

(60118)

<b>Medical Benefit</b>		<b>Effective Date:</b> 10/01/11	<b>Next Review Date:</b> 05/15
<b>Preauthorization</b>	No	<b>Review Dates:</b> 05/10, 05/11, 05/12, 05/13, 05/14	

*The following Protocol contains medical necessity criteria that apply for this service. It is applicable to Medicare Advantage products unless separate Medicare Advantage criteria are indicated. If the criteria are not met, reimbursement will be denied and the patient cannot be billed. **Preauthorization is not required but is recommended if, despite this Protocol position, you feel this service is medically necessary.** Please note that payment for covered services is subject to eligibility and the limitations noted in the patient's contract at the time the services are rendered.*

### Description

Scintimammography refers to the use of radiotracers with nuclear medicine imaging as a diagnostic tool for abnormalities of the breast. Breast-specific gamma imaging (BSGI), or molecular breast imaging (MBI), refer to specific types of imaging machines that are used in conjunction with scintimammography to improve diagnostic performance.

### Background

Scintimammography is a diagnostic modality using radiopharmaceuticals to detect tumors of the breast. After injection of a radiopharmaceutical, the breast is evaluated with planar imaging. Scintimammography is performed with the patient lying prone and the camera positioned laterally, which increases the distance between the breast and the camera. Scintimammography using conventional imaging modalities has relatively poor sensitivity in detecting smaller lesions (e.g., smaller than 15 mm), because of the relatively poor resolution of conventional gamma cameras in imaging the breast. Breast-specific gamma imaging (BSGI) and molecular breast imaging (MBI) were developed to address this issue. Breast-specific gamma cameras acquire images while the patient is seated in a position similar to that in mammography, and the breast is lightly compressed. The detector head(s) is immediately next to the breast, increasing resolution, and the images can be compared with the mammographic images. Breast-specific gamma imaging and molecular breast imaging differ primarily in the type and number of detectors used (multi-crystal arrays of cesium iodide or sodium iodide versus semiconductor materials, such as cadmium zinc telluride, respectively). In some configurations, a detector is placed on each side of the breast and used to lightly compress it. The maximum distance between the detector and the breast is therefore from the surface to the midpoint of the breast. Much of the research on BSGI and MBI has been conducted at the Mayo Clinic. The radiotracer usually utilized is technetium Tc99m sestamibi. MBI imaging takes approximately 40 minutes. (1)

Breast-specific gamma imaging and molecular breast imaging have been suggested for a variety of applications. In practice guidelines for breast scintigraphy with breast-specific gamma cameras, the Society for Nuclear Medicine provides a list of common uses, as follows:

1. Among patients with recently detected breast malignancy, initial staging; detecting multicentric, multifocal, or bilateral disease; and assessing response to neoadjuvant chemotherapy.
2. Among patients at high risk for malignancy, evaluating suspected recurrence or using it when a mammogram is limited or a previous malignancy was occult on mammogram.

3. Among patients with indeterminate breast abnormalities and remaining diagnostic concerns, evaluating lesions identified by other breast imaging techniques, palpable or non-palpable, aiding in biopsy targeting, and a number of others.
4. Among patients with technically difficult breast imaging, such as radiodense breast tissue or implants, free silicone, or paraffin injections.
5. Among patients for whom breast magnetic resonance imaging (MRI) is indicated but contraindicated, e.g., patients with implanted pacemakers or pumps, or as an alternative for patients who meet MRI screening criteria, such as BRCA1, BRCA2 mutations.
6. Among patients undergoing preoperative chemotherapy, for monitoring tumor response in order to determine the impact of therapy of plan for residual disease.

The guideline also mentions other efforts, such as the American College of Radiology's Appropriateness Criteria and the American College of Surgeons' Consensus Conference III. (2) Less emphasis is placed on detecting positive axillary lymph nodes with BSGI or MBI than with scintimammography because with current configurations, these lymph nodes are frequently out of view. Selected studies on these modalities are discussed below.

The primary radiopharmaceutical used with BSGI or MBI is technetium Tc99m sestamibi (marketed by Draxis Specialty Pharmaceuticals Inc.; Cardinal Health 414, Dublin, Ohio; LLC, Mallinckrodt Inc., and Pharmalucence, Inc., Bedford, MA). The labeling states that technetium-99m sestamibi is "indicated for planar imaging as a second-line diagnostic drug after mammography to assist in the evaluation of breast lesions in patients with an abnormal mammogram or a palpable breast mass. Technetium Tc99m sestamibi is not indicated for breast cancer screening, to confirm the presence or absence of malignancy, and it is not an alternative to biopsy."

Several scintillation or gamma cameras have general 510(k) marketing clearance from the U.S. Food and Drug Administration (FDA), which states that they are cleared for "use in imaging the distribution of radionuclides in the human body using planar imaging techniques." Two examples of gamma cameras used in BSGI or molecular breast imaging are Dilon 6800® (Dilon Technologies, Newport News, VA) and LumaGEM™ (Gamma Medica Instruments, Northridge, CA).

The radiation dose associated with BSGI is substantial for diagnostic breast imaging modalities. According to the American College of Radiology (ACR) Appropriateness Criteria, the radiation dose from BSGI is 10 to 30 mSv, which is 15-30 times higher than the dose from a digital mammogram. (3) According to the ACR Appropriateness Criteria, at these levels BSGI is not indicated for breast cancer screening.

According to another study, (4) the radiation dose to the breast from the 20 mCi (740 MBq) technetium Tc99m sestamibi used for BSGI at this center is 0.13 rad or 1.3 mGy, less than the 0.75 rad the authors report for mammography, except that the dose is given to the entire body. The authors assert that this dose poses an "extremely low risk of harmful effects to the patient" but that it should be reduced by a factor of five to 10 if BSGI were to be used as a regular screening technique. The authors also estimate that the cost of BSGI is three to four times that of mammography.

Another article published online in August 2010 calculated mean glandular doses, and from those, lifetime attributable risk of cancer (LAR) for film mammography, digital mammography, BSGI, and positron emission mammography (PEM). (5) The author, who is a consultant to GE Healthcare and a member of the medical advisory boards of Koning (which are working on dedicated breast computed tomography [CT]) and Bracco (MR contrast agents), used BEIR VII Group risk estimates (6) to gauge the risks of radiation-induced cancer incidence and mortality from breast imaging studies. The estimated lifetime attributable risk of cancer for a patient with the average-sized compressed breast during mammography of 5.3 cm (it would be higher for larger breasts) for a single breast procedure at age 40 is:

- five per 100,000 for digital mammography (breast cancer only),
- seven per 100,000 for screen film mammography (breast cancer only),
- 55-82 per 100,000 for BSGI (depending on the dose of technetium Tc99m sestamibi), and
- 75 for 100,000 for PEM.

The corresponding lifetime attributable risk of cancer mortality at age 40 is:

- 1.3 per 100,000 for digital mammography (breast cancer only),
- 1.7 per 100,000 for screen film mammography (breast cancer only),
- 26-39 per 100,000 for BSGI, and
- 31 for 100,000 for PEM.

A major difference in the impact of radiation between mammography, on the one hand, and BSGI or PEM, on the other, is that for mammography, the substantial radiation dose is limited to the breast. With BSGI and PEM, all organs are irradiated, which adds to the risks associated with BSGI and PEM. A lower dose version of molecular breast imaging (MBI) has been developed and is being tested at the Mayo Clinic among 1,000 women with dense breast tissue on mammography who are at increased risk of cancer. (1) According to the authors, all of whom are from the Mayo Clinic, this new approach will “make MBI comparable with screening mammography in terms of radiation exposure.” It is not clear whether this statement refers to breast exposure or whole body exposure.

**NOTES:** The term “molecular breast imaging” is used in different ways, sometimes for any type of breast imaging involving molecular imaging, including positron emission mammography (PEM), and sometimes limited to imaging with a type of breast-specific gamma camera, as is used in this report.

### Policy (Formerly Corporate Medical Guideline)

Scintimammography, breast-specific gamma imaging and molecular breast imaging are considered **investigational** in all applications, including but not limited to their use as an adjunct to mammography or in staging the axillary lymph nodes.

---

Services that are the subject of a clinical trial do not meet our Technology Assessment Protocol criteria and are considered investigational. *For explanation of experimental and investigational, please refer to the Technology Assessment Protocol.*

It is expected that only appropriate and medically necessary services will be rendered. We reserve the right to conduct prepayment and postpayment reviews to assess the medical appropriateness of the above-referenced procedures. **Some of this Protocol may not pertain to the patients you provide care to, as it may relate to products that are not available in your geographic area.**

### References

We are not responsible for the continuing viability of web site addresses that may be listed in any references below.

1. O'Connor M, Rhodes D, Hruska C. Molecular breast imaging. *Expert Rev Anticancer Ther* 2009; 9(8):1073-80.

2. Society for Nuclear Medicine (SNM). The SNM procedure guideline for breast scintigraphy with breast-specific gamma cameras 1.0. 2010. Available online at: [http://interactive.snm.org/docs/BreastScintigraphyGuideline\\_V1.0.pdf](http://interactive.snm.org/docs/BreastScintigraphyGuideline_V1.0.pdf). Last accessed October 2010.
3. American College of Radiology (ACR). Breast cancer screening. 2012. Available online at: <http://www.acr.org/~media/ACR/Documents/AppCriteria/Diagnostic/BreastCancerScreening.pdf>. Accessed April 2013.
4. Hruska CB, Boughey JC, Phillips SW et al. Scientific Impact Recognition Award: Molecular breast imaging: a review of the Mayo Clinic experience. *Am J Surg* 2008; 196(4):470-6.
5. Hendrick RE. Radiation doses and cancer risks from breast imaging studies. *Radiology* 2010; 257(1):246-53.
6. Health risks from exposure to low levels of ionizing radiation: BEIR VII, Phase 2. Washington, DC: National Research Council of the National Academies Press; 2006. Available online at: <http://www.nap.edu/openbook.php?isbn=030909156X>. Last accessed April 2013.
7. Blue Cross and Blue Shield Association Technology Evaluation Center (TEC). Breast-specific gamma imaging (BSGI), molecular breast imaging (MBI), or scintimammography with breast-specific gamma camera. TEC Assessments 2013; Volume 28; in press.
8. Blue Cross and Blue Shield Association Technology Evaluation Center (TEC). Screening Asymptomatic Women with Dense Breasts and Normal Mammograms for Breast Cancer. TEC Assessments 2013; Volume 28; in press.
9. Brem RF, Fishman M, Rapelyea JA. Detection of ductal carcinoma in situ with mammography, breast specific gamma imaging, and magnetic resonance imaging: a comparative study. *Acad Radiol* 2007; 14(8):945-50.
10. Brem RF, Ioffe M, Rapelyea JA et al. Invasive lobular carcinoma: detection with mammography, sonography, MRI, and breast-specific gamma imaging. *AJR Am J Roentgenol* 2009; 192(2):379-83.
11. Kim BS. Usefulness of breast-specific gamma imaging as an adjunct modality in breast cancer patients with dense breast: a comparative study with MRI. *Ann Nucl Med* 2012; 26(2):131-7.
12. Keto JL, Kirstein L, Sanchez DP et al. MRI versus breast-specific gamma imaging (BSGI) in newly diagnosed ductal cell carcinoma-in-situ: a prospective head-to-head trial. *Ann Surg Oncol* 2012; 19(1):249-52.
13. Taillefer R. The role of 99mTc-sestamibi and other conventional radiopharmaceuticals in breast cancer diagnosis. *Semin Nucl Med* 1999; 29(1):16-40.
14. Schillaci O, Scopinaro F, Spanu A et al. Detection of axillary lymph node metastases in breast cancer with Tc-99m tetrofosmin scintigraphy. *Int J Oncol* 2002; 20(3):483-7.
15. Spanu A, Dettori G, Nuvoli S et al. (99mTc-tetrofosmin SPET in the detection of both primary breast cancer and axillary lymph node metastasis. *Eur J Nucl Med* 2001; 28(12):1781-94.
16. Xu HB, Li L, Xu Q. Tc-99m sestamibi scintimammography for the diagnosis of breast cancer: meta-analysis and meta-regression. *Nucl Med Commun* 2011; 32(11):980-8.
17. Killelea BK, Gillego A, Kirstein LJ et al. George Peters Award: How does breast-specific gamma imaging affect the management of patients with newly diagnosed breast cancer? *Am J Surg* 2009; 198(4):470-4.
18. Rhodes DJ, Hruska CB, Phillips SW et al. Dedicated dual-head gamma imaging for breast cancer screening in women with mammographically dense breasts. *Radiology* 2011; 258(1):106-18.
19. Brem RF, Rapelyea JA, Zisman G et al. Occult breast cancer: scintimammography with high-resolution breast-specific gamma camera in women at high risk for breast cancer. *Radiology* 2005; 237(1):274-80.

20. Berrington de Gonzalez A, Berg CD, Visvanathan K et al. Estimated risk of radiation-induced breast cancer from mammographic screening for young BRCA mutation carriers. *J Natl Cancer Inst* 2009; 101(3):205-9.
21. Ernestos B, Nikolaos P, Koulis G et al. Increased chromosomal radiosensitivity in women carrying BRCA1/BRCA2 mutations assessed with the G2 assay. *Int J Radiat Oncol Biol Phys* 2010; 76(4):1199-205.
22. Spanu A, Sanna D, Chessa F et al. The clinical impact of breast scintigraphy acquired with a breast specific gamma-camera (BSGC) in the diagnosis of breast cancer: incremental value versus mammography. *Int J Oncol* 2012; 41(2):483-9.
23. Spanu A, Chessa F, Sanna D et al. Scintimammography with a high resolution dedicated breast camera in comparison with SPECT/CT in primary breast cancer detection. *Q J Nucl Med Mol Imaging* 2009; 53(3):271-80.
24. Spanu A, Cottu P, Manca A et al. Scintimammography with dedicated breast camera in unifocal and multifocal/multicentric primary breast cancer detection: a comparative study with SPECT. *Int J Oncol* 2007; 31(2):369-77.
25. Hruska CB, Phillips SW, Whaley DH et al. Molecular breast imaging: use of a dual-head dedicated gamma camera to detect small breast tumors. *AJR Am J Roentgenol* 2008; 191(6):1805-15.
26. Spanu A, Chessa F, Meloni GB et al. The role of planar scintimammography with high-resolution dedicated breast camera in the diagnosis of primary breast cancer. *Clin Nucl Med* 2008; 33(11):739-42.
27. Brem RF, Petrovitch I, Rapelyea JA et al. Breast-specific gamma imaging with 99mTc-Sestamibi and magnetic resonance imaging in the diagnosis of breast cancer--a comparative study. *Breast J* 2007; 13(5):465-9.
28. Brem RF, Floerke AC, Rapelyea JA et al. Breast-specific gamma imaging as an adjunct imaging modality for the diagnosis of breast cancer. *Radiology* 2008; 247(3):651-7.
29. Park JS, Lee AY, Jung KP et al. Diagnostic Performance of Breast-Specific Gamma Imaging (BSGI) for Breast Cancer: Usefulness of Dual-Phase Imaging with 99mTc-sestamibi. *Nucl Med Mol Imaging* 2013; 47(1):18-26.
30. Weigert JM, Bertrand ML, Lanzkowsky L et al. Results of a multicenter patient registry to determine the clinical impact of breast-specific gamma imaging, a molecular breast imaging technique. *AJR Am J Roentgenol* 2012; 198(1):W69-75.
31. Sun Y, Wei W, Yang HW et al. Clinical usefulness of breast-specific gamma imaging as an adjunct modality to mammography for diagnosis of breast cancer: a systemic review and meta-analysis. *Eur J Nucl Med Mol Imaging* 2013; 40(3):450-63.
32. Whiting P, Rutjes AW, Reitsma JB et al. The development of QUADAS: a tool for the quality assessment of studies of diagnostic accuracy included in systematic reviews. *BMC Med Res Methodol* 2003; 3:25.
33. Whiting PF, Rutjes AW, Westwood ME et al. QUADAS-2: a revised tool for the quality assessment of diagnostic accuracy studies. *Ann Intern Med* 2011; 155(8):529-36.
34. American College of Obstetricians and Gynecologists (ACOG). Breast cancer screening, ACOG Practice Bulletin no. 122. Washington, DC: American College of Obstetricians and Gynecologists (ACOG); Aug 2011. Available online at: <http://guidelines.gov/content.aspx?id=34275&search=scintimammography>. Accessed April 2013.
35. American College of Radiology (ACR). Breast microcalcifications — Initial diagnostic workup 2009. ACR Appropriateness Criteria®. Available online at <http://www.acr.org/~media/ACR/Documents/AppCriteria/Diagnostic/BreastMicrocalcifications.pdf>. Accessed April 2013.

36. American College of Radiology (ACR). Palpable breast masses 2012. Available online at:  
<http://www.acr.org/~media/ACR/Documents/AppCriteria/Diagnostic/PalpableBreastMasses.pdf>. Accessed  
April 2013.