Advancements in Molecular Breast Imaging

Paula R McPeak, MSRS, R.T.(R)(M)

Breast cancer is the second most deadly type of cancer affecting women, accounting for nearly 1 in 3 cancers in women. An estimated 2830 000 women are living with breast cancer in the United States.1 The mortality rate from breast cancer has decreased, largely because of increased awareness and advancements in medical imaging technology such as molecular breast imaging (MBI) that aid in early detection (see Figure 1).2,3

Although breast cancer is common among women, the disease does not discriminate between the sexes. Approximately 1% of all new breast cancer cases each year occur in men.4 Molecular breast imaging, sometimes referred to as breast-specific gamma imaging (BSGI), is a nuclear medicine procedure—specifically breast scintigraphy—that is cost-effective and improves lesion detection, especially in dense breasts. A nuclear medicine technologist or physician injects the patient with technetium Tc 99m sestamibi, a radiopharmaceutical that accumulates in tumor cells more than in other body cells because of tumor cells’ high metabolic activity. Cancer cells are highly metabolic with a higher cytoplasmic mitochondrial density, which causes them to uptake the majority of the tracing agent. When the radioactive tracers attach to cells with increased metabolic activity, the results show a highlighted area on the nuclear medicine image.5-8

A mammography unit first was used in the United States in 1969, and although the technology remains the most important tool used for breast cancer detection, the risk of radiation-induced breast cancer from mammography still is debated.9 As with mammography and all diagnostic medical imaging examinations that use radiation, physicians must weigh the risks of radiation dose with the benefits a test will provide when scheduling an MBI procedure.

In applying the ALARA (as low as reasonably achievable) principle, radiologic technologists are tasked with keeping their patients’ radiation dose as low as possible while maintaining diagnostic confidence.
Advancements in Molecular Breast Imaging

quality in imaging results; this principle also guides MBI examinations. Because MBI uses a radioactive tracer that is introduced into the body, some critics are concerned with the radiation dose and lifetime attributable risks associated with the examination. When the recommended amount of technetium Tc 99m sestamibi is administered for an MBI examination, a patient receives the approximate equivalent of a whole-body dose of 6 mSv. Hendrick noted that the lifetime risk of inducing a fatal cancer from a single BSGI or positron emission mammography (PEM) examination is greater than or comparable to the risk from a lifetime of annual screening mammography in women who begin screening at age 40 years.

Breast Anatomy

The structures of the breast are surrounded by a complex layer of adipose tissue. Overall, the female breast is a semicomplex structure consisting of 12 to 20 mammary lobes made up of smaller lobules that produce milk in women who are nursing. Milk ducts carry breast milk to the nipple. Breast cancers usually start to form in the lobes, lobules, or ducts. The breast also contains blood and lymph vessels, fibrous glandular tissue, nerves, and ligaments (see Figure 2).

The breast is conical in shape with many overlapping structures, which poses a challenge when imaging the various portions of breast anatomy. Because these overlapping structures vary in density, a malignancy can easily be disguised within dense breast tissue. In addition, breast tissue is located anterior to the pectoralis major muscle, which poses an additional imaging challenge to visualize abnormalities located along the chest wall. The breast tissue extends into the axilla, which contains lymph nodes (see Figure 3). The axillary lymph nodes should be imaged for accurate diagnosis and are commonly displayed on mediolateral oblique (MLO) mammograms.

Figure 1. Cancer sites include invasive cases only unless otherwise noted. Rates are per 100,000 and are age adjusted to the 2000 U.S. standard population (19 age groups – Census P25-1130). Regression lines are calculated using the Joinpoint Regression Program Version 4.0.3, April 2013, National Cancer Institute. Mortality source: U.S. Mortality Files, National Center for Health Statistics, Centers for Disease Control and Prevention.

Figure 2. Breast anatomy.

Figure 3. Lymph node locations.
Breast Composition

The American College of Radiology (ACR) has provided terminology to identify breast density by categories and instructs radiologists to include this information when describing a patient’s breast composition in interpretive reports. Dense breast tissue is an important risk factor for breast cancer because increased density represents a higher proportion of fibroglandular tissue than fatty tissue, and it has not yet been proven whether glandular tissue is more likely to develop cancer or whether it just obscures more tumors on imaging. In general, younger women who have not yet reached menopause have denser breasts than women who are older and have reached menopause. Mammography’s sensitivity decreases with highly dense tissue. In addition, adipose tissue is radiolucent, appearing dark on a mammogram, yet connective and epithelial tissues appear radiologically dense.

Breast cancer also appears radiologically dense on a mammogram, so other methods of imaging could improve detection. MBI yields a high sensitivity for patients with extremely dense breast tissue. Radiopharmaceutical uptake by the mitochondria is not affected by breast tissue density, which makes MBI both highly sensitive and specific for imaging dense breasts. The ACR’s Breast Imaging Reporting and Data System (BI-RADS) categories describe mammography findings, and BI-RADS classifies the percentage of glandular tissue and fatty tissue in a breast’s composition (see Table 1 and Figure 4).

Table 1

| American College of Radiology BI-RADS Categories of Mammographic Breast Density |
|---------------------------------|---------------------------------|
| BI-RADS Category | Characteristics |
| 1 | Predominately fat breast tissue. Fibrous and glandular tissue make up < 25% of the breast. |
| 2 | Scattered densities in the breast tissue. Fibrous and glandular tissue make up 25%-50% of the breast. |
| 3 | Heterogeneously dense breast tissue made up of 51%-75% of fibrous and glandular tissue, making it difficult to see small masses on a mammogram. |
| 4 | Extremely dense breast tissue made up of ≥ 75% fibrous and glandular tissue, which can lead to some missed cancers. |

Figure 4. Examples of variation in mammographic density. A. 0%. B. Less than 10%. C. Less than 25%. D. Less than 50%. E. Less than 75%. F. More than 75%. G. A computer-assisted measure. The outer (red) line shows the edge of the breast; the inner (green) line shows the edge of dense tissue. Percent density is calculated by dividing the dense area by the total area and multiplying by 100. Reprinted with permission from Boyd NF, Martin LJ, Bronskill M, Yaffe MJ, Duric N, Minkin S. Breast tissue composition and susceptibility to breast cancer. J Natl Cancer Inst. 2010;102(16):1224-1237.
Breast Disease

Breast cancer is any classification of primary cancer located within the breast. There are multiple types of breast cancer, however, and patients with each type present with unique signs and symptoms (see Table 2). Patients with newly detected breast cancers have an increased risk of occult cancers or cancer in the ipsilateral or contralateral breast that cannot be seen using mammography or ultrasonography. This is concerning because mammography is the primary screening method for early breast cancer detection.

One of the most common types of breast cancer, infiltrating lobular carcinoma, is less distinguishable on a mammogram during its earliest stages and is difficult to detect even when mammography is combined with ultrasonography. The sensitivity of MBI is reportedly greater than 90% for detecting infiltrating lobular carcinoma lesions less than 1 cm. One study reported that MBI revealed additional malignant findings in the ipsilateral or contralateral breast in 10.9% of recently diagnosed breast cancer patients.

Genetics

Inherited genetic mutations can increase risk for breast cancer. Some mutations, such as those in ATM, TP53, and CHEK2 genes, are rare. Normal BRCA1 and BRCA2 genes prevent an individual from developing breast and ovarian cancer by producing proteins that prevent abnormal cell growth. However, if a person inherits a mutation of one or both of these genes, the

| Table 2 | Breast Cancer Types
<table>
<thead>
<tr>
<th>Type</th>
<th>Characteristics</th>
<th>Statistics</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Common Types</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ductal carcinoma in situ</td>
<td>Cells that line the ducts resemble cancer cells but have not spread through the ducts into breast tissue.</td>
<td>1 in 5 new breast cancers are ductal carcinoma in situ.</td>
</tr>
<tr>
<td>Invasive (or infiltrating) ductal carcinoma</td>
<td>Begins in a milk duct and grows through the duct wall to the fatty tissue. Can metastasize to other body organs and structures via the lymph and vascular systems.</td>
<td>8 of 10 invasive breast cancers are invasive (or infiltrating) ductal carcinoma.</td>
</tr>
<tr>
<td>Invasive (or infiltrating) lobular carcinoma</td>
<td>Begins in the milk-producing glands, or lobules, and can metastasize to other organs.</td>
<td>1 in 10 invasive breast cancers are invasive (or infiltrating) lobular carcinoma.</td>
</tr>
<tr>
<td><strong>Less Common Types</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inflammatory breast cancer</td>
<td>Usually no single lump or tumor, but skin erythema and warmth are present, and breast skin might look like an orange peel as cancer cells block lymph vessels and cause diffuse edema.</td>
<td>1% to 3% of all breast cancers</td>
</tr>
<tr>
<td>Triple-negative breast cancer</td>
<td>An aggressive form of cancer in which the cancer cells do not have estrogen or progesterone receptors or excess ERBB2 (formerly HER2 or HER2/neu) protein on their surfaces.</td>
<td>About 15% to 20% of all breast cancers</td>
</tr>
<tr>
<td>Paget disease of the nipple</td>
<td>Begins in the breast ducts and spreads to the skin of the nipple and areola. The nipple’s skin can become crusted, scaly, and red with some bleeding. Burning or itching sensations might be present.</td>
<td>Accounts for only about 1% of breast cancers</td>
</tr>
<tr>
<td>Phyllodes tumor</td>
<td>Develops in the connective tissue. Surgery often is the only treatment required unless the cancer has metastasized.</td>
<td>Rare</td>
</tr>
<tr>
<td>Angiosarcoma</td>
<td>Develops in cells that line the blood or lymph vessels. It can occur 5-10 years after breast radiation therapy.</td>
<td>Rarely occurs in the breast but might occur in the arms after lymph node surgery or radiation therapy for breast cancer</td>
</tr>
</tbody>
</table>
individual is at an increased risk for both cancers. BRCA1 and BRCA2 gene mutations are linked to breast cancers that usually affect both breasts in younger women.20,21

Each year, approximately 10% of newly diagnosed breast cancers in women aged younger than 50 years occur in women who have a BRCA mutation.21 The American Cancer Society (ACS) reported that a BRCA1 mutation can increase an individual’s risk of breast cancer by as much as 80%, but the average risk ranges from 55% to 65%. A BRCA2 mutation increases breast cancer risk by approximately 45%.20

Understanding risk factors for developing breast cancer can help patients make decisions about whether to undergo genetic testing and can help physicians advise women on the best course of action for screening and diagnostic examinations. If a close blood relative has had breast cancer, a woman’s risk is doubled, and if 2 first-degree relatives have had breast cancer, the risk is further increased. Nevertheless, 85% of women who develop breast cancer have no family history of the disease.20

Breast Imaging

Breast imaging is part of a comprehensive approach to breast cancer screening and diagnosis. The intention of screening for breast cancer in asymptomatic women is to identify breast cancer before it is clinically apparent. Mammography still is the mainstay of breast cancer screening.22 ACS screening guidelines recommend that women have a clinical breast examination every 3 years between the ages of 20 and 39 and annually beginning at age 40.23 The ACS also recommends annual screening mammograms for women aged 40 years and older. Women who have high breast cancer risk based on specific factors such as family history or known BRCA1 or BRCA2 mutations, or women who have not had genetic testing but have known first-degree relatives with BRCA mutations, should have annual mammograms and magnetic resonance (MR) breast imaging.24 Screening mammography and advanced medical imaging of the breast are essential in finding breast cancers while they are smaller and still confined to the breast.20

Although screening and diagnostic mammography are the most important and common imaging procedures used for breast evaluation, breast tomosynthesis, ultrasonography, MR imaging, and scintimammography all are used in breast imaging for detecting or defining breast cancer and for planning treatment for the disease.

Mammography

Mammography is the most common screening modality for breast cancer, and a screening mammogram is the only breast imaging examination for which a woman can self-refer.22,23,24 Multiple studies have shown that mammography effectively detects breast cancers and actively contributes to lower mortality rates from the disease. The compression device that flattens the breast anatomy is one feature that makes mammography an excellent tool for screening.

During a routine screening mammogram, a mammographer acquires bilateral images of the patient’s breasts, typically with 2 projections per breast: a cranio-caudal (CC) and an MLO projection. If the patient has signs or symptoms of breast cancer, a diagnostic mammogram might be ordered for the affected breast that includes the routine CC and MLO projections, along with additional projections such as coned compression, exaggerated CC, cleavage, and 30° oblique projections as requested by the radiologist.26

Although statistics repeatedly verify mammography’s effectiveness in breast cancer detection, the screening and diagnostic method is not 100% accurate. The sensitivity for mammography is reported to be approximately 87% to 97% in women with more fatty tissue in the breast and as low as 30% to 48% in patients with a higher ratio of dense breast tissue.25 Figure 5 demonstrates a comparison between digital mammography and a molecular breast imaging study. Because mammography has limitations, research to find a better imaging tool for the breast continues.27

Digital Breast Tomosynthesis

Exerting force onto the breast with a compression paddle during screening or diagnostic mammography helps prevent overlapping of anatomical structures, yet even with appropriate compression, it is impossible to completely eliminate structural superimposition. The ability to display the breast in 3-D can overcome the limitations of structural superimposition in breast imaging.
Digital breast tomosynthesis was approved by the U.S. Food and Drug Administration (FDA) in 2011 with the intention of supplementing mammography, but the technology has the potential to replace 2-D mammography. A breast tomosynthesis unit obtains a traditional mammographic image while subsequently acquiring approximately 10 to 25 slices of the breast from varying angles. The slices are combined to create a 3-D image of the breast. Breast tomosynthesis allows earlier detection and accuracy in determining size, shape, and location of breast tumors. The breast is positioned and compressed in the methods for tomosynthesis as it is for conventional mammography.

The average glandular dose from digital breast tomosynthesis is comparable to that of conventional digital mammography. Studies have shown that sensitivity from combined mammography and tomosynthesis could be as high as 92.9%. Specificity for tomosynthesis was slightly lower (84.4%) than for mammography alone (86.1%).

**Breast Ultrasonography**

Breast ultrasonography provides diagnostic images of the breast using sound waves. Breast ultrasonography commonly is used as a supplemental examination along with diagnostic mammography when a suspicious abnormality is detected. Breast ultrasonography is particularly useful for examining palpable areas of concern that are not detected on a mammogram and for imaging the breasts of younger women, which are more radiosensitive.

Ultrasonography can help physicians determine whether a palpable lesion or mammographic area of concern is solid or cystic in nature. Because there is no ionizing radiation used with ultrasonography, critics often have questioned why the modality has not replaced mammography as the breast imaging examination of choice. However, breast ultrasonography is not as sensitive as mammography at detecting many findings of concern that can indicate breast cancer in its earliest stages, such as microcalcifications.

Another limitation to breast ultrasonography relates to the anatomy of the breast. Because the breast is a large mass of tissue with no defined central landmarks, it is difficult to scan an entire breast and remain confident that all of the breast has been imaged. A proposed option known as automated whole-breast ultrasonography is a more recent advancement in medical imaging. Automated whole-breast ultrasonography acquires and records images of the entire breast with a transducer attached to a computer-guided mechanical arm. The system creates a cine loop of the images, which is then viewed and interpreted by the radiologist.

Whether ultrasonography becomes the solution to improving detection of breast cancer remains to be seen. An American College of Radiology Imaging Network trial reported that cancer was missed in 8 of 40 high-risk patients with dense breasts and negative screening findings. This emphasizes the need for additional diagnostic imaging modalities in the workup of patients with breast density and abnormal findings on mammography.
mammography findings when mammography and ultrasonography were combined; these results helped to emphasize the need for improved breast imaging technology.12

**Breast Magnetic Resonance Imaging**

Breast MR imaging helps physicians examine structures of the breast by displaying the breast’s form along with vascular activity. Breast MR imaging displays a particularly high sensitivity (88%-99%) but a reported specificity as low as 37%, which has caused critics to question the modality’s efficacy.35 Breast MR uses high-energy magnetic fields and an enhancing contrast medium to highlight the hydrogen atoms located within breast tissue.35 Because the breast comprises varying tissue densities, MR imaging is effective at displaying cancers that might have been otherwise undetectable on a mammogram.

Breast MR is more expensive than mammography and is not easily justified as a breast screening examination unless a patient fits the specific criteria outlined by the ACS.27 MR is particularly helpful for women who are at high risk for breast cancer, who have heterogeneously dense breast tissue, and who are undergoing breast cancer treatment planning or staging.27 Breast MR imaging can assist in assessing lumpectomy sites following surgery for breast cancer, evaluating changes in scars, detecting recurrent cancers, or assessing tumor changes after chemotherapy.27

The ACS has not found sufficient evidence to suggest that breast MR should replace mammography as a screening tool; however, evidence suggests MR’s usefulness as an adjunct screening tool in select patient populations.38 Limitations to breast MR include cost, insurance coverage, and less accessibility to MR scanners than to mammography units.39 Because the equipment is large and an expensive investment, it might not be practical for all women’s imaging centers to offer the examination on site.

MBI could emerge as a solution for many limitations of mammography and breast MR imaging. The advantages of MBI compared to breast MR include40:

- Patient comfort.
- Shorter interpretation times.
- A higher specificity rating.

Studies have suggested that because an MBI examination acquires fewer images than a breast MR examination, there is less room for error during interpretation of MBI.35 Additional research should be conducted to determine whether MBI should be used as an adjunct to mammography and ultrasonography instead of breast MR.

**Nuclear Medicine Breast Imaging Techniques**

With breast cancer awareness on the rise and statistics proving that early detection can improve survival, many technological advances are aimed at improving breast imaging sensitivity. Nuclear medicine technology helps physicians evaluate both anatomy and function when accumulation of an injected radioactive tracer highlights areas within the body that have high vascularity or metabolic activity.6,39,41

**Scintimammography**

Scintimammography is the term that commonly describes a nuclear medicine examination of the breast. Scintimammography was first introduced in the early 1990s and uses a general large field of view nuclear medicine γ-camera and technetium Tc 99m methoxyisobutylisonitrile (Tc 99m MIBI). The technologist acquires images with the patient in the prone, breast-pendant position. The use of the large field of view camera makes detector positioning challenging and compromises spatial resolution because the pendant breasts are 4 to 6 cm from the surface of the collimator.5

Although the specificity for primary breast lesions in scintimammography is high (86%-89%), sensitivity for detecting lesions less than 1 cm is low. Large field of view γ-cameras have a 35% to 65% sensitivity rate when imaging cancers less than or equal to 1 cm.7 Research in nuclear medicine imaging of the breast began to focus on early detection and developing a camera with higher resolution that could display minute breast lesions. As a result, the use of conventional γ-cameras decreased.4 As technology has developed, 3 specific nuclear medicine techniques related to scintimammography have emerged.5
Positron Emission Mammography

Positron emission mammography (PEM) uses fluoro- deoxyglucose F 18. The technologist acquires images of patients for a 10-minute period 1 hour after injection of the radiopharmaceutical. Positioning of the patient and breast for PEM is similar to mammography, and slight compression is used. PEM has shown a high sensitivity rate (90%) and the ability to display breast lesions that are not visible on mammograms or ultrasonograms.41 PEM images are acquired in the same projections as screening and diagnostic mammograms, which improves the radiologist’s ability to correlate findings on mammograms and PEM images.41

A study comparing MR imaging of the breast with PEM concluded that MR imaging had better lesion-level sensitivity, but PEM had greater specificity at the breast and lesion levels. Fourteen women in the study (3.6%) had tumors that were not visible on MR scans but could be seen on PEM images.42

Breast-Specific Gamma Imaging

Breast-specific gamma imaging (BSGI) often also is included with the general term MBI. The interchangeable terms can be confusing, however, because of differences in technology. Both use small field of view γ-cameras specially designed for breast imaging, but BSGI uses a sodium-iodide scintillation detector, and MBI uses cadmium-zinc-telluride digital detectors.43 The first BSGI camera became commercially available in 2004,42 and more than 250 000 patients have had a BSGI procedure worldwide as of 2011, according to Dilon Technologies Inc (March 2014).

Many health care providers have recognized the important contribution that scintigraphy can make in breast imaging and have continued to introduce a form of scintimammography into the health care setting over the past 10 years with the common goal of early breast cancer detection. The term breast-specific gamma imaging has been questioned because use of the word gamma tends to intimidate or alarm the public. More recently, companies have begun to use molecular breast imaging as a more palatable term.44

Molecular Breast Imaging

MBI uses a breast-optimized small field of view γ-camera with technetium Tc 99m MIBI. Image acquisition can begin about 5 to 10 minutes after injection.45 The technologist acquires images with the patient in a seated position with the breast slightly compressed, and the specially designed camera allows the technologist to maneuver the detector into positioning options to acquire images of the maximum amount of breast tissue.45 The small field of view γ-camera improves signal-to-noise ratio and spatial resolution. The introduction of small field of view cameras for molecular imaging of the breast has greatly improved lesion localization and detection of small occult breast cancers.50 The MBI camera can be equipped with a 15° slanted collimator that allows imaging of lesions close to the chest wall.23

MBI produces high-contrast images of lesions as small as less than 1 cm. The sensitivity rate of imaging lesions less than or equal to 0.7 cm was reported at 88.5% in one study.5,46 The high-resolution cameras have high photon sensitivity and are offered in different sized detectors for different sized breasts.

The MBI detector makes it possible to minimize the object-to-image distance by allowing the patient’s breast to rest virtually on the detector. The detector is small and portable, making it easy for small imaging centers to add MBI without adding a separate nuclear medicine department. The detector’s range of motion allows the technologist to image the breast with angles similar to mammography so that image comparison is more accurate for diagnosis and localization.4 This range of motion also allows for precise imaging of the axilla.

Practice Guidelines and Clinical Indications

The Society of Nuclear Medicine and Molecular Imaging (SNMMI) is the professional organization that provides guidance on the application of nuclear medicine studies. This professional organization comprises physicians, technologists, and scientists who are dedicated to continuing research and developing competencies related to the field of nuclear medicine.5,6,47 Guidelines for breast scintigraphy with breast-specific γ-cameras have been developed to ensure quality examinations to facilitate diagnostic interpretation. The guidelines are to educate and offer general practice suggestions and can be altered by the overseeing practitioner if warranted.47 The current guidelines developed
by the SNMMI were adopted in 2010 and cover clinical indications, qualifications of personnel, an explanation of the procedure, documentation policies, equipment specifications, quality control policies, and radiation safety practices."

The SNMMI clinical guidelines, along with ACR appropriateness criteria, are intended to help breast imaging practitioners and referring physicians when they are selecting patients for MBI procedures. For example, the ACR rates BSGI appropriateness low and relative radiation risk level high for BSGI with Tc 99m MIBI (ie, MBI) for screening, even in high-risk women.6 When a breast cancer has been identified, MBI can be used to assess whether the disease is multicentric, multifocal, confined to one or both breasts, or extended to more than one quadrant and whether the cancer has metastasized to the lymph nodes (ie, initial staging).67

MBI also can assist in evaluating the response of a breast tumor to neoadjuvant chemotherapy and is a noninvasive monitoring method.68 In addition, MBI is helpful for detecting suspected recurrence of breast cancer, as a follow-up examination when the initial mammogram was limited, or if a previous malignancy was not found on a mammogram. Patients who have tested positive for the BRCA1 or BRCA2 gene mutation also are good candidates for MBI.67

An MBI study conducted on patients with known malignancies showed radiotracer uptake in additional areas of concern for 18 of 82 patients. Seventeen of the 18 patients underwent additional biopsies in which 9 areas of concern were found and excision was determined necessary. Of the 9 areas identified, 6 were diagnosed as cancer. This study showed that MBI is effective in detecting new occult cancers that could alter the course of a patient’s treatment.69

Patients who have had a lumpectomy for a prior breast cancer are monitored closely with surveillance mammograms because of concerns about recurrence near the lumpectomy site. A research study involving 513 women with breast-conserving surgery following a breast cancer diagnosis reported that 42 of the 513 women developed recurrence in close proximity to their lumpectomy site. Because women with a prior history of breast cancer have a higher incidence of recurrence and scar tissue that makes imaging more difficult, MBI is valuable in the early detection of recurrence.47,50

Often a patient has an indeterminate abnormality within a breast, such as nipple discharge, palpable abnormalities not visible with mammography or sonography, multiple masses, or unexplained architectural distortion.47 When these conditions occur, it is the physician’s responsibility to determine the cause.

Even if a mammographic finding is normal, nipple discharge indicates further testing. Underlying breast cancer has been reported in 5% to 12% of patients who presented with nipple discharge.48 Not all forms of nipple discharge are a concern. The color, presence of blood, ductal location, and whether the discharge is from one or both breasts can indicate malignancy but are not final determining factors. Nipple discharge can be caused by hormones, bacteria, a small benign mass in the breast, or by breast cancer. If mammogram findings are negative and nipple discharge is present, ductography usually is indicated.48 If a ductography examination is unsuccessful, an MBI study is indicated to evaluate the nipple discharge.49

When a physician discovers a new palpable lesion that cannot be seen on mammograms or ultrasonograms, MBI might be warranted to evaluate the abnormality. MBI could be beneficial in evaluating multiple areas of concern, such as masses or clusters of microcalcifications, and to aid in biopsy targeting. If an area of concern is seen on only one mammographic projection, ultrasonography or spot imaging can help in evaluation, but MBI could be used to assess the metabolic activity of the lesion. When axillary lymph node metastases are present but the primary tumor location is unknown, MBI can be useful in evaluating the breast for occult disease.

MBI is recommended in patients who have extremely dense breasts and patients with augmented breasts. Approximately two-thirds of premenopausal women in their 40s have extremely dense breast tissue. Although digital mammography has greatly improved the quality of mammograms when imaging dense breast tissue, some radiologists believe that mammography is ineffective for imaging extremely dense breasts.64 Because MBI overcomes the limitations presented by dense breast tissue, this technology can be a useful adjunct for younger patients and all women with dense breasts.25,49

The number of breast implant procedures performed in 2005 was reported to be 364 610, and more than half of the implants were placed in women aged younger
Concerns have been raised for many years regarding the limitations of mammography when imaging breast implants (see Figure 6). Patients who have augmented or surgically altered breasts do not have a decreased likelihood of early breast cancer detection with mammography.

Because mammography is not recommended in asymptomatic women until 40 years of age, not all women receiving implants have a baseline mammogram before their surgery. The lack of baseline images of the preaugmented breasts to compare with future mammograms is a disadvantage when a woman has her first mammogram following augmentation because it is difficult to distinguish between scar tissue and dense breast tissue; a baseline mammogram before augmentation helps to distinguish scar tissue from dense tissue when compared with mammograms following augmentation. Breast implant mammography can be performed using the Eklund technique to image as much breast tissue as possible during a routine mammogram. However, silicone implants, silicone breast injections, and subglandular and subpectoral implant placement make it virtually impossible to image all breast tissue properly using mammography. With MBI, there are no known limitations to imaging patients with breast implants and injected silicone.

Some patients are not candidates for breast MR imaging as an adjunct to mammography. Patients with pacemakers or certain implanted devices usually are contraindicated for MR because of concerns regarding the magnet’s potential effects on the implant. Although there is much debate regarding whether pacemakers can withstand an MR scan, a survey of radiologists at Cleveland Clinic reported that 97% of the physicians would not allow an MR scan on a patient with an implanted pacemaker. The recent development of devices compatible with MR technology, such as Medtronic SureScan pacemakers and leads, allows these patients to have an MR scan.

Patients with compromised renal function might not be good candidates for an MR scan using gadolinium contrast. Gadolinium can cause nephrotoxicity in patients with suspected renal disease. Researchers believe that the use of gadolinium during routine MR examinations could be the cause of a systemic disorder known as nephrogenic systemic fibrosis. Therefore, an MBI examination could be a better alternative for these at-risk patients.

Another indication for choosing MBI over a breast MR is body habitus. During an MR examination, the patient must be able to fit inside the MR bore while resting atop the dedicated breast coil. In addition, the patient’s breasts must be small enough to fit within the breast coil for imaging. Therefore, the main limitations of MR for obese patients are bore size and weight limits. Newer MR systems have up to 70-cm bores and weight limits.

Figure 6. Left MLO projection of an augmented breast on mammogram (A) and breast-specific gamma imaging (B). High-intensity abnormal focal activity in the left breast and a palpable mass were consistent with invasive malignancy. Ultrasonography-guided biopsy confirmed infiltrating ductal carcinoma. Image courtesy of Dilon Technologies Inc.
limits between 400 lb and 550 lb. MR image quality is somewhat affected by obesity; increased body habitus can cause noise, and the necessity for a large field of view decreases resolution. Patient contact with the bore can degrade MR images, and open bore systems usually have a lower field strength, which also degrades image quality and requires longer examination times.

MBI might be a better option for patients who have claustrophobia and might be unwilling or unable to undergo an MR scan without sedation. Using sedation does not guarantee a successful MR scan free of motion in patients with claustrophobia. Premedication for sedation requires that a patient make transportation arrangements and sign the informed consent form before being medicated. Further, staff at a facility performing an MR scan with sedation must be qualified to handle a patient who has taken these medications. Because MBI is a shorter procedure requiring no sedation, it is a more appropriate choice for these patients.

When a patient presents with breast cancer requiring chemotherapy, research has suggested that the chemotherapy be started before surgery or as neoadjuvant therapy. Following neoadjuvant chemotherapy with medical imaging allows physicians to determine tumor shrinkage or growth and whether the chosen chemotherapy regimen is optimal for a particular patient. MBI can be used to monitor tumor response to neoadjuvant chemotherapy. In a study by Mitchell et al, the authors showed that MBI images acquired 3 to 5 weeks after neoadjuvant chemotherapy were accurate in predicting the presence or absence of residual disease after patients had completed the chemotherapy regimen.

Finally, sometimes an MBI examination could be used to set a patient’s mind at ease by providing information to accurately describe a significant finding.

Clinical Contraindications

MBI is considered a safe examination for virtually the entire patient population. There is a rare incidence of allergic reaction including anaphylactic events, angioedema, and generalized hives with itching for some patients following the administration of technetium Tc 99m MIBI. In clinical breast imaging trials involving 673 women, 19.2% reported alterations in taste and 1.6% reported headache. No anaphylaxis, chest pain, or ST segment changes on electrocardiography were reported among study participants (see Table 3). Another study performed in Europe over a 2-year period reported allergic reactions in fewer than 0.025% of cases.

The SNMMI Procedure Guidelines for the Use of Radiopharmaceuticals 4.0 state that “female patients who are postmenarcheal and premenopausal should be asked about pregnancy, lactation, and breast feeding” before receiving radiopharmaceuticals. In addition, the guidelines recommend that pregnancy testing be performed before using any radiopharmaceutical that could expose an embryo or fetus to 50 mSv of radiation or more. If possible, women who are pregnant should refrain from nuclear medicine scans, including MBI.

| Selected Adverse Events in Women Who Received Technetium Tc 99m Sestamibi |
|-----------------------------|-------------------|
| Adverse Effect on* | N = 673 (%) |
| Special senses | 132 (19.6) |
| Taste alteration | 129 (19.2) |
| General body effects | 21 (3.1) |
| Head (headache) | 11 (1.6) |
| Cardiovascular system | 9 (1.3) |
| Digestive system | 8 (1.2) |
| Smell (parosmia, or distorted odor perception) | 8 (1.2) |
| Gastrointestinal system (nausea) | 4 (0.6) |

*Events reported in more than 0.5% of women who received the radiopharmaceutical as part of a clinical study.
Advancements in Molecular Breast Imaging

Examination

The MBI examination typically takes place in a designated nuclear medicine suite. The nuclear medicine technologist introduces an intravenous line in the patient’s arm on the contralateral side of the breast to be imaged and administers the radiopharmaceutical. Imaging can begin approximately 5 to 10 minutes after injection. The patient is seated, and the technologist places the breast onto the detector’s supportive device. The breast compression used for MBI is minimal, about one-third that used in conventional mammography, which might alleviate some anxiety associated with mammography. An upper paddle on the MBI unit lightly supports the superior breast tissue and minimizes radiation scatter from the injected pharmaceutical. The technologist acquires a craniocaudal and mediolateral oblique projection of each breast, each with a scan time of 10 minutes, for a total time of 40 minutes.

Jones et al describe an injection technique for imaging the axillary lymph nodes that reduces the possibility of extravasation and vascular trapping. Extravasation occurs when an injected fluid leaks under the skin, and vascular trapping occurs when a concentration of the radiopharmaceutical remains along the walls of the veins for more than 5 minutes after injection. Both conditions can be visible on MBI and can cause artifacts on the images (see Figure 7).

Instead of a straight-stick injection, Jones et al recommend using an intravenous line with a “test, push, and flush technique.”

The technologist should begin by injecting 3 mL to 5 mL of saline through the line to verify patency. Next, the entire dose of technetium Te 99m MIBI is administered, followed by the rest of the saline. After injection is complete, the patient should be instructed to raise his or her arm straight above the head so that the elbow is above the ear and told to squeeze a ball for 1 minute. Jones reports that this technique can significantly reduce the frequency of extravasation and vascular trapping artifacts. If there are no complications, the patient can return to normal activity immediately following the MBI examination.

Future Uses

Molecular imaging for breast disease is a relatively new technology and one that holds promise as researchers and clinicians evaluate and resolve the limitations of molecular imaging techniques and develop potential new applications. For example, future clinical research might address methods for reducing radiation dose from the examination and establishing clinical relevance.

Dual-Head Cameras

Development of a dual-head MBI system incorporates a second detector mounted at the superior breast tissue. The breast tissue is compressed lightly between the 2 detectors, which can be rotated to obtain the craniocaudal and mediolateral oblique projections. A study involving 150 patients showed a sensitivity of 80% for breast cancer detection with a single-head camera and a sensitivity of 90% with use of a dual-head camera. In addition, the dual-head system’s sensitivity for detecting cancers of less than 10 mm was 82%, and the single-head system was 68%. Thirteen additional cancers were detected on dual-head images.

Biopsy

At the time this article was written, only one FDA-approved biopsy device for dedicated γ-cameras using stereotactic localization was available (GammaLoc, Dilon Technologies Inc). The device uses a sliding...
slant-hole collimator to obtain 2 separate gamma images that facilitate localization. The patient sits upright in the imaging position, and the physician inserts a needle into the lesion through a grid-support and needle positioning block, which is also the compression paddle. 69

This biopsy device makes it possible to sample a suspicious area displayed on a patient’s MBI examination without having to use mammography or ultrasonography correlation to locate the suspicious lesion. The procedure takes about 90 minutes. 69 A research study conducted on 25 patients undergoing the new biopsy procedure yielded 6 malignancies and 16 high-risk lesions. Of the 6 malignancies detected, all were confirmed as ductal carcinoma in situ. 70, 71

**Breast Density and Mammography Reporting Act**

Because mammography is less effective in women with dense breasts—the sensitivity of the examination decreases from an average of 66% to 85% to as low as 30%—it is important that women with dense breasts be aware that their mammogram could result in a false-positive result. 17, 54 The Breast Density and Mammography Reporting Act of 2013, also known as HR 3404, is a federal bill that would mandate how a mammography report is dictated and delivered to a patient with dense breast tissue.

Under the bill, radiologists would be required to include “information regarding the patient’s breast density and language communicating that individuals with more dense breasts may benefit from supplemental screening tests.” 72 The bill had not been passed at the time this article was written, but many states were diligently working on the bill, and several states have already enacted their own mandatory breast density legislation (see **Figure 8**). The Breast Density and Mammography Reporting Act could be a driving force for the advancement of MBI technology. Both mammography and ultrasonography have limitations when it comes to dense breast tissue. When patients are more informed of the composition of their breasts, they might choose to request an additional study such as an MBI, which is not limited by dense breast tissue. 12

**Conclusion**

MBI has shown promising results for evaluation of breast disease in several patient populations, but researchers must continue to investigate the modality’s limitations and potential in larger populations. The technology’s efficacy in imaging dense breasts is particularly important for the early detection of breast cancer and decreased mortality and morbidity from the disease.

Paula R McPeak, MSRS, R.T.(R)(M), is an instructor of radiography and mammography for the Riverside School of Health Careers in Newport News, Virginia.

Reprint requests may be mailed to the American Society of Radiologic Technologists, Communications Department, at 15000 Central Ave SE, Albuquerque, NM 87123-3909, or e-mailed to communications@asrt.org.

© 2014 American Society of Radiologic Technologists

**References**


Advancements in Molecular Breast Imaging


Advancements in Molecular Breast Imaging

2007;120(7 suppl 1):705-80S. doi:http://dx.doi.org/10.1136/bmj.f2399.


Advancements in Molecular Breast Imaging

To earn continuing education credit:

- Take this Directed Reading quiz online at www.asrt.org/drquiz.
- Or, transfer your responses to the answer sheet on Page 544M and mail to ASRT, PO Box 51870, Albuquerque, NM 87181-1870.

New and rejoining members are ineligible to take DRs from journal issues published prior to their most recent join date unless they have purchased access to the quiz from the ASRT. To purchase access to other quizzes, go to www.asrt.org/store.

*Your answer sheet for this Directed Reading must be received in the ASRT office on or before this date.

Read the preceding Directed Reading and choose the answer that is **most correct** based on the article.

1. Molecular breast imaging (MBI):
   1. is cost-effective.
   2. is a first-line screening modality.
   3. improves lesion detection in dense breasts.
   
   a. 1 and 2
   b. 1 and 3
   c. 2 and 3
   d. 1, 2, and 3

2. When the recommended amount of technetium Tc 99m sestamibi is administered for an MBI examination, a patient receives the approximate equivalent of a whole-body dose of ______ mSv.
   
   a. 3
   b. 5
   c. 6
   d. 7

3. Breast cancers usually start to form in the breast’s:
   1. lobes.
   2. lobules.
   3. ducts.
   
   a. 1 and 2
   b. 1 and 3
   c. 2 and 3
   d. 1, 2, and 3

4. Dense breast tissue is an important risk factor for breast cancer; increased fibroglandular density is associated with an increased cancer risk.
   
   a. true
   b. false

5. A *BRCA2* mutation increases breast cancer risk by approximately ______ %.
   
   a. 30
   b. 35
   c. 40
   d. 45

*continued on next page*
6. A diagnostic mammogram might include coned compression views along with which additional projections?
   - exaggerated craniocaudal
   - cleavage
   - 30° oblique
   a. 1 and 2
   b. 1 and 3
   c. 2 and 3
   d. 1, 2, and 3

7. Limitations to ultrasonography as a breast imaging tool include:
   - inability to differentiate between solid and cystic lesions.
   - poor detection of microcalcifications.
   - difficulty ensuring that the entire breast has been scanned.
   a. 1 and 2
   b. 1 and 3
   c. 2 and 3
   d. 1, 2, and 3

8. Some critics have questioned breast magnetic resonance (MR) imaging’s efficacy because of its:
   - high false-positive results.
   - low specificity.
   - low sensitivity.
   - poor resolution.
   a. high false-positive results.
   b. low specificity.
   c. low sensitivity.
   d. poor resolution.

9. Breast-specific gamma imaging differs from general MBI in:
   - positioning.
   - detector type.
   - camera type.
   - radiopharmaceutical administered.

10. In MBI, image acquisition can begin approximately ______ minutes after injection of the radiopharmaceutical.
    a. 5 to 10
    b. 15 to 20
    c. 30 to 45
    d. 60 to 90

11. With the development of small field of view cameras, MBI has improved:
    - localization of tumors.
    - signal-to-noise ratio.
    - detection of small occult breast cancers.
    a. 1 and 2
    b. 1 and 3
    c. 2 and 3
    d. 1, 2, and 3

12. The MBI detector’s range of motion allows the technologist to image the breast with angles similar to mammography so that image comparison is more accurate for diagnosis and localization.
    a. true
    b. false

13. Currently, MBI is appropriate for all of the following except:
    - assessing whether breast disease is multifocal or multicentric.
    - evaluating tumor response to chemotherapy.
    - screening for breast cancer in women who have a high risk of developing cancer.
    - detecting suspected recurrence.
14. According to the article, a molecular breast imaging study may be indicated in patients with nipple discharge:
   a. only if a mammography finding is abnormal.
   b. after ductography is unsuccessful.
   c. when a fine-needle biopsy is unsuccessful.
   d. if breast MR is contraindicated.

15. Approximately ______ of premenopausal women in their 40s have extremely dense breast tissue.
   a. one-quarter
   b. one-third
   c. one-half
   d. two-thirds

16. Indications for choosing molecular breast imaging instead of MR imaging of the breast include:
   1. the presence of an implanted medical device in the patient.
   2. compromised renal function in the patient.
   3. a patient with small body habitus.
   a. 1 and 2
   b. 1 and 3
   c. 2 and 3
   d. 1, 2, and 3

17. For best results, women undergoing an MBI examination should schedule the examination between the ______ day preceding the onset of menstruation.
   a. 1st and 5th
   b. 2nd and 14th
   c. 3rd and 10th
   d. 4th and 8th

18. During an MBI examination, the radiopharmaceutical is administered in the ______ side being examined.
   a. leg of the ipsilateral
   b. leg of the contralateral
   c. arm of the ipsilateral
   d. arm of the contralateral

19. According to Jones et al, which of the following techniques can reduce the possibility of extravasation and vascular trapping in a molecular breast imaging procedure?
   a. straight-stick injection
   b. test, push, flush
   c. Seldinger technique
   d. continuous fluid drip

20. Mammography has a higher false-positive rate in women with dense breasts, yielding a sensitivity rate as low as ______%.
   a. 10
   b. 30
   c. 66
   d. 85