MEDICAL POLICY

MEDICAL POLICY DETAILS	
Medical Policy Title	**Nuclear Breast Imaging**
Policy Number	**6.01.02**
Category	**Technology Assessment**
Original Effective Date	**10/18/01**
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Product Disclaimer	• *Services are contract dependent; if a product excludes coverage for a service, it is not covered, and medical policy criteria do not apply.* • *If a commercial product (including an Essential Plan or Child Health Plus product), medical policy criteria apply to the benefit.* • *If a Medicaid product covers a specific service, and there are no New York State Medicaid guidelines (eMedNY) criteria, medical policy criteria apply to the benefit.* • *If a Medicare product (including Medicare HMO-Dual Special Needs Program (DSNP) product) covers a specific service, and there is no national or local Medicare coverage decision for the service, medical policy criteria apply to the benefit.* • *If a Medicare HMO-Dual Special Needs Program (DSNP) product DOES NOT cover a specific service, please refer to the Medicaid Product coverage line.*

POLICY STATEMENT

I. Based upon our criteria and assessment 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, therefore, is considered **investigational** in **ALL** applications, including, but not limited to:
   A. Adjunct to mammography for imaging of breast tissue;
   B. Detection of axillary metastases;
   C. Staging of the axillary lymph nodes in patients with breast cancer;
   D. Assess the need for a biopsy;
   E. Assess response to adjuvant chemotherapy in patients with breast cancer;
   F. Screening for breast cancer.

Refer to Corporate Medical Policy #11.01.03 Experimental or Investigational Services

DESCRIPTION

Methods used 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 magnetic resonance imaging (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 they are unable to detect small lesions and, thus, have low sensitivity and specificity for this indication. BSGI and PEM

are modifications of both of these modalities and have led to improvements in detection of smaller lesions of breast cancer, as discussed more fully below.

Scintimammography is a diagnostic modality that uses radiopharmaceuticals to provide tumor-specific imaging of the breast. Radiopharmaceuticals, including, but not limited to, technetium-99m sestamibi (Miraluma), thallium-201, indium-111 satumomab pendetide (Oncoscint CR/OV), indium–111 pentetreotide (OctreoScan), 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. As cancer cells absorb more technetium, and absorb it faster than other cells, 99mTc Sestamibi images help the 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 scintimammography.

Dilon Technologies introduced a dedicated scintimammography system for BSGI in 2007. The Dilon 6800 gamma camera is a small-field-of-view unit that was proposed to serve as an adjunct to mammography, as distinguished from scintimammography with whole-body units. Dilon proposed that a dedicated gamma camera would allow better resolution and more views than a standard whole-body SPECT unit and that this technology may eliminate the need for biopsy. Gamma Medica of Northridge, CA also markets a camera, the LumaGEM 3200S, as does IS2 Medical systems of Ottawa, Ontario, which markets its Breast Cancer Camera (BCC).

Whole Breast Positron Emission Tomography (WBPET) is used to stage breast cancer and to monitor response to treatment. The agent ^{18}FDG is introduced into the body via intravenous injection, and then transported to the cells, where it undergoes phosphorylation. In cancer cells, ^{18}FDG cannot be metabolized, and it accumulates. Differences in metabolism of ^{18}FDG allows the WBPET scanner to distinguish between normal and tumor cells; however, it is not able to distinguish lesions less than one centimeter due to its spatial resolution, which limits its sensitivity.

Positron Emission Mammography (PEM) utilizes the principles of WBPET, but PEM is able to detect lesions that are much smaller than those detected by WBPET because the detectors are located closer to the breast. The whole-body radiation dose that 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.

In March 2009, the FDA approved the Naviscan PEM Flex Solo II High Resolution PET Scanner (Naviscon, Inc.). 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. 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

The National Comprehensive Cancer Network's guidelines on breast cancer screening and diagnosis (V.3.2023) state: For screening/follow-up, consider contrast-enhanced mammography (CEM) or molecular breast imaging (MBI) for those who qualify for but cannot undergo MRI.

Scintimammography

A key diagnostic statistic of scintimammography for use as an adjunct to mammography is the negative predictive value (NPV), i.e., 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 failing

to identify breast cancer, the NPV of scintimammography would have to be extremely high to influence treatment decisions. NPV 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 that are highly suggestive of breast cancer, the NPV will be lower than in a population of patients with mammographic abnormalities that are 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 NPV of scintimammography are not high enough to influence treatment decisions. The benefits of avoiding the minor harms of a negative biopsy do not appear to outweigh the harms of undetected malignancy.

In 2012, the Federal Agency for Healthcare Research and Quality published an update to its February 2006 comparative effectiveness report on the accuracy of non-invasive diagnostic tests in women presenting with breast abnormalities (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's theorem and the summary estimates of accuracy suggest that only women with a pre-scintimammography suspicion of malignancy of five 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 that the use of non-invasive imaging, in addition to standard work-up 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%) pre-test suspicion of malignancy. When choosing which non-invasive imaging technology to use for this purpose, the evidence appears to suggest that diagnostic B-mode grayscale US and MRI are more accurate than PET, scintimammography, or Doppler US. The utility of these findings, however, depends on whether clinicians can identify women with a pre-test suspicion of malignancy in the ranges necessary for the tests to affect management. Several of the expert reviewers of this report did not think that this is currently possible.

The American College of Radiology (ACR) Appropriateness Criteria for Breast Cancer Screening (2016) stated that there is insufficient evidence to support the use of other imaging modalities, such as thermography, BSGI, PEM, and optical imaging, for breast cancer screening. Radiation doses from BSGI and PEM are 15 to 30 times higher than the dose from digital mammography, and they are not indicated for screening in their present form.

Miraluma (technetium-99m sestamibi) has specific 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, US or MRI. Although 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.

Appropriateness Criteria from the American College of Radiology rated breast-specific gamma imaging a one or two (indicating "usually not appropriate" for breast cancer screening), in patients with high or intermediate breast cancer risk (last reviewed in 2017), palpable breast masses (last reviewed in 2016), and workup of breast pain (last reviewed in 2018). Guidelines on screening for breast cancer in above average-risk patients (last reviewed in 2018) do not recommend the use of molecular breast imaging (MBI) for breast cancer screening in any higher-risk population. The guidelines state, "further advances in detector technology to allow lower dosing, more widespread penetration of MBI-guided biopsy capabilities, and additional large prospective trials (to include incidence screening results) will be needed before MBI can be embraced as a screening tool, even in women at elevated risk." In a 2021 guideline for supplemental breast cancer screening based on breast density, MBI is categorized as "usually not appropriate" regardless of breast density and breast cancer risk.

Positron Emission Mammography (PEM)

A multi-center study of 388 women eligible for breast-conserving surgery, with newly diagnosed breast cancer detected by core-needle or vacuum-assisted biopsy, comparing MRI and PEM, was reported by Berg et al. (2011). Among the 386 lesion 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% versus 94.5%, respectively; p = 0.004). The sensitivity in identifying additional lesions was 60 percent (95% CI = 48%, 70%) for MRI and 51 percent for PEM (95% CI = 40%,62%; p = 0.24). Of the additional lesions, 26 percent were detected with MRI only, 17 percent 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 percent of women with additional disease. Adding PEM to DCIS would increase the sensitivity from 39 percent with MRI alone to 57 percent 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% versus 64%, p = 0.025). MRI was more sensitive than PEM in dense breasts (57% versus 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

- *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).*

CPT Codes

Code	Description
78800	Radiopharmaceutical localization of tumor, inflammatory process or distribution of radiopharmaceutical agent(s) (includes vascular flow and blood pool imaging, when performed); planar, single area (e.g., head, neck, chest, pelvis), single day imaging
78801	Radiopharmaceutical localization of tumor, inflammatory process or distribution of radiopharmaceutical agent(s) (includes vascular flow and blood pool imaging, when performed); planar, 2 or more areas (e.g., abdomen and pelvis, head and chest), 1 or more days imaging or single area imaging over 2 or more days

Code	Description
78803	Radiopharmaceutical localization of tumor, inflammatory process or distribution of radiopharmaceutical agent(s) (includes vascular flow and blood pool imaging, when performed); tomographic (SPECT), single area (e.g., head, neck, chest, pelvis), or acquisition, single day imaging
78811	Positron emission tomography (PET) imaging; limited area (e.g., chest, head/neck)
78999	Unlisted miscellaneous procedure, diagnostic nuclear medicine

HCPCS Codes

Code	Description
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 (radioimmunoscintigraphy of the breast), unilateral, including supply of radiopharmaceutical

ICD10 Codes

Code	Description
C50.0-C50.929	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)
R92.0-R92.8	Abnormal and inconclusive findings on diagnostic imaging of breast (code range)

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*Key Article

KEY WORDS

BSGI, Breast Specific Gamma Camera, Molecular Breast Imaging, Radioimmunoscintigraphy, Scintimammography, Scintigraphy, Gammagram.

CMS COVERAGE FOR MEDICARE PRODUCT MEMBERS

Based upon our review, Scintimammography, Breast Specific Gamma Imaging and Positron Emission Mammography are not addressed in National or Regional Medicare coverage determinations or policies.