

# Detection of bilateral, multifocal breast cancer and assessment of tumour response to neoadjuvant chemotherapy by Tc-99m sestamibi imaging – a case report

Mariano Grosso<sup>1</sup>, Muhammad Babar Imran<sup>2</sup>, Duccio Volterrani<sup>1</sup>,  
Manuela Roncella<sup>3</sup>, Khalid Abufalgha<sup>4</sup>, Gaia Grassetto<sup>5</sup>,  
Adil Al-Nahhas<sup>6</sup>, Domenico Rubello<sup>5</sup>, Giuliano Mariani<sup>1</sup>

<sup>1</sup>Regional Centre of Nuclear Medicine, University Hospital of Pisa, Pisa, Italy  
<sup>2</sup>Punjab Institute of Nuclear Medicine, Faisalabad Hospital, Faisalabad,  
Pakistan

<sup>3</sup>Breast Surgery Unit, University Hospital of Pisa, Pisa, Italy

<sup>4</sup>Department of Radiology and Medical Imaging, Misurata Central  
Hospital, University Medical School, Misurata, Libya

<sup>5</sup>Department of Nuclear Medicine, "S. Maria della Misericordia" Hospital,  
Rovigo, Italy

<sup>6</sup>Department of Nuclear Medicine, Hammersmith Hospital, London, United  
Kingdom

[Received 14 XI 2008; Accepted 08 II 2009]

## Abstract

In breast cancer, neoadjuvant chemotherapy needs early indication for responsiveness. Tc-99m sestamibi scintimammography provides comprehensive information about the extent of disease including multiple foci in one or both breasts and possible involvement of nodes.

In the present case, X-mammography was positive for a suspicious mass in the upper quadrant of the left breast only. On the

other hand, Tc-99m Sestamibi scintimammography was able to depict the full extent of the disease, including its spread to the axillary lymph node, and gave useful information on the effectiveness of neoadjuvant chemotherapy.

The case reported here demonstrates that Tc-99m sestamibi scintimammography was useful in detecting bilateral breast cancer and could provide additional information on possible axillary lymph node involvement. Furthermore, Tc-99m sestamibi scintimammography was effective in monitoring response to chemotherapy in the studied case.

**Key words:** breast cancer, chemotherapy, Tc-99m sestamibi

Nuclear Med Rev 2008; 11, 2: 70–72

## Introduction

Breast carcinoma is a serious health problem for women, with a strong socioeconomic impact [1]. Early diagnosis is achieved by routine physical examination and programmed screening with mammography. Both procedures are known to have certain diagnostic limitations [2].

Tc-99m sestamibi imaging has been used as a complementary test to diagnose primary breast cancer. Its role for axillary lymph node involvement has also been evaluated [3]. Tc-99m Sestamibi is a substrate for the P-glycoprotein transport mechanism, which is responsible for multidrug resistance (MDR) expression, and Tc-99m Sestamibi uptake can be significantly decreased in tumour cells overexpressing the MDR1 gene. Therefore, in addition to its diagnostic role, Tc-99m Sestamibi can provide important information for the evaluation of the susceptibility of a breast cancer to chemotherapeutic agents [4]. This report reveals the role of

Correspondence to: Domenico Rubello  
Department of Nuclear Medicine, PET Centre  
'S. Maria della Misericordia' Hospital  
Viale Tre Martiri, 140, I: 45100, Rovigo, Italy  
Tel.: (+39 425) 394 427 44–31, fax: (+39 425) 394 434  
email: domenico.rubello@libero.it

Tc-99m sestamibi for the evaluation of multifocal bilateral breast cancer, lymph node involvement, and its possible role in the selection of treatment and in prognosis.

## Case report

A 49-year-old woman with a mammography showing clusters of microcalcifications in the external upper quadrant of the left breast underwent Tc-99m sestamibi imaging.

Lateral prone and anterior supine images were acquired 20 minutes after intravenous injection of 740 MBq of Tc-99m sestamibi. Imaging was performed using a dual-head LFOV gamma camera (ELGEMS Millennium, GE) equipped with a high-resolution parallel-hole collimator.

As shown in the upper panel of Figure 1, scintimammography showed increased tracer concentration with tumour to background ratio (T/B) > 2.4 in the upper and lower quadrants of the right breast and in the upper quadrants of the left breast with extension to the equatorial low region (T/B = 2.7). There was also another area of increased tracer uptake in the left axilla. These findings were suggestive of bilateral malignancy with left axillary metastases.

The patient received four cycles of neoadjuvant chemotherapy (CAF protocol: cyclophosphamide, doxorubicin, and fluorouracil) followed by a second Tc-99m sestamibi scintimammography three weeks after completion of chemotherapy. The second scan (lower panel of Figure 1) showed no abnormal uptake in the right breast, in the lower quadrants of the left breast, or in the left axilla. Although still detectable, uptake in the upper quadrants of the left breast was remarkably reduced compared with the previous scan, confirmed by semiquantitation (T/B = 1.29 vs. 2.7 pre-treatment), suggesting that most of the tumour foci responded favourably to chemotherapy.

The patient underwent bilateral radical mastectomy plus bilateral axillary lymphadenectomy one month after chemotherapy, and histology revealed microfoci of lobular in situ carcinoma

in the left breast, multifocal infiltrative lobular carcinoma with neoplastic lymphangiosis in the right breast, and left axillary involvement (1/14 nodes positive). After surgery the patient received adjuvant chemotherapy consisting of five alternate cycles of CAF and CMF (cyclophosphamide, methotrexate, and fluorouracil).

## Discussion and conclusions

The diagnosis of breast carcinoma poses a dilemma in certain circumstances, such as in younger women with dense breasts, in severe dysplastic disease, in the presence of microcalcifications, or in patients evaluated following breast surgery or radiotherapy. In such circumstances, the diagnostic accuracy of mammography is quite low. Moreover, neoadjuvant chemotherapy (which ensures a better outcome) needs early indication for responsiveness [5]. Scintimammography provides comprehensive information about the extent of disease including multiple foci in one or both breasts, and possible involvement of nodes. Change in uptake after initial chemotherapy can give an indication as to the effectiveness of therapy.

In the present case, mammography was positive for a suspicious mass in the upper quadrant of the left breast. Scintimammography explored the full extent of the disease including its spread to the axillary lymph node.

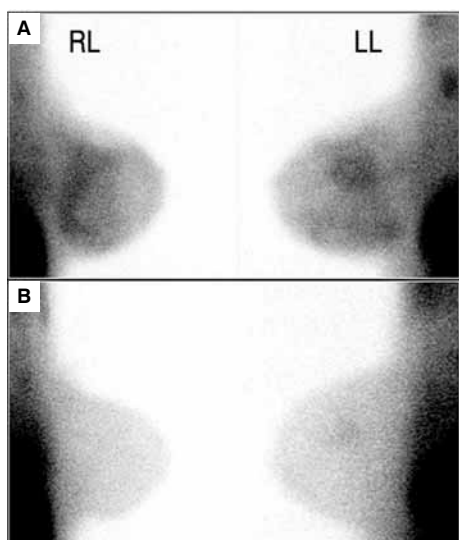
Tc-99m sestamibi has good physical characteristics for scintimammography, and consequently high diagnostic accuracy [6]. This lipophilic cation is retained in cells by electronegative cellular and mitochondrial membrane potentials [7]. Its increased uptake is due to the high density of mitochondria and increased blood flow in tumours (angiogenesis) in comparison with the normal breast, and is inversely related to necrosis. It has been observed that Tc-99m sestamibi scans may allow in vivo visualization of the level of MDR1 expression, which can represent an important factor in the evaluation of response to chemotherapy [8–9].

Assessment of axillary lymph nodes for the spread of cancer is important for planning treatment. A non-invasive technique to detect breast cancer with axillary lymph node metastases could permit a better selection of patients for axillary dissection. Taking advantage of the whole-body distribution of Tc-99m sestamibi, detection of foci in the axillae would facilitate treatment planning without sentinel lymph node mapping.

This case report demonstrates that scintimammography may be useful in detecting bilateral breast cancer and can provide additional information on possible axillary lymph node involvement. Furthermore, scintimammography was effective in monitoring response to chemotherapy.

## Reference

1. Cancer facts and figures 1995. American Cancer Society, Atlanta, Georgia 1995.
2. Donnegan WL. Evaluation of a palpable breast mass. *N Engl J Med* 1992; 327:937–942.
3. Taillefer R, Robidoux A, Turpin S, Lambert R, Cantin J, Leveille J. Metastatic axillary lymph node Technetium-99m-MIBI imaging in primary breast cancer. *J Nucl Med* 1998; 39: 459–464.
4. Moretti JL, Duran Cordobes M et al. Involvement of glutathione in loss of Technetium-99m-MIBI accumulation related to membrane MDR pro-



**Figure 1.** Tc-99m sestamibi scintimammography. **A.** Before treatment. **B.** After neoadjuvant chemotherapy. LL — left lateral; RL — right lateral.

- tein expression in tumor cells. *J Nucl Med.* 1998; 39: 1214–1218.
5. Booser DJ, Hortobagyi GN. Treatment of locally advanced breast cancer. *Semin Oncol* 1992; 19: 278–85.
6. Khalkhali I, Cutrone J, Mena I et al. Technetium-99m-sestamibi scintimammography of breast lesions: clinical and pathological follow-up. *J Nucl Med* 1995; 36:1784–1789.
7. Chiu ML, Kronauge JF, Piwnica-Worms D. Effect of mitochondrial and plasma membrane potentials on accumulation of hexakis (2 methoxy-isobutyl isonitrile) technetium in cultured mouse fibroblast. *J Nucl Med* 1990; 31: 1646–1653.
8. Piwnica-Worms D, Chiu ML, Budding M, Kronauge JF, Kramer RA, Groop JM. Functional imaging of multidrug resistant P-glycoprotein with an organotechnetium complex. *Cancer Res* 1993; 53: 977–984.
9. Del Vecchio S, Ciarmiello A, Pace L et al. Fractional retention of technetium-99m-sestamibi as an index of P-glycoprotein expression in untreated breast cancer patients. *J Nucl Med* 1997; 38: 1348–1351.