

PET-Guided Breast Biopsy

A Case Study

Positron emission mammography helps verify that targeted tissues are sampled

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Image-guided percutaneous vacuum-assisted core biopsy plays a crucial role in the initial diagnosis and subsequent pre-surgical planning of women with breast cancer. Stereotactic X-rays, ultrasonography and magnetic resonance imaging (MRI) have been used to guide biopsies. The choice of the imaging modality used is typically based on the modality that visualizes the lesion best, the size and location of the target lesion, and equipment availability.

Functional imaging with positron emission tomography (PET) using fluorodeoxyglucose (FDG) has an advantage in that it relies on differences in cellular metabolic activity. One could then hypothesize that if this form of molecular imaging achieved high enough spatial resolution, it could be used to guide the tissue sampling and may allow for a more reliable sampling of viable tumor tissue.

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Positron emission mammography (PEM), a high-resolution breast PET scanner, relies on differences in glucose metabolism to identify breast cancers from normal breast cells. Using PEM, we have an opportunity to find cancers at an even earlier stage than that detected with breast MRI, and we may even have the opportunity to find atypia because it changes cellular metabolism prior to the advent of neoangiogenesis. PEM has been shown in recently published prospective data to have similar sensitivity and superior specificity to breast MRI.

PEM Biopsy Provides Quick Feedback

The Naviscan PEM scanner is a small, compact, mobile device, similar in size to conventional ultrasound devices. It uses plates that house detectors which are able to mimic mammographic views and permit imaging in the CC and MLO projections, as

well as visualization of the axilla with mere gentle immobilization. Since 2008, the Stereo Navigator PEM-guided biopsy accessory has been approved by the U.S. Food and Drug Administration (FDA). This necessary additional tool allows biopsy of lesions down to 1.3 mm, which may only be visible or accessible on PEM.

The biopsy procedure is similar to an upright stereotactic biopsy, with the patient seated with her head resting on the paddle. In our experience, this procedure seems to be well-tolerated by patients, particularly if they are claustrophobic, kyphotic or otherwise contraindicated for MRI. After the procedure is completed, specimens are imaged to confirm

uptake above level of background with immediate feedback that biopsy has been successful. This is unlike MRI biopsy, where we are required to wait for final pathologic diagnosis by the pathologist to determine concordance.

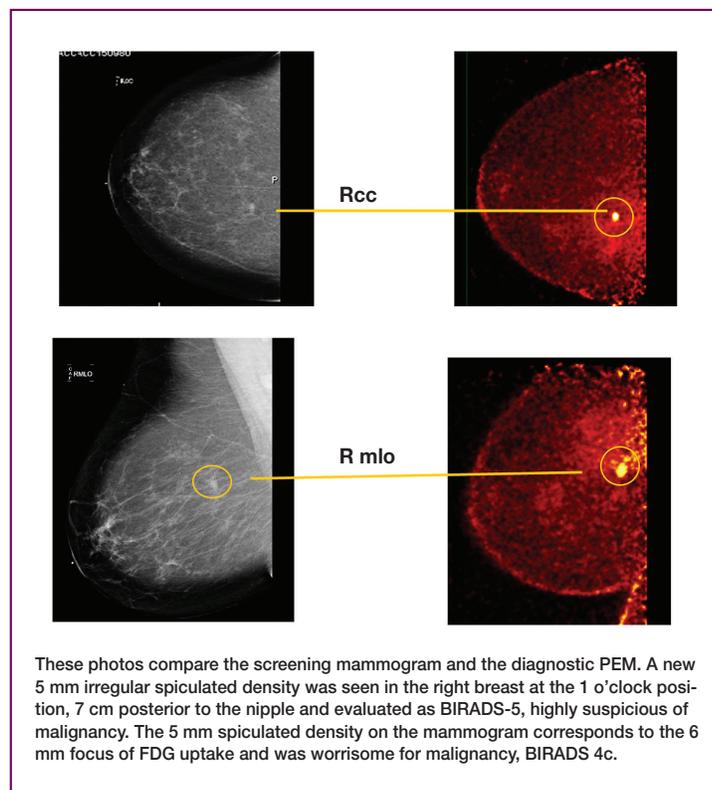
A Case Study Illustrates this Approach

The following case study demonstrates the strength of this PET-guided biopsy approach. A 55-year-old post-menopausal woman presented for routine screening mammogram. Bilateral mammography showed scattered fibro-glandular densities. A new 5 mm irregular spiculated density was seen in the right breast at the 1 o'clock position, 7 cm posterior to the nipple, and

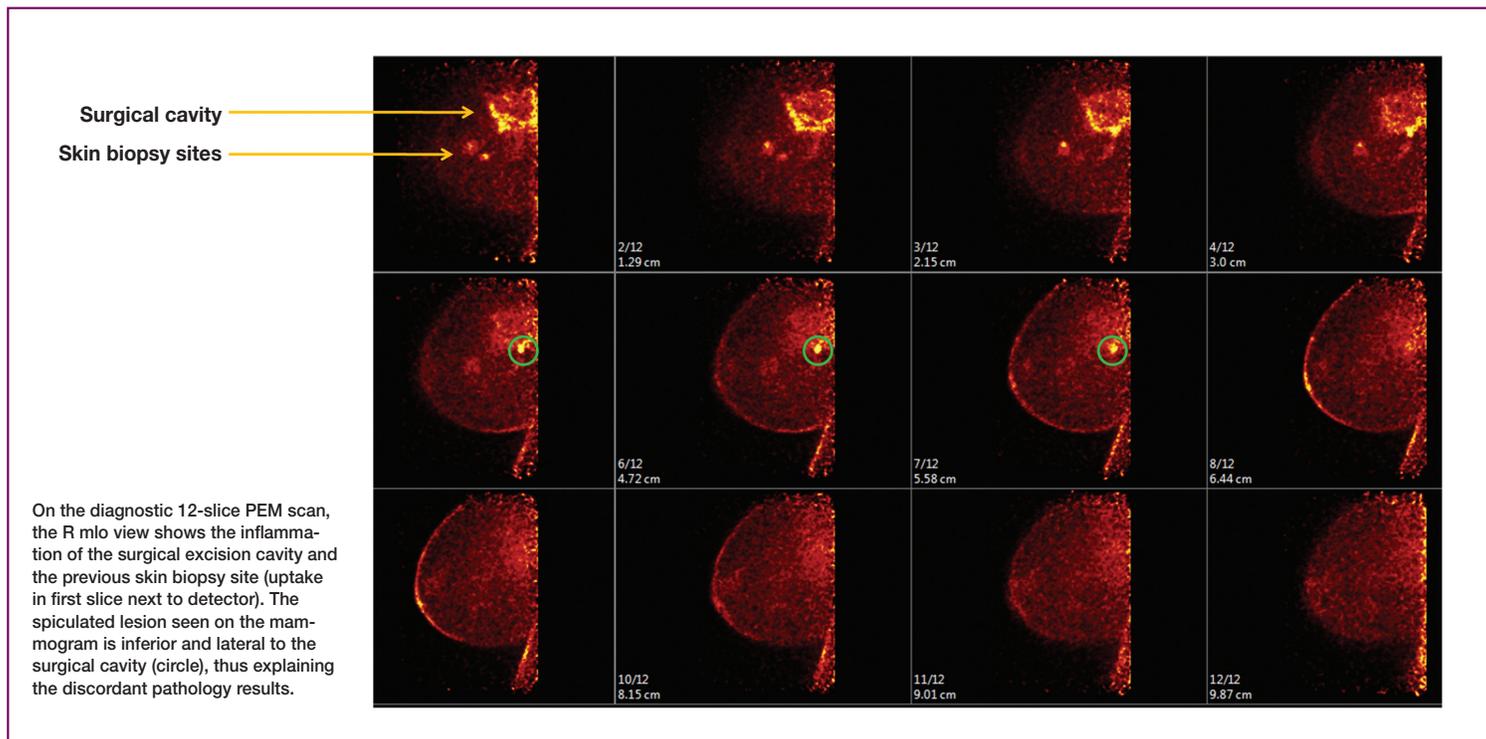
evaluated as BIRADS-5, highly suspicious of malignancy. (See photos at left.) A targeted ultrasound failed to identify the lesion. A biopsy under stereotactic guidance was recommended.

The pathology from the stereotactic biopsy was benign glandular tissue, which was thought to be discordant. In addition, the patient suffered a large hematoma. A delayed right breast needle-localized excisional biopsy of the tissue marker was performed after resolution of the hematoma and development of two new areas of fat necrosis. Pathology yielded discordant benign results once again, but the patient remained BIRADS-5. MRI could not be performed due to the patient's weight.

Subsequent organ-specific breast PET



These photos compare the screening mammogram and the diagnostic PEM. A new 5 mm irregular spiculated density was seen in the right breast at the 1 o'clock position, 7 cm posterior to the nipple and evaluated as BIRADS-5, highly suspicious of malignancy. The 5 mm spiculated density on the mammogram corresponds to the 6 mm focus of FDG uptake and was worrisome for malignancy, BIRADS 4c.



or PEM imaging showed a post-surgical rim of 18 F-FDG uptake consistent with granulation at the site of excisional biopsy with modest uptake of FDG. In addition, a 9 mm oval lesion of intense FDG uptake was identified contiguous with the inferior aspect of the biopsy cavity consistent with suspected malignancy. (See photo above.) Two adjacent areas of mild FDG uptake were consistent in location and activity with areas of fat necrosis seen mammographically. The patient then underwent one of the first PET-guided breast biopsies as part of a clinical trial.

High-resolution breast PET-guided biopsy was performed using Naviscan's Stereo Navigator software to target the lesion and provide direction on the best approach for vacuum-assisted biopsy (done using a Suros ATEC 9 gauge from Hologic). The four-scan biopsy process typically takes about 20 minutes.

The Stereo Navigator targets the lesion in three dimensions. Two biopsy passes were made to ensure adequate sampling. The biopsy cores were imaged on the PEM scanner and showed high levels of FDG uptake, confirming that the lesion had been

accurately sampled, similar to how calcifications are imaged using stereotactic methods.

Histopathology of the core biopsy found Grade III infiltrating ductal carcinoma, finally, concordant pathology. The patient was referred for definitive surgical excision. Final surgical pathology showed residual high-grade intraductal carcinoma.

This patient's case illustrates how PEM confirmed that the lesion seen on anatomical imaging, which was worrisome for malignancy, can be localized confidently by the high FDG uptake levels. It

MBI Effective for Surgical Treatment Planning

According to a new study, molecular breast imaging (MBI) is effective in the preoperative evaluation of women with biopsy-proven breast cancer. Published in the April issue of *Journal of Nuclear Medicine*, the study shows MBI can detect invasive ductal cancer (IDC), ductal carcinoma in situ (DCIS) and invasive lobular cancer (ILC), and can play a valuable role in evaluating the extent of disease and presence of multifocal disease in the breast for surgical treatment planning.

The study goals were to determine whether MBI is more sensitive than mammography in detecting additional foci of breast cancer in the ipsilateral and contralateral breasts and in the evaluation of disease extent of biopsy-proven disease.

Patients with biopsy-proven breast cancer scheduled for surgery were offered enrollment in the study. All patients had a diagnostic mammogram and an MBI study prior to surgery. Patients with MBI studies showing additional sites of disease underwent additional diagnostic studies.

At the time of operation, the pathologic findings were correlated with the MBI results. MBI studies were performed using a Gamma Medica Luma-GEM MBI system, which comprises dual-head pixilated cadmium zinc telluride (CZT) detectors mounted on a modified mammographic gantry. For MBI, patients were injected with 296 MBq Tc-99m sestamibi and the standard CC and MLO views were acquired of each breast.

A total of 98 patients with biopsy-proven breast cancer were enrolled and underwent preoperative MBI and completed surgical resection. MBI detected additional disease greater than that identified by the combination of mammogram and ultrasound, which altered the surgical treatment in 12 patients (12/98 = 12.2%).

In 7 of 98 patients, MBI detected additional foci of cancer not seen on mammography (7.1%). This resulted in change of surgical treatment plan from breast conservation to mastectomy. Final pathology confirmed that mastectomy

was warranted.

One patient (1%) had a contralateral breast cancer detected on MBI that was not detected with mammography. Second-look mammogram and ultrasound with biopsy demonstrated invasive breast cancer, and the patient underwent surgery on both breasts.

Two patients (2%) had uptake in the contralateral breast on MBI. Surgical excision demonstrated atypical ductal hyperplasia and atypical lobular hyperplasia. Another patient had an abnormality detected on MBI which, at the time of planned bilateral mastectomy, was found to represent atypical ductal hyperplasia.

In 3 out of 98 patients, MBI detected a significantly greater extent of disease than mammography (3%), which resulted in change of surgical treatment plan from breast conservation to mastectomy.

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also demonstrates the accuracy of PEM-guided biopsy to localize, target and verify that targeted tissues have been sampled. Further, this case highlights how molecular imaging, PEM in particular, can be used to problem-solve, even when a women's imaging center has access to stereotactic-, ultrasound- and MRI-guided biopsy

approaches.

"This case beautifully shows how PEM not only identifies lesion location, but also can assist in identifying lesion pathology by assessing the quantitative uptake of FDG," said Schilling. "In this case, we absolutely knew exactly which area of uptake corresponded to the suspected cancer.

This patient, although not well suited for MRI, was successfully diagnosed using our newest tool, PEM."

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Outlook Good for Low-Dose MBI

The possibility of low-dose molecular breast imaging (MBI) looks promising, according to recent clinical evidence revealed at the National Institutes of Health (NIH). Marcela Bohm-Velez, M.D., and colleagues from Associates in Pittsburgh, Penn., shared preliminary results from a prospective study on low-dose MBI, specifically breast-specific gamma imaging (BSGI), at the Society of Nuclear Medicine's "Breast Cancer Imaging: State of the Art 2011" event. They suggest it may be possible to reduce the radiation dose patients get from a BSGI procedure by up to 60%.

The tracer used, Technetium Tc99m Sestamibi (MIBI), has been used in cardiac studies for years and was cleared by the FDA in the mid-1990s for diagnostic breast imaging. The recommended dose (20–30 mCi) was established using an older, larger, less sensitive whole body imaging system. Newer breast-optimized imaging systems have an inherently higher photon sensitivity which may allow a lesser dose to be used.

At the Weinstein Imaging Center, BSGI has become a valuable diagnostic tool, especially for patients with dense breast tissue that limits the effectiveness of mammography. "In order to optimize care and use BSGI to screen specific populations, we wanted to examine the possibility of using a lesser dose," said Bohm-Velez. "The present challenge for the clinician is that the use of lower doses is currently an off-label use of the pharmaceutical."

Their study compared breast tissue uptake at low-dose levels of 5, 10 and 15 mCi to those obtained with the conventional 20 mCi (740 MBq) injections. Bohm-Velez said, "Although these are early results, we were quite surprised to see that we can reduce the dose to 15 mCi without any substantial impact on breast tissue uptake or image quality. In addition, a 10 mCi image still provided a very good, clinically viable image. The good news is that at lower doses, the breast tissue uptake is still sufficient, leading us to believe that a dose of 8 mCi is likely possible with the current instrumentation."

Bohm-Velez said investigations are underway at the University of Virginia to potentially allow doses as low as 2–4 mCi to be used, making the radiation dose from a BSGI/MBI study equivalent to that from a mammogram.



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In Shreveport, Louisiana, Willis-Knighton Cancer Center has established a model stereotactic radiation therapy program for community-based practices. Hundreds of patients have been treated since 2003, including one of the largest groups of patients receiving stereotactic body radiation therapy (SBRT) for lung cancer at a single institution in the United States.

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