

North Pacific Surgical Association

# Real-world application of breast-specific gamma imaging, initial experience at a community breast center and its potential impact on clinical care

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## KEYWORDS:

Scintimammography;  
BSGI;  
Breast imaging;  
Breast cancer

## Abstract

**BACKGROUND:** Breast-specific gamma imaging (BSGI) has brought scintimammography back to the forefront by using a dedicated small field-of-view system designed to detect and localize lesions down to 2 mm. Initial studies have reported sensitivity equaling that of magnetic resonance imaging, but with improved specificity. We reviewed our initial experience to evaluate the impact of this technology at our community breast center.

**METHODS:** We performed a retrospective review of the initial 176 patients who underwent BSGI.

**RESULTS:** A total of 128 patients underwent BSGI because of suspicious imaging, abnormal physical examination, or high risk with dense breasts. BSGI was positive in 12 of 107 patients with breast imaging reporting and data system (BI-RADS) 1, 2, or 3. Two of these were cancer. Of the 21 patients with BI-RADS 4, 18 were BSGI negative (11 with benign biopsy, 7 observed), and 3 were BSGI positive with 2 being cancer. Forty-eight patients with a new diagnosis of cancer obtained BSGI for further work-up. It was positive at a new location in 6 cases: 2 cases were new cancers in the contralateral breast, 1 was in the ipsilateral breast, and the remaining 3 had benign pathology. Of the 176 initial patients, clinical management was changed significantly in 14.2%, with another 6.3% in whom a negative BSGI could have prevented a biopsy.

**CONCLUSIONS:** BSGI has played an important role in our clinical management of breast patients with complex breast tissue. BSGI is also a good adjunctive imaging tool in the work-up of newly diagnosed breast cancer patients.

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Breast cancer is the leading site of new cancer cases and the second leading cause of cancer deaths in females in the United States.<sup>1</sup> Current screening and diagnostic imaging modalities include mammography (MM), ultra-

sound (US), and magnetic resonance imaging (MRI). All of these imaging modalities convey mostly anatomic data (abnormalities). Scintimammography, in contrast, provides purely physiologic data via detection of cellular uptake of a radioactive tracer (sestamibi). Hundreds of studies have been conducted since the late 1990s evaluating the clinical utility of scintimammography. The sensitivity and specificity of this modality from the largest study conducted (n = 1,734) were 93% and 87%, respectively, and appeared not to be affected by breast density.<sup>2</sup>

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Manuscript received October 23, 2007; revised manuscript January 7, 2008

This was better than the reported sensitivity and specificity of the largest breast MRI study ( $n = 821$ ) of 88% and 68%, respectively.<sup>3</sup>

The sensitivity of mammography suffers greatly with increasing breast density (87%–97% down to 48%–63%).<sup>4,5</sup> Despite the promising results of scintimammography, it has not caught on in this country as a diagnostic modality for breast cancer. Several reasons account for this, including difficulty in spatially correlating images obtained from the large gamma cameras and a lack of sensitivity for subcentimeter lesions (35%–64%).<sup>6</sup> These limitations are a function of the large field-of-view gamma cameras and not the radiopharmaceutical used. The development of a dedicated breast gamma imaging system has overcome these limitations and has brought scintimammography back to the forefront of breast imaging.<sup>7</sup> This study reviews the impact of this technology on the clinical management of breast patients at a community breast center.

## Materials and Methods

### Patients

This was a retrospective review of the first 176 patients who were referred for breast-specific gamma imaging (BSGI) at a single tertiary community breast health center that performed 11,451 mammograms in 2006. Reasons for evaluation were as follows: (1) new biopsy-proven breast cancer undergoing BSGI for further work-up, (2) suspicious imaging on MM, US, and/or MRI, (3) abnormal physical examination with dense breast tissue, and (4) high risk for breast cancer with dense breast tissue.

### Imaging

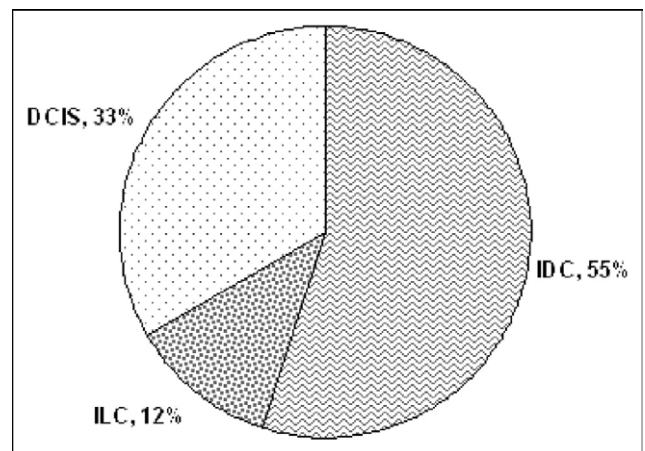
Patients were injected with 25 to 30 mCi (925–1110 MBq) of technetium-99m sestamibi into an arm vein contralateral to the breast of interest. A dorsalis pedis vein was used if no suitable arm veins were found. Imaging began after 10 minutes. Craniocaudal and mediolateral views were performed of both breasts with 10 minutes per view (total time, 40 min). Images were obtained with a high-resolution, small field-of-view, breast-specific gamma camera (Dilon 6800 Gamma Camera; Dilon Technologies, Newport News, VA).

### Image evaluation

All images were read by 1 of 4 dedicated breast radiologists. The images were classified as either negative, no further work-up recommended; or positive, further work-up such as additional imaging or biopsy recommended.

### Data collection and analysis

Data were collected retrospectively and stored in Microsoft Excel 2003 (Microsoft Corporation, Redmond,



**Figure 1** Distribution of pathologic diagnoses of the 48 known cancer patients. ILC = invasive lobular carcinoma.

WA). Statistical analysis was performed with Microsoft Excel.

## Results

Data on the first 176 patients who underwent BSGI between December 2006 and May 2007 were reviewed. The mean age was 53 years (range, 27–86 y). Forty-eight patients (26.7%) with a mean age of 57 years (range, 41–77 y) had a known diagnosis of breast cancer and were undergoing BSGI for further work-up (Fig. 1). The remaining 128 patients had a mean age of 51 years (range, 27–86 y).

Table 1 reviews the breast imaging reporting and data system (BI-RADS) lexicon established by the American College of Radiology.<sup>8</sup> The 176 patients were separated into 3 groups according to their pre-BSGI imaging BI-RADS category (Table 2).

One hundred and seven patients had BI-RADS 1, 2, or 3. Twelve (11.2%) had positive BSGI. Eight of these patients underwent a biopsy. Two (1.9%) of these were positive for cancer (invasive ductal carcinoma [IDC], 1; ductal carcinoma in situ [DCIS], 1). In the remaining 4 patients, 3 had follow-up US and 1 had a follow-up MRI; all returned as benign.

Twenty-one patients had BI-RADS 4, for which biopsy is recommended by the established guidelines. Three (14.3%) of these patients had positive BSGI, all of these patients underwent a biopsy and 2 (9.5%) returned as cancer (IDC). The remaining 18 patients had negative BSGI. Eleven of these patients underwent a biopsy, the results of which were benign. One patient biopsy was attempted but aborted because the suspicious lesions found previously could not be visualized. In 6 patients a biopsy was avoided. Follow-up information is available for 3 of the 6 patients. One patient had a 5-month follow-up MRI, 1 patient had a 5-month follow-up MM and US, and the third patient had a 9-month follow-up MM; all results were benign.

**Table 1** BI-RADS lexicon established by the American College of Radiology

BI-RADS category	Assessment	Clinical management recommendations
0	Assessment incomplete	Need to review prior studies and/or complete additional imaging
1	Negative	Continue routine screening
2	Benign finding	Continue routine screening
3	Probably benign finding	Short-term follow-up mammogram at 6 months, then every 6–12 months for 1–2 years
4	Suspicious abnormality	Perform biopsy, preferably needle biopsy
5	Highly suspicious of malignancy; appropriate action should be taken	Biopsy and treatment, as necessary
6	Known biopsy-proven malignancy, treatment pending	Ensure that treatment is completed

In the 48 patients with a known diagnosis of breast cancer (Fig. 1), BSGI was positive at new foci in 6 patients (12.5%): 4 in the contralateral breast, 2 in the ipsilateral breast. Three patients (6.3%) had additional cancer that was confirmed on biopsy (DCIS, 1; IDC, 2). Of the remaining 3 patients, 2 underwent a biopsy and the results were benign, the other patient had a follow-up US that showed a benign cyst.

The clinical impact noted over our initial 176 BSGI studies was the detection of 6 (3.4%) additional foci or new diagnosis of cancer not found by other imaging modalities. In 6 (3.4%), a negative BSGI prevented a biopsy. In addition, 11 patients with BI-RADS 4 could have avoided a biopsy because of a negative BSGI. In newly diagnosed breast cancer patients undergoing further imaging, there was a false-positive rate of only 6.3%.

## Comments

Screening mammography has been the gold standard for breast cancer detection for the past 30 years and is the only screening tool proven to reduce breast cancer mortality. One of the major limitations as mentioned previously is its dramatic decrease in sensitivity with increased breast density.<sup>4,5</sup> This limitation is magnified by the fact that an increase in breast density is an independent risk factor for developing cancer.<sup>9</sup> MRI currently is recommended by the American Cancer Society in patients with high risk, but its sensitivity is undone by its problems with increased false-positive rates leading to numerous benign biopsies.<sup>10</sup> In the

case of a new diagnosis of breast cancer, MRI overcalls can lead to a decision for mastectomy in patients who actually could have had breast conservation.<sup>11</sup>

Scintimammography provides physiologic data in breast cancer imaging via 2 mechanisms. First, the radioactive tracer sestamibi is distributed evenly throughout the circulatory system, but because malignant tumors induce neoangiogenesis to support their hyperproliferation, pharmaceutical delivery to these lesions is enhanced.<sup>12</sup> Second, sestamibi specifically binds mitochondria within cells and because cancer cells have a higher cytoplasmic mitochondrial density than the surrounding breast tissue, they retain more of the radiopharmaceutical.<sup>13</sup> These 2 mechanisms make scintimammography highly sensitive and specific.<sup>2</sup> New advances in scintimammography, in particular the development of a dedicated BSGI, has overcome the 2 major limitations of this imaging modality: tumor localization and detection of subcentimeter lesions.<sup>7</sup> BSGI also has the advantage of not being affected by breast density similar to MRI, but comes at a fraction of the cost (BSGI is 37% of the cost of MRI). There is current ongoing research on the role of BSGI and where it fits in the imaging armamentarium for breast cancer.

Reviewing our initial experience, we were impressed with 3 areas in which BSGI had a meaningful impact in our clinical practice. The first and major group is in patients with newly diagnosed breast cancer. In the age of breast MRI, there is continual debate regarding its utility in the preoperative evaluation of newly diagnosed breast cancer patients. Although MRI has a very high sensitivity, its poor specificity and high false-positive rate results in numerous

**Table 2** Three groups of patients undergoing BSGI

BI-RADS category	BSGI positive	Biopsy/imaging follow up	Pathology
1, 2, 3 (N = 108)	N = 12	Excisional, 3; US-guided core, 4; FNA, 1; US, 3; MRI, 1	IDC, 1; DCIS, 1; benign, 10
4 (N = 21)	N = 3	Excisional, 1; US-guided core, 1; FNA, 1	IDC, 2; benign, 1
6 (N = 48)	N = 6 (positive at a new location)	US-guided core, 5; US, 1	IDC, 2; DCIS, 1; benign, 3

FNA = fine-needle aspiration.

unnecessary biopsies, additional imaging, and patient anxiety.<sup>14</sup> In our series, BSGI found 3 (6.4%) additional foci of cancer not seen with other imaging modalities, with 2 in the contralateral breast. The false-positive rate was only 6.3%. This compares favorably with MRI studies in this setting that have reported false-positive rates of up to 78%.<sup>14</sup>

The second group is patients with BI-RADS 1, 2, or 3 with an abnormal physical examination, high risk, and/or MM dense breasts. BSGI is not affected by breast density and in our patient population it proved to be a useful adjunctive imaging study. In our group of 107 patients with otherwise benign imaging (BI-RADS 1, 2, or 3), a positive BSGI led to the detection of 2 occult malignancies. There were 10 false-positive findings with a final diagnosis of benign fibrocystic changes, fibroadenoma, and papilloma. This is consistent with published reports by Brem et al<sup>6</sup> who looked at 94 patients with BI-RADS 1, 2, or 3. In this series, 16 patients had positive BSGI with 2 confirmed cancers with biopsy. The overall calculated sensitivity and specificity was 100% and 85%, respectively (the high sensitivity in that study was caused in part by small sample size, and larger series are needed to confirm these findings).

The third group who may benefit from BSGI is patients with BI-RADS 4, a category for which biopsy is recommended. At our community breast center with 4 dedicated mammographers there were 11,451 diagnostic and screening MMs performed in 2006, with 229 patients eventually undergoing biopsy. In our review, we had 21 patients with a BI-RADS 4 designation. Eighteen had negative BSGI studies and 3 had positive BSGI, 2 were malignant. All the patients with negative BSGI were confirmed negative by biopsy or follow-up imaging (except for 3 whose follow-up information was not available). This is an exciting area in which BSGI could play an extremely valuable role. If BSGI can determine reliably that MM findings are benign, we potentially can avoid unnecessary biopsies for a majority of patients. Lumachi et al<sup>15</sup> reported on a series of 73 patients with MM suspicious breast lesions evaluated with sestamibi scintimammography before biopsy. The positive predictive value was 95.7%. Age did not affect the sensitivity of sestamibi scintimammography, which reached 100% in patients with breast lesions 8 mm or larger in size. They concluded that sestamibi scintimammography in conjunction with mammography potentially may reduce unnecessary invasive biopsy. There have been other studies looking at this group of patients to see if sestamibi scintimammography can avoid unnecessary biopsy. Unfortunately, they all were conducted with the old large field-of-view gamma cameras and cannot be compared with results from the new dedicated small field-of-view gamma cameras. Larger series of patients in this category using a small field-of-view breast gamma camera will be needed to verify this promising finding in our small group of patients.

At our institution, the total cost of a MRI is approximately \$3,400, the total cost of BSGI is \$1,259, and the total cost of MM is \$340. BSGI can be performed easily in

patients with obesity, claustrophobia, metal implants, and other conditions that limit the use of MRI. This, in combination with the reported improved sensitivity and specificity of BSGI compared with MRI,<sup>2,3,16,17</sup> makes BSGI a viable alternative.

## Conclusions

BSGI has played an important role in our management of patients with complex breast tissue and newly diagnosed breast cancer. Potential roles for BSGI in the current paradigm of breast imaging include screening and diagnosis. BSGI has the ability to pick up MM occult breast cancers and can be especially useful in high-risk patients with dense breasts in whom the sensitivity and specificity of MM suffers significantly. Another promising use of BSGI could be further evaluation of BI-RADS 4 patients to see if invasive biopsy can be avoided. A larger series of patients is needed to confirm this hypothesis.

## Acknowledgment

The authors acknowledge Gerald Green, M.D., and Sam Gruner, M.D.

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## Discussion

**David Maccabee, M.D.** (Hood River, OR): As a new member I would like to take this opportunity to thank the President, Dr. Orrom, officers, and members of the association, for the invitation to join the NPSA. I would like to thank the authors for preparing the manuscript in a timely fashion and also for producing material that I believe is clinically relevant and may change the way we practice surgery in the near future.

Summarizing the available statistics regarding breast cancer, this disease affects one eighth of women in the United States, about 200,000 new cases per year, and is the most commonly diagnosed cancer in women in the North American continent. The past 10 years, and indeed the last 5, have seen the popularization of 2 new technologies that are now used everyday for diagnosis and treatment of breast cancer; specifically MRI for tumor imaging and SLNBx for surgical staging.

For the majority of American women, breast cancer screening consists of a physical exam and a yearly mammogram. Increasingly, a positive finding then leads to another imaging study, either ultrasound or MRI, prior to biopsy or surgical extirpation of a suspected malignancy. These additional imaging studies may confirm or shed doubt

on the initial mammogram or may discover altogether new areas of suspicion. These additional studies are costly in both patient and physician time and resources. Widespread introduction of another imaging modality that is cost effective and accurate should be broadly accepted in our technologically advanced but cost-conscious medical system.

This paper represents early experience with a technology that has not gained popularity in the United States, unlike the other 2 new technologies mentioned above. Since the implication of this paper is that BSGI may supplant MRI for diagnosis of BrCa, can you compare and contrast those 2 studies with respect to patient tolerance for the procedure and difficulty of interpretation by the radiologist or surgeon?

Would you please comment on how performance of BSGI may interfere with your ability to perform sentinel node biopsy, which typically uses technetium-tagged sulfur colloid? How long do you wait between studies and have you noted any problems? Also, would the authors please comment on the differences in sensitivity of this technique for infiltrating ductal versus lobular carcinoma versus DCIS?

With respect to the data: how many of the 48 patients with known diagnosis of malignancy (with their primary tumor still intact) had their primary tumor detected by BSGI imaging? This information will provide an internal control in your study to determine the true sensitivity of this technique at your center.

Finally, regarding your conclusions, given the time and technologic sophistication required for BSGI, it seems better suited to confirming suspected diagnoses rather than screening large numbers of patients (as in the BI-RADS 1–3 group). It seems likely that the BI-RADS 4 suspicious group will benefit most from this technique, which could spare patients a surgical procedure. You report on 21 patients in the BI-RAD 4 group, 18 of whom could have been spared surgery. Of the 3 positive studies in this group, only 2 proved to have malignancy. Although these numbers are small, how will you improve on the specificity of this study?

In conclusion, the authors have presented information which represents their experience with a less popular but possibly better imaging modality useful in the treatment of breast cancer. I would like to applaud the authors for their fine work and courage to innovate and introduce new techniques for care—clearly this is an extra burden for those who spend the majority of time in the arena of clinical practice and they should be recognized.