

# MEDICAL POLICY



<b>SUBJECT: NUCLEAR BREAST IMAGING</b>	<b>EFFECTIVE DATE: 07/02/99</b>
<b>POLICY NUMBER: 6.01.02</b>	<b>REVISED DATE: 05/17/01, 03/21/02, 03/20/03, 01/15/04, 01/20/05, 01/19/06, 11/16/06, 09/20/07, 08/21/08, 08/20/09, 10/28/10, 04/21/11, 03/15/12, 05/23/13, 02/20/14</b>
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<ul style="list-style-type: none"><li>• <i>If the member's subscriber contract excludes coverage for a specific service it is not covered under that contract. In such cases, medical policy criteria are not applied.</i></li><li>• <i>Medical policies apply to commercial and Medicaid products only when a contract benefit for the specific service exists.</i></li><li>• <i>Medical policies only apply to Medicare products when a contract benefit exists and where there are no National or Local Medicare coverage decisions for the specific service.</i></li></ul>	

## **POLICY STATEMENT:**

Based upon our criteria and review of the peer-reviewed literature, nuclear breast imaging including Scintimammography, breast-specific gamma imaging (BSGI), and Positron Emission Mammography (PEM), has not been medically proven to be effective and is considered **investigational** in all applications, including but not limited to:

- I. Use as an adjunct to mammography for imaging of breast tissue; or
- II. The detection of axillary metastases, or
- III. Staging the axillary lymph nodes in patients with breast cancer; or
- IV. To assess the need for a biopsy; or
- V. To assess response to adjuvant chemotherapy in patients with breast cancer; or
- VI. Screening for breast cancer.

## **POLICY GUIDELINES:**

The Federal Employees Health Benefit Program (FEHBP/FEP) requires that procedures, devices or laboratory tests approved by the U.S. Food and Drug Administration (FDA) may not be considered investigational and thus these procedures, devices or laboratory tests may be assessed only on the basis of their medical necessity.

## **DESCRIPTION:**

Methods to image the breast can be divided into either anatomical or functional modalities. Anatomical modalities differentiate normal tissue from cancerous tissue based on structural differences between tissues while functional modalities rely on the differences in the physiological uptake of radiopharmaceuticals between normal and tumor tissue. Examples of anatomic imaging modalities include but are not limited to, mammography and MRI. Both modalities have limitations thus other modalities are being explored. Scintimammography and whole body positron emission tomography (WBPET) are two functional imaging modalities that can be used to image the breast but are unable to detect small lesions, thus have low sensitivity and specificity for this indication. Breast-specific gamma imaging (BSGI) and positron emission mammography (PEM) are modifications of both of these modalities and have led to improvements in detection of smaller lesions of breast cancer. Both breast-specific gamma imaging (BSGI) and positron emission mammography (PEM) will be discussed in more detail.

Scintimammography is a diagnostic modality that uses radiopharmaceuticals to provide tumor specific imaging of the breast. Radiopharmaceuticals such as, but not limited to, technetium-99m sestamibi (Miraluma®), thallium-201, indium-111 satumomab pendetide (Oncoscint CR/OV®), indium-111 pentetate (OctroScan®), and technetium-99m arcitumomab (CEA-Scan®) are injected intravenously to identify abnormal cells based on the difference in metabolic characteristics between benign and malignant cells. Since cancer cells absorb more technetium and absorb it faster than other cells, 99mTc Sestamibi images help radiologist determine whether a lesion is benign or malignant. After injection of the radiopharmaceutical, the breast is evaluated with planar or single positron emission computed tomography (SPECT) radionuclide imaging.

Breast-specific gamma imaging (BSGI) uses the same principles as scintimammography but contains a gamma camera to detect emission. The gamma camera is smaller and much closer to the patient's breast, thus having the ability to detect smaller lesions than what is detected with scintimammography.

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Dilon Technologies has introduced a dedicated scintimammography system for BSGI. The Dilon 6800 gamma camera is a small-field-of-view unit that is proposed to serve as an adjunct to mammography as a distinction between this technology and scintimammography with whole-body units. Dilon proposes that a dedicated gamma camera allows better resolution and more views in comparison to a standard whole-body SPECT unit and hopes that this technology may eliminate the need for biopsy. Gamma Medica of Northridge, CA markets a camera, the LumaGEM 3200S. IS2 Medical systems of Ottawa, Ontario is marketing it Breast Cancer Camera (BCC).

Whole breast positron emission tomography (WBPET) is used to stage breast cancer and to monitor response to treatment. <sup>18</sup>FDG is introduced into the body via intravenous injection. There is it transported to the cell and undergoes phosphorylation. In cancer cells, the <sup>18</sup> FDG cannot be metabolized and accumulates. Differences in metabolism of <sup>18</sup>FDG allows the PET scanner to distinguish between normal and tumor cells. However WBPET is not able to distinguish lesions less than 1 cm due to its spatial resolution which limits its sensitivity.

Positron emission mammography (PEM) utilizes the principles of WBPET but is able to detect lesions that are much smaller than those detected by WBPET due to the location of the detectors closer to the breast. The whole body radiation dose a patient receives may be up to three times that of mammogram, making PEM less likely to be used as a screening modality. However the dose is not more than what is delivered to patients receiving radiation therapy and may be useful for those already diagnosed with breast cancer. Because PEM is limited to views of the breast only, it cannot replace WBPET for staging of breast cancer patients.

The FDA approved the Naviscan PEM Flex Solo II High Resolution PET Scanner (Naviscon, Inc) in March 2009. The scanner is described by the manufacturer as a “high spatial resolution, small field-of-view Pet imaging system specifically developed for close range, spot, i.e., limited field, imaging”.

Both BSGI and PEM utilize breast compression between two plates to stabilize the breast tissue. In addition, the detectors are located on the compression plates making them closer in proximity to the radiation source (the breast) which enables high resolution images to be taken. These procedures are proposed for use primarily as an adjunct to mammography and physical examination in patients with palpable masses, suspicious mammograms or dense breasts as a technique to improve patient selection for biopsy. It is not intended to be a substitute for mammography screening.

### **RATIONALE:**

Scintimammography. A key diagnostic statistic of scintimammography for use as an adjunct to mammography is the negative predictive value; whether patients who have negative scintimammography test results can reliably forego breast biopsy. Given the relative ease and diagnostic accuracy of the gold standard of biopsy coupled with the adverse consequences of missing breast cancer, the negative predictive value (NPV) of scintimammography would have to be extremely high to influence treatment decisions. The negative predictive value is determined partially by the sensitivity of the test; the higher the sensitivity, the higher the NPV. The NPV will also vary according to the prevalence of disease. Among a population of patients with mammographic abnormalities highly suggestive of breast cancer, the NPV will be lower than in a population of patients with mammographic abnormalities not suggestive of breast cancer. Therefore, the clinical utility of scintimammography as an adjunct to mammography may vary according to the type of mammographic abnormalities included in the studies. Considerations regarding the use of scintimammography as a technique to evaluate axillary lymph nodes are similar.

Clinical evidence does not demonstrate that the use of scintimammography in differentiating between benign and malignant breast lesions, or for detecting and/or staging axillary lymph node metastases in patients with proven breast cancer, improves net health outcomes. As a second-line diagnostic test after mammography, the sensitivity and corresponding negative predictive value of scintimammography are not high enough to influence treatment decisions. It does not appear that the benefits of avoiding the minor harms of a negative biopsy outweigh the harms of undetected malignancy.

The Federal Agency for Healthcare Research and quality published an update (2012) to the comparative effectiveness report in February 2006 on the accuracy of noninvasive diagnostic tests in women presenting with breast abnormalities

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(either by mammography or physical examination), specifically comparing ultrasound (US), positron emission tomography (PET), scintimammography, and magnetic resonance imaging (MRI). Ten studies of scintimammography were identified. The summary sensitivity of scintimammography was 84.7 percent (95% CI: 78.0 to 89.7%) and the summary specificity was 77.0 percent (95% CI: 64.7 to 85.9%). The estimate of accuracy was judged to be supported by a Low strength of evidence. Bayes' theorem and the summary estimates of accuracy suggest that only women with a pre-scintimammography suspicion of malignancy of 5 percent or less will have their post-scintimammography suspicion of malignancy change sufficiently to suggest that a change in patient management may be appropriate. The summary concluded the use of noninvasive imaging, in addition to standard workup of women recalled for evaluation of an abnormality detected on breast cancer screening, may be clinically useful for diagnostic purposes only for women with a low (less than 12%) pretest suspicion of malignancy. When choosing which noninvasive imaging technology to use for this purpose, the evidence appears to suggest that diagnostic B-mode grayscale ultrasound and MRI are more accurate than PET, scintimammography, or Doppler ultrasound. The utility of these findings, however, depend on whether clinicians can identify women with a pretest suspicion of malignancy in the ranges necessary for the tests to affect management. Several of the expert reviewers of this report did not think this is currently possible.

The ACR Appropriateness Criteria for Breast Cancer Screening (2013) rated BSGI and FDG-PEM as 2, usually not appropriate for women with BRCA mutations, previous irradiation to the breast, and greater than or equal to a 20% life-time risk of breast cancer because there is insufficient evidence to support the use of these modalities. A rating of 1, usually not appropriate was given for average-risk women. Furthermore, radiation doses from BSGI and positron emission mammography (PEM) are 15 to 30 times higher than the dose from digital mammography, thus these two imaging modalities are not indicated for screening in their present form.

Only Miraluma® (technetium-99m sestamibi) has specific U.S. Food and Drug Administration (FDA) approval for use in breast imaging. Product labeling states that the agent is not indicated for breast cancer screening, to confirm the presence or absence of malignancy, and it is not an alternative to biopsy. While the labeling only applies to planar imaging, studies have also reported results using SPECT radionuclide imaging. In June 1997 an FDA warning letter was issued to the manufacturers of Miraluma® stating that information published regarding Miraluma's® efficacy and superiority over mammography was unsubstantiated.

Breast specific gamma imaging (BSGI). Estimates of sensitivity and specificity in available studies are not high enough to preclude breast biopsy. To evaluate how BSGI might be used in the diagnosis of breast cancer, it must be compared to other breast-imaging modalities, such as traditional mammography, ultrasound or MRI. Although some comparative studies have been published, they are limited by the retrospective nature of most study designs, small sample sizes, patient populations with mixed indications for imaging, and a high prevalence of cancer.

Clinical evidence is not sufficient to determine the role of scintimammography in monitoring neoadjuvant chemotherapy in local advanced breast cancer.

A 2013 Blue Cross Blue Shield Technical Assessment concluded the published literature on BSGI, Molecular Breast Imaging (MBI), and scintimammography with breast-specific gamma camera is limited by a number of factors. Studies include populations that usually do not represent those encountered in clinical practice and that have mixed indications. The studies have medium to high risk of bias and lack information on the impact on therapeutic efficacy. The relatively high dose of radiation associated with this imaging modality also limits the clinical situations in which it might be used. The American College of Radiology explicitly notes that at the current dose, BSGI is not indicated for breast cancer screening. Therefore, consideration of the potential use of BSGI for screening women with dense breasts or at high risk of breast cancer should await the development of a lower dose regimen, and if warranted, larger, higher quality studies with study populations representative of those encountered in clinical practice. In addition, a large, high-quality head-to-head comparison of BSGI and MRI would be needed, especially for women at high risk of breast cancer, for whom MRI is currently the recommended screening technique alternated with mammography. Another BSGI indication considered in the Assessment, besides screening, is its use for women with suspicious lesions. The evidence currently available is insufficient. No studies were identified that address the health outcomes of interest for the Assessment, nor is there

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sufficient indirect evidence to infer that the use of BSGI would produce changes in health outcomes. Thus breast-specific gamma imaging (BSGI), molecular breast imaging (MBI), or scintimammography with breast-specific gamma camera does not meet the TEC criteria.

Positron emission mammography (PEM). A multi-center study of 388 women with newly diagnosed breast cancer detected by core-needle or vacuum-assisted biopsy of women eligible for breast-conserving surgery comparing MRI and PEM was reported by Berg, et al (2011). Among the 386 lesions sites confirmed during surgery, there was no statistically significant difference in the sensitivity of PEM (92.5%) and MRI (89.1%) when only tumor sites were included. When both tumor and biopsy sites were included, MRI had a higher sensitivity than PEM (98.2% vs. 94.5%, respectively; p = 0.004). The sensitivity in identifying additional lesions were 60% (95% CI = 48%, 70%) for MRI and 51% for PEM (95% CI = 40%, 62%; p = 0.24). Of the additional lesions, 26% were detected with MRI only, 17% with PEM only, and 8.5% with conventional imaging only. There was no statistically significant difference between PEM and MRI in accuracy or area under the receiver operating characteristic (ROC) curve. The authors found that MRI was less sensitive for detection of DCIS foci (39% [22/56]) than for detection of any invasive cancer. Cancer was not detected by any means in 3.6% of women with additional disease. Adding PEM to DCIS would increase the sensitivity from 39% with MRI alone to 57% combined (p = 0.001). MRI is more sensitive than PEM in detecting invasive cancer, but the two combined would still have a higher sensitivity than MRI alone (73% vs. 64%, p = 0.025). MRI was more sensitive than PEM in dense breasts (57% vs. 37%, respectively, p = 0.031).

The radiation dose associated with PEM is larger than with mammography and is an important consideration when using this modality. Studies are ongoing to determine the effects on sensitivity and specificity of PET when the radiation dose is reduced and to find alternate radiopharmaceutical tracers.

**CODES:**      Number                      Description

*Eligibility for reimbursement is based upon the benefits set forth in the member's subscriber contract.*

**CODES MAY NOT BE COVERED UNDER ALL CIRCUMSTANCES. PLEASE READ THE POLICY AND GUIDELINES STATEMENTS CAREFULLY.**

Codes may not be all inclusive as the AMA and CMS code updates may occur more frequently than policy updates.

Code Key: Experimental/Investigational = (E/I), Not medically necessary/ appropriate = (NMN).

<b><u>CPT:</u></b>	78800	Radiopharmaceutical localization of tumor or distribution of radiopharmaceutical agent(s); limited area
	78801	multiple areas
	78803	tomographic (SPECT)
	78811	Positron emission tomography (PET) imaging; limited area (eg chest, head/neck)
	78999	Unlisted miscellaneous procedure, diagnostic nuclear medicine

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<b><u>HCPCS:</u></b>	A9500	Technetium tc- 99m sestamibi, diagnostic, per study dose
	A9552	Fluorodeoxyglucose F-18 FDG, diagnostic, per study dose, up to 45 millicuries
	S8080 (E/I)	Scintimammography (radioimmunosintigraphy of the breast), unilateral, including supply of radiopharmaceutical

**ICD9:**      **The following ICD-9 codes are investigational for all diagnoses with HCPCS A9500**

	174.0-174.9	Malignant neoplasm of female breast-code range
	196.3	Secondary malignant neoplasm, axilla, axillary
	198.81	Secondary malignant neoplasm of other specified sites - breast

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	233.0	Carcinoma in situ of breast
<b>ICD10:</b>	C50.011-C50.919	Malignant neoplasm of breast (code range)
	C77.3	Secondary and unspecified malignant neoplasm of axilla and upper limb lymph nodes
	C79.81	Secondary malignant neoplasm of breast
	D05.00-D05.92	Carcinoma in situ of breast (code range)

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**KEY WORDS:**

BSGI, Breast specific gamma camera, Molecular breast imaging, Radioimmunoscintigraphy, Scintimammography, Scintigraphy, Gammagram.

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## **CMS COVERAGE FOR MEDICARE PRODUCT MEMBERS**

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There is currently no National Coverage Determinations (NCD) or Local Coverage Determinations (LCD) for Scintimammography, breast specific gamma imaging or positron emission mammography.