

Scintimammography with dedicated breast camera in unifocal and multifocal/multicentric primary breast cancer detection: A comparative study with SPECT

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Abstract. The aim of this study was to assess the usefulness of planar scintimammography (SM) with a high-resolution dedicated breast camera (DBC) compared to SPECT in unifocal and multifocal/multicentric primary breast cancer (BC) detection. DBC planar SM and conventional SPECT were acquired using ^{99m}Tc-tetrofosmin as radiotracer in 85 consecutive patients suspect for BC at conventional imaging and clinical examination. Scintigraphic data were related to histology in all cases. BC was proven in 74/85 patients, unifocal in 56/74 cases and multifocal/multicentric in 18/74; 90 carcinomas were ascertained. Benign lesions were found in 12 cases, including one who also had BC in the contralateral breast. DBC planar SM and SPECT were true-positive in 72/74 and in 70/74 BC patients, respectively, and globally detected 96.7% and 92.2% of carcinomas. DBC and SPECT sensitivity were, respectively, 90.3% and 80.6% in ≤ 10 -mm carcinomas and 100% and 98.3% in larger ones; sensitivity values in non-palpable carcinomas were 92.6% and 77.8%, respectively, and 98% for both procedures in palpable ones. DBC planar SM and SPECT correctly assessed multifocality/multicentricity in 91.7% and 83.3% of cases, respectively. Sensitivity differences were not significant. Both procedures showed only a false-positive result. DBC planar SM and SPECT proved highly sensitive and specific in BC detection, representing a useful complementary tool to mammography. However, DBC planar SM showed technical advantages and better clinical performance than SPECT in both subcentrimetric carcinoma detection and multifocal/multicentric disease assessment. Thus, DBC planar SM should be preferred, but SPECT remains a useful alternative when DBC is unavailable.

Introduction

During the last decade, scintimammography (SM) has emerged as a useful complementary tool to mammography in the diagnosis of primary breast cancer, with significantly higher specificity values in respect of the latter.

At present, its employment, more frequently with the cationic lipophilic radiotracers ^{99m}Tc MIBI and ^{99m}Tc-tetrofosmin as tumour-seeking agents, is especially indicated in patients with dense breast or with fibrocystic disease in whom the sensitivity of mammography markedly decreases (1), the radiotracer uptake being independent of breast density (2). SM can also be used in the presence of microcalcification, parenchymal distortion or iatrogenic scars in which mammography can often be doubtful or inconclusive as well as in patients with prosthetic implants (3). In addition, SM may be helpful in assessing a multifocal/multicentric disease in patients with proven biopsy primary breast cancer and in the detection of an occult primary cancer sited in the breast in patients with negative mammography but with axillary lymph node metastases (3).

SM, usually performed with the planar acquisition method using a conventional general purpose gamma camera, has demonstrated an important limitation, that is a low sensitivity (in the range of 30-60%) in the detection of non-palpable and small-size carcinomas of ≤ 10 mm (4-7), which represent the more frequent cancers detected by screening mammography, due to the limited intrinsic resolution of the gamma camera. This low sensitivity value means that conventional planar SM markedly limits its employment in the diagnosis of a primary breast cancer in an early stage.

To overcome this limitation, over recent years there has been a growing interest in the employment of other acquisition scintigraphic procedures. In particular, several studies have been carried out using single photon emission computed tomography (SPECT). However, the superiority of SPECT over planar SM in breast cancer detection remains controversial; the tomographic procedure has proved less sensitive than planar SM in some comparative studies (8-10), while more recently it proved able to increase planar sensitivity (11-16), especially in the detection of non-palpable and small-size carcinomas in which it also maintains a very high

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specificity (15,16). Furthermore, SPECT also proved more sensitive than planar SM in detecting multifocal/multicentric carcinomas (17).

More recently, several types of small field of view cameras specifically designed for the imaging of the breasts have also been developed. These systems are characterized by a more favourable energy resolution and a higher intrinsic spatial resolution than that achieved by a conventional gamma camera and they also present several technical advantages in image acquisition.

Preliminary comparative studies have demonstrated that the dedicated breast cameras (DBC) are able to significantly increase the sensitivity of conventional planar SM particularly in patients with non-palpable and ≤ 10 -mm carcinomas (18,19) as well as in the cases with occult carcinoma and in those with dense breast at risk of cancer (20,21), while no data have been reported in multifocal/multicentric disease assessment.

In the present study we have compared the diagnostic performance of SM obtained with a new advanced DBC based on a cadmium-zinc-telluride (CZT) detector mounted in a mammographic gantry with that of SPECT, using ^{99m}Tc -tetrofosmin as tumour-seeking radiotracer, in a series of patients with unifocal and multifocal/multicentric breast lesions suspected to be cancer and scheduled to undergo biopsy.

Materials and methods

From November 2005 to October 2006 we studied 85 consecutive female patients, aged 33 to 82 years (mean age, 62 ± 12.3 years), scheduled to undergo breast biopsy because of suspect primary breast cancer on the basis of clinical examination and/or conventional diagnostic imaging procedures (mammography/ultrasonography).

Three of the patients had already undergone contralateral mastectomy and axillary lymph node dissection for infiltrating ductal carcinomas 5, 6 and 12 years, respectively, before scintigraphy, while one patient had undergone omolateral excisional biopsy for an adenoepithelioma 13 years previously.

All patients had previously undergone clinical examination and mammography, and in the majority of cases also ultrasonography. The clinical examination had been performed by an experienced clinician.

In all patients, two-view (mediolateral and craniocaudal) film-screen mammograms of both breasts were obtained with a dedicated unit; if necessary, additional views were obtained, as well as magnified mammograms. All mammography studies were read by one experienced radiologist and the mammographic findings were classified as follows: highly suggestive of malignancy in the presence of breast cancer features (i.e. dominant or speculated opacity with or without microcalcification, irregular borders of the opacity in fatty breast), suspect in the presence of indirect diagnostic signs of cancer (i.e. microcalcification without mass, focal architectural distortions, asymmetrical breasts), indeterminate in the presence of high breast density and negative in the absence of any abnormalities. The mammographic findings were considered highly suggestive of malignancy in 50/85 patients, suspect in 27/85 cases, indeterminate in 6 cases and negative in 2 cases. Each of the 8 patients with indeterminate/negative mammography had one hypoechoic nodule each at ultrasonography.

The final diagnosis was obtained in all 85 patients within 1 week of scintigraphy, by surgical biopsy in 19 cases and by percutaneous biopsy in 66 cases; in the latter the biopsy was performed by ultrasound guidance in 53 cases and by stereotactic guidance in 13 cases.

^{99m}Tc -tetrofosmin scintimammography protocol. All patients underwent both planar SM with a dedicated breast camera and SPECT using ^{99m}Tc -tetrofosmin (Myoview, Amersham Health - GE Healthcare) as radiotracer.

Radiolabelling and quality control procedures of the radiotracer were carried out according to the manufacturer's instructions. Labelling efficiency was always $>95\%$. In all patients, 740 MBq of ^{99m}Tc -tetrofosmin were injected intravenously in a pedal vein.

Written informed patient consent was always obtained before scintigraphy.

Planar scintimammography with dedicated breast camera. Planar SM was acquired starting 10 min after the i.v. injection of the radiotracer using the LumaGEM 3200S/12k (Gamma Medica Ideas Inc.), high-resolution solid-state dedicated breast camera which represents the latest advance of LumaGEM breast cameras.

The detector is attached to an adaptor mounted on a modified mammographic unit, replacing the radiographic Bucky, permitting projections very similar to those of mammography. The camera head measures $22.5 \times 27.7 \times 6.64$ cm ($8.87 \times 10.9 \times 2.62$ inches) and weighs 14 pounds. The dead space between the outside edge of the head and the active area of the field of view is <1 cm (0.4 inches). The field of view is 20×15 cm. The camera head is composed of a pixelated (12,288 pixels) array of CZT (pixel size, $1.5 \times 1.5 \times 5$ mm) semiconductor detector coupled to an array of amplifiers, the signals from which are conveyed on an electronics readout board. The system is equipped with a highly sensitive (HSEN, LEAP) long-bore low-energy collimator (hole shape, hex; hole length, 25.4 mm; hole diameter, 2 mm; septal thickness, 0.3 mm) matched to the CZT elements. The system is modeled to have an intrinsic spatial resolution of 1.6 mm; moreover, it has an energy resolution of $<5\%$ (average 4.6% at 140 Kev) which is markedly more favourable than that of a conventional gamma camera, thus reducing scattering radiation in the image data and improving the image contrast.

In all cases the breast images were acquired both in craniocaudal and mediolateral oblique projections (600 sec/view), using a 128×128 matrix size, with the breast positioned between the detector and the compression paddle of the mammographic unit to ensure a light compression of the breast parenchyma, reducing its thickness, limiting movement artefacts and improving lesion contrast. Additional projections were acquired in 4 patients because the breast was bigger than the field of view (1 case) or there were areas of increased uptake at the border of the field of view (3 cases), given the flexibility of mammographic gantry in positioning.

SPECT scintimammography. SPECT SM was acquired immediately after the planar acquisition using a dual head gamma camera (Helix, Elscint or Millennium VG, GE) equipped with low-energy high-resolution parallel hole collimators.

SPECT images were acquired over 360° (180° per head), the patient lying in supine position, the arms raised over the head, with both breasts and axillae included in the field of view. A 64x64 matrix size, a 3° angular step and 30 sec/frame were used. The zoom factor ranged from 1 to 1.2 according to the individual patient. A 10% window and a 140-KeV photopeak were selected. The body contouring system was always used in order to ensure the minimum distance between the patient and the collimator.

Reconstruction was performed with the back projection filter method (with a count-optimized Metz filter) without attenuation correction, including both breasts and axillae in the reconstruction ROI to obtain transaxial, coronal and sagittal slices; 3D images were also obtained in all cases.

Data analysis. Planar and SPECT images of the breasts were independently evaluated by two experienced nuclear medicine physicians who were blinded to the clinical findings, to all the other diagnostic imaging procedure data and to the final histopathological diagnoses.

Scintigraphy was considered positive for tumor in the presence of one or more areas of focally increased tetrofosmin uptake with definable borders in the breast compared to the surrounding tissue.

Interobserver variability was extremely low; disagreement was observed in one case at the qualitative analysis of DBC planar SM and in 2 cases at SPECT and was resolved by consensus.

Planar SM results were compared to those of SPECT, and both of these were related to the other diagnostic imaging data and subsequently to the histopathological findings obtained from surgical samples.

Histopathological diagnosis. The pathological diagnosis was obtained in all patients. Breast surgical specimens were fixed in 10% buffered formalin and stained with haematoxylin and eosin. The size of the carcinomas was determined according to the largest dimension ascertained at surgery. Surgical cancer specimens were also evaluated for tumor histological type and grading. A further immunohistochemical analysis was performed on malignant breast specimens, including oestrogen and progesterone receptor status and proliferation index (MIB-1). According to the number of tumor foci, the carcinomas were classified as unifocal (only one focus) or multifocal/multicentric (two or more tumor foci within a single quadrant of the breast or within different quadrants of the same breast). According to size, the pathological T stage of both unifocal and multifocal/multicentric carcinomas was determined following the AJCC criteria (22). On the basis of these criteria, the largest primary carcinoma was used to designate T classification in multiple simultaneous ipsilateral primary carcinomas.

Statistical analysis. ^{99m}Tc-tetrofosmin planar and SPECT images were classified as true-positive, true-negative, false-positive or false-negative considering histology as the 'gold standard'. Sensitivity, specificity, accuracy, and positive and negative predictive values were then calculated on this basis.

McNemar's test was used to assess the statistical differences in sensitivity and specificity between planar and SPECT scintimammography. The statistical differences between the

Table I. Histopathologic findings and T stage of 74 patients with primary breast carcinoma.

	Histology	No. of cases	T stage
Patients with unilateral unifocal cancer (n=56)	IDCa	54	3 T1a 15 T1b 25 T1c 11 T2
	ILCa	2	2 T2
Patients with unilateral multifocal/multicentric cancer (n=16)	IDCa	8	1 T1b 5 T1c 2 T2
	ILCa	3	1 T1c 2 T2
	Mixed IDCa/ILCa	1	1 T1c
	DCIS	3	3 Tis
	LCIS	1	1 Tis
Patients with bilateral cancer (n=2)	IDCa	1	T1c right, T1c left
	LCis	1	Tis right, Tis left

IDCa, infiltrating ductal carcinoma; ILCa, infiltrating lobular carcinoma; DCIS, ductal carcinoma *in situ*; LCIS, lobular carcinoma *in situ*. T1a, ≤5 mm; T1b, >0.5 and ≤1 cm; T1c, >1 and ≤2 cm; T2, >2 and ≤5 cm; Tis, multifocal/multicentric microscopic carcinoma *in situ*.

sensitivity of the two procedures was calculated taking into account overall primary breast carcinomas and also after subdividing the carcinomas according to palpability (palpable vs non-palpable) and size (≤10 mm and >10 mm). The results were considered significant when P was <0.05.

Results

Histopathological findings. Primary breast cancer was ascertained at biopsy in 74/85 patients, unilateral in 72 cases and bilateral in two cases, while benign lesions were diagnosed in the remaining 11 patients. Moreover, in one of the 72 patients with unilateral breast cancer, a benign condition was ascertained at biopsy in the contralateral breast where suspect microcalcification for cancer was present at mammography.

All 74 patients with malignant breast lesions were then submitted to surgery: quadrantectomy in 53 patients, mastectomy in 20 patients, bilaterally in one with bilateral breast cancer, and mastectomy in one breast and quadrantectomy in the contralateral breast in the remaining patient with bilateral breast cancer.

Of 72 breast cancer patients with unilateral cancer, 56 had a unifocal carcinoma, palpable in 47 cases and non-palpable in 9 cases. The remaining 16/72 patients had multifocal

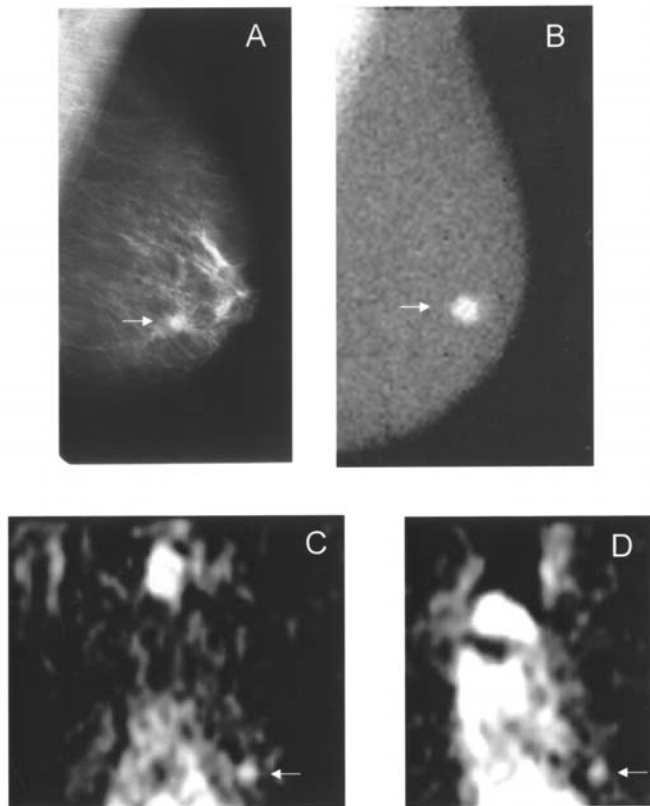


Figure 1. An 81-year-old patient with a palpable T1b (10 mm) infiltrating ductal carcinoma sited in the left breast highly suggestive of cancer at mammography which in medio-lateral oblique projection (A) showed a nodular speculated opacity (arrow). The carcinoma was clearly positive (arrow) at both DBC planar SM in medio-lateral (B) view (arrow) and at SPECT in coronal (C) and sagittal (D) slices.

(n=10)/multicentric (n=6) disease; among the latter 16 patients there were 12 palpable with multiple simultaneous ipsilateral invasive primary carcinomas and 4 non-palpable with multiple microscopic foci of carcinoma *in situ*.

Of the two patients with bilateral cancer, one had two distinct foci of invasive carcinoma, one palpable and one non-palpable, in the right breast and a further palpable invasive focus in the left breast, while the other patient had non-palpable bilateral multifocal microscopic carcinoma *in situ*.

The histopathologic findings of the 74 breast cancer patients are reported in Table I which also includes the pathologic T stage.

In the 5 patients with multifocal/multicentric microscopic carcinoma *in situ* (Tis), including the one with bilateral cancer, the tumor extension ranged from 2 to 5 cm.

In total, 90 primary breast carcinomas were ascertained at surgery, 63 palpable and 27 non-palpable; moreover, 31 were ≤ 10 mm and 59 were >10 mm in size.

Globally, 12 benign lesions, 5 palpable and 7 non-palpable, were ascertained in 12 patients, including the aforementioned patient who also had breast cancer in the contralateral breast. Adenosis was ascertained in 6/12 cases, fibrocystic disease in 3 cases, papillomatosis in 1 case, a mixed pattern of papillomatosis/adenosis in 1 case and a mixed pattern of chronic mastitis, atypical ductal hyperplasia and sclerohyaline fibrosis in the remaining case, the lesions ranging from 7 to 12 mm.

Scintigraphic findings. Planar scintigraphy acquired with DBC was true-positive for cancer in 72 of the 74 patients with primary breast carcinoma globally considered (per-patient overall sensitivity: 97.3%), and false-negative in 2 cases with

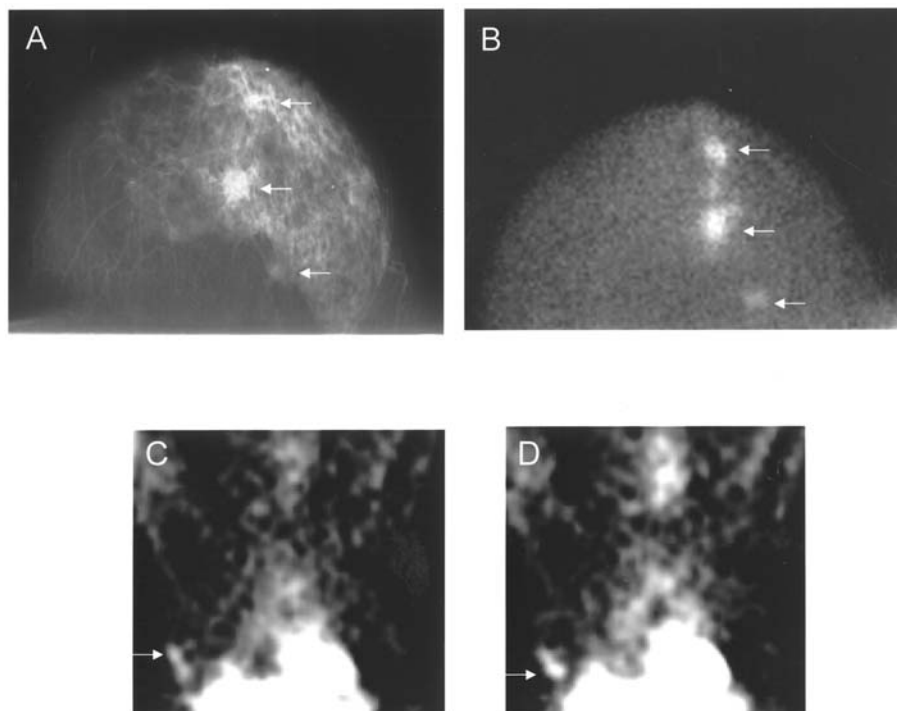


Figure 2. A 58-year-old patient with a T1c (the largest focus measuring 15 mm) multicentric infiltrating ductal carcinoma in the right breast, positive for cancer and for multicentric disease at mammography in cranio-caudal projection (A), which showed multiple nodular speculated opacity (arrows). Both DBC planar SM in cranio-caudal (B) view and SPECT in coronal (C and D) slices were positive. However, SPECT underestimated the number of tumor foci, evidencing only two of these (arrows), while DBC planar SM showed multiple focal areas (arrows) corresponding to mammographic findings.

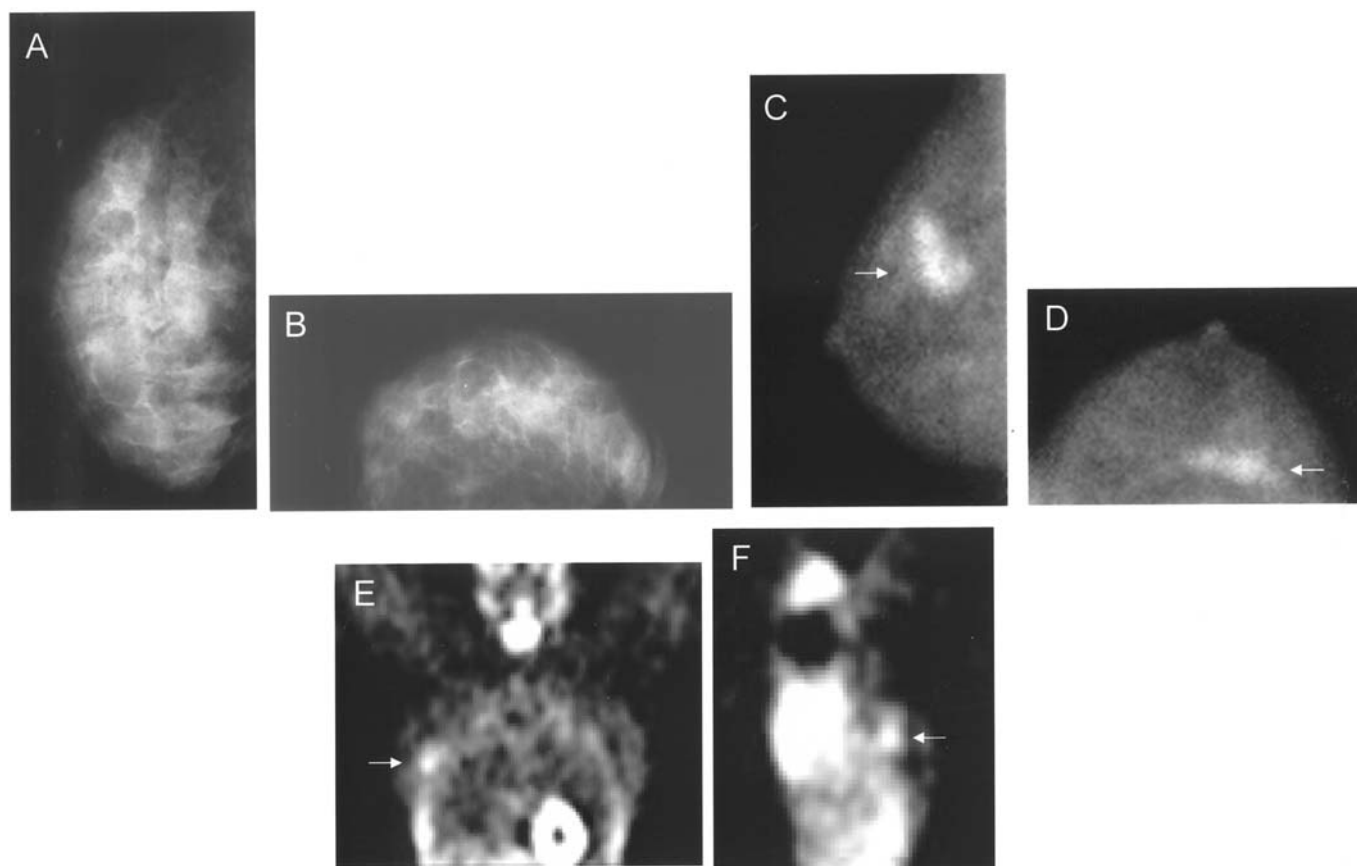


Figure 3. A 44-year-old patient with a non-palpable multiple microscopic lobular carcinoma *in situ* (tumor extension: 30 mm) sited in the upper quadrants of the right breast with diffuse microcalcification without masses at mammography in medio-lateral oblique (A) and cranio-caudal (B) projections. The carcinoma is clearly positive (arrow) at both DBC planar SM in medio-lateral (C) and cranio-caudal (D) projections, and at SPECT in coronal (E) and sagittal (F) slices, but the former better determined tumor extension.

unifocal cancer who had one T1b infiltrating ductal carcinoma each; one of these 2 carcinomas was non-palpable, measured 7 mm in size and was sited in the internal upper quadrant of the left breast, while the other was palpable, measured 6 mm in size and was sited in the internal upper quadrant of the right breast.

SPECT was true-positive in 70/74 patients (per-patient overall sensitivity: 94.6%) and false-negative in 4 cases; the latter included the 2 cases also false-negative at DBC, a further patient with unifocal cancer who had a non-palpable 6-mm T1b infiltrating ductal carcinoma sited in the internal lower quadrant of the right breast and a patient with a non-palpable multifocal microscopic ductal carcinoma *in situ* (2 cm in tumor extension) in the external upper quadrant of the right breast. A unifocal primary breast carcinoma positive at both DBC planar SM and SPECT is shown in Fig. 1.

DBC planar SM and SPECT correctly assessed multifocal/multicentric disease in 11/12 (91.7%) and in 10/12 (83.3%) patients with multiple simultaneous ipsilateral invasive primary carcinomas. Both procedures failed the diagnosis of multifocality in one patient with 2 distinct foci of infiltrating ductal carcinomas of 10 and 5 mm in size, only identifying the larger palpable focus and missing the smaller non-palpable one, while SPECT did not ascertain multifocality in one further case, missing a non-palpable 10-mm infiltrating ductal carcinoma. Moreover, SPECT underestimated the number of invasive foci in another patient with multicentric infiltrating ductal

carcinoma who had 3 distinct foci of 15, 7 and 6 mm in size, missing the latter non-palpable one (Fig. 2).

In the 4 patients with unilateral multiple microscopic foci of carcinoma *in situ*, all were positive at DBC planar SM and 3 at SPECT. DBC planar SM gave a more accurate visualization of tumor extension than SPECT in all concordantly positive cases (Fig. 3).

Moreover, both procedures correctly assessed bilaterality and local tumor extension in the two patients with bilateral cancer.

Among the patients true-positive for cancer at both DBC planar SM and SPECT, 6 unifocal cases were indeterminate for dense breast and 1 multifocal was negative at mammography. One of these unifocal cases is illustrated in Fig. 4. Furthermore, DBC planar SM and SPECT were determinant in assessing multicentric/multifocal disease missed by mammography in 4 and in 3 cases, respectively, with multiple simultaneous ipsilateral invasive carcinomas. Moreover, DBC planar SM and SPECT showed distinct focal areas in 4 and in 3 further patients, respectively, with multifocal microscopic ductal carcinoma *in situ*, including the case with bilateral disease, in all of whom mammography only evidenced microcalcification without masses.

Both DBC and SPECT were true-negative in 11/12 patients with benign disease, all with findings (i.e. microcalcification without mass, architectural distortions, asymmetrical breasts) suspect of cancer at mammography; DBC and SPECT were

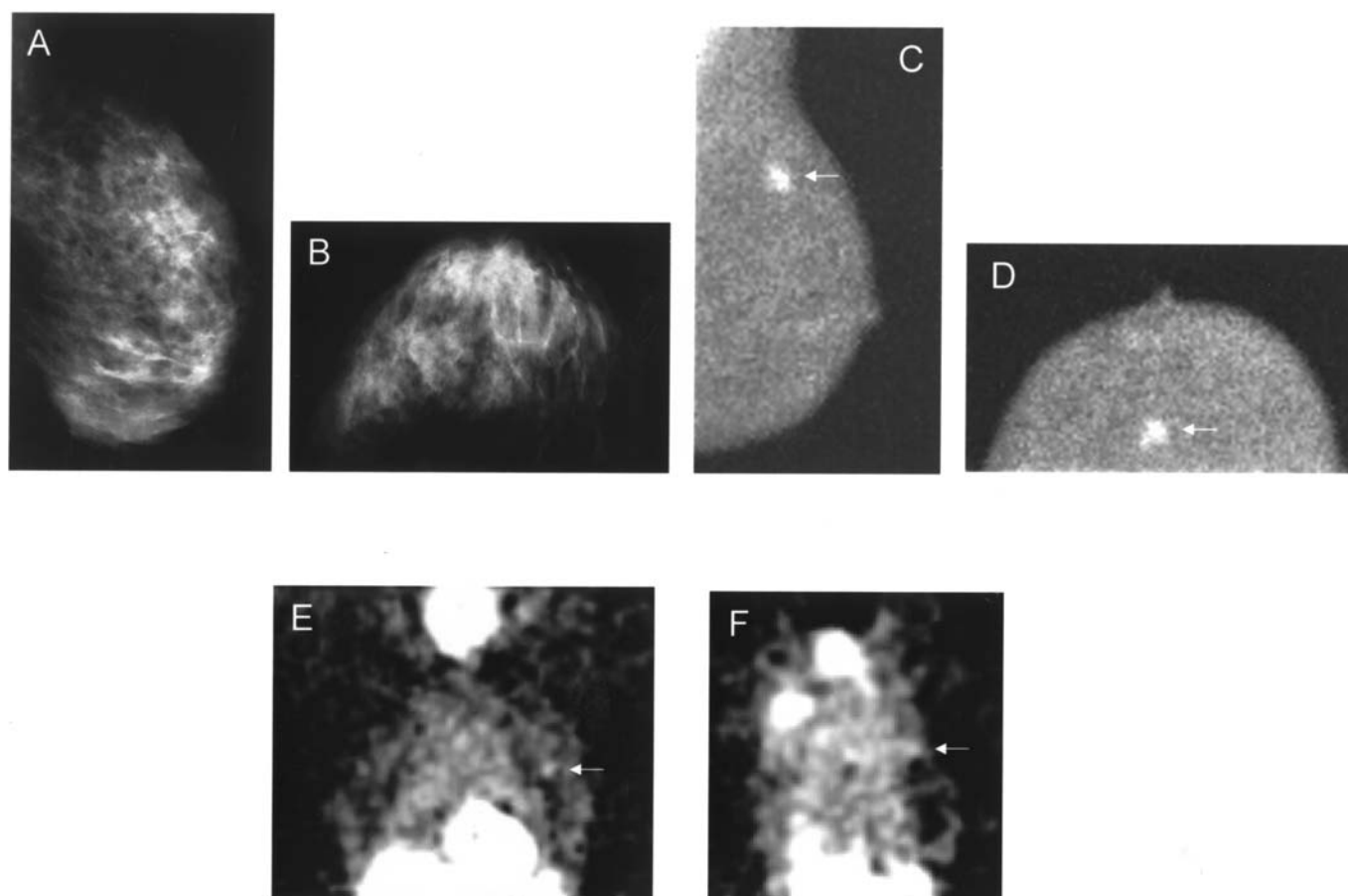


Figure 4. A 50-year-old patient with a non-palpable T1b (8 mm) infiltrating ductal carcinoma sited in the external upper quadrant of the left breast negative at mammography in cranio-caudal (A) and medio-lateral (B) views, but positive at both DBC planar SM in cranio-caudal (C) and medio-lateral (D) views (arrow), and SPECT in coronal (E) and sagittal (F) slices (arrow).

Table II. DBC planar SM and SPECT imaging: overall results calculated on a per-lesion basis (90 carcinomas and 12 benign lesions).

	DBC planar SM	SPECT
True positive	87	83
True negative	11	11
False positive	1	1
False negative	3	7
Sensitivity	96.7% (87/90)	92.2% (83/90)
Specificity	91.7% (11/12)	91.7% (11/12)
Accuracy	96.1% (98/102)	92.1% (94/102)

Table III. DBC planar SM and SPECT sensitivity according to palpability and size of carcinomas.

	DBC planar SM sensitivity	SPECT sensitivity
Palpable carcinomas (n=63)	98.4% (62/63)	98.4% (62/63)
Non-palpable carcinomas (n=27)	92.6% (25/27)	77.8% (21/27)
≤10-mm carcinomas (n=31)	90.3% (28/31)	80.6% (25/31)
>10-mm carcinomas (n=59)	100% (59/59)	98.3% (58/59)

false-positive, concordantly with mammography, in the remaining patient with a mixed pattern of chronic mastitis, atypical ductal hyperplasia and sclerohyaline fibrosis (per-patient overall specificity: 91.7%).

Per-patient overall accuracy values were 96.5% for DBC planar SM and 94% for SPECT; positive predictive value was 98.6% for both procedures, while negative predictive value was 84.6% for DBC planar SM and 73.3% for SPECT.

According to the number of lesions, DBC planar SM globally detected 87/90 primary breast carcinomas ascertained at surgery, while SPECT detected 83/90 (Table II). DBC planar SM showed a higher per-lesion overall sensitivity than SPECT, but not significantly, while specificity values were the same for both procedures which were true-negative in 11/12 benign

lesions. DBC planar SM also showed a higher overall accuracy than SPECT in differentiating malignant from benign breast lesions (Table II).

The sensitivity of both procedures according to palpability and size are reported in Table III. DBC planar SM showed a higher sensitivity than SPECT in both ≤ 10 -mm and >10 -mm carcinomas as well as in non-palpable ones, but not significantly, while both procedures had the same sensitivity value in palpable carcinomas.

Finally, the quality of images was excellent in all cases with DBC used for planar SM, giving a more precise quadrant localization of lesions than SPECT and thus showing a better correlation with mammographic images; moreover, DBC planar SM also gave a clearer visualization of carcinomas, especially when small in size. In addition, the light compression used with DBC was well tolerated, with minimal discomfort for patients.

Discussion

Planar SM acquired with a conventional general purpose gamma camera has proven to be limited in the detection of non-palpable and small size (≤ 10 mm) breast carcinomas, with sensitivity values generally $<60\%$ (4-7).

This poor sensitivity has been explained by the low intrinsic spatial resolution of the gamma camera as well as by technical factors affecting the imaging, such as the large distance between the detector and the breast, the reduced accessibility to some sites, such as the posterior and medial mammary areas, and the impact of scatter radiation from near organs, in particular the myocardium and liver.

Both SPECT, especially when acquired in supine position with the arms up, and planar SM performed with high resolution compact DBC have demonstrated in comparative studies to significantly improve the sensitivity of conventional planar SM in non-palpable and ≤ 10 -mm carcinomas, reaching values $>80\%$ in some series (5,16,21,23).

Moreover, in multifocal/multicentric carcinoma detection, conventional planar SM has obtained sensitivity values in the range of 55-62% (24,25), while SPECT, in preliminary comparative studies, has been shown to increase planar sensitivity from 55.3% to 81.2% (17); however, no specific data using DBC planar SM have been reported in detecting multifocal/multicentric disease in breast cancer.

In the present prospective study we performed a patient-by-patient comparative evaluation between DBC planar SM and SPECT in the detection of both unifocal and multifocal/multicentric primary breast carcinomas using ^{99m}Tc -tetrofosmin as tumor seeking radiotracer. All patients enrolled in the study were suspected to have cancer and were scheduled to undergo biopsy.

DBC planar SM was acquired with the latest advanced Lumagem breast camera system based on a solid-state semiconductor ultra-high resolution CZT detector which presents both energy and spatial resolutions more favourable than those given by other dedicated systems employed until now in clinical studies. Moreover, the detector, mounted on a mammography unit replacing the radiographic Bucky, permitted the same projections as mammography in combination with pain-free mild compression during acquisition and the exclusion

of nearby organs from the field of view. In this way, the intrinsic technical limitations of a conventional gamma camera in breast imaging were greatly reduced, improving the detection of both smaller and deep lesions.

In all cases the scintigraphic data were related to histology and the prevalence of cancer in our series was 87%. A definitive diagnosis of unifocal carcinoma was made in 76% of cancer patients, while multifocal/multicentric disease was ascertained in 24%.

Both DBC planar SM and SPECT proved highly sensitive methods in the detection of primary breast cancer, being globally true-positive in 97.3% and 94.6% of patients, respectively.

The sensitivity obtained with the two procedures was similarly high in both patients with unifocal and multifocal/multicentric carcinomas, without false-negative findings for DBC planar SM in carcinomas >10 mm.

DBC planar SM detected 4 carcinoma foci more than SPECT in 4 breast cancer patients, one of whom had a unifocal carcinoma and 3 with multifocal/multicentric disease.

However, DBC planar SM increased SPECT sensitivity, although not significantly, especially in small ≤ 10 -mm carcinomas and non-palpable ones, reaching 90.3% sensitivity value in the former and 92.6% in the latter. The corresponding values of SPECT were 80.6% and 77.8%, respectively.

Furthermore, the sensitivity values achieved by DBC in the present study in carcinomas of ≤ 10 mm using a CZT detector were markedly higher than those obtained in other clinical studies using different types of high resolution detectors, such as multicrystal sodium iodine (NaI) and multicrystal cesium iodine (CsI) solid-state crystals, in which sensitivity values ranged from 67% to 81% (18,22). The superiority of a CZT detector in respect of these other two types of detectors has also been demonstrated in a phantom study, since it obtained the best energy resolution and a better visualization of simulated <10 -mm breast tumors (26).

In addition, the sensitivity value achieved with a CZT detector of the new DBC system employed in this study was also slightly more elevated in respect to the 86% value reported by other authors using another type of CZT detector connected to a different system (23), most likely due to the higher intrinsic spatial resolution and better energy resolution of the former.

DBC planar SM also showed a slightly higher sensitivity than SPECT (91.7% vs 83.3%) in multifocal/multicentric disease assessment, missing one case, while SPECT two.

Although SPECT proved less sensitive than DBC planar SM in our study, on the whole the former tomographic procedure confirmed its usefulness in both non-palpable and small-size carcinoma detection as well as in multifocal/multicentric disease assessment, with a better performance in respect to conventional planar SM when taking into account the data reported in literature in different series of patients (4-7,24,25).

Moreover, although the present study was not designed to perform a comparative evaluation with mammography, it is interesting to note that in our series DBC planar SM and SPECT gave additional information to mammography in almost 31% and 28% of cases, respectively. In particular, the two procedures detected cancer in all 6 patients with indeterminate mammography for dense breast; they assessed

a higher number of multifocal/multicentric diseases, and also correctly classified patients with doubtful mammographic patterns as affected by malignant or benign lesions, including those cases with microcalcification without masses.

The low performance of mammography is well recognized in detecting cancer in dense breast, with sensitivity values dropping to 44% in cases with extremely dense breast tissue (27); the limited specificity of mammography is also well established, leading to a high number of unnecessary biopsies. These data assume even more importance when considering clinical practice, given the increasing employment of mammographic screening in young women, since a higher and higher number of indeterminate mammograms is to be expected; valid non-invasive complementary tools are thus required to increase the sensitivity of mammography while maintaining a high specificity.

Moreover, mammography has proved poorly sensitive in assessing multifocal/multicentric disease with values ranging from 14% to 44% (28-31). In the era of breast conserving surgery, however, the preoperative assessment of local disease extension is crucial for an appropriate surgical planning, incomplete excision representing a significant risk factor for local recurrence.

Dynamic contrast enhanced magnetic resonance (DCE-MRI) of the breast has been proposed by some authors as a useful alternative diagnostic imaging modality in both dense breast and multifocal/multicentric disease due to its extremely high sensitivity values (31,32). However, like mammography, MRI is also characterized by a low specificity which may cause overtreatment.

In our series, taking into account both DBC planar SM and SPECT findings, biopsy could have been avoided in almost 13% of overall cases.

On the basis of our data it is possible to deduce that both DBC and SPECT could play a complementary role to mammography in primary breast cancer detection. In particular, very high positive predictive values were obtained in this study (96%), positive lesions corresponding to the presence of carcinomas not only when mammography was true-positive but also when the latter was equivocal or indeterminate due to dense breast. In only one case were both DBC and SPECT as well as mammography false-positive.

Moreover, negative predictive value was also high for both procedures, especially for DBC (84.6%), which missed carcinomas in only 2 cases, and SPECT missed carcinomas in 4, most of which were non-palpable and subcentrimetric and sited in internal upper quadrants, while all benign lesions except one were true-negative.

The encouraging results we obtained with both DBC and SPECT as acquisition methods, if confirmed in a larger series of patients, seem to suggest that SM could be employed more widely in the future, in particular in small lesion detection. Furthermore, some authors have recently demonstrated that DBC planar SM is capable of depicting subcentrimetric, mammographically occult carcinomas in women at high risk for breast cancer (21).

Thus, both high resolution planar SM and SPECT might also find a useful employment in the detection of early-stage primary breast cancer; conventional planar SM, on the other hand, is not recognized at present as capable of playing such

a role given its unsatisfactory sensitivity in small carcinoma detection, 90.3% of which by DBC and 80.6% by SPECT were detected in this study.

In our experience, both DBC planar SM and SPECT proved simple to perform, well tolerated and easy to read, although a more adequate training is necessary for SPECT. However, the images acquired with DBC were more resolute in respect of SPECT, especially in small size ≤ 10 -mm carcinomas and in multifocal/multicentric disease, were more easily comparable to those of mammography and also permitted a more precise quadrant localization of the lesion site. Thus, DBC planar SM should be preferred to SPECT. However, since at present DBC systems are still not widely used and are in a continuous stage of development, SPECT maintains an important role when DBC is not available. The performance of SPECT may be further improved by using the hybrid SPECT/TC systems recently employed in clinical practice by means of which anatomical mapping together with functional imaging can be obtained.

Both ^{99m}Tc -tetrofosmin DBC planar SM and SPECT were characterized in our study by an extremely high sensitivity and specificity in both unifocal and multifocal/multicentric breast cancer detection. Their performance appears better than that reported in literature for conventional planar SM acquired with a general purpose gamma camera, in particular in small-size carcinomas. Thus, a larger clinical application of these two procedures as a complementary tool to mammography could be suggested.

Moreover, DBC planar SM showed more technical advantages and a better clinical performance in respect to SPECT in our study and thus it should be preferred in clinical practice. However, SPECT can maintain its current important role as a useful alternative method to DBC, also considering that it is present in most nuclear medicine centres while DBC is not as yet widely available.

Our data clearly need to be confirmed by studies with a larger cohort.

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