Interest in nuclear medicine-based breast imaging is increasing as advances in technology allow for lower dose of radiotracer and confirm high sensitivity for the detection of in-breast cancers. These tools may have roles as we develop tailored breast imaging in our efforts to provide personalized, value-based care for our patients. Breast molecular imaging currently utilizes two radiotracers to evaluate breast cancer: the gamma-emitting 99mTc-sestamibi and the positron-emitting 18-F-fluorodeoxyglucose (18F-FDG) (Table 1). Dedicated breast gamma camera imaging can be performed with a single detector scintillating crystal system termed “breast specific gamma imaging” (BSGI) or through the use of a dual head cadmium-zinc-telluride detector system that is often called “molecular breast imaging” (MBI). Both approaches obtain imaging in craniocaudal (CC) and mediolateral oblique (MLO) views similar to mammography, with the breast
stabilized between a compression paddle and detector (BSGI) or between two detectors (MBI). Imaging is obtained within 5 minutes of intravenous injection of radiotracer and includes 10 minute acquisitions in both CC and MLO projections of both breasts for a minimum of 40 minutes of imaging, not including additional views as needed. MBI demonstrates 91% overall sensitivity for detection of invasive cancers (1) and outperforms BSGI for the detection of small cancers, identifying 76% of invasive cancers in the 6-10 mm range and 71% of cancers ≤ 5 mm (2).

Dedicated breast positron emission tomography (PET, also known as positron emission mammography or PEM) devices have been developed and the most widely validated unit uses positioning similar to mammography with the breast stabilized between a compression paddle and the detector and 10 minute acquisitions per view. The patient must be fasting for 4-6 hours and one-hour resting time is required prior to imaging. Positron emission mammography (PEM) has been shown to have greater in-breast sensitivity for detection of small cancers when compared to whole body PET or PET-CT (3, 4). Given the coincidence requirement for counting positron emissions (at 180 degrees from each other), the posterior 1 cm of breast tissue is not well evaluated with PEM; however, dedicated prone tables may improve visualization of posterior tissues.

It is imperative to reduce the dose of ionizing radiation as low as possible while still providing adequate diagnostic information for medical imaging. Reported
typical BSGI doses range from 15 to 30 mCi (555-1110 MBq). However, MBI with optimized collimator and energy levels have utilized doses averaging 8.1 mCi (300 MBq) while maintaining diagnostic performance (5). The radiation exposure with these nuclear medicine agents is to the whole body. The greatest accumulation of sestamibi is seen in the colon, kidneys, bladder and gallbladder. The effective dose from an 8.1 mCi (300 MBq) sestamibi injection is 2.4 mSv as compared to 0.4 mSv for mammography (6). For PEM, the typical 10 mCi dose of 18F-FDG results in an effective dose of 6.2 to 7.1 mSv (7) with the highest exposure to the bladder.

Indications for dedicated nuclear breast imaging are evolving. The role of sestamibi-based breast imaging for the evaluation of extent of disease may merit additional study, as PPV ranges from 35 to 60% (8) and a small study revealed improved specificity for BSGI as compared to breast MRI (9). BSGI may underestimate DCIS (10). In a study of 286 women with known invasive breast cancer, invasive lobular carcinoma showed less intense radiotracer uptake with resulting reduced sensitivity of 38/55 (69%) compared to 210/227 (92.7%, p=0.0062) for invasive ductal carcinoma (2). In a multicenter study, PEM was comparable to MRI in identifying ipsilateral disease with a slightly lower sensitivity (with 61/116 additional malignant foci, 53%, seen on MRI and 47, 41%, seen on PEM, p=0.043) and higher specificity than breast MRI (11). MRI outperformed MBI for the identification of contralateral disease (12). Neither sestamibi- nor 18-F-FDG-based imaging are reliable at identifying metastatic
axillary disease and there are no data regarding the role of nuclear medicine tracers in identifying residual disease in patients with positive margins at surgery.

Dense breast tissue reduces sensitivity and specificity of mammography (13, 14) but has not been shown to reduce the sensitivity of sestamibi-based imaging (15). Sestamibi-based breast imaging using BSGI has been explored for screening high-risk women who cannot tolerate MRI (16); however, radiation exposure is of concern in young women and in BRCA1 or -2 or TP53 mutation carriers with impaired DNA repair. The Mayo Clinic group has explored using sestamibi with a dual head camera for supplemental screening in women with dense breasts (17, 18). Cost analysis revealed that the cost per cancer diagnosis for mammography with MBI was lower than mammography alone (19). Table 2 summarizes the cancer detection rate and recall rates by modality after digital mammography. However, dose remains of concern, as whole body rather than breast-only exposure occurs with MBI.

In efforts to standardize interpretive criteria, lexicons have been developed to describe findings identified on gamma camera imaging (20) and breast PET (21), with ease of use and substantial reproducibility demonstrated for most terms (22,23). Interpretation of breast molecular imaging must include review of current mammography and other breast imaging studies as well as patient history and should be performed with or by a radiologist who meets experience requirements for breast imaging. A PEM-MRI trial revealed 9% of breasts with additional tumor
were identified on review of mammography and US, highlighting the importance of breast imaging expertise during evaluation (11). Focal radiotracer uptake should be considered suspicious in the absence of known benign correlate. For sestamibi-based imaging, a method of quantification has been described (24) but cannot routinely be performed with current software. For PEM, uptake can be quantified by drawing a region of interest with comparison to a region of uptake in normal background parenchyma; quantification, called PEM-uptake value or PUV, is similar for PET-CT and PEM despite lack of attenuation correction for PEM.

In addition to the aforementioned concerns regarding radiation exposure, licensing requirements, and long imaging times that hamper patient throughput have tempered interest in use of molecular imaging for screening. No method for direct biopsy of imaging findings detected by MBI is available at this time, though one approach has been submitted to the Food and Drug Administration; BSGI and PEM-guided methods for biopsy are available. The cancer detection rates from annual or biennial sestamibi-based incidence screening have not been reported to date.

Additional study is needed regarding indications and outcomes of breast molecular imaging techniques. Future areas of study may include use of targeted radiotracers to evaluate response to neoadjuvant therapy. Many novel radiotracers are being investigated in both preclinical and clinical settings to
determine feasibility and role of such agents in breast imaging as we continue to improve personalized and value-based breast imaging.
Table 1. Radiotracers Utilized in Breast Imaging

<table>
<thead>
<tr>
<th>Radiotracer</th>
<th>Energy (KeV)</th>
<th>Half-life</th>
<th>Decay Mode</th>
</tr>
</thead>
<tbody>
<tr>
<td>99mTc-sestamibi</td>
<td>140</td>
<td>6 hr</td>
<td>Gamma-emitter</td>
</tr>
<tr>
<td>18F-FDG</td>
<td>511</td>
<td>2 hr</td>
<td>Positron emitting glucose analog</td>
</tr>
</tbody>
</table>
Table 2. Summary of Prevalence Screening Cancer Detection and Recall Rates by Modality After Digital Mammography\(^a\)

<table>
<thead>
<tr>
<th>If 1000 Women With Dense Breasts Are Screened With</th>
<th>Number of Additional Women Found to Have Cancer</th>
<th>Technology/Relative Cost(^b)</th>
<th>Number of Women Recalled for Additional Testing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular Breast Imaging</td>
<td>8</td>
<td>Intravenous radioactive agent $400</td>
<td>+65</td>
</tr>
<tr>
<td>Tomosynthesis</td>
<td>1-2</td>
<td>Ionizing radiation $60</td>
<td>-18 to -30</td>
</tr>
<tr>
<td>Ultrasound (US)</td>
<td>2-4</td>
<td>Sound waves $300</td>
<td>+130</td>
</tr>
<tr>
<td>Contrast-enhanced MRI</td>
<td>10</td>
<td>Magnetic field and intravenous contrast $1000</td>
<td>+90</td>
</tr>
</tbody>
</table>

\(^a\) Courtesy Wendie A. Berg, MD, PhD, adapted from [www.DenseBreast-info.org](http://www.DenseBreast-info.org), accessed on August 9, 2015.

\(^b\) Based on estimated average reimbursement as of August 2015.

References


