability of cancer was certainly higher than ours. Indeed, in our group 2, recurrence was frequently suspected on the basis of TD alone—that is, in asymptomatic women. Therefore, the tumor prevalence is lower, as is the overall diagnostic accuracy of SM, which is in accordance with results of the multicentric study (22). It is foreseeable that in a clinical setting in which women are followed more closely by systematic imaging, SM will be ordered more frequently for cases with doubtful TD, in the absence of any clinical manifestation. The diagnostic performance of SM will be influenced by these changing inclusion criteria, as shown by our results. Moreover, we systematically used SPECT acquisition, as opposed to planar imaging alone used by many authors. Cwikla et al. reported 89% sensitivity and 88% specificity using planar imaging in a series of 18 patients (6). In our study, 7 of 11 false-positive findings in group 2 were positive only on SPECT images. Planar imaging was found to be more specific (79.5%) than SPECT (67%), but the difference was not statistically significant. The use of a scoring system of the SPECT images might perhaps increase our accuracy in these particularly difficult cases of suspected local tumor relapse.

Twenty-six patients (group 3) were referred to SM for evaluation tumor extent—that is, multifocality, multicentricity, and bilaterality. SM diagnosed multicentricity in 2 patients and bilaterality in 2 patients. SM confirmed bilaterality or multicentricity in 4 patients. Multicentricity was missed in 3 cases: false-negative cases were small lesions (3- and 4-mm invasive and one in situ carcinoma). SM showed only one tumor in 7 patients, although TD was suggestive for a multicentric disease. Our results are in accordance with those of Cwikla et al., who reported that SM was more efficient in assessing multifocality and multicentricity than morphologic techniques (11). In 8 additional patients, SM was able to detect a larger tumor local spread than TD, and histopathology confirmed that TD had underestimated the actual tumor size.

Seven patients were diagnosed with metastatic axillary lymph nodes of unknown primary. SM-SPECT was able to detect 3 primary breast cancers (9, 18, and 13 mm) but was false-negative in 1 patient. It is difficult to determine the place of SM in such patients because of the lack of published studies (7).

Lobular carcinoma is a diagnostic challenge for triple conventional assessment (24–26). Indeed, in our series, lobular carcinoma was present in 21 patients (18% of the total population) with an inconclusive triple procedure. SM-SPECT was true-positive in 18 of them (sensitivity, 86%). In a series of 46 patients, Leidenius et al. found that SM
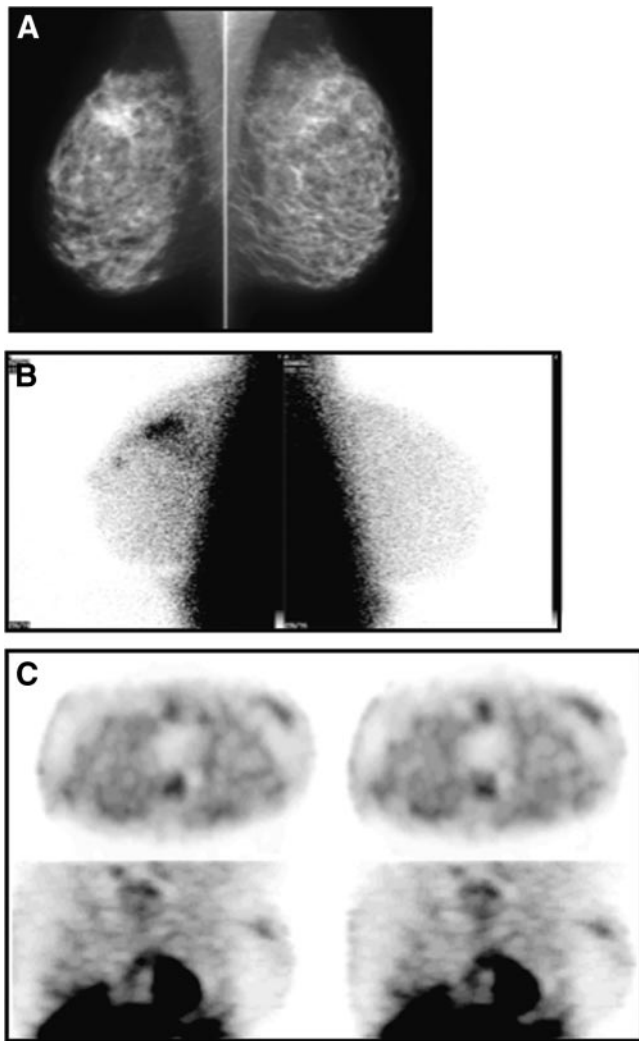
FIGURE 3. Highly dysplastic breasts in 48-y-old woman. (A) X-ray mammogram showed dense tissue in superoexternal part of left breast (class III). Ultrasound-guided FNA shows benign material. (B) SM (planar lateral views) shows high uptake of 99mTc-MIBI in upper external part of left breast. Invasive lobular carcinoma was confirmed at surgery. (C) SM-SPECT acquisition. Axial (top) and coronal (bottom) slices show tumor in left breast.

detected 3 of 6 lobular carcinomas (sensitivity, 50%) (*18*). SM was positive for all 3 lobular carcinomas in Prats et al. (*10*) and in 7 of 9 cases of Buscombe et al. (*13*). The present series is larger, with 17 invasive lobular and 4 mixed invasive ductal and lobular carcinomas, and 86% sensitivity clearly suggests that SM-SPECT can accurately detect lobular carcinoma (Fig. 3).

As used in our study—that is, systematically when TD is inconclusive and regardless of the clinical situation (initial diagnosis, suspicion of recurrence, questionable tumor extension, or search for a breast primary)—SM-SPECT has a significant impact on patient management. The results of SM-SPECT altered the management in 58 patients (49%) by

diagnosing cancer in 30, modifying the extent of disease in 5, and ruling out cancer in 28. An interesting point would be to select, on the basis of SM, the patients who deserve an invasive diagnostic procedure such as microbiopsy or surgical exploration. It has been suggested that SM could reduce the need for biopsies in patients with a low or intermediate suggestion of cancer (*10*). We were not able to test this hypothesis in our study: Because of its retrospective design, the decision to refer the patient for biopsy was not systematically taken on the basis of the TD plus SM-SPECT results. Therefore, we believe that this must be addressed in a prospective study.

CONCLUSION

SM-SPECT is useful for initial diagnosis of breast cancer, detection of recurrence, and evaluation of tumor extent when TD is doubtful or discordant. This population represents a daily challenge for the breast imaging community. In such a selected population, the sensitivity of SM-SPECT is 89% and its overall accuracy is 80%. SM-SPECT is also efficient for diagnosing lobular carcinoma, with a sensitivity of 86%. Overall, SM-SPECT altered the patient management in 49% of cases.

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