

Tc-99m MIBI MAMMOSCINTIGRAPHY : A FUNCTIONAL IMAGING FOR BREAST CANCER

Molrudee EKMAHACHAI, M.D.,¹ Nonglak VILASDECHANON, M.Sc.,¹
Chanpen VONGBOONTAN, Cert. in Rad.Tech.,¹ Sombut BOONYAPRAPA, M.D.¹

ABSTRACT

Drug resistance of malignant cells is a major cause of failure in cancer chemotherapy. Multidrug resistance (MDR) mediated by the transmembrane pump P-glycoprotein (Pgp) is an important mechanism of tumor resistance against chemotherapy. Recent study by Ciarmiello et al reported that Tc-99m MIBI efflux from the breast cancers with high levels of Pgp was significantly faster than that observed in cancers with low Pgp levels. The purpose of our study was to evaluate the pattern and characteristic of Tc-99m MIBI uptake in the breast cancers.

METHODS

The Tc-99m MIBI mammoscintigraphies were performed in 16 female patients with suspected of breast cancer, age range 32-73 years, mean 52 years. The early and delayed planar images of the breasts were obtained at 20 minutes and 1 hour after injection with 20 millicuries of Tc-99m MIBI intravenously. The Tc-99m MIBI tumor indices were also calculated and analyzed.

RESULTS

All patients had the final diagnosis of infiltrating ductal carcinoma of the breast. Our results revealed two different patterns of Tc-99m MIBI uptake within the breast carcinomas. Of the 16 patients, 15 patients (93.75%) had negative value of the MIBI tumor index (washout pattern) and one patient (6.25%) had the positive value (accumulation pattern).

CONCLUSION

From our study, we found different patterns

of Tc-99m MIBI biokinetic changes within the breast cancers. Therefore, we consider that the Tc-99m MIBI mammoscintigraphy may not only be useful for the diagnosis, but also for the prediction of chemotherapeutic response in the patients with breast cancer.

INTRODUCTION

Drug resistance of malignant cells is a major cause of failure in cancer chemotherapy. Multidrug resistance (MDR) mediated by the transmembrane pump P-glycoprotein (Pgp) is an important mechanism of tumor resistance against chemotherapy. Pgp is a 170 kDa membrane transport protein present in many normal tissue and tumors, which appears to function as a cellular efflux pump of a variety of potent chemotherapeutic agents.^{1,2}

Technetium-99m Sestamibi (Tc-99m MIBI) is a lipophilic cationic isonitrile analog that has been used for myocardial perfusion imaging as an alternative to Thallium-201 since 1989.³ Later,

¹ Department of Radiology, Faculty of Medicine, Chiang Mai University, Chiang Mai 50200, THAILAND

Tc-99m MIBI has been accepted as a tumor imaging agent for detection a number of benign and malignant tumors in clinical imagings.⁴⁻⁷ The use of Tc-99m MIBI as a new agent for mammoscintigraphy was initially reported by Campeau et al in 1992.⁸ In the past several years, a number of reports have indicated that Tc-99m MIBI mammoscintigraphy is an effective procedure in the diagnosis of breast carcinomas.⁹⁻¹⁵ Recent publications have shown that breast imaging with Tc-99m MIBI has a high sensitivity and improved the specificity of conventional mammography for the diagnosis of breast cancer.^{9,12,16,17} It was recently reported that Tc-99m MIBI is a Pgp transport substrate, and thus Tc-99m MIBI scintigraphy may be used as a noninvasive imaging to detect the Pgp expression in human tumors in vivo.^{1,18,19} The study by Ballinger et al also supported the potential use of Tc-99m MIBI for functional imaging of Pgp activity in patients undergoing chemotherapy.² Interestingly, recent study by Ciarmiello et al which performed the Tc-99m MIBI mammoscintigraphy in patients with breast cancer, showed that Tc-99m MIBI efflux from the breast cancers with high levels of Pgp was significantly faster than that observed in cancers with low Pgp levels.²⁰

We proposed Tc-99m MIBI mammoscintigraphy as a functional imaging for breast cancers and the purpose of our study was to evaluate the pattern and characteristic of Tc-99m MIBI uptake within the breast cancers.

MATERIALS AND METHODS

Sixteen female patients with suspected of breast carcinoma aged 32 - 73 years, mean 52 years were referred for the Tc-99m MIBI mammoscintigraphy. All patients had palpable breast masses. The lesion size ranged from 2.0-8.0 cm in diameter (mean 4.2 cm) by mammographic or physical findings. Five of these also had ipsilateral palpable axillary nodes, and one had both ipsilateral axillary and supraclavicular node palpable. All of them underwent surgery and/or fine needle aspiration biopsy of the breasts for the final diagnosis.

The mammoscintigraphy were performed with intravenous injection of 20 mCi of Tc-99m MIBI in the arm contralateral to the abnormal breast. Planar anterior imagings were obtained including both breasts and axillary regions at 20 minutes (early image) and 1 hour (delayed image) after injection, with the patients in supine position, the arms were raised and the hands were placed behind the head. Additional posterior oblique views of the breast were also imaged in the upright position. The Tc-99m MIBI mammoscintigraphies were acquired with a preset time of 2 minutes for each image in 256 x 256 matrix, using a large-field-of-view gamma camera (Apex-SP4 Elscint), equipped with low energy general purpose collimator.

Furthermore, the regions of interest were drawn over areas of increased Tc-99m MIBI uptake in the primary tumors, in order to get the numbers of counts from both early and delayed images in every patient. Then, the Tc-99m MIBI tumor indices were calculated and analyzed by using the following formula.

$$\text{MIBI tumor index} = \frac{(\text{Counts at 1 hour} - \text{Counts at 20 min})}{\text{Counts at 20 min}} \times 100 \%$$

RESULTS

All patients had the final diagnosis of infiltrating ductal carcinoma of the breast, proven by surgery and/or biopsy.

The early and delayed Tc-99m MIBI mammoscintigraphic results demonstrated focal areas of increased uptake that corresponded to the palpable breast masses in all patients. In addition to the uptake of Tc-99m MIBI in primary breast tumors, 5 of these also revealed other focal areas of increased uptake in the palpable axillary nodes, and one showed positive MIBI uptake in the regional axillary and supraclavicular lymph node metastases. However, the breast cancers in our study were all palpable and rather big in size, with the smallest is 2.0 cm in diameter.

As compared the two interval early and delayed mammoscintigraphic findings in each patient, and also from the analysis of the MIBI tumor indices, we found that there were two types of Tc-99m MIBI uptake within the breast tumors, which were classified as washout and accumulation patterns. Of the 16 patients, 15(93.75%) had negative value of the MIBI tumor index (washout pattern), which ranged from -12.77% to -40.07%, mean -23.56%. The remainder one patient(6.25%) had positive value of the MIBI tumor index (accumulation pattern), which was +1.26%.

DISCUSSION

Tc-99m MIBI is a lipophilic cationic agent, which accumulates within the mitochondria and cytoplasm of cells on the basis of electrical potentials generated across the cell membranes.³ The exact mechanism of Tc-99m MIBI uptake in tumor cells is not yet clearly understood. However, it is considered to be multifactorial, including regional blood flow, viability, cellularity, metabolic activity, mitochondrial activity, plasma membrane potentials and Pgp expression in tumor cells.^{3,21-23} The Pgp is an energy-dependent

transmembrane efflux pump, which decreases the accumulation of a broad spectrum of chemotherapeutic drugs, including anthracyclines, vinca alkaloids, podophylotoxins, actinomycin-D, and mitomycin within the tumor cells.²⁴ The presence of Pgp overexpression represents an expression of MDR in patients with cancer.^{21,25} Previous study from France found that Tc-99m MIBI uptake by cells expressing no immunodetectable levels of Pgp was significantly higher than that by cells expressing high Pgp levels.¹⁹ Ballinger et al from Canada performed Tc-99m Sestamibi imaging study in a rat breast tumor cell line and its doxorubicin-resistant variant, and found that Tc-99m MIBI washed out of the resistant tumors at three times the rate of non-resistant tumors.² Therefore, the mammoscintigraphy using Tc-99m MIBI has been proposed as a noninvasive imaging method in demonstrating Pgp expression or MDR tumor in many recent series.^{20,25}

Conventional mammography is still the only imaging examination recommended for breast cancer screening. However, Tc-99m MIBI scintigraphy plays an important role as a complementary imaging to mammography especially in patients with dense breast or equivocal mammographic findings.¹⁰ Tc-99m MIBI mammoscintigraphy is well accepted as a sensitive test in detecting primary breast carcinoma, moreover it can detect the axillary lymph node metastases as well.^{11,26,27} Like in our study, in addition to uptake in the primary breast tumors, we found Tc-99m MIBI uptake in the axillary node metastases in 5 patients, and in one patient we found Tc-99m MIBI uptake in the primary left breast cancer, left axillary nodes, and also in left supraclavicular node metastases as well.

The MIBI tumor index were derived from percent difference between the early and delayed tumor counts, thus the MIBI tumor index represented the Tc-99m MIBI washout from or accumulation within the tumors. From the

literature review, we found that Tc-99m MIBI uptake related to the Pgp levels within the tumor cells.^{2,19,20} Therefore, we consider that the Tc-99m MIBI tumor index, may relate to the difference of Pgp levels within the tumor cells as well. Of the 16 patients, one patient with positive value of MIBI tumor index represented Tc-99m MIBI accumulation within the breast tumor, may probably associate with no Pgp expression of the tumor cells. The remainder 15 patients with varying range of negative MIBI tumor index indicated different rate of washout of Tc-99m MIBI from those breast tumors. In contrast to the former assumption, the washout pattern may probably relate to the different Pgp expression within the tumor cells in those patients.

However, further studies are required to confirm whether the Tc-99m MIBI tumor index relates to the difference of Pgp levels within the tumor cells or not, and if so this finding will be very helpful in the prediction of chemotherapeutic response in the patients with breast cancer.

In conclusion, Tc-99m MIBI mammoscintigraphy is a simple, noninvasive and useful imaging in the detection of breast carcinoma. Our results revealed different patterns of Tc-99m MIBI biokinetic changes within the breast cancers. Therefore, we consider that the Tc-99m MIBI mammoscintigraphy may not only be useful for the diagnosis, but also for the prediction of chemotherapeutic response in the patients with carcinoma of the breast.

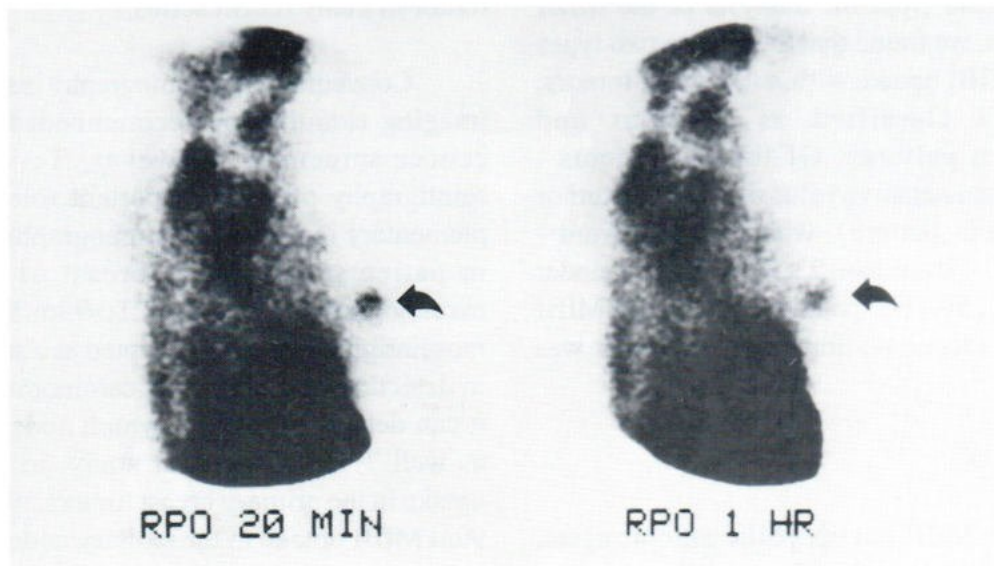


Fig. 1. A 44-year-old woman presented with a palpable right breast mass. Physical examination revealed a 4-cm right breast mass at the upper outer quadrant. Right posterior oblique views of Tc-99m MIBI mammoscintigraphy performed at 20 minutes and 1 hour after injection, show definite focal increased uptake in the right breast tumor (curve arrows). The MIBI tumor index was -20.93% , which represented washout of the Tc-99m MIBI from the breast tumor. Biopsy findings corresponded to infiltrating ductal carcinoma.

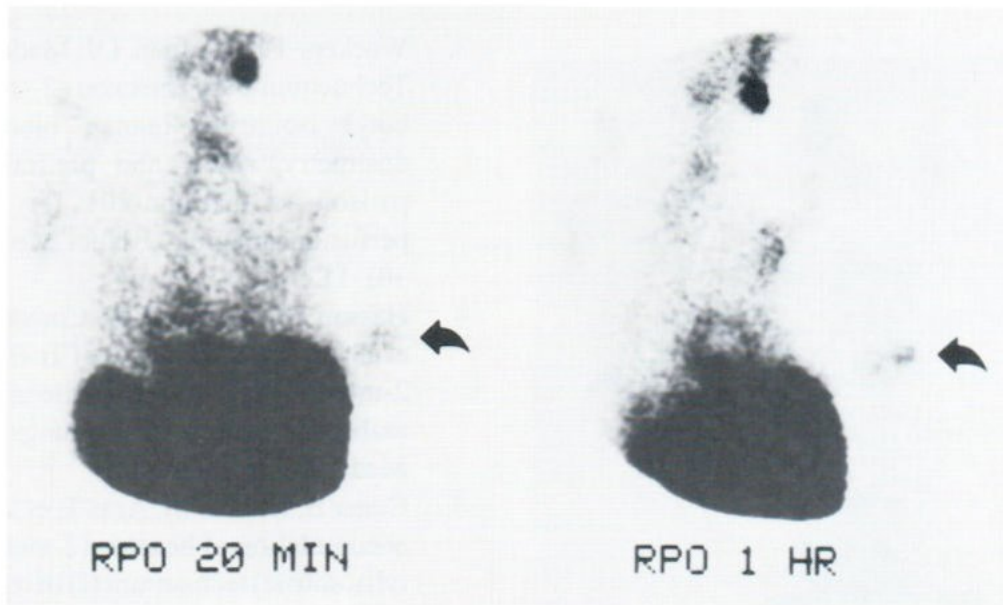


Fig. 2. A 48-year-old woman presented with a palpable right breast mass. Physical examination revealed a 6-cm right breast mass at the central portion. Early and delayed images of Tc-99m MIBI mammoscintigraphy obtained in the right posterior oblique view reveal an area of focal increased uptake in the right breast tumor (curve arrows) that corresponded to the palpable breast mass, with accumulation pattern. The MIBI tumor index was +1.26%. The final diagnosis was infiltrating ductal carcinoma, proven by surgery.



Fig. 3. Anterior view of Tc-99m MIBI mammoscintigraphy performed at 20 minutes after injection, demonstrates definite focal increased uptake in the primary right breast tumor (thick arrow) and ipsilateral axillary lymph node metastases (curve arrow). Moreover, diffuse increased uptake in the soft tissue of right breast surrounding the primary tumor (thin arrow) is also noted, represents skin involvement of the cancer. These scintigraphic findings corresponded to the physical examination. Biopsy of the right breast mass revealed an infiltrating ductal carcinoma.



Fig. 4. Early anterior image of Tc-99m MIBI mammoscintigraphy reveals focal areas of increased uptake in the primary left breast tumor (arrow head), ipsilateral axillary node (curve arrow) and supraclavicular lymph node metastases (thin arrow), corresponding with the physical findings. Biopsy of the left breast mass indicated infiltrating ductal carcinoma.

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