Breast-Specific γ-Imaging: Molecular Imaging of the Breast Using ^{99m}Tc-Sestamibi and a Small-Field-of-View γ-Camera*

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Breast-specific γ-imaging (BSGI), also known as molecular breast imaging, is breast scintigraphy using a small-field-of-view γ-camera and ^{99m}Tc-sestamibi. There are many different types of breast cancer, and many have characteristics making them challenging to detect by mammography and ultrasound. BSGI is a cost-effective, highly sensitive and specific technique that complements other imaging modalities currently being used to identify malignant lesions in the breast. Using the current Society of Nuclear Medicine guidelines for breast scintigraphy, Legacy Good Samaritan Hospital began conducting BSGI, breast scintigraphy with a breast-optimized γ-camera. In our experience, optimal imaging has been conducted in the Breast Center by a nuclear medicine technologist. In addition, the breast radiologists read the BSGI images in correlation with the mammograms, ultrasounds, and other imaging studies performed. By modifying the current Society of Nuclear Medicine protocol to adapt it to the practice of breast scintigraphy with these new systems and by providing image interpretation in conjunction with the other breast imaging studies, our center has found BSGI to be a valuable adjunctive procedure in the diagnosis of breast cancer. The development of a small-field-of-view γ-camera, designed to optimize breast imaging, has resulted in improved detection capabilities, particularly for lesions less than 1 cm. Our experience with this procedure has proven to aid in the clinical work-up of many of our breast patients. After reading this article, the reader should understand the history of breast scintigraphy, the pharmaceutical used, patient preparation and positioning, imaging protocol guidelines, clinical indications, and the role of breast scintigraphy in breast cancer diagnosis.

Key Words: breast-specific gamma imaging (BSGI); molecular breast imaging (MBI); mammography; ultrasound; scintimammography; breast scintigraphy

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According to the National Cancer Institute, in 2008 more than 180,000 new cases of breast cancer were diagnosed in the United States. Breast cancer is second only to skin cancer as the most common type of cancer affecting women in this country. Mammography provides an excellent screening tool for the early detection of breast cancer and is highly sensitive in most cases, but the sensitivity of mammography diminishes with increasing tissue density (*1*). Breast scintigraphy has demonstrated the ability to detect breast cancer regardless of breast density (*2*).

There are many types of breast cancer, and all have unique characteristics. Several types of breast cancer present additional challenges for the radiologists interpreting the breast studies. Infiltrating lobular carcinoma is the second most common form of breast malignancy, representing 10% of the diagnosed cases (*3*). Because of the growth characteristics of infiltrating lobular carcinoma, early detection is less probable for that form than for infiltrating ductal carcinomas. Infiltrating lobular carcinoma is often detected at a later stage with larger tumors and nodal involvement (*4*). Ultrasound is also limited in detecting small infiltrating lobular carcinoma lesions. Multifocality is more common with infiltrating lobular carcinoma than with infiltrating ductal carcinoma, and these additional lesions are often mammographically occult (*5*). Breast scintigraphy has demonstrated a high sensitivity to infiltrating lobular carcinoma, even lesions under 1 cm in size. The sensitivity has been reported to be in excess of 90% for infiltrating lobular carcinoma (*6,7*).

Patients with newly diagnosed breast cancer have an increased risk of occult, synchronous ipsilateral or contralateral breast cancers. These cancers are often not appreciated by mammography or ultrasonography. The rate for additional lesions is between 11% and 57% (*8*). Additional studies may be warranted for these patients before surgical intervention to determine the extent of disease and to identify occult lesions, the presence of which could modify treatment planning. Several studies have reported on the role of breast-specific γ-imaging (BSGI) in presurgical planning. In a study conducted at our institution, Zhou et al. reported additional or more extensive malignancy in the

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same or contralateral breast in 10.9% of newly diagnosed breast cancer patients (*9*).

There are several imaging studies that look at the structural makeup of the breast tissue. Mammography is the standard of care for screening studies of the breast and is usually the first step in the diagnostic workup for patients with a questionable finding on screening mammography. Mammography is accomplished by compressing the breast tissue and using x-rays to create the images in several different projections. This modality is highly sensitive but has a relatively low positive predictive value, especially in dense breast tissue (*1*). Ultrasound, a study that uses sound waves instead of ionizing radiation to evaluate the structures in the breast, can determine whether a structure is solid or fluid-filled and evaluates characteristics such as size, shape, and orientation.

Breast scintigraphy, also known as scintimammography or molecular breast imaging, has been performed for more than a decade using general large-field-of-view nuclear medicine γ-cameras. Although this method has produced a high specificity for primary breast lesions, 86%−89% (*2*), the lack of sensitivity for subcentimeter lesions resulted in decreased use of this imaging modality. In addition, correlation of the scintimammography images with the views obtained during a mammogram is difficult. Figure 1 is an example of breast images obtained with a standard γ-camera. These imaging limitations are the result of poor detector positioning achieved with the prone, breast-pendent position required for large cameras. Because the pendent breast is between 4 and 6 cm from the surface of the collimator, spatial resolution is significantly compromised. In addition, because the large camera design greatly limits the number of possible views and cannot accommodate organ views from the superior, inferior, or medial aspects of the breast, visualization of lesions in these areas is compromised. Figure 2 shows the table design for breast imaging with the standard γ-camera. The compact camera designs used in BSGI allow the breast to be imaged while in contact with the detector, minimizing detector-to-target distance and allowing the breast to be imaged from a variety of angles similar to mammography. Figure 3 is a picture of a small-field-of-view γ-camera design. Resolution is optimized, and the images can be easily correlated with the mammograms and other imaging studies. Figure 4 is an example of images obtained with the BSGI camera.

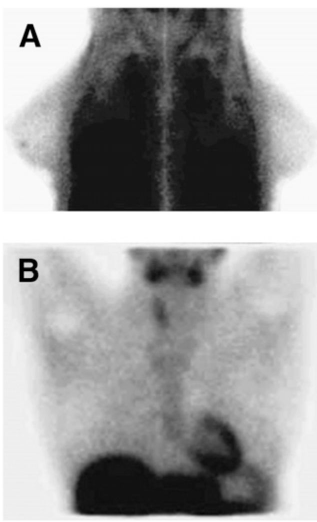

FIGURE 1. Typical views from standard scintimammography study with general large-field-of-view γ-camera: lateromedial (A) and anterior (B).

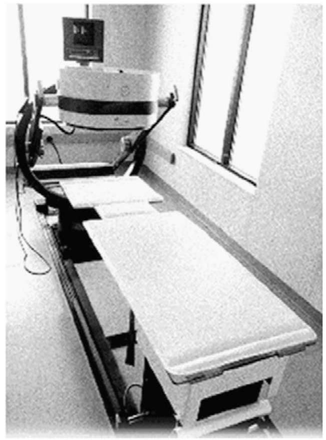

FIGURE 2. Large-field-of-view γ-camera with table modification for prone breast positioning.

EQUIPMENT

The Dilon 6800, manufactured by Dilon Technologies, is the small-field-of-view γ-camera used at our institution for this form of breast imaging. The detector has a pixilated

FIGURE 3. Dilon 6800 γ-camera (Dilon Technologies).

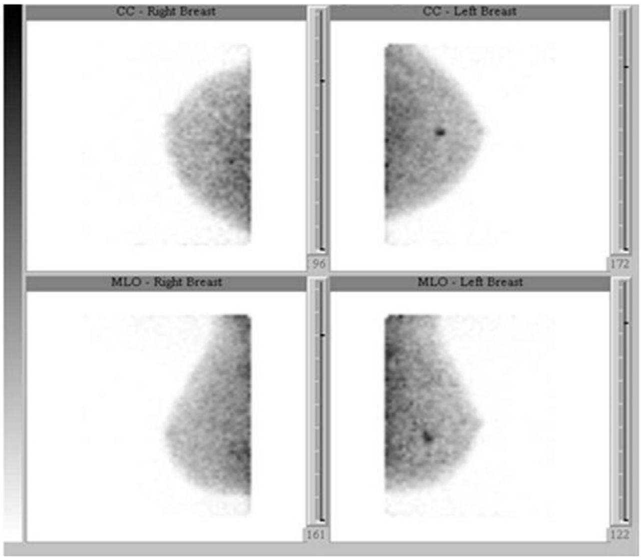

FIGURE 4. Typical views from breast-optimized detector: biopsy-proven 3-mm cancer of left breast.

NaI crystal design with more than 3,000 individual 3-mm-square detector crystals. There is an 8 × 6 array of 1-in (2.54-cm)-square mini position-sensitive photomultiplier tubes under the crystal array. The manufacturer spent several years optimizing the system resolution to provide maximum contrast for subcentimeter breast lesions and has constructed systems with a resolution of as fine as 1.4 mm but found that the optimal system resolution for breast imaging was approximately 3 mm (*10*). The maneuverability of the detector allows numerous positioning options to mimic mammographic views and to maximize the amount of breast tissue imaged during the study. The Smartshield paddle opposite the detector stabilizes the breast during the image acquisition and contains shielding to reduce image contamination from other organs. Currently, there are 3 different collimators available for this γ-camera. The collimators can be interchanged easily as necessary. In breast imaging, the low-energy general-purpose collimator is used for the standard images and the slant-hole collimator is an option for additional views when lesions are near the chest wall. A high-resolution collimator is also an option for limited general nuclear medicine imaging (e.g., bone imaging of hands or feet).

PROCEDURE

BSGI is an adjunctive procedure for patients requiring additional studies to evaluate breast health. Our institution adapted the current scintigraphy protocol to breast imaging with the new camera design. The study requires no preparation by the patient and is well tolerated.

Patient Preparation

The patient should remove all clothing from the waist up and be given a cape or gown. If the patient is premenopausal, imaging should be conducted between days 2 and 14 of her menstrual cycle for optimal results. Legacy Good Samaritan attempts to image patients between days 5 and 12. Imaging of lactating patients should be delayed until 3 mo after cessation of lactation.

Acquisition Protocol

Breast images should be acquired for 5–10 min each, and axillary images should be acquired for 3 min.

Collimator and Energy Window

The collimator is low-energy general-purpose, and the energy window is ±10% centered on 140 keV for ^{99m}Tc-sestamibi.

Radiopharmaceutical and Dose

According to the Bristol-Myer Squibb's drug safety sheet, 740–1,110 MBq (20–30 mCi) of ^{99m}Tc-sestamibi may be used for breast imaging (*11*).

Administration Technique

Place an indwelling catheter or butterfly catheter in the contralateral upper limb, if possible. Most injections are into either the antecubital vein or the dorsal aspect of the hand. A foot vein may be used. In addition, if placement of the intravenous line is too difficult, a straight stick may be used. Administer 740–1,110 MBq (20–30 mCi) of ^{99m}Tc-sestamibi, and flush with 10–20 mL of normal saline. Remove the intravenous line and have the patient raise her arm overhead and squeeze a ball for a full minute. This technique may reduce vascular trapping for some patients. Have the patient expose the breast to be imaged. At this point, the patient is ready for imaging to begin.

Patient Positioning and Views

Positioning. Our nuclear medicine technologists were trained in breast positioning by the camera manufacturer, with follow-up assistance by our institution's mammography technologists. The patient is seated for the examination, and standard mammographic views are obtained as well as axillary images. The patient may sit forward or stand for images if a protruding abdomen makes imaging difficult. The detector can be rotated to accommodate a protruding abdomen on larger patients.

Standard Imaging Views. Lower the shield to apply light compression to the breast. This will improve image quality and reduce the number of patient movement artifacts. The possible imaging projections are as follows. (Because these obtained images are to be compared with the mammographic findings, we use x-ray mammography nomenclature when describing the image positions.)

- Right craniocaudal—detector inferior to the breast.
- Left craniocaudal—detector inferior to the breast.
- Right mediolateral oblique—detector positioned at an oblique inferior/lateral position at an angle aligning with that of the pectoralis muscle.
- Left mediolateral oblique—detector positioned at an oblique inferior/lateral position at an angle aligning with that of the pectoralis muscle.

- Right axilla—detector placed in the axilla (use the hair line as a reference) at an oblique angle to the torso.
- Left axilla—detector placed in the axilla (use the hair line as a reference) at an oblique angle to the torso.

Additional Views

- Right mediolateral—detector placed at the lateral aspect of the breast.
- Right lateromedial—detector placed at the medial aspect of the breast.
- Left mediolateral—detector placed at the lateral aspect of the breast.
- Left lateromedial—detector placed at the medial aspect of the breast.
- Right exaggerated craniocaudal—a modified craniocaudal view typically obtained by rotating the patient to obtain better positioning for lateral breast tissue.
- Left exaggerated craniocaudal—a modified craniocaudal view typically obtained by rotating the patient to obtain better positioning for lateral breast tissue.

INDICATIONS FOR USE

BSGI should be used in patients who have radiodense breast tissue, breast implants, or unexplained architectural distortion or in whom MRI is indicated but not possible. Other uses include evaluation of indeterminate areas identified by mammography or ultrasound, evaluation of multiple lesions or clusters of microcalcifications to aid in biopsy target selection, evaluation of the axillary region for node status in breast cancer patients, and postsurgical or posttherapeutic evaluation of mammographic tissue changes. In addition, BSGI can be used to investigate a palpable mass not demonstrated on mammogram or ultrasound, detect multicentric and multifocal disease or bilateral disease, determine the extent of the primary lesion, and screen a high-risk population.

CASE REVIEW

Legacy Good Samaritan added BSGI as a breast imaging modality in 2007. This functional study has been helpful in identifying cancers and is used regularly for patient treatment planning. The following is an example case study.

A morbidly obese woman with a newly diagnosed left breast cancer was being worked up for surgical planning and treatment options. Her left breast cancer was found through clinical examination, and she also had a questionable contralateral clinical examination. The patient underwent an ultrasound of the right breast, and the findings were reported as normal. The patient was then referred for a BSGI study before surgery. Figure 5 shows the patient's left mammogram, and Figure 6 shows the left BSGI image with the known cancer and the right BSGI image with a focal enhancement present.

FIGURE 5. Mammogram of left breast, with known malignancy circled.

Pathology reported the left breast mass to be an invasive ductal carcinoma measuring 3.9 cm. The right breast contained a 1.1-cm invasive ductal carcinoma with a focus of ductal carcinoma in situ. This mass was discovered by BSGI. The right sentinel node was positive, with a 2-mm cancer in 1 of 3 nodes evaluated.

DISCUSSION

BSGI has proven to be an important adjunct for patients with inconclusive breast studies or who have a known cancer and are undergoing surgical and treatment planning. After Food and Drug Administration approval in 2004, the Dilon 6800 was put into clinical use, and our institution acquired the camera in December 2006. We have performed more than 1,000 BSGI studies to date, and considering the high sensitivity and specificity, 93% and 87%, respectively (*12*), of the camera, it has proven to be an important component of our breast program. BSGI is likely to become more widely available as the benefits are understood by radiologists, referring physicians, and the public. In a study by our institution (*13*), 176 patients underwent BSGI with the following selection criteria: preoperative work-up, inconclusive mammography findings, high risk with dense breasts, and palpable mass with negative mammography findings. In that study, management changed for 14% of the patients. Cancer was detected in

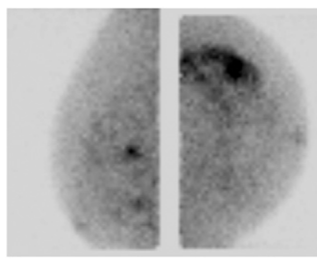

FIGURE 6. (Left) BSGI image of right breast showing focal abnormality. (Right) BSGI image of left breast confirming extent of known disease.

2% of patients with negative mammography findings, and additional cancers were found in 6% of the patients with a known primary. BSGI correctly ruled out the need for biopsy in 86% of the Breast Imaging Reporting and Data System 4 patients, with only a 6.3% false-positive rate (*13*). The nuclear medicine technologists perform all quality control procedures, injections, patient positioning, and image acquisition in the breast center. Breast positioning was an integral component of the training, and we used the expertise of the mammography technologists for challenging cases during our early experience.

CONCLUSION

Because of the higher cost of MRI and patient limitations (e.g., implanted devices, claustrophobia, body habitus, and renal insufficiency), BSGI has established itself as a viable diagnostic imaging alternative at our facility.

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