Detection of Occult Foci of Breast Cancer Using Breast-Specific Gamma Imaging in Women with One Mammographic or Clinically Suspicious Breast Lesion

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Rationale and Objectives: The aim of this study was to determine how often breast-specific gamma imaging (BSGI) identifies occult cancerous lesions in women with one suspicious lesion detected on mammography or physical exam.

Materials and Methods: A retrospective review was performed of the records of all patients who underwent BSGI between January 1, 2004, and June 4, 2007. Included in the study were 159 women who had one suspicious breast lesion on physical exam and/or mammography and who underwent BSGI to evaluate for occult lesions in the breast. All patients had one or more foci of cancer proven pathologically. BSGI findings were classified as normal or abnormal on the basis of the presence of focal radiotracer uptake.

Results: BSGI detected additional suspicious lesions occult to mammography and physical exam in 46 of 159 women (29%). BSGI identified occult cancer in 14 of 40 women (35%) who underwent biopsy or excision because of BSGI findings and in 14 of the 159 (9%) women in this study. In nine women, the occult cancer was present in the same breast as the index lesion (6%), and in five women, the occult cancer was found in the contralateral breast (3%).

Conclusions: BSGI is an effective imaging modality in the identification of mammographically and clinically occult cancer in women with one suspicious breast lesion.

Key Words: Breast cancer; breast-specific gamma imaging; breast cancer imaging; nuclear medicine imaging of the breast.

Breast conservation surgery has replaced mastectomy as the preferred treatment for early-stage breast cancer (1,2). However, when two or more primary tumors are located in different quadrants of the breast, breast-conserving therapy is contraindicated (3). Routine physical examinations and mammography are the most common methods for early cancer detection, but they have diagnostic limitations. A study of 282 mastectomy specimens (performed for unifocal breast cancer) found that 63% of breasts had additional sites of cancer not detected by clinical examination or mammography, including 7% with additional foci of cancer in a different quadrant of the breast (4). Additional analyses of the pathology of mastectomy specimens have shown sites of cancer other than the index lesion in 20% to 63% (5–9). To achieve the highest possible level of diagnostic accuracy in the preoperative radiologic assessment, additional imaging techniques may be used. These include ultrasound, magnetic resonance imaging (MRI), and breast-specific gamma imaging (BSGI). Ultrasound, the primary diagnostic adjunct to mammography, aids in the diagnostic evaluation of mammographic findings and is used to guide interventional procedures (10,11). Houssami et al (12) reported sensitivity of 96% and specificity of 79% for the combination of mammography and breast ultrasound in the identification of breast cancer.

Although mammography and ultrasound are predominantly anatomic in their approach to breast cancer diagnosis, MRI and BSGI rely on physiologic changes for the evaluation of breast cancer. Molecular breast imaging, or BSGI, uses

Acad Radiol 2010; 17:735–743

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doi:10.1016/j.acra.2010.01.017

a high-resolution, small–field of view gamma camera specific to breast imaging (13), which has demonstrated improved sensitivity for the detection of breast cancer (14). The sensitivity of BSGI ranges from 78.6% to 100% for detecting breast cancer, which is comparable to that of MRI (73%–100%) (15–19). Breast MRI and BSGI are similar in their ability to detect intraductal cancer, with sensitivities reported ranging from 88% and 92% for breast MRI (16,20) and 91% to 94% for BSGI (15,19). Additionally, both breast MRI and BSGI can detect breast cancers that are mammographically and clinically occult (19,21). BSGI can detect subcentimeter occult cancers as small as 1 mm (18,19). The reported specificities of BSGI and breast MRI are also similar, ranging from 59.5% to 93.3% for BSGI (17,19) and from 37% to 97% for breast MRI (22). Although BSGI and MRI are similar in their ability to detect breast cancer, BSGI has advantages in ease of performing the examination for patients and in interpretation for radiologists. Although MRI may be difficult for patients with claustrophobia and not possible in patients with renal insufficiency, implantable devices, or large body habitus, BSGI can be performed in any woman with venous access. A breast MRI examination often generates >1000 images, compared to four to 10 images with BSGI, with a concomitant decrease in interpretation time. Although formal cost analysis studies are needed to further evaluate the relative costs, both the equipment and the cost of the study are lower with BSGI.

Several studies have shown that breast MRI, in the preoperative evaluation of known breast cancer, can detect multifocal, multicentric, and bilateral disease that was previously unsuspected, which facilitates preoperative planning (22,23–26). Breast MRI has identified additional sites of cancer occult to initial mammography and physical examination in the ipsilateral breast in 6% to 34% of women and in the contralateral breast in 4% to 24% of women (23,24).

The purpose of this study was to determine how often BSGI identifies clinically and mammographically occult breast cancer in women with one suspicious or cancerous lesion detected on mammography or physical exam.

MATERIALS AND METHODS

Subjects

A retrospective review was performed of the records of all patients who underwent BSGI from January 1, 2004, through June 4, 2007. Among these, 159 women met the following criteria: (1) one suspicious breast lesion was found on physical exam and/or mammography, (2) BSGI was performed to evaluate for occult cancerous lesions in the breasts, and (3) the patient was proven by pathology to have one or more foci of breast cancer. Institutional review board approval and Health Insurance Portability and Accountability Act full waiver of informed consent were obtained for this study.

BSGI Technique and Interpretation

BSGI examinations were performed with the patients in a seated position with a breast-dedicated, small–field of view breast-specific gamma camera (Dilon 6800; Dilon Technologies, Newport News, VA). Each patient received an injection of 20 to 37 mCi ^{99m}Tc sestamibi in an antecubital vein. Immediately after injection of the radiotracer, imaging began. Initially, craniocaudal and mediolateral oblique projections were obtained. Additional projections were performed as deemed necessary by the interpreting radiologist. The acquisition time for each image was approximately 6 to 10 minutes, with a minimum of 100,000 counts, for a total imaging time of approximately 40 minutes per study.

BSGI examinations were read by a radiologist with expertise in BSGI interpretation. Images were interpreted in conjunction with clinical history and other breast imaging studies, including mammograms and sonograms. BSGI findings were prospectively classified as normal or abnormal on the basis of the presence of focal radiotracer uptake. For nonpalpable, mammographically occult, BSGI-detected lesions warranting further workup, directed, second-look ultrasound with a focused examination in the region of the increased radiotracer uptake was performed. If no lesion was identified with directed ultrasound, the patient underwent breast MRI to identify the lesion for MRI-guided biopsy. Further imaging following abnormal findings on BSGI was performed at the discretion of the radiologist to further characterize the area of abnormal radiotracer uptake as well as to target biopsy. Biopsy of additional suspicious lesions occult to physical exam and mammography were performed by one or more of the following methods: ultrasound-guided fine needle aspiration, ultrasound-guided core needle biopsy, MRI-guided vacuum-assisted needle biopsy, surgical excision with ultrasound-guided wire localization, or stereotactic-guided core needle biopsy if the lesion was seen on repeat mammography but not identified at initial mammographic interpretation.

Data Collection and Analysis

One hundred fifty-nine women (mean age, 54 years; range, 29–93 years) who had one suspicious lesion on physical exam and/or mammography and underwent BSGI to evaluate for occult cancerous lesions in the breasts were included. Of these 159 women, 123 (77%) had known breast cancer at the time of BSGI. Thirty-six women (23%) had at least one suspicious lesion that did not have a tissue diagnosis at the time of imaging but was later proven by pathology to have one or more foci of breast cancer. Personal history of breast cancer and family history, including whether the relative who had breast cancer was a first-degree relative (mother, sister, or daughter), was noted. Mammographic parenchymal density was determined by subjective assessment by an expert mammographer and was recorded according to the Breast Imaging Reporting and Data System lexicon as class 1 (almost entirely fat), class 2 (scattered fibroglandular density), class 3, (heterogeneously dense), or class 4 (extremely dense) (27).

Medical records and mammograms were reviewed to determine the locations of the index lesion and whether the index lesion was palpable on physical exam and/or evident on mammography. Findings on ultrasound, if performed, were also reviewed to assess for the presence of correlative findings. The index tumor size, if determined, and pathology were also recorded. Pathology of the mastectomy or partial mastectomy specimens was used unless the biopsy had a higher grade lesion than identified at surgery or if the final pathology was unavailable because of patient had definitive surgery at another institution.

BSGI studies and interpretations were reviewed to determine the frequency of additional sites of abnormal uptake in one or both breasts as well as the frequency of detecting occult pathology-proven cancerous sites. BSGI-detected lesions were considered to be additional sites if they were in a different breast or quadrant than the index lesion, if they were in the same quadrant but separate from the index lesion, or if they were in the same quadrant and contiguous with the index lesion but extended ≥4.0 cm beyond the site of the index lesion. The latter instance was included because this finding would affect surgical management. The location of an additional site of abnormal uptake, the presence of an ultrasound or MRI correlate of the additional site, the biopsy method, if performed, the size, and the pathology, if cancerous, were recorded. The likelihood of detecting mammographically and clinically occult cancerous lesions was calculated as a function of family history of breast cancer, personal history of breast cancer, breast density, menopausal status, and index cancer size and histology.

Data were entered into a spreadsheet (Excel 2003; Microsoft Corporation, Redmond, WA) for analysis. Statistical analyses were performed using χ- and Fisher's exact tests, with P value < .05 considered significant.

RESULTS

Baseline Characteristics

One hundred fifty-nine women with one suspicious lesion on physical exam or mammography who underwent BSGI were included. Sixty-two of the women (39%) were premenopausal and 97 (61%) were postmenopausal. Nineteen of these women (12%) had personal histories of breast cancer. Family histories of breast cancer were present in 68 women (43%), of whom 35 women had family histories of breast cancer in first-degree relatives. One woman was adopted, and her family history was unknown.

The Breast Imaging Reporting and Data System mammographic parenchymal density in these 159 women was class 4 in 17 (11%), class 3 in 98 (62%), class 2 in 33 (21%), and class 1 in three (<2%). The parenchymal density was unknown in eight women (5%) because the mammograms of these eight women were not available for re-review, and their densities were not noted in the mammographic reports.

Of the 159 suspicious index lesions, 84 (53%) were palpable, two presented with bloody nipple discharge, one presented with an eczematous rash of the nipple due to Paget's disease, and one presented with nipple retraction. At the time of BSGI, 123 of the 159 suspicious index lesions (77%) were biopsy proven to be cancer, and 36 of the lesions (23%) were suspicious findings that did not yet have tissue diagnoses but were later proven by pathology to have one or more foci of breast cancer. The index lesion was suspicious on mammography in 152 (96%) women. Of the 71 suspicious index lesions (45%) not detected on physical exam, all were evident on mammography.

The pathologic findings of the index lesions included infiltrating ductal carcinoma in 111 lesions (69.8%), 78 of which were associated with ductal carcinoma in situ (DCIS), infiltrating lobular carcinoma in 10 lesions (6%) and infiltrating ductolobular carcinoma in three (2%), one of which included DCIS. There were two mucinous adenocarcinomas (1%), one with DCIS with a dense inflammatory background (<1%). Finally, pure DCIS was present in 31 lesions (19.5%), and one lesion was benign (<1%). In the latter case, the index lesion was benign but the occult lesion was malignant. Of the 127 infiltrating cancers, nuclear grade was known in 116 cancers and was high grade in 49 cancers (42%), intermediate grade in 53 cancers (46%), and low grade in 14 cancers (12%). Of the 31 pure DCIS lesions, grade was known in 30 lesions and was high grade in nine lesions (30%), intermediate grade in 18 lesions (60%), and low grade in three lesions (10%). Size, known in 112 of 127 infiltrating cancers (88%), ranged from 0.3 to 8.5 cm (mean, 1.87 cm).

BSGI-detected Additional Suspicious Lesions

BSGI detected 56 foci or areas of abnormal radiotracer uptake other than the index lesions in 46 women. "Second-look" ultrasound was performed to evaluate 53 of these 56 additional lesions and revealed suspicious correlates in 44 (83%). Breast MRI was performed on 12 women to evaluate 14 of the additional BSGI-detected lesions. MRI demonstrated correlates in 12 of these 14 lesions (85.7%).

Biopsy was performed on 46 of the 56 additional lesions (82%). Four of these lesions (7%) had percutaneous biopsies followed by excisional biopsies, and six of these lesions (11%) had two percutaneous biopsy sites, yielding 56 total biopsies. Percutaneous biopsy of the lesions was performed by ultrasound guidance in 45 biopsies (80.4%), stereotactic guidance in four biopsies (7.1%) (based on mammographic findings identified only after the BSGI information), and MRI guidance in three biopsies (5.4%). Excisional biopsy was performed with MRI-guided needle localization in one (1.8%) and ultrasound-guided needle localization in three (5.4%).

Ten of the 56 additional lesions (18%) were not biopsied. Of these 10 lesions, three (30%) were excised during bilateral mastectomies per the patients' choice. The pathologic results of these prophylactic mastectomies proved two of these lesions to be benign and one lesion to be cancerous. Seven of the 56

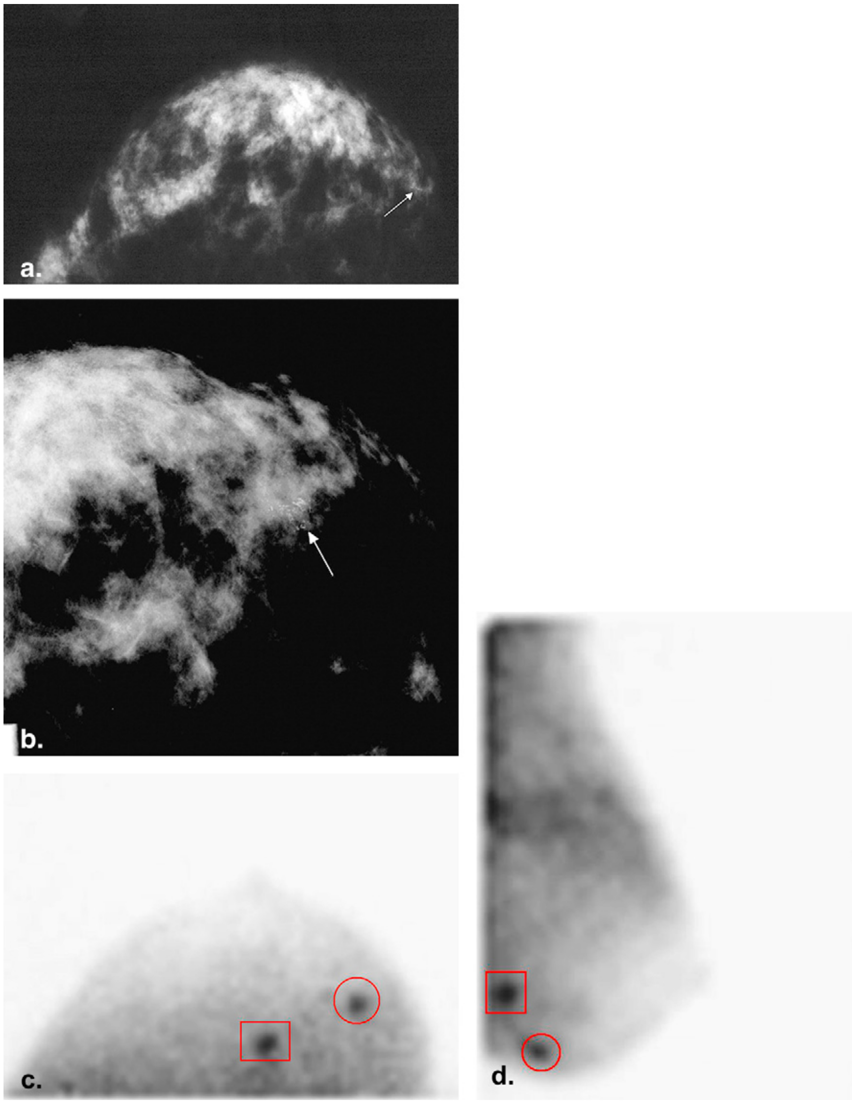

Figure 1. Mammography and breast-specific gamma imaging (BSGI) in a 48-year-old woman with infiltrating ductal carcinoma of the left breast. **(a)** Left craniocaudal and **(b)** left magnified craniocaudal mammographic images demonstrated a 6-mm area of pleomorphic calcifications concentrated in the lower inner posterior left breast (white arrow). BSGI **(c)** left craniocaudal and **(d)** left mediolateral oblique views demonstrated two abnormal foci of increased radiotracer uptake in the inferior of the left breast, the index cancer (black circle) and a second occult focus of increased radiotracer uptake (black rectangle). Pathology revealed two wire-localized foci measuring 1.2 and 1.0 cm of high-grade infiltrating ductal carcinoma at the 8:00 and 6:00 axes of the left breast.

BSGI-detected additional suspicious lesions (13%) were not biopsied or excised. None of these seven lesions had suspicious correlates on ultrasound. Five of these seven lesions were proven benign on the basis of their routine imaging the following year. Data for the last two lesions remain unavailable, because the patients did not return for further imaging.

Breast biopsy or surgery yielded cancer in 14 lesions, constituting 14 of 56 (25%) additional lesions detected on BSGI and 14 of 40 women (35%) who underwent biopsy or excision because of BSGI findings (Fig 1). Directed ultrasound was performed to evaluate 13 cancers and revealed suspicious correlates in 12 cancers (92%). MRI was performed to evaluate four cancers identified initially with BSGI and revealed suspicious correlates in all four (100%). One of these MRI examinations was performed to evaluate the lesion that did not undergo "directed" ultrasound.

Four ultrasound-guided core needle biopsy specimens and one excisional biopsy specimen with ultrasound-guided wire localization, which had benign pathology initially, were later proven cancerous. Three of the four ultrasound-guided core needle biopsies underwent excisional biopsy because of radiologic-pathologic discordance, and pathology of the surgical specimens with wire localization by ultrasound guidance demonstrated the lesions to be cancer. The remaining two of the five benign biopsy specimens were initially diagnosed as intraductal papillomas and underwent surgical excision, which demonstrated DCIS.

Breast biopsy or surgery yielded benign pathology in 35 lesions, constituting 63% (35 of 56) of additional lesions detected on BSGI and 71% (35 of 49) of lesions for which biopsy or surgery was performed. Originally, one of these lesions was assumed benign because it did not have a suspicious correlate on ultrasound and was not biopsied. However, subsequent imaging, including mammography, ultrasound, and BSGI, the following year led to a biopsy in the same lesion. An additional seven lesions were assumed benign on the basis of their ultrasound findings and were followed up. Five of these lesions were proven benign on the basis of

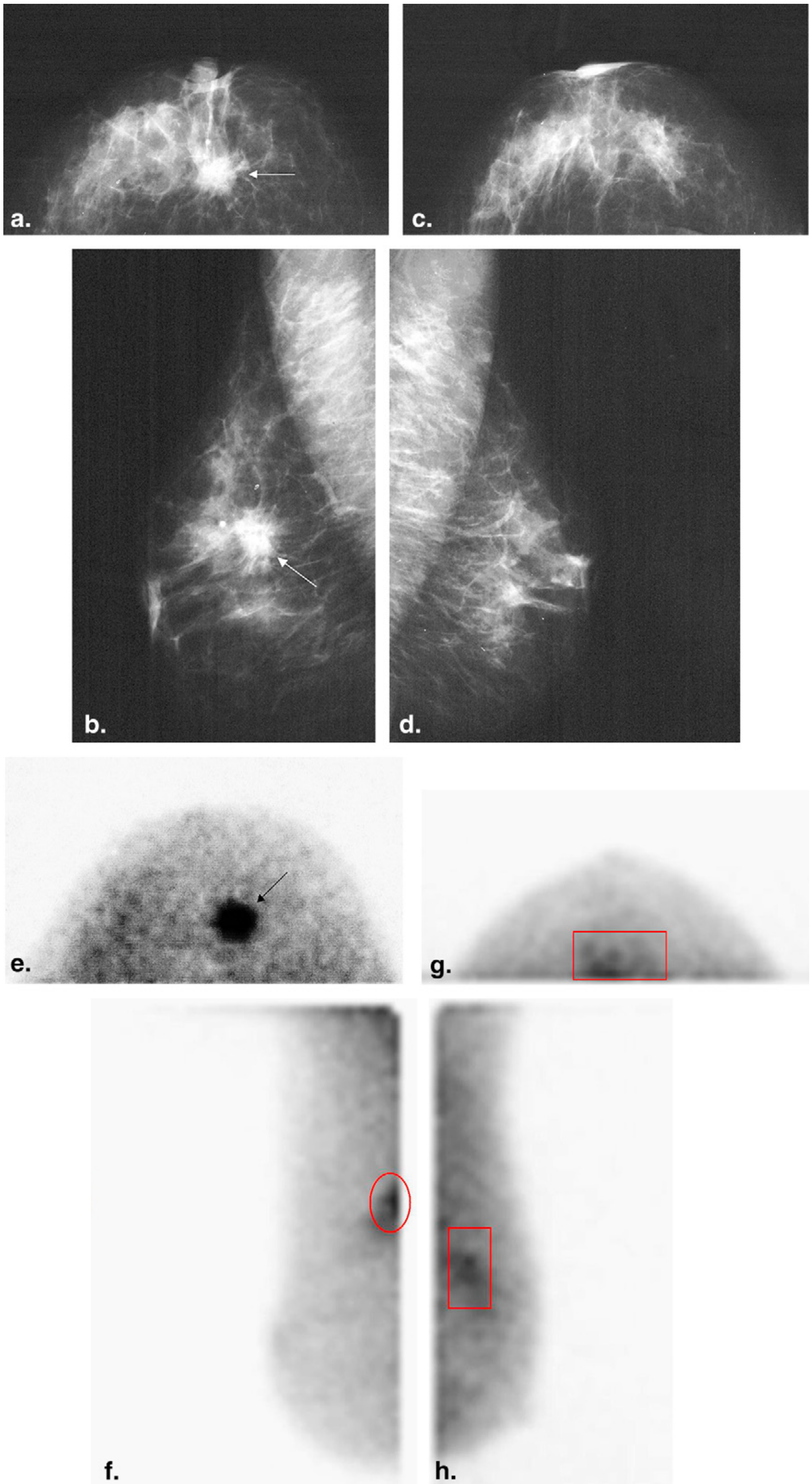

Figure 2. Mammography and breast-specific gamma imaging (BSGI) in a 39-year-old woman who presented with a palpable abnormality of the left breast. **(a)** Left craniocaudal and **(b)** left mediolateral oblique mammographic images demonstrated a spiculated mass in the 12:00 axis (white arrow). **(c)** Right craniocaudal and **(d)** right mediolateral oblique mammographic failed to demonstrate a new mass, area of distortion, or suspicious cluster of microcalcifications. BSGI **(e)** left craniocaudal and **(f)** left mediolateral oblique views demonstrated one focus of abnormal uptake in the left breast corresponding to the spiculated mass (black arrow). BSGI **(g)** right craniocaudal and **(h)** right mediolateral views revealed an occult focus of focal increased radiotracer uptake (black rectangle). Ultrasound-guided core biopsy yielded infiltrating carcinoma in the left breast at the 11:30 axis and in the right breast at the 1:00 axis.

imaging the following year, and two lesions had incomplete data because the patients did not return for evaluation. The pathology of the noncancerous lesions with increased radiotracer uptake included fibrocystic change, fibroadenoma, papillomatosis, atypical ductal hyperplasia, and fat necrosis (17).

BSGI-detected Occult Cancerous Lesions and Comparison with Index Lesion

BSGI detected 14 sites of nonpalpable, mammographically occult cancer in the ipsilateral or contralateral breast in 14 of

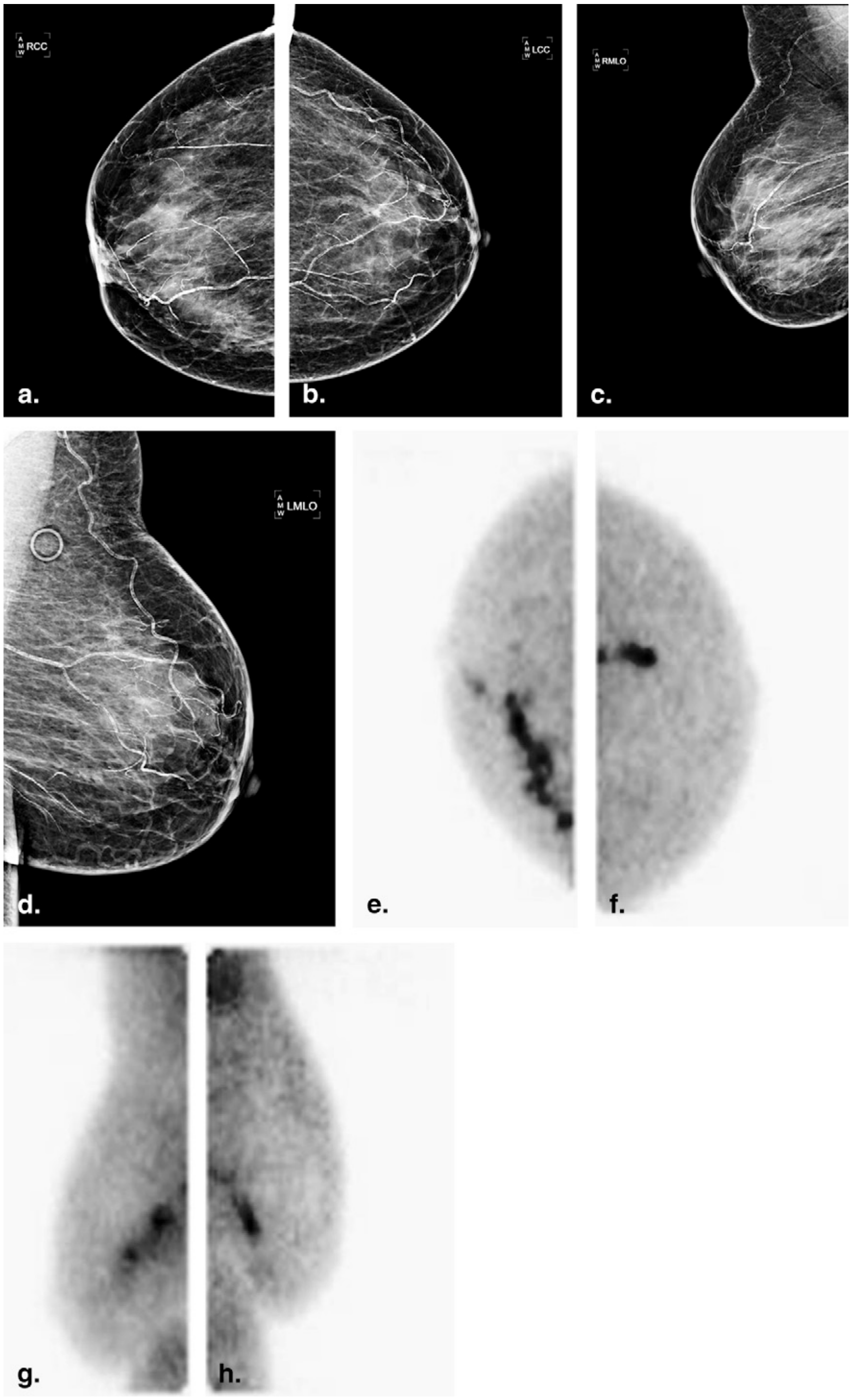

Figure 3. Breast-specific gamma imaging (BSGI) in a 69-year-old woman who presented with new left breast nipple discharge. **(a)** Right and **(b)** Left Cranio-caudal and **(c)** Right and **(d)** Left Medio-lateral Oblique mammograms demonstrate scattered heterogenous fibroglandular tissue with vascular calcifications and no other findings. Ultrasound was normal **(e)** Right and **(f)** Left Cranio-caudal and **(g)** Right and **(h)** Left Medio-lateral oblique BSGI demonstrates linear clumped radiotracer uptake bilaterally, greater on the right than the left. Second look ultrasound demonstrated a vague area of prominent ducts, which on biopsy demonstrated bilateral DCIS.

159 women (9%), including 9 of 159 women (6%) in whom the occult cancer was present in the same breast (Fig 2) as the index lesion and five of 159 women (3%) in whom the occult cancer was found in the contralateral breast (Figs 3 and 4). Of the nine ipsilateral cancers, six (67%) were in the same quadrant and three (33%) were in different quadrants from the index lesion. In the six women with cancers detected in the same quadrant as the index cancer, pathology showed that the additional cancers were separate from the index cancer in five women (83%) and contiguous with the index cancer in one woman (17%), with extent beyond the index cancer of >4.5 cm.

The pathologic features of the BSGI-detected occult sites of cancer in these 14 women are listed in Table 1, and descriptions of the sizes of these cancers are listed in Table 2. The pathologic features of the index tumors and the occult cancerous lesions were the same in 11 of these 14 women (79%): ductal in 10 and lobular in one. In three women (21%), the pathologic findings of the index lesions

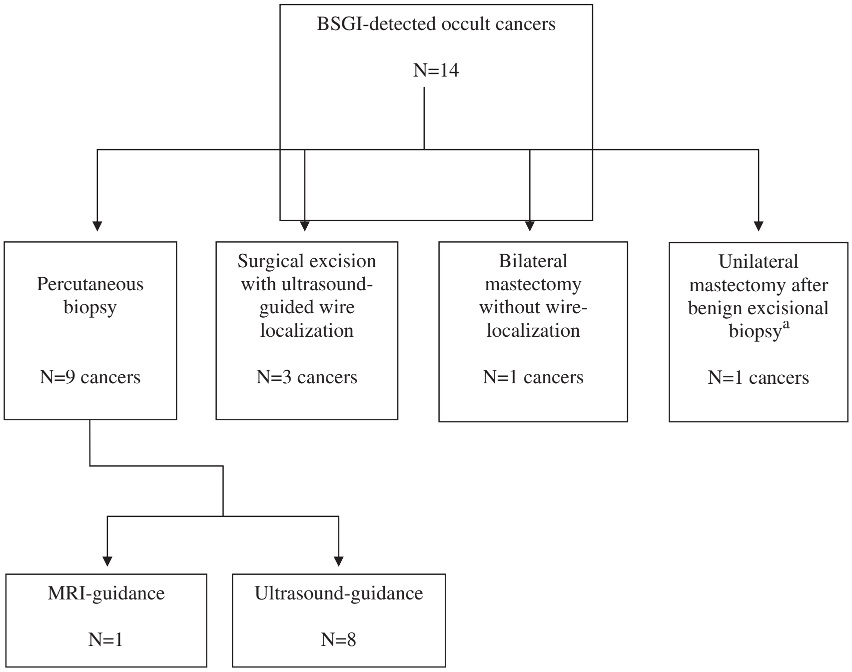

Figure 4. Method of cancer diagnosis of breast-specific gamma imaging (BSGI)–detected occult cancers. *Ductal carcinoma in situ was found on mastectomy specimen adjacent to the site of a previous excisional biopsy with wire localization performed for the BSGI-detected lesion. MRI, magnetic resonance imaging.

TABLE 1. Pathologic Features of BSGI-detected Occult Cancers

Pathology	Total Frequency	Contralateral Frequency	Ipsilateral Frequency
Infiltrating ductal carcinoma	6/14 (43%)	2/5 (40%)	4/9 (44%)
Intermediate grade	3/6		
High grade	3/6		
Associated with DCIS	4/6		
Infiltrating lobular carcinoma*	3/14 (14%)	2/5 (40%)	1/9 (11%)
Low grade	1/3		
Associated with DCIS	1/3		
DCIS	5/14 (36%)	1/5 (20%)	4/9 (44%)
Low grade	1/5		
Intermediate grade	1/5		
High grade	3/5		

BSGI, breast-specific gamma imaging; DCIS, ductal carcinoma in situ.
*One infiltrating lobular carcinoma had unknown grade.

TABLE 2. Sizes of BSGI-detected Occult Cancers

Size Description	All Cancers	Contralateral Cancers	Ipsilateral Cancers
Mean size of occult infiltrating cancers (cm)*	1.16	0.58	1.6
Range of sizes of infiltrating cancers (cm)	0.15–3.6	0.15–1.0	0.8–3.6
Number of cancers <1 cm	7†	4†	3

BSGI, breast-specific gamma imaging.
*Two of the nine infiltrating carcinomas were of unknown size.
†Includes the one pure ductal carcinoma in situ lesion with known size, which measured 0.4 cm.

and BSGI-detected additional lesions differed, including one woman with duct and lobular features in the index lesion and an invasive ductal carcinoma in the contralateral lesion, one invasive ductal carcinoma in the index lesion with the occult cancer demonstrating ductal and lobular features in the contralateral breast, and one woman with benign pathology in the index lesion and invasive lobular cancer in the ipsilateral additional BSGI-detected lesion occult to

TABLE 3. Frequency of BSGI Detection of Occult Cancer Versus Various Parameters

Parameter	Frequency of Detection	*P*
Menopausal status		
Premenopausal	7/62 (11%)	.38
Postmenopausal	7/97 (7%)	
Personal history of breast cancer		
Yes	1/19 (5%)	1
No	13/140 (9%)	
Family history of breast cancer		
Yes	7/68 (10%)	.58
No	7/90 (8%)	
Breast density pattern		
4 (extremely dense)	1/17 (6%)	.74*
3 (heterogeneously dense)	9/98 (9%)	
2 (scattered fibroglandular density)	4/33 (12%)	
1 (almost entirely fat)	0/3 (0%)	
Pathology of index cancer		
Infiltrating lobular carcinoma	1/10 (10%)	.25‡
Infiltrating ductal carcinoma	8/111 (7%)	
Infiltrating ductolobular carcinoma	1/3 (3%)	
Ductal carcinoma in situ	3/31 (10%)	
Other†	0/4 (0%)	
Size of index cancer§		
>0.2 cm	5/37 (14%)	.29
<0.2 cm	5/75 (7%)	

BSGI, breast-specific gamma imaging.

*For comparison of classes 4 and 3 versus classes 2 and 1.

†Includes mucinous adenocarcinoma, carcinoma with dense inflammatory background, and a benign lesion.

‡For comparison of infiltrating lobular versus other pathologies of index cancer.

§For 112 index cancers in which size could be measured pathologically.

mammography and physical exam. Of the 11 women in whom the pathologic features of the two tumors were the same, nuclear grade was the same in eight (73%), higher in the occult lesions in one (9%), and lower in two (18%).

The occult infiltrating cancers detected ranged in size from 0.15 to 3.6 cm (mean, 1.16 cm). Of the tumor grades in the occult, BSGI-detected cancers, two (14.2%) were low grade, four (28.5%) were intermediate grade, and six (42.8%) were high grade. The grade was unknown for two (14.2%) of the occult, BSGI-detected cancers.

There was no significant difference in the likelihood of detection of occult cancer as a function of menopausal status, personal or family history of breast cancer, mammographic parenchymal density, index cancer pathology, or size (Table 3).

DISCUSSION

The detection of multifocal, multicentric, and bilateral breast cancer is important because it alters the surgical management of the patient (28). The identification of all foci of breast cancer is a critical component of optimal patient care. BSGI is a novel, physiologically based adjunct imaging modality for the diagnosis of breast cancer that is increasingly being used. BSGI has been shown to reliably detect breast cancers, including subcentimeter cancers, as well as difficult-to-detect cancers such as DCIS and invasive lobular cancers (15,19,29). This study was undertaken to evaluate BSGI as an adjunct imaging modality for the diagnosis of occult breast cancer in women with one pathologically proven cancer or suspicious lesion.

In our study of 159 women with one suspicious lesion on physical exam and/or mammography, BSGI detected additional foci of increased radiotracer uptake occult to mammography and physical exam in 29% of women. BSGI detected occult cancer in 35% of women who underwent biopsy or surgical excision because of additional suspicious lesions detected on BSGI and detected occult cancer in 9% of women.

Of the occult cancers detected with BSGI, six (42%) were <1 cm and ranged in size from 0.15 to 0.9 cm. Of the occult cancers detected, nine (64.2%) were invasive and five (35.7%) were DCIS. This is consistent with previously published studies demonstrating that BSGI is sensitive for the reliable detection of subcentimeter cancers as small as 1 mm (15,17–19). Our study confirms what others have reported: BSGI has high sensitivity in the detection of small invasive cancers as well as DCIS (91%–94%) (15,19).

BSGI and MRI are both physiologically based imaging modalities used to assess women with known breast cancer for occult disease. Our study demonstrates that the detection of occult foci of breast cancer with BSGI is comparable to that reported for MRI (23,24). However, studies have supported the greater specificity of BSGI compared to MRI, as well as other advantages of BSGI, including ease of exam for patients, with the patients sitting upright; more rapid physician interpretation, with BSGI generating four to 10 images compared to hundreds or more for breast MRI; and lower equipment and study costs (15,19,29). This coupled with the ability to perform BSGI in essentially all patients makes it a viable option in evaluating women with newly diagnosed breast cancer for the identification of additional, occult foci of disease. Additional larger, prospective, and multi-institutional studies are needed to compare the detection of additional occult foci of breast cancer detected with BSGI and MRI.

In our study, the likelihood of BSGI detecting clinically and mammographically occult cancers was not affected by menopausal status, family or personal history of breast cancer, pathology, or the size of the index lesion. Interestingly, parenchymal density did not affect the likelihood of occult cancer detection, as BSGI detected occult breast cancer in women with dense as well as nondense and fatty breasts. This is consistent with previous reports that BSGI is beneficial in women with dense as well as nondense breasts (18). However, the number of women with nondense breasts was smaller than that of those with dense breasts in this study, and therefore further studies are needed.

Second-look ultrasound identified suspicious correlates in 92% of occult, BSGI-detected cancers. In a study by LaTrenta et al (31), who examined directed second-look ultrasound of MRI-detected breast lesions, ultrasound correlates were demonstrated in 47% of MRI-detected cancers. It is unclear why our experience differed from that reported. Perhaps with the increased use and concomitant increased expertise of directed second-look ultrasound with both BSGI-directed and MRI-detected lesions since LaTrenta et al's report, more lesions can now be identified. Nevertheless, there is undoubtedly a need to directly localize and biopsy lesions identified with BSGI. This would obviate the expense of using MRI to biopsy all suspicious lesions seen with BSGI, particularly because BSGI can be used in women who cannot undergo MRI. With the recent US Food and Drug Administration approval of a Gamma Loc (Dilon Technologies, Newport News, VA) (32), a device to localize and subsequently biopsy BSGI-detected lesions, the last hurdle in the integration of this approach in clinical practice has been overcome.

However, until Gamma Loc is widely used, our study demonstrates that by using multimodality imaging, foci of increased radiotracer uptake identified with BSGI can be localized and undergo biopsy with a combination of directed second-look ultrasound and, if necessary, MRI-guided breast biopsy.

Limitations of this study include its small sample size and its single-institution and retrospective design.

In conclusion, BSGI detected additional suspicious lesions occult to mammography and physical exam in 29% of women (46 of 159) with one suspicious or cancerous lesion detected on mammography and/or physical exam. Breast biopsy or surgery demonstrated occult cancer in 35% of women who underwent biopsy because of findings on BSGI, which constituted 9% of all women in this study. Considering the advantages of BSGI over MRI, including cost, ease of study for patients, time of interpretation for radiologists, and the ability to image all women, BSGI is an effective imaging modality in the identification of occult breast cancer.

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