Diagnostic value of $^{99m}$Tc MIBI scintimammography in patients with breast lesions

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Summary.—This study has aimed to determine the diagnostic value of the scintimammography with $^{99m}$Tc-MIBI in the detection of primary breast cancer and to verify its clinical usefulness. Sixty-three female patients (age range 27-83) with breast lesions detected by physical examination, ultrasonography, and/or mammography were prospectively included in this study. An anterior and prone lateral planar $^{99m}$Tc-MIBI scintimammography was performed on all patients. The final diagnosis was achieved by histopathological examination in 49 patients and clinical follow-up (at least one year) in 14 patients. Histopathological diagnosis confirmed that 15 lesions were malignant and 34 lesions were benign. All the malignant lesions were larger than 1 cm. The $^{99m}$Tc-MIBI scintimammography showed increased focal uptake in 17 lesions (two of them were benign and the other 15 were malignant). The diffuse heterogeneous uptake pattern was considered as benign. The sensitivity, specificity, positive predictive value, negative predictive value, and accuracy values for breast carcinoma were calculated as 100%, 96%, 88%, 100%, 97%, respectively. We concluded that $^{99m}$Tc-MIBI scintimammography could be a valuable method in the differentiation of malignant breast neoplasm larger than 1 cm size from benign ones, especially when the uptake pattern was considered.

KEY WORDS: Scintimammography. $^{99m}$Technetium-MIBI. Breast cancer.

PALABRAS CLAVE: Scintimammografía. $^{99m}$Tecnecium-MIBI. Carcinoma de mama.

INTRODUCTION

Prognosis of breast cancer depends on early detection of primary tumor. Standard screening tests for early detection of breast cancer include breast self-examination, breast examination by a physician and mammography. Mammography is successfully used in breast cancer screening. However, it has low specificity with a positive predictive value of 10%-35%.$^1$ This low specificity causes low cancer yield in breast biopsies thus the majority of biopsies can be considered unnecessary. It is also less reliable method in patients with fibrocystic disease (FCD), dense breasts, dysplastic disease and breast implants.$^2$ New imaging techniques such as $^{99m}$technetium-methoxyisobutylisonitrile ($^{99m}$Tc MIBI) scintimammography, positron emission tomography, contrast enhanced dynamic magnetic resonance imaging, Doppler ultrasonography and digital computerized mammography have been used to overcome this diagnostic limitations.$^3$ In par-
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Ticular, a promising new approach using $^{99m}$Tc MIBI could enhance the specificity of mammography. However, lesion size and uptake pattern of MIBI that are important factors may affect diagnostic accuracy.

The purpose of this study was to evaluate the diagnostic value of $^{99m}$Tc MIBI scintimammography in the detection of primary breast cancer with special emphasize on uptake pattern of MIBI and size of the lesions.

MATERIALS AND METHODS

Patients

A total of 63 female patients (age range 27-83) with suspicious lesions for breast cancer detected by physical examination, ultrasound and/or mammography were included in this prospective study. In the total patient group, there were 21 nonpalpable and 42 palpable lesions.

Scintimammography

Patients were injected with 740 MBq $^{99m}$Tc MIBI into the arm contralateral to the breast with the suspected lesion. The study consisted of two prone lateral breast images and an anterior view that were obtained 15 minutes after the injection. Image acquisition time was 10 minutes, using a low energy, general-purpose collimator and a 256 x 256 matrix.

Image interpretation

The images obtained were subjectively assessed by two experienced nuclear medicine specialists (AY and FG) who gave a consensus. All focal uptake of $^{99m}$Tc MIBI higher than the background of the breast was considered as positive for malignancy. Diffuse heterogeneous uptake (DHU) was considered as negative result. All focal uptake were graded from 0 to 3:

Grade 0: There is no focal uptake (Normal).
Grade 1: Focal uptake intensity is slightly higher than the breast background.
Grade 2: Focal uptake intensity is clearly higher than the breast background, but lower than the myocardium.
Grade 3: Focal uptake intensity is equal to or higher than the myocardium.

MIBI uptake in axillary lymph node was also evaluated as positive or negative.

RESULTS

A total of 63 lesions were evaluated in this study. Histopathologic diagnosis was done in 49 lesions and confirmed that 15 of 49 lesions were malignant and 34 of 49 lesions were benign. The other 14 of 63 lesions that were in clinical follow-up were accepted as benign, since there was no evidence of malignancy in the follow-up period. Thirty-eight patients were diagnosed as FCD. Histopathological examination proved FCD in 24 of 38 patients. The rest of 14 patients who were in clinical follow-up were also diagnosed as FCD by the combination of clinical follow-up, ultrasonographic and mammographic findings. While 8 of 38 FCD showed DHU (Fig. 1), the rest of 30 FCD showed no MIBI uptake and were evaluated as grade 0. Twenty-five patients who have histopathologic examination apart from FCD are summarized in table I.

Fig. 1.—Diffuse heterogeneous uptake pattern of $^{99m}$Tc MIBI in the left lateral prone view in a patient with fibrocystic disease which was confirmed by biopsy.
All 15 malignant lesions showed MIBI uptake. Six of 15 patients were evaluated as grade 1, six were grade 2, and the rest of three were grade 3. Figure 2 shows an example for grade 3 lesion (patient no: 12) which was located in the left breast. Only one malignant lesion (patient no: 2) was nonpalpable even the size of the lesion was 3 × 1 cm. This patient had been presented with a 2 × 2 cm right axillary lymph node and the malignant epithelial tumor metastasis was proved by the biopsy. Physical examination of the breast was normal. Ultrasonography and mammography were not able to show any breast mass. 99mTc MIBI scintimammography showed grade 1 uptake in the right breast adjacent to the chest wall (Fig. 3). The rest of 20 nonpalpable lesions were benign.

Ten benign lesions proved by histopathological examination apart from FCD are also showed in table I. Two of them were grade 1 (patient no: 16, 17), one of them was with DHU (patient no: 18), and the rest of them were grade 0. Figure 4 shows an example for grade 1 benign lesion (patient no: 17) in the left breast. While 20 of 48 benign lesions were nonpalpable, 28 of them were palpable.

Axillary lymph node involvement has been proved by histopathologically in 8 patients. Four of them (50%) showed MIBI uptake.

The overall lesion size range was 3-50 mm. The smallest malignant lesion had a maximal diameter of 10 mm.

Sensitivity, specificity, positive predictive value, negative predictive value, and accuracy value were 100%, 96%, 88%, 100%, 97%, respectively.

### DISCUSSION

Scintimammography with 99mTc-MIBI have shown high sensitivity and specificity for palpable breast cancer, with a reported sensitivity of 80-90%, and a specificity of 83-100%.

### Table I

**SUMMARIZED OF 25 PATIENTS WHO HAD HISTOPATHOLOGICAL EXAMINATION EXCEPT FIBROCYSTIC DISEASE**

<table>
<thead>
<tr>
<th>Patient No</th>
<th>p/np</th>
<th>MIBI uptake</th>
<th>Pathologic size (cm)</th>
<th>Operation</th>
<th>Histopathology</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>p</td>
<td>Grade 1</td>
<td>4</td>
<td>RM</td>
<td>IDC +</td>
</tr>
<tr>
<td>2</td>
<td>np</td>
<td>Grade 1</td>
<td>3</td>
<td>MRM</td>
<td>IDC +</td>
</tr>
<tr>
<td>3</td>
<td>p</td>
<td>Grade 3</td>
<td>4</td>
<td>RM</td>
<td>IDC -</td>
</tr>
<tr>
<td>4</td>
<td>p</td>
<td>Grade 2</td>
<td>5</td>
<td>RM</td>
<td>IDC +</td>
</tr>
<tr>
<td>5</td>
<td>p</td>
<td>Grade 2</td>
<td>3</td>
<td>MRM</td>
<td>IDC -</td>
</tr>
<tr>
<td>6</td>
<td>p</td>
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<td>4</td>
<td>MRM</td>
<td>IDC +</td>
</tr>
<tr>
<td>7</td>
<td>p</td>
<td>Grade 1</td>
<td>4</td>
<td>RM</td>
<td>IDC +</td>
</tr>
<tr>
<td>8</td>
<td>p</td>
<td>Grade 1</td>
<td>3</td>
<td>MRM</td>
<td>IDC -</td>
</tr>
<tr>
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<td>9</td>
<td>MRM</td>
<td>IDC +</td>
</tr>
<tr>
<td>10</td>
<td>p</td>
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<td>3</td>
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<td>IDC -</td>
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<tr>
<td>11</td>
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<tr>
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<td>5</td>
<td>MRM</td>
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<td>1</td>
<td>MRM</td>
<td>DCIS -</td>
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<tr>
<td>15</td>
<td>p</td>
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<td>2</td>
<td>MRM</td>
<td>IDC -</td>
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<tr>
<td>16</td>
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</tr>
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<td>p</td>
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<td>2</td>
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<td>18</td>
<td>p</td>
<td>DHU</td>
<td>2</td>
<td>Biopsy</td>
<td>Lactation -</td>
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<td>1</td>
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<td>Lipoma -</td>
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<tr>
<td>20</td>
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<td>Grade 0</td>
<td>0.3</td>
<td>Biopsy</td>
<td>Intaductal papilloma -</td>
</tr>
<tr>
<td>21</td>
<td>p</td>
<td>Grade 0</td>
<td>1</td>
<td>Biopsy</td>
<td>Fa -</td>
</tr>
<tr>
<td>22</td>
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<td>2</td>
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<td>Fa -</td>
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<td>p</td>
<td>Grade 0</td>
<td>1</td>
<td>Biopsy</td>
<td>Fa -</td>
</tr>
<tr>
<td>24</td>
<td>p</td>
<td>Grade 0</td>
<td>2</td>
<td>Biopsy</td>
<td>Fa -</td>
</tr>
<tr>
<td>25</td>
<td>p</td>
<td>Grade 0</td>
<td>2</td>
<td>Biopsy</td>
<td>Fat necrosis -</td>
</tr>
</tbody>
</table>

scintimammography is not affected by the density of the breast tissue, contrary to mammography\(^6\). However, intensity of MIBI uptake varies from mild to very intense depending on several factors such as the size, type, location and hormonal factors\(^9\). Lesion size is an important factor that affects the sensitivity. The sensitivity of lesion size less than 1 cm is low. Therefore, it could not be considered as a screening test\(^4\). The sensitivity for palpable abnormalities is significantly higher than that of nonpalpable lesions\(^10\). We observed that the localization of lesion was also important. In our study, a nonpalpable, \(3 \times 1\) cm sized breast cancer which localized adjacent to the chest wall had been demonstrated only by scintimammography (patient no 2).

In our study, the sensitivity was 100% and the specificity was 96%. Our results were comparable to reported series by the others. Waxman et al and Palmedo et al also found 100% sensitivity in palpable lesions with a diameter larger than 1 cm sized\(^6, 11\). The smallest malignant lesion size was 1 cm might be the reason of the high sensitivity in our study. The variation in sensitivity may result from different proportions of small tumors in other studies\(^11\).

The studies emphasized that in lesions with a low or intermediate mammography and with a diameter >1 cm, the inclusion of scintimammography may have important consequences in reducing the number of biopsies\(^8, 12, 13\). Forty-nine of 63 patients had histopathological examination in our study. Even 32 lesions that were diagnosed as benign by histopathologically and had no MIBI uptake, biopsy was performed on these patients. If we were to apply scintimammography in the diagnostic protocol to our patients, it would not have been necessary to perform biopsies in 32 of 49 patients (65%).

In our study, sensitivity was higher than specificity (100% vs 95%). We observed 2 false positive results that 1 in glandular hyperplasia and 1 in glandular adenosis. In some studies, it was shown that increased uptake of MIBI was detected in benign breast lesions, such as fibroadenoma, mastitis, scar tissue and FCD\(^14, 15\). Prats et al demonstrated that fibroadenomas larger than 3 cm could show pathological MIBI uptake due to the increased metabolic activity\(^14\). Four fibroadenomas which size ranged between 1 to 2 cm were showed no MIBI uptake in our study.

When we evaluated the lesions according to the grade, six of 15 malignant lesions (40%) were rated as grade 1. Two false positive lesions were also rated as grade 1 (patient no: 16, 17). Although high uptake of Grade 2 or 3 is likely to correspond to ma-

**Fig. 2.**—Left lateral prone view shows well-defined pathological concentration of \(^{99m}\)Tc MIBI (grade 3) in an infiltrating ductal carcinoma (patient no: 12).

**Fig. 3.**—Right lateral prone view shows grade 1 \(^{99m}\)Tc MIBI accumulation in the right breast adjacent to the thorax wall (patient no: 2).
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lignancy, there was considerably overlapping of benign and malignant lesions for grade 1 in our study. Similar data has been reported previously.

The use of specific criteria than a positive focus of increased uptake in the breast would greatly improve the specificity of MIBI scintimammography in the differentiation between benign and maligant lesions. In this study not all uptake patterns considered as positive, instead only focally intense uptake of MIBI was regarded as malignant lesion. This might be reason of lower false positive uptake yield than the most of the other studies. It is important to recognize uptake patterns of MIBI for discriminating benign patterns from malignant ones in these patients. When we consider these findings as positive, the specificity was decreased from 96% to 79%.

A series with a high prevalence of benign lesions, primarily with hyperproliferative breast disorders have been higher proportion of false positive results. The prevalence of benign lesions in the different series varies ranging from 16%-59%. Although 77% of our patients had benign lesions, we observed only two false positives.

Generally, MIBI uptake in hyperproliferative diseases can be seen more diffuse than focal, often bilateral, not well-delineated contours and often presenting a patchy uptake. Lactating breasts with suspected breast lesion could result false positive finding due to false positive uptake in this hyperproliferative situation. We have seen heterogeneous intense uptake of MIBI in the lactating breasts. However, if it is considered these uptake patterns as negative, it can cause false negative uptake for obscured malignant lesion in and around this benign uptake.

In our study, 4 of 8 (50%) patients with malignant axillary lymph node involvement showed MIBI uptake. The sensitivity of $^{99m}$Tc MIBI scintimammography (44%-79%) is various and not high as shown in a large number of studies. Inherent low resolution of scintigraphy for the detection of small volume of lymph nodes and considerably more background uptake in the axillary region could be the reasons. However, it could not be disadvantage because of the information from axillary imaging is concomitantly obtained from standard scintimammography.

**CONCLUSION**

$^{99m}$Tc MIBI scintimammography can be valuable complementary method in the differentiation of malignant breast neoplasm from benign ones. When uptake pattern and size of the lesions was considered, higher accuracy can be obtained. The adoption of scintimammography in diagnostic protocol could reduce the number of biopsies performed in patients with suspicious of malignancy.

**BIBLIOGRAFÍA**


