Detection of DCIS using ^{99m}Tc-MIBI scintimammography in patients with suspected primary breast cancer, comparison with conventional mammography

Jarosław B. Ćwikła, John R. Buscombe, Andrew J.W. Hilson
Department of Nuclear Medicine, Royal Free Hospital, London, UK

Abstract

BACKGROUND: Scintimammography using Tc-99m MIBI (SMM) is often used clinically as a second line diagnostic test for the detection of breast cancer in cases where there is concern about the results of x-ray mammography (XMM) and ultrasound. Both of these methods, but particularly XMM, may miss a significant proportion of ductal carcinoma in situ (DCIS).
MATERIAL AND METHODS: This study was performed to determine the possible accuracy of SMM in finding DCIS and comparing this with the accuracy of XMM in the same patient. Over a 3 year period 353 patients with no previous history of breast cancer were imaged with both XMM and SMM. The histology of any suspect area was verified by pathological examination of biopsy material. There were 203 malignant breast tumours.
RESULTS: In those 203 cancers there were 15 pure DCIS cancers. SMM correctly diagnosed 12 of these (sensitivity was 80%). XMM diagnosed correctly 8 DCIS (sensitivity 53%) and was equivocal in 2. Combining of both SMM and XMM provided the best result with all but one DCIS identified (sensitivity 93%).
CONCLUSIONS: This study shows that the SMM is helpful in detecting DCIS in those cases where XMM failed to detect DCIS or was equivocal. The combination of the two techniques produces a higher sensitivity result than either modality alone.
Key words: breast imaging, DCIS, scintimammography

Correspondence to: Dr John R. Buscombe
Department of Nuclear Medicine,
Royal Free Hospital, London NW3 2QG
fax: (+44 20) 78302469; e-mail: buscombe@rfhsm.ac.uk

Introduction

In most western countries breast cancer is one of the commonest malignancies among women. England and Wales have one of the highest mortality rates in Europe, and this cancer accounts for about 27 deaths per 100000 women per year (1–3). One of the histological types of breast cancer is DCIS (ductal carcinoma in situ), which unfortunately may be missed by conventional imaging. Though at diagnosis there may be no invasive component to the cancer, some types, such as the comedo type, are more aggressive and often have a poor prognosis (3, 4).

DCIS is normally identified by the particular appearance of microcalcification on mammography and may be classified by its mammographic appearance more than its nature on histology (3–6).

The mammographic features commonly seen at diagnosis of DCIS are rod shaped calcification and a ductal distribution of calcification, also predominantly punctuate calcification, granular calcifications and more than 10 calcifications in a single cluster (1, 3, 7, 8). All of them are often marks for cancer growth and should be the trigger for further exploration. There are however some cases of DCIS without microcalcification or any architectural distortion of the breast. In those cases XMM and ultrasound often fail to detect these (7–9).

Functional imaging uses Tc-99m sestaMIBI, which is an agent of metabolic activity and has significant uptake in a range of

tumours including breast cancer, which was previously described (10–17). Previously performed studies have shown that scintimammography (SMM) has a sensitivity and specificity of 72––100% for the diagnosis of breast cancer (15–17). There has not been a specific study using Tc-99m MIBI SMM to identify DCIS but in a series of 150 patients with suspected primary disease a small group of DCIS was included and these were all identified on SMM (18).

The aim of the study

The aim of this study was to assess the diagnostic accuracy of Tc-99m-MIBI in detection of DCIS in patients with suspected primary malignancy of the breast.

Material and methods

Patients

Patients were recruited from symptomatic breast clinics. Overall 353 female patients were enrolled in this study. The mean age of the patients was 53 years (SD 12; range 28–85). 147 patients were younger than 50 years old (39%). Each patient had a physical examination by a surgeon in supine and upright positions, all had conventional XMM and SMM.

Mammography

Patients with suspected breast cancer were imaged using a standard 2-view XMM before SMM. XMM was performed in standard projections, using a dedicated mammography unit (IGE, DMR, Paris, France). A standard two view protocol, caudal-cranial and lateral-oblique, was used with variable range from 26–28 keV and automatic exposure control (AEC). The images were interpreted by trained specialist radiologists, with knowledge of the patient's history, clinical presentation and the results of any previous mammograms. Cancer was described, when there were suspicious microcalcifications, a spiculated or irregular dense lesion, or when other changes in breast tissue architecture were seen, compared to previous examinations. The clinical reports of all patients were reviewed and graded using a simple 5 point grading system as follows: grade 1: definitely normal or benign; grade 2: probably normal or benign; grade 3: equivocal; grade 4: probably cancer; grade 5: definitely cancer.

Scintimammography

The radionuclide imaging was performed 5–10 minutes after intravenous injection of 740 MBq Tc-99m sestaMIBI (DuPont, Billerica, MA., USA) in a foot vein. All patients were imaged using standard Diggles–Khalkhali method (19) using a two-head gamma camera (Picker Prism 2000XP, Picker, Cleveland, OH, USA). A high resolution, low energy collimator was used in each case. Studies were reported by a specialist in Nuclear Medicine using the same 5 grades as was used in the reporting of the XMM. All SMM images were interpreted blinded to the clinical presentation and mammographic result. Focal or abnormal diffuse uptake in at least one planar image of the breast was the criterion for evaluating a picture as suspicious or malignant. Diffuse uptake without focal accumulation was scored as equivocal. Homogeneous uptake of tracer in both breasts was classified as normal.

Confirmation of pathology

All patients with suspicious breast lesions had limited incisional biopsy, fine needle aspiration biopsy (FNAB), definitive wide local excision or mastectomy confirmed on final diagnosis. All histology and cytology slides were read by a specialist of pathology with an interest in breast cancer.

Data Analysis

Images were interpreted as true-positive when cancer was confirmed by the histological examination, and the images had been scored as probably or definitely cancer (grade 4 and 5). False negative result was when cancer was present but the images had been reported definitely or probably benign or normal or as equivocal (grades 1–3). The examination was interpreted as true negative when cancer was excluded by histopathology and the images were scored as definitely or probably normal or benign (grades 1 and 2). A false positive result was defined when the images were reported as probably or definitely cancer or equivocal (grades 3–5) but there were no malignant tumours. As only a selected group of patients was analysed with known breast cancer, specificity was not analysed.

Results

Malignancy of all types was found in 205 patients and this included 15 pure DCIS. The final classification of the DCIS was as follows: 6 comedo type DCIS (mean size 17.5 mm), 4 cribriform (mean size 28.7 mm) 2 solid type (mean size 20 mm) and last 3 mixed texture DCIS (mean size 28.7 mm) (Table 1). There were 6 poorly differentiated (mean size 24 mm), 6 intermediate differentiated (mean size 16.5 mm) and 3 well differentiated DCIS (mean size 34 mm).

SMM correctly diagnosed 12 of 15 DCIS (Figure 1, Table 2). The sensitivity in the group of DCIS lesions was 80%. XMM diagnosed correctly 8 DCIS and in 2 cases it was equivocal (Figure 2). The sensitivity of the XMM for detection of DCIS was 53%. The combination of both tests (SMM followed by XMM) provides best results with sensitivity 93%. In 7 cases XMM was negative or equivocal, there were 3 cases of high grade, 3 intermediate and 1 low grade DCIS. Three of them were cribriform, 2 represented mixed solid comedo and solid-cribriform types. There was also a single comedo and a single solid type. The sizes of the tumours ranged from 7mm to 26mm. SMM was not helpful in 3 cases which were assessed as normal, two of them were with suspicious microcalcification and further confirmed in histology as solid and comedo type of DCIS.

Only one DCIS (cribriform, size 20 mm) was not detected using sequence imaging, where SMM was followed by XMM. The 3 tumours missed on SMM had a low Ki-67 count and medium to high expression of oestrogen and progesterone receptors evaluated in histochemistry.

Discussion

This study shows that scintimammography is able to find more cases of DCIS than mammography This is not unexpected as SMM has a higher sensitivity than XMM in a range of breast cancers (10–18).

Table 1. Size and type of DCIS found in 15 patients

patient	age	size (mm)	type	grade
1	43	25	cribrifom	high
2	61	23	solid	intermediate
3	68	20	comedo	high
4	51	10	cribriform	intermediate
5	55	15	comedo	high
6	30	7	comedo	intermediate
7	69	18	solid	low
8	52	60	cribriform	low
9	29	14	comedo	intermediate
10	42	25	comedo	intermediate
11	75	26	solid + comedo	high
12	57	20	cribriform	intermediate
13	54	24	comedo	low
14	70	40	solid + cribriform	high
15	56	20	solid + cribriform	high

Table 2. Results of imaging with XMM and SMM, with additional TBR, ER, PR and Ki-67 results

patient	xmm	smm	TBR	ER	PR	Ki-67
1	2	5	1.35	1	1	10
2	4	1	1.21	4	3	5
3	5	5	1.79	3	4	5
4	1	5	1.64	1	1	20
5	4	1	1.10	4	1	10
6	1	5	1.78	2	1	25
7	1	5	1.42	2	2	10
8	4	4	1.25	3	3	10
9	5	4	1.32	4	3	1
10	4	5	1.41	2	1	25
11	3	4	1.71	4	4	5
12	2	4	1.45	2	2	5
13	5	5	1.56	3	2	15
14	4	5	1.47	3	3	10
15	3	1	1.02	3	3	5

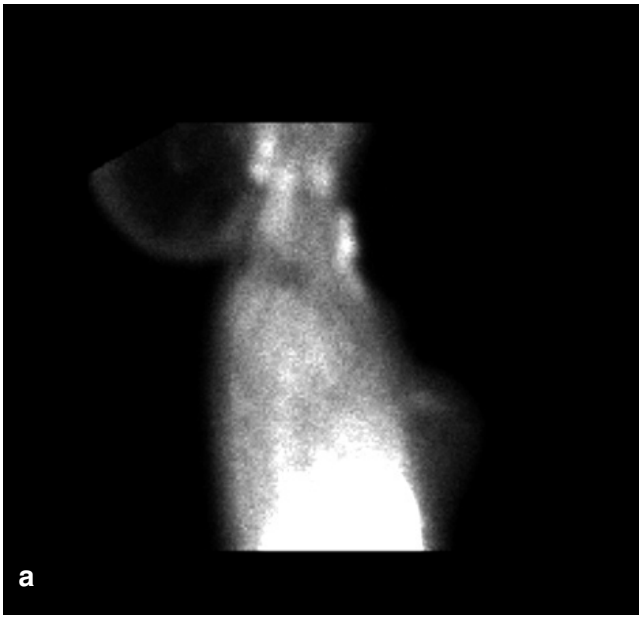
key: XMM is x-ray mammography, SMM is scintimammography, the number denotes the grade of report, 1= definitely normal or benign, 2= probably normal or benign, 3= equivocal, 4= probably cancer, 5= definitely cancer. TBR = tumour to background ratio. ER = oestrogen receptor status (the higher the number the greater the receptor density, PR = progesterone receptor, Ki-67 is a measure of cell replication: the higher the number the more cell mitosis

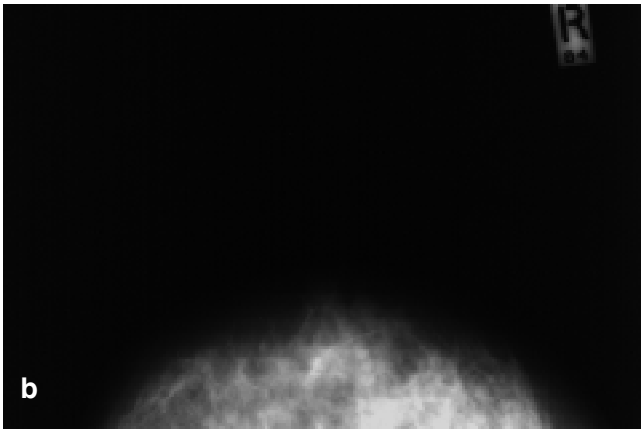
A more conventional second line test when XMM is negative or equivocal is breast US, which seems to complement mammography in the detection of breast cancer (21). However results in DCIS are rather limited (21, 22). A review of mammography and US in 335 cancers indicated that most of the missed tumours on US were DCIS and microinvasive ductal carcinomas dominated by DCIS (22), though other series have suggested it may have a role in the non-calcified DCIS (23).

Unfortunately XMM is dependent on the presence and pattern of microcalcification. In our series 4/15 patients had no microcalcification detectable and these were reported as negative or equivocal. In one patient there was macrocalcification and appearance of benign changes, but on histology this was found to be an area of DCIS.

As SMM does not depend on the presence or absence of microcalcifications and there is evidence that it is not affected by changes in breast density, it is a method which can complement the use of XMM in patients with DCIS. A previous study on a series of mixed primary cancers has suggested this is the case with 8/8 cases of DCIS identified by Tc-99m MIBI (15). However this study did not give concise information about histological type and nuclear grade of the tumours. Therefore direct comparison of the results between this and our study is difficult. Functional imaging can indicate metabolic exchange of the tumour which may not correspond with morphological picture (24–26). Using functional imaging SMM as an additional test, the diagnostic accuracy of this approach in those cases with suspected DCIS produces a higher accuracy than each test alone, which is a similar result to that obtained in all primary breast cancers (27).

It is interesting to note how cellular factors affect the accuracy of SMM in DCIS. For example in previous studies the size of the lesion appeared to be a major factor (28). However in this series the smaller DCIS were seen on SMM but missed on XMM, suggesting that size is less important than function. Indeed it appears





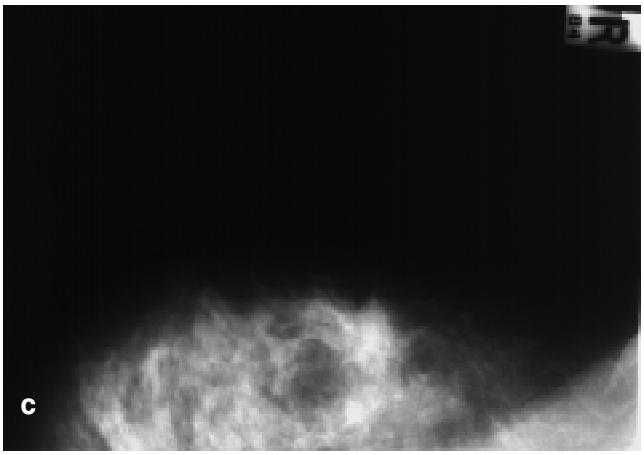
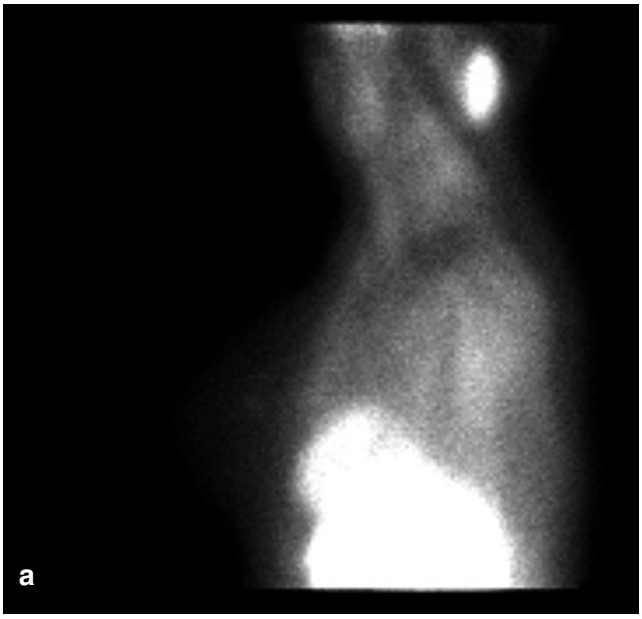
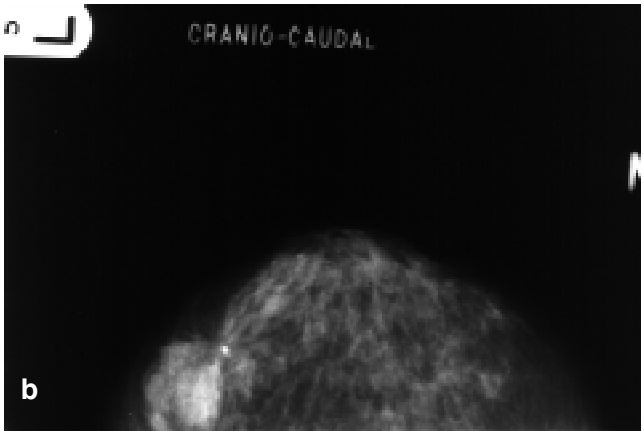


Figure 1. A 30 years old woman with some local increased tissue density in upper segment of the right breast in oblique lateral view (a) but no definitive mass no microcalcification and no worring futures in both crano-caudal and oblique views (a, b). Slightly increase uptake in right lateral view with Tc-99m sestaMIBI (c). Histology small 7 mm comedo type DCIS intermediate grade.





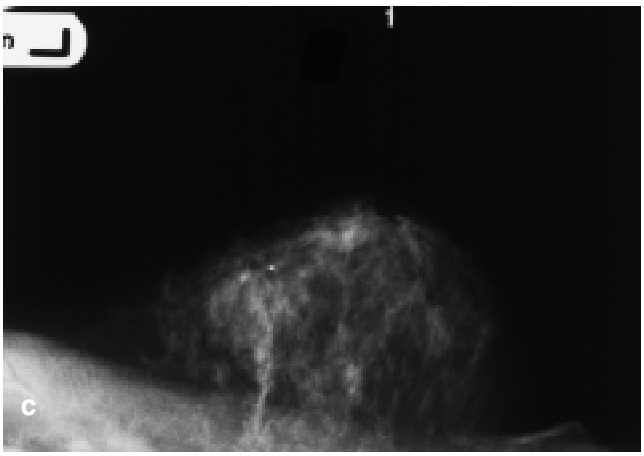


Figure 2. A 57 year old lady with prominent focus of calcification in the supero-lateral segment of the left breast, equivocal result with suspicous of fat necrosis, both standard projections of XMM (a, b). In Tc-99m sestaMIBI focal uptake within left breast (c). Histology cofirmed presence of 20 mm cribriform DCIS intermediate grade.

that those cancers with cellular factors suggesting a non-aggressive cancer with a good prognosis (high level of oestrogen and progesterone receptors, and low Ki-67) are the ones less likely to be seen with Tc-99m MIBI. It is known from previous studies that the most aggressive cancers are those with the greatest uptake of Tc-99m MIBI (29). This will mean that Tc-99m MIBI is finding those cancers in which urgent treatment is required. This is especially important if they are mammographically negative.

Conclusion

This initial study indicated that Tc-99m sestaMIBI is able to detect different types of DCIS even if conventional mammography is negative or equivocal. The combination of the two techniques finds 93% of DCIS and Tc-99m MIBI identifies the most malignant of these.

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