The Role of Technetium Tc 99m Sestamibi in the Early Detection of Breast Carcinoma

Leonard R. Coover, MD

Technetium Tc 99m sestamibi (MIBI), a radionuclide, has been utilized for more than a decade as a myocardial imaging agent. The success of this agent in evaluating myocardial ischemia is based on the fact that tissue distribution of MIBI is a linear function of blood flow.[1] MIBI was approved by the United States Food and Drug Administration in December 1990 for use in cardiac imaging and in May 1997 for use in breast imaging. Scintimammography, a recently introduced nuclear medicine procedure that utilizes MIBI, can be used to detect breast cancer. Scintimammography is a highly sensitive adjunct to the self–breast examination, clinical breast examination, and film screen mammography.[1–5] This new diagnostic option may improve the selection process for biopsy and facilitate early detection of breast carcinoma and/or prevent unnecessary biopsies. Appropriate and cost-effective use of scintimammography requires an understanding of basic imaging parameters as well as the mechanism of MIBI concentration in tumors.

MECHANISM OF ACTION

MIBI concentrates in tissue in proportion to blood flow, metabolic activity, and desmoplastic activity (written communication, MW Graves, MD, July 1998). Soon after injection, MIBI localizes in most tumors in greater concentration than in the surrounding tissues because tumors generally have a greater blood supply per gram of tissue compared with surrounding tissues. Malignant tumors also display greater metabolic activity than benign tumors or surrounding breast tissues.[6] In addition, most tumors have a higher intracellular mitochondrial concentration and MIBI accumulation is roughly proportional to mitochondrial concentration.[6] These factors allow localization of the radionuclide in most breast tumors.

SENSITIVITY AND SPECIFICITY

The sensitivity of MIBI for the detection of breast tumors is dependent on the lesion size. A recent European study has shown that the sensitivity of MIBI for detection of malignancy in small lesions is poor.[2] Approximately 25% of lesions less than 1 cm in diameter and 78% of lesions 1 to 1.5 cm were detected.[1] Most importantly, 94% of lesions greater than 1.5 cm in diameter were detected.[1] The specificity of MIBI for the detection of breast tumors is approximately 80%.[2,4,5,7] Because of the loss of contrast from the soft tissue attenuation, medial lesions that are farther from the detector are more difficult to detect.

PATIENT SELECTION

Patient selection is of pivotal importance for the use of MIBI. In general, a physician should only refer patients with lesions found on physical examination or mammography for MIBI imaging. Physicians must be aware that scintimammography is not a screening examination.[8,9] If scintimammography is used to evaluate highly suspicious clinical or mammographic findings, such as category 5 mammograms (**Table 1**) or microcalcifications that are not associated with a mass, a negative test result should not preclude biopsy. In these cases, scintimammography may reveal previously unrecognized synchronous lesions or metastases to lymph nodes.

Scintimammography is most appropriate for patients with a palpable or radiographic abnormality that is greater than 1 cm in diameter and is not clearly malignant or benign. New cameras are currently being developed that will permit detection of much smaller tumors

Dr. Coover is Section Chief, Nuclear Medicine Section, Division of Radiology, Department of Medicine, Hamot Medical Center, Erie, PA.

Table 1. Assessment Categories for the Results of Mammography

Category	Interpretation
0	Additional evaluation of the image is necessary
1	Negative finding
2	Benign finding
3	Probably benign finding; short interval follow-up suggested
4	Suspicious abnormality; biopsy should be considered
5	Highly suggestive of malignancy; appropriate action should be taken

American College of Radiology (ACR). *Breast Imaging Reporting and Data System (BI-RADS™).* Third Edition. Reston [VA]. American College of Radiology; 1998.

Table 2. Appropriate and Inappropriate Uses for Technetium Tc 99m Sestamibi Imaging

Appropriate uses
Breast lesions that are not clearly malignant or benign
Breast abnormalities on mammogram after breast irradiation
Breasts that are difficult to examine by palpation and mammography
Breast implants
Patients uncomfortable with the approach of waiting and reevaluating at a 6-month follow-up
Inappropriate uses
Highly suspicious breast lesions (ie, category 5 mammograms)
Breast microcalcifications that are not associated with a mass
Breast lesions that are less than 1 cm in diameter

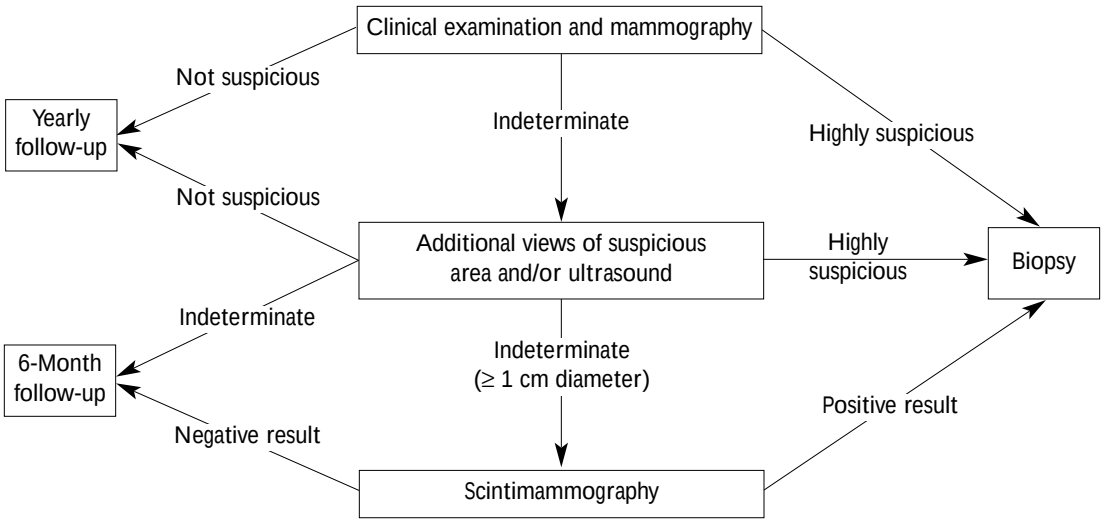

Figure 1. Algorithm illustrating the relation of scintimammography to the management of patients with suspected breast carcinoma.

through improved spatial and contrast resolution as well as improved flexibility in detector positioning. Scintimammography may also be used for patients with smaller lesions, with an awareness that the sensitivity is reduced. In addition, scintimammography may be useful in evaluating patients with breast implants, patients with breast abnormalities that have questionable status after breast irradiation, and patients whose breasts are difficult to examine by palpation and mammography. Patients who are uncomfortable with the approach of waiting and reevaluating at a 6-month follow-up can also benefit from the use of scintimammography. Before ordering scintimammography, physicians must be aware of the appropriate utilization of MIBI imaging (**Table 2, Figure 1**).

Use of MIBI to Determine the Need for Biopsy

The acceptable positive predictive values for biopsies are approximately 25% for palpable nodules and 30% for mammographically suspicious lesions.[5] MIBI allows the clinician or radiologist the opportunity to use MIBI as a sensitive examination for determining the appropriateness of biopsy. Patients with lesions that previously would have been reevaluated at follow-up could be referred for biopsy after scintimammography, thus allowing earlier detection. Conversely, patients with lesions that would have been biopsied may be followed with the knowledge that the incidence of malignancy in this subgroup of patients is approximately 5%.[2] Thus, the use of MIBI for these patients can

Figure 2. Photograph of a patient in position for scintimammography. The patient is in a prone position and the breast that is being examined hangs down. This position allows the image of the breast to be undistorted and minimizes the background radiographic activity in the patient's body.

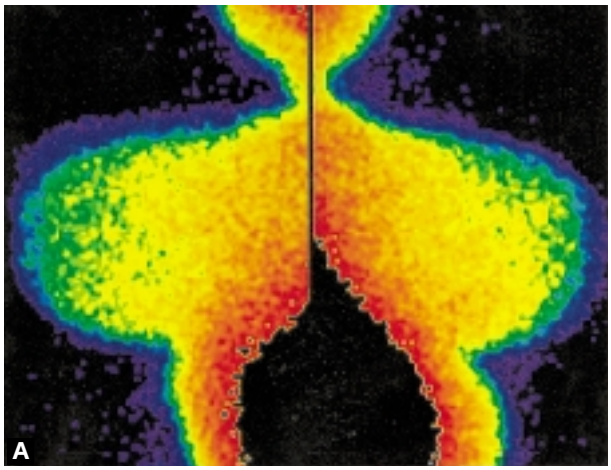

Figure 3. Scintimammograms illustrating negative results of technetium Tc 99m sestamibi imaging. A) Lateral view. B) Anterior view. The *curved black arrow* indicates the thyroid gland, and the *white arrow* indicates the left ventricular myocardium.

increase the true positive rate of biopsy for breast lesions as well as increase the absolute number of malignancies detected.

The MIBI evaluation of equivocal findings allows the examiner to move the biopsy threshold forward (ie, use a less conservative management approach), while permitting evaluation of less suspicious lesions that would not normally undergo biopsy. Thus, referring MIBI evaluation for patients with lesions that are appropriate for MIBI imaging as an alternative to biopsy, as well as referring patients with less suspicious lesions that may be dismissed as category 2 or 3 mammograms, not only reduces the number of inappropriate biopsies but also selects a second group of patients for biopsy with lesions that would normally be observed or possibly dismissed as benign. Thus, scintimammography can identify a more appropriate patient population for biopsy.

PROCEDURE

Ideally, the patient is injected with 30 mCi of MIBI into a vein on the dorsum of the foot. If this injection site is not possible, a vein in the arm on the contralateral side of the suspected breast lesion is injected through an

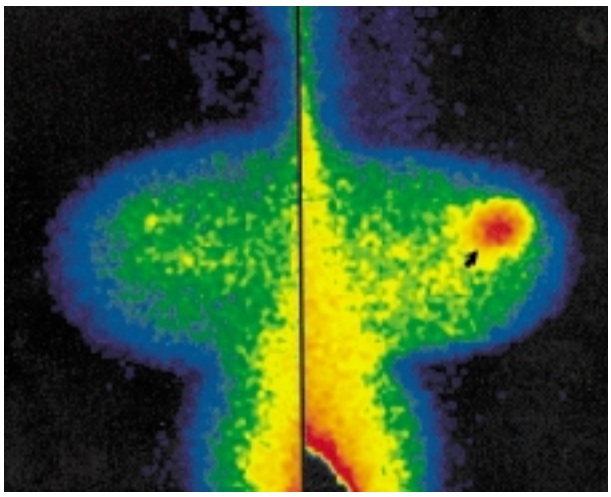

Figure 4. Lateral scintimammograms with a positive finding indicating focally increased activity in the breast (*arrow*).

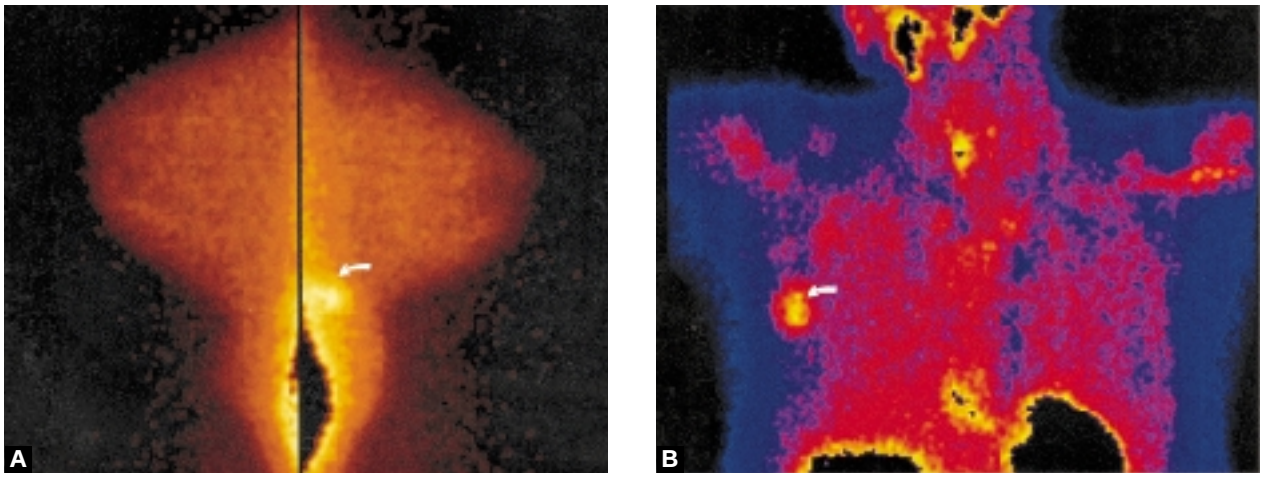

Figure 5. Scintimammograms with a positive finding. A) Lateral scintimammograms with a positive finding (*arrow*). B) The anterior view demonstrates increased activity in the left axilla (*arrow*). This finding indicates metastasis to axillary lymph nodes.

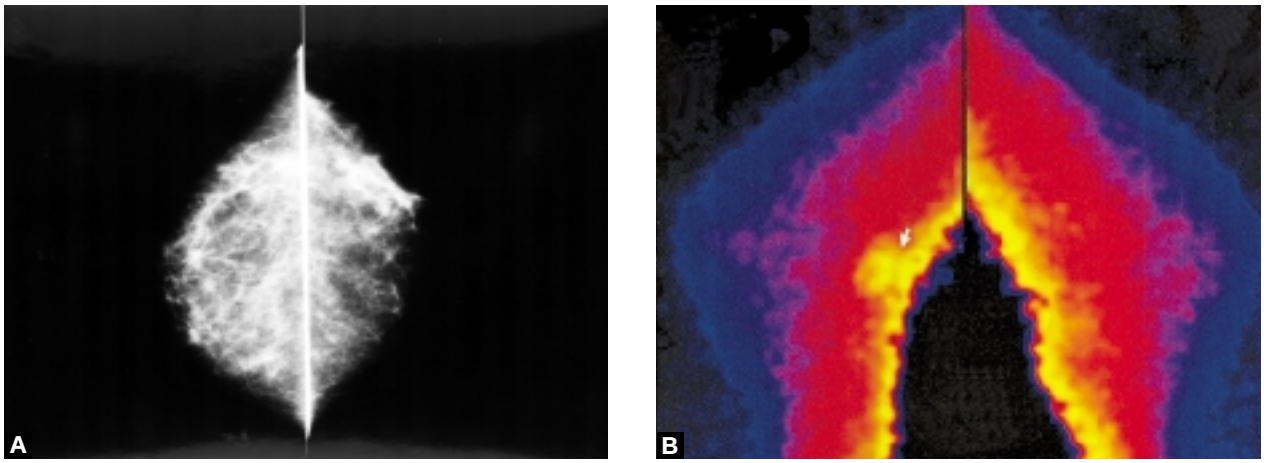

Figure 6. Mammogram and scintimammograms in a patient with a palpable lesion in the left breast. A) The patient's mammogram shows no evidence of malignancy. The sensitivity of mammography is reduced by the presence of dense fibroglandular tissue. B) Lateral scintimammograms reveal a positive finding (*arrow*).

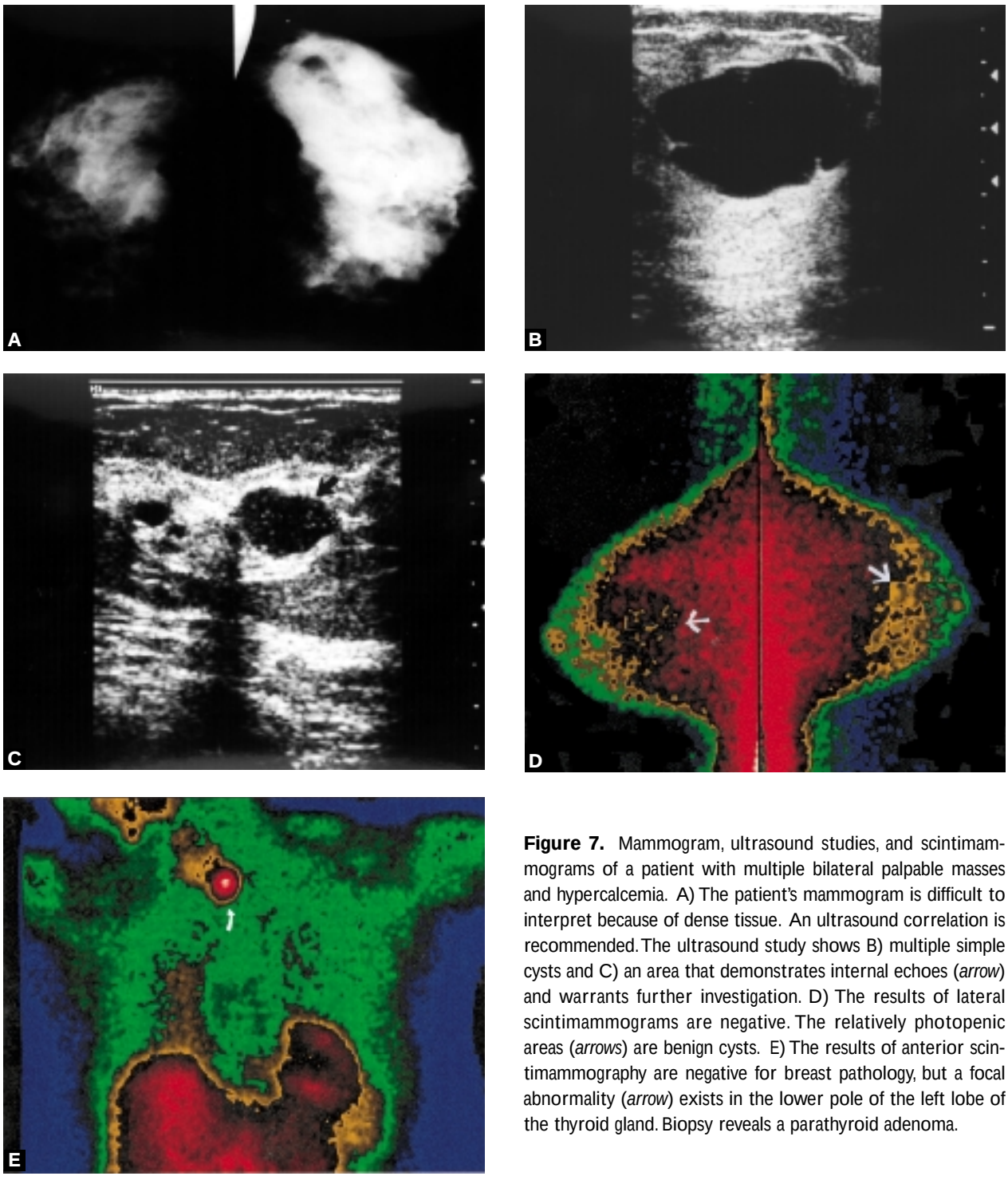

Figure 7. Mammogram, ultrasound studies, and scintimammograms of a patient with multiple bilateral palpable masses and hypercalcemia. A) The patient's mammogram is difficult to interpret because of dense tissue. An ultrasound correlation is recommended. The ultrasound study shows B) multiple simple cysts and C) an area that demonstrates internal echoes (*arrow*) and warrants further investigation. D) The results of lateral scintimammograms are negative. The relatively photopenic areas (*arrows*) are benign cysts. E) The results of anterior scintimammography are negative for breast pathology, but a focal abnormality (*arrow*) exists in the lower pole of the left lobe of the thyroid gland. Biopsy reveals a parathyroid adenoma.

indwelling intravenous catheter. The arm on the side of the abnormality is not injected to avoid confounding imaging data (ie, uptake in normal lymph nodes that may occur when a portion of the dose is infiltrated). The patient is placed in a prone position and the breast that is being examined hangs down (**Figure 2**). This position allows the image of the breast to be undistorted and minimizes the background radiographic activity in the patient's body.

Imaging begins 10 minutes after injection. The views are: first, a lateral view of the involved breast; second, a lateral view of the contralateral breast; and third, an anterior view of the chest and axilla. Each image is acquired for 10 minutes. The images are then processed and reviewed by the nuclear medicine physician who determines if additional views are necessary. The entire MIBI study can be completed in less than 1 hour.

IMAGE INTERPRETATION

Interpretation of the MIBI image is simple. A negative result is depicted in the lateral and anterior views in **Figure 3**. Positive studies reveal focally increased activity in the breast (**Figure 4**). The axillae are also examined on the anterior projection for lymphadenopathy (**Figure 5**). The entire study is then examined for any incidental relevant findings. **Figure 6** illustrates the radiographic studies undertaken for a patient with a palpable lesion in the left breast. **Figure 7** illustrates the series of radiographic studies that are undertaken for a patient with multiple bilateral palpable masses and hypercalcemia.

Conditions that cause difficulties in interpreting mammograms, such as postsurgical or postradiation scarring or breast implants, have little or no effect on MIBI images. False-positive results on MIBI imaging may be caused by benign tumors that have unusually high rates of metabolism.

CONTRAINDICATIONS AND SIDE EFFECTS

No known contraindications or major side effects have been reported with MIBI. Approximately 20% of patients experience a transient metallic taste or other transient minor sensations including headache, flushing, nausea, and pruritus. (These side effects have been reported in clinical trials but are rare or have not occurred in this author's experience.)

SUMMARY

MIBI imaging is recommended for patients with indeterminate breast lesions that are greater than 1 cm in diameter. The practical goals of scintimammography are two-fold: improving early detection of breast carcinoma and/or preventing unnecessary biopsies. Achievement of these goals is dependent upon the referring physician's knowledge of the procedure and appropriateness of patient selection. This author is hopeful that this brief overview will aid physicians in deciding the next best step in response to an abnormal result on a screening breast examination. **HP**

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