Scintimammography with a Hybrid SPECT/CT Imaging System

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Abstract. Background: Planar scintimammography is useful for characterizing breast lesions >10 mm. Our aim was to evaluate Tc-99m sestamibi scintimammography with a hybrid (SPECT/CT) device for functional anatomical mapping (FAM).

Patients and Methods: Three planar images and a chest SPECT/CT were performed with a hybrid device in 53 patients with mammographically suspicious lesions. The final histopathological diagnosis was obtained after surgery. Results: The planar images were positive in 27 out of 37 carcinomas (sensitivity 73%) and the SPECT/CT in 33 (sensitivity 89.2%). The sensitivity of planar imaging and SPECT/CT was 42.9% and 71.4% in cancers ≤10 mm, and 91.3% and 100% in cancers >10 mm, respectively. The specificity was 93.8% for both planar and SPECT/CT imaging; accuracy was 79.2% for planar scans and 90.6% for SPECT/CT. FAM was useful in providing a precise anatomical localisation of the SPECT findings. Conclusion: SPECT/CT scintimammography using a hybrid device is able to detect breast cancer, showing a sensitivity higher than that of planar images, especially for small cancers.

Breast cancer is the most common malignancy in women: it represents 32% of all invasive tumours in the female population in the U.S.A., and it accounts for 15% of all women’s cancer deaths. In 2005, the American Cancer Society estimated 211,240 new cases and 40,410 female deaths from this disease. Trends in incidence and mortality show that there has been a small but steady annual increase in breast carcinoma incidence over the last 30 years, whereas the mortality rate has declined steadily since the beginning of 1990. This improvement is attributed to earlier detection of breast cancer using mammographic screening.

Till now, mammography is the best imaging modality for the early identification of breast cancer. Nevertheless, this technique has some limitations: not all breast carcinomas are evident on mammograms, especially in dense or dysplastic breasts; moreover, its specificity and positive predictive value are low because it cannot always differentiate benign lesions from malignant ones. The drawbacks of mammography have led to the development of complementary modalities for breast cancer imaging, including scintimammography, a nuclear medicine technique that uses radiopharmaceuticals to detect malignant breast tumours.

Scintimammography is conventionally performed with planar acquisitions, which have a low sensitivity for lesions ≤10 mm. Recently, a new imaging device combining a dual-head, variable angle gamma camera with a low-dose X-ray tube has been introduced: this hybrid gamma camera/CT scanner provides cross-sectional X-ray transmission images that facilitate anatomical localisation of radiotracer uptake, because the acquired tomoscintigraphic and CT images are co-registered by means of the hardware in the same session.

The aim of this study was to evaluate the usefulness of this new imaging system for functional anatomical mapping (FAM) in patients with suspected breast cancer submitted to scintimammography with Tc-99m sestamibi, and if FAM is able to improve the accuracy of conventional planar images in breast cancer diagnosis.

Patients and Methods

Fifty-three female patients (age range: 27-78 years) with suspicious breast lesions on mammography were evaluated. The final histopathological diagnosis was obtained in all the cases after surgery. Each patient gave written informed consent to participate in the study. Patients were injected with ~740 MBq of Tc-99m sestamibi into an antecubital vein of the opposite arm to the known mammary lesion. The labelling and quality control procedures were carried out according to the manufacturer’s instructions. All scintigraphic images were acquired using a combined SPECT/CT system (Millenium VG & Hawkeye; General Electric Medical Systems, Milwaukee, WI, USA) composed of a dual-head, variable angle gamma-camera and an X-ray tube with a set of detectors mounted on opposite sides of the gamma-camera gantry. This system enables the sequential interchangeable acquisition of nuclear medicine and CT images. The CT scanner has a fixed anode oil-cooled X-ray tube operating at 140 kV and 2.5 mA during the acquisition of each image.
Table I. Histopathological findings.

<table>
<thead>
<tr>
<th>Histology</th>
<th>Lesion (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Malignant lesions</td>
<td>37</td>
</tr>
<tr>
<td>Infiltrating ductal carcinoma</td>
<td>29</td>
</tr>
<tr>
<td>Mixed ductal and lobular carcinoma</td>
<td>4</td>
</tr>
<tr>
<td>Infiltrating lobular carcinoma</td>
<td>3</td>
</tr>
<tr>
<td>Infiltrating mucinous carcinoma</td>
<td>1</td>
</tr>
<tr>
<td>Benign conditions</td>
<td>16</td>
</tr>
<tr>
<td>Fibrocystic disease</td>
<td>8</td>
</tr>
<tr>
<td>Fibroadenoma</td>
<td>6</td>
</tr>
<tr>
<td>Papilloma</td>
<td>1</td>
</tr>
<tr>
<td>Cyst</td>
<td>1</td>
</tr>
</tbody>
</table>

Table II. Overview of the results.

<table>
<thead>
<tr>
<th></th>
<th>Planar</th>
<th>FAM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity</td>
<td>73% (27/37)</td>
<td>89.2% (33/37)*</td>
</tr>
<tr>
<td>Specificity</td>
<td>93.8% (15/16)</td>
<td>93.8% (15/16)</td>
</tr>
<tr>
<td>PPV</td>
<td>96.4% (27/28)</td>
<td>97.1% (33/34)</td>
</tr>
<tr>
<td>NPV</td>
<td>60% (15/25)</td>
<td>78.9% (15/19)</td>
</tr>
<tr>
<td>Accuracy</td>
<td>79.2% (42/53)</td>
<td>90.6% (48/53)*</td>
</tr>
</tbody>
</table>

FAM=functional anatomical mapping; PPV=positive predictive value; NPV=negative predictive value.
*p<0.05 vs. planar.

Results

According to the histopathologic results, the patients were divided into two groups as malignant and benign breast lesions (Table I). There were 37 cancers (four different histologic types, palpable in 21 cases and non-palpable in 16 cases) and 16 benign lesions (four different histologic diagnoses, palpable in 11 cases and non-palpable in 5 cases). According to the American Joint Committee on Cancer (AJCC) tumour (T) pathologic classification, three carcinomas were classified as T1a, 11 as T1b, 18 as T1c and five as T2.

SPECT/CT scintimammography detected 33 out of 37 primary breast carcinomas, planar imaging 27/37, and both procedures were true-negative in 15/16 benign mammary lesions. Table II reports the overall sensitivity, specificity, accuracy, positive and negative predictive values of SPECT/CT and planar scintimammography, calculated on the basis of true-positive, false-negative, true-negative and false positive results.

SPECT/CT was positive in 1/3 T1a, in 9/11 T1b, in 18/18 T1c and in 5/5 T2 carcinomas, while planar images were positive in 0/3, in 6/11, in 16/18 and in 5/5, respectively. When considering palpability, SPECT/CT in all the palpable cancers and in 12 out of 16 of the non-palpable ones, whereas planar imaging was positive in 19/21 and in 8/16, respectively. SPECT/CT sensitivity values were significantly
higher than those of the planar scans both in cancers sized <10 mm (71.4% vs. 42.9%, p<0.05) and in non-palpable ones (75% vs. 50%, p<0.05). Moreover, in all the malignant tumours positive both at SPECT7CT and planar imaging, SPECT/CT gave a better anatomical localization of the lesions. Figures 1 and 2 illustrate two patients with two T1b carcinomas, both positive at SPECT/CT and negative at planar imaging.

SPECT/CT scintimammography was false-negative in four breast cancers: two T1a non-palpable invasive ductal carcinomas and two T1b non-palpable invasive carcinomas (one ductal and one lobular). Planar images were false-negative in all the above mentioned four cases missed by SPECT/CT and also in 6 further malignant lesions: 1 T1a non-palpable invasive ductal carcinoma, three T1b invasive ductal carcinomas (two non-palpable and one palpable), two T1c cancers (one non-palpable invasive ductal carcinoma and one palpable invasive lobular carcinoma).

The only false-positive case observed with both SPECT/CT and planar imaging was a palpable fibroadenoma (size 14 mm), highly suspicious for malignancy at mammography, which showed moderate signs of inflammation and a high proportion of proliferating cells at histopathology.

**Discussion**

The capacity of visualizing small carcinomas is critical for the clinical development and acceptance of scintimammography, because the other breast imaging modalities are increasingly used for the early identification of small suspicious abnormalities. Mammography is currently the imaging modality of choice in detecting early, non-palpable breast cancer: however, false-negative results are reported, as well as false-positive findings, and scintimammography has proved to be a very useful adjunct to a non-diagnostic or difficult mammography (5).

Nevertheless, the literature data clearly indicate that the sensitivity of conventional planar scintimammography is strictly dependent on the size of lesions. A multi-centre study on 420 patients with 449 breast lesions (355 carcinomas) has reported sensitivity of 26%, 56%, 95% and 97% for T1a, T1b, T1c and T2 breast cancers, respectively (9); in particular, sensitivity was significantly different between malignant lesions >10 mm (96%) and those ones sized ≤10 mm (46.5%). Similar findings regarding sensitivity are obtained when breast lesions are grouped in palpable and non-palpable, which always show a lower sensitivity on breast scintigraphy, as confirmed by Liberman *et al.* (10), who, in a recent meta-analysis considering 64 unique studies with data on 5,340 patients with 5,354 breast lesions (malignant n=3024), have reported sensitivity of 87.8% for patients with a palpable breast mass and of 66.8% for patients without a palpable lesion. Moreover, the results of a North American multi-centre trial involving 673 patients in 42 institutions (11) have indicated a sensitivity for breast cancer detection of 87% and 61% for palpable and non-palpable abnormalities, respectively.

Technical considerations for scintimammography should be taken into account to obtain good results; in particular, the acquisition of tomographic images, by means of SPECT, could play a role in increasing the sensitivity of planar images. An experimental study carried out on a breast phantom demonstrated a statistically significant gain in the detection rate of small size lesions using SPECT imaging when compared to planar scans (12). However, in clinical practice, SPECT acquisition is not routinely performed, and the value of this imaging method has not yet been definitively established (5). Therefore, the potential role of SPECT in increasing the sensitivity of planar scintimammography, especially for small-sized tumours, is still controversial. In comparative studies using SPECT for primary breast cancer detection, discordant findings have been reported: SPECT sensitivity has been found to be lower than planar images by some authors (13-15) and higher by other investigators (16-18). To this end, it is important to highlight that good quality SPECT imaging can be obtained only with the patient in the supine position and the arms up, because SPECT with patients in the prone position is limited by geometric constraints of the patient, the imaging table and the gantry (5).

The main drawback of SPECT scintimammography is the absence of precise anatomical landmarks that renders localisation efforts difficult and often inaccurate (19). In fact, although SPECT provides better contrast resolution than planar images, it can be difficult to obtain accurate localisation of breast lesions. Fusion imaging can solve this problem by combining the functional information of nuclear medicine studies with the anatomical details of CT or MRI, so allowing a precise localisation of sites of increased radiopharmaceutical uptake: anatomic landmarks are important in order to precisely identify the sites of abnormal uptake and the structures containing normal activity. These are the basis for the growing interest in the development of multi-modality devices combining structural and functional images. These hybrid systems are able to acquire data in the same scanning session, and therefore to reduce the problems often observed with software approaches to image fusion (20). In particular, the first clinical reports indicate that the dual-modality data acquired using a device combining a dual-head, variable angle gamma camera with a low-dose X-ray tube, is clinically useful in cancer imaging with single-photon radiopharmaceuticals, including Tc-99m sestamibi (21, 22).

The present study was performed with this hybrid SPECT/CT imaging system in a series of patients with suspected breast cancer. The data obtained have clearly indicated the clinical usefulness of Tc-99m sestamibi
SPECT/CT scintimammography. The comparative evaluation of FAM and planar acquisitions have demonstrated the greater effectiveness of SPECT/CT. In particular, a marked difference in sensitivity both in non-palpable primary breast cancers and in those sized ≤10 mm, the two categories that are most difficult to detect and to distinguish from benign lesions with conventional diagnostic procedures was found. Planar images missed more than 50% of these lesions, and they were never positive in carcinomas negative on FAM. These results suggest that the use of SPECT/CT must be preferred for small non-palpable breast cancers, because its sensitivity is significantly higher than that of planar scans. Moreover, also in malignant lesions of >10 mm the planar imaging detection rate was slightly lower than that of FAM.

In our series, both SPECT/CT and planar scintimammography demonstrated high specificity (93.8% for both) and positive predictive value (97.1% and 96.4%, respectively), with the same single false-positive result in

Figure 1. Sixty-one years old patient with a proven non-palpable 6 mm infiltrating ductal carcinoma in the external quadrants of the right breast. Mammography in the mediolateral oblique projection (A) demonstrates a nodular spiculated opacity (black arrow). Tc-99m sestamibi planar scintimammography (right prone lateral view) is negative (B). SPECT (C, center) shows a focal uptake (white arrow) that SPECT/CT (C, right) demonstrates corresponding to the carcinoma (white arrow); the respective CT scan is on the left.
one palpable high-proliferating fibroadenoma with signs of inflammation. This outcome is in accordance with the findings of a recent paper aimed of assessing the tissue-specific effects on uptake of Tc-99m sestamibi by breast lesions, with a targeted analysis of false scintigraphic diagnoses; overall, the uptake pattern was determined by a combination of factors, with the extent of the inflammatory component of benign lesions playing a major role (23).

In conclusion, this study confirms the high specificity of Tc-99m scintimammography in differentiating malignant from benign breast lesions in patients with suspected breast carcinoma. Moreover, our findings indicate that SPECT/CT with a hybrid device is useful for breast imaging: it improves

Figure 2. Fifty-six years old patient with a proven non-palpable 10 mm infiltrating ductal carcinoma in the lower quadrants of the left breast. Mammography in the craniocaudal projection (A) demonstrates a nodule with irregular borders (black arrow). Tc-99m sestamibi planar imaging (left prone lateral view) is negative (B), while SPECT (C, center) shows a focal area of increased uptake (white arrow) that SPECT/CT (C, right) precisely localizes in the breast (white arrow); the corresponding CT scan is on the left.
the diagnostic accuracy of conventional planar scintimammography. In particular, FAM is more sensitive than planar scintigraphy, especially in the detection of non-palpable and/or sized ≤10 mm breast cancers. Therefore, a more extensive use of this new technology for breast imaging with scintimammography is suggested; however, we are aware that further studies in larger series are needed to confirm our data.

References


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