Seminars in ULTRASOUND CT and MRI

Molecular Breast Imaging: A Comprehensive Review

Ashley I. Huppe, MD, Anita K. Mehta, MD, and Rachel F. Brem, MD, FACR, FSBI

Molecular breast imaging (MBI), also called breast-specific gamma imaging (BSGI), has been an integral component of our breast imaging practice for over a decade. Unlike mammography and ultrasound that are based on anatomy, MBI is a physiologic approach to breast cancer detection. MBI detects additional foci of occult breast cancer in 9.0% of women with newly diagnosed breast cancer, has a high sensitivity for detecting high-risk lesions, and detects 98% of invasive breast cancer and 91.0% of ductal carcinoma in situ. Furthermore, in surveillance of high-risk women, BSGI/MBI detects occult cancer in up to 16.5 per 1000 women. This modality is increasingly being used to assess response to treatment in women undergoing neo-adjuvant chemotherapy and for adjunct screening in women with dense breasts. It has been shown to influence surgical management in nearly a quarter of women with newly diagnosed breast cancer. The Society of Nuclear Imaging has established clinical indications and The American College of Radiology has established appropriateness criteria as well as an accreditation program for MBI. A BIRADS-like lexicon for MBI has also been described. Initially, MBI utilized 10-20 mCi of 99 mTc sestamibi, however, recent studies have reported the use of 5-10 mCi with equal sensitivity to the higher dose of radiotracer. There are over 300 studies in the literature about MBI/BSGI with increasing integration of MBI into clinical practice. This chapter will describe the history, current literature and indications, clinical use, approach to biopsy and integration of MBI into clinical practice.
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History and Current Use

Breast cancer-related mortality, currently the second leading cause of cancer death in the United States,[1] has declined over the last 30 years by over 30%,[2] in large part due to mammographic screening. Although breast cancer mortality has decreased, mammography, which relies on the anatomic differences between cancer and normal breast parenchyma, remains an imperfect examination. The overall sensitivity of screening mammography is 75%-85%. However, in women with dense breast tissue, the sensitivity is significantly reduced to 42%-68%.[3-5] Furthermore, dense breast tissue is an independent risk factor for the development of breast cancer.[6] Ultrasound, the second most common modality in breast imaging, also utilizes an anatomic approach to finding breast cancer. It too has limitations, including a high false positive rate. Adjunct imaging modalities are now available that rely on physiologic and not purely anatomic findings to improve breast cancer detection.

Molecular breast imaging (MBI), also referred to as breast-specific gamma imaging (BSGI), is a modality that utilizes dedicated gamma cameras and an injected radiopharmaceutical to identify breast cancer. In MBI, the radiotracer uptake is proportional to blood flow and mitochondrial activity as well as other physiologic factors, resulting in preferential uptake by cancer cells. The Food and Drug Administration initially approved the use of technetium-99m sestamibi for scintimammography in 1997, and although a conventional gamma camera was employed to image the breast at that time, the technology demonstrated good sensitivity and specificity for tumors larger than 15 mm.[7,8] However, the inability to reliably image subcentimeter cancer and to directly compare to mammography markedly limited the integration of scintimammography into clinical practice. With the development of compact, high-resolution breast-specific gamma camera systems, the limitations of conventional gamma cameras were

George Washington University, Comprehensive Breast Care Center, Washington, DC.

Address reprint requests to Ashley I. Huppe, MD, George Washington University, Comprehensive Breast Care Center, 2300 M Street NW, 8th Floor, Washington, DC 20037. E-mail: ahuppe@mfa.gwu.edu

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resolved, and MBI can now reliably image subcentimeter cancers[9] as well as image in projections comparable to mammography, resulting in the meaningful integration of MBI into clinical practice.

There are several different configurations of breast-specific gamma cameras, including single-headed and dual-headed gamma cameras.[10] Currently, the commercially available detectors use sodium iodide crystals or a cadmium zinc telluride (CZT) semiconductor. In the research environment, the parameters of the different types of detectors vary.[10] However, numerous studies confirm that both types of detectors reliably image subcentimeter cancers and have comparable sensitivity and specificity.[9,11-13] The ability to detect subcentimeter cancers is not impacted by whether a single- or dual-headed camera is used, however, with a dual-headed camera, the time for image acquisition may be shorter and the cost of the equipment may substantially increase. Another difference between a single- and dual-headed camera is that with a second detector, positioning may become more difficult due to the inability to visualize the breast during positioning.[14]

MBI is performed by injecting the radiopharmaceutial technetium-99m sestimibi, called Miraluma when used for breast imaging, into the venous system. In a patient with known breast cancer, the injection should be performed in the contralateral arm to avoid lymphatic uptake from extravasation of the radioisoptope during injection, as this will be imaged as axillary uptake and can be mistaken for lymphatic involvement.[15] The patient is positioned while seated with the breast gently compressed between the gamma detector and compression plate or the 2 gamma detectors in a dual-headed camera. Bilateral conventional craniocaudal and mediolateral oblique views are obtained that allow for direct correlation with mammography. For the Dilon Camera, the detector is on an articulating arm that can be rotated to obtain addition projections. With the Gamma Medica and GE Cameras, the detectors are on a gantry, similar to a mammography unit and additional images can be obtained by angling the gantry. The radiologist, in a manner comparable to diagnostic mammography, reviews the initial images. Additional images can be acquired as deemed necessary and may include exaggerated craniocaudal, true lateral, or in the case of a single detector camera, imaging with the detector on the opposite side of the breast. No additional radiotracer is administered when additional images are obtained. Imaging in projections comparable to mammography allows for multimodality correlative imaging. "Second-look" mammography is frequently utilized to identify MBI-detected lesions with subtle mammographic findings that might not have been appreciated before the MBI findings (Fig. 1).

A complete MBI study consists of 4-12 images (significantly fewer than MRI), which allows for rapid interpretation and efficient workflow. In our experience, the time for interpretation of MBI is far less than that of MRI. With the current emphasis on workflow and efficiency, the markedly fewer images and shorter interpretation time allows for efficient as well as effective integration into clinical practice.

While MRI is commonly utilized in many clinical scenarios, we find that approximately 15% of patients are unable to undergo evaluation by MRI due to implantable devices/metallic foreign bodies, body habitus, renal insufficiency, patient positioning, and claustrophobia. Reticence to undergo MRI is a significant issue with the ACRIN 6666 trial demonstrating that 48% of women at substantially increased risk of breast cancer refused MRI, even when it was offered at no cost.[16,17] Additional concerns with MRI include gadolinium accumulation in the brain, particularly with repeated studies. In our practice, it is critical to have MBI to offer to women who cannot or will not undergo MRI as an alternative physiologic imaging modality to detect cancers that are not visible with mammography or ultrasound.

MBI has a high sensitivity, comparable to that of MRI, of 89%-96.4% (97% for invasive cancers and 93.8% for ductal carcinoma in situ [DCIS]).[18-20] Of note, the sensitivity of MBI is independent of breast density, with sensitivities of 95.1% in dense breasts and 95.8% in nondense breasts.[22,22] Not only can MBI detect cancer, but MBI can also detect high-risk lesions such as ADH and ALH.[23] This can be of clinical importance especially as the risk of developing breast cancer in young women with ADH and in women with multiple foci of ADH has recently been shown to be as high as 50%.[24] In this high-risk population, risk reduction strategies are often considered and may include chemoprevention. Therefore, the identification of ADH and other high-risk lesions is clinically important.

MBI has many advantages, however, as with all imaging modalities, there are disadvantages. The disadvantages of MBI include the lack of anatomy included when compared to MRI and the radiation required for MBI. Initially, MBI was performed using 20-30 mCi (740-1100 megabecquerels [MBq]) of technetium sestamibi. Recently, a number of studies have demonstrated the use of 5-10 mCi, a 2.5-fold reduction in injected dose, with maintenance of sensitivity and specificity.[19,20,25] The ability to utilize lower dose radiotracer has been demonstrated with both NaI detectors[19] and CZI detectors.[25] While both mammography and MBI incur radiation, the former involves exposure to the breast, while MBI is associated with whole-body radiation. A MBI examination using 8 mCi of technetium sestamibi has an estimated dose to the breast of 0.07 mGy/mCi,[26] or approximately 0.53 mGy. However, the effective whole-body dose of MBI is approximately 0.325 mSv/mCi, or 2.5 mSv for an administered activity of 8 mCi.[26] In comparison, the effective dose from 2-view digital mammography is 0.5 mSv. Although the use of MBI for generalized screening is not recommended, its use for diagnostic evaluation, in patients with contraindications to MRI, in women with newly diagnosed breast cancer and in women with dense breast tissue is reasonable.[27] It is important to note that the MBI dose is significantly lower than the annual exposure limit of 50 mSv set by the U.S. federal government for radiation workers, and comparable to that of other cancer screening modalities.

The purpose of this chapter is to provide a comprehensive review of MBI to include current indications and limitations, imaging technique, diagnostic performance of MBI including