

Molecular Imaging and Breast Cancer

Breast cancer is the most common cancer in women, and the second leading cause of cancer death in women.¹ Molecular imaging can help diagnose and stage breast cancer. Early diagnosis improves patient outcomes, and accurate TNM staging is critical for optimizing treatment strategies for patients with breast cancer.

What is molecular imaging and how does it help people with breast cancer?

Molecular imaging can provide detailed information about disease activity at the molecular and cellular levels. Conventional anatomic imaging — such as mammography, ultrasound, and computed tomography (CT) — predominantly provides structural information. Molecular imaging such as positron emission tomography (PET) allows for noninvasive visualization of a physiologic process, such as glucose metabolism with 18F-fluorodeoxyglucose (FDG); tumor receptor status, such as estrogen receptor status in 18F-fluoroestradiol (FES); or osteoblastic activity with 18F-Sodium Fluoride (NaF) bone scans.

In breast cancer, molecular imaging can:

- Screen for and characterize primary tumors in the breast (molecular breast imaging (MBI), dedicated breast PET (dbPET). [Visit this link for a listing of U.S. MBI Centers.](#)
- Provide systemic staging in a single examination (FDG PET/CT), which may be more cost-effective and accurate than conventional imaging with bone scan and CT. [2-6](#)
- Predict the likelihood of response to endocrine therapy in patients with estrogen-positive (ER+) tumors (FES PET/CT). [7-9](#)
- Provide early assessment of response to systemic therapy (MBI and FDG PET/CT). [10, 11](#)
- Identify early evidence of disease recurrence in patients with a personal history of treated breast cancer (FDG PET/CT). [12](#)

How does oncologic molecular imaging work?

Molecular imaging excels at detecting the cellular changes that occur in malignancies, in many cases before structural or anatomic changes can be seen on conventional imaging.

Nuclear medicine is a branch of molecular imaging that uses a [radiotracer](#) (typically a biologically relevant compound labeled with a radioactive isotope that is administered to a patient in very small quantities) and a camera to detect radioactivity emitted from the patient. Once the radiotracer is introduced into the body, it accumulates in a target organ or attaches to specific cells. Images created by the camera show how the radiotracer is distributed in the body, and this distribution pattern maps the sites of disease.

What molecular imaging technologies are used for breast cancer?

Molecular imaging technologies currently being used for breast cancer include tools to evaluate:

- **The whole body**
 - Positron emission tomography (PET), usually in conjunction with computed tomography (CT) (PET/CT)
 - [Bisphosphonate bone scans](#)

- **Regional lymph nodes:** radiotracer-guided sentinel lymph node biopsy
- **The breast:** [Molecular breast imaging \(MBI\)](#), dedicated breast PET (dbPET)

What is PET?

PET is an imaging technique that is able to localize and quantify the amount of positron emitting radiotracer that accumulates in the body after intravenous injection. The most frequently used PET radiotracer is FDG, a glucose analogue and a small amount of radioactive [fluorine](#). It usually takes between 30 and 60 minutes for the FDG to distribute throughout the body.

Once the radiotracer accumulates in the body, its natural decay includes emission of [positrons](#) that react with [electrons](#) in the body. This reaction, known as [annihilation](#), produces energy in the form of a pair of high energy [photons emitting in opposite direction from each other](#). The patient is placed in a PET scanner, which detects these photons and creates images that show the distribution of FDG in the body. Because malignant cells are often more metabolically active than other cells, they accumulate more FDG and appear more intense than surrounding tissue on PET images (Figure 1).

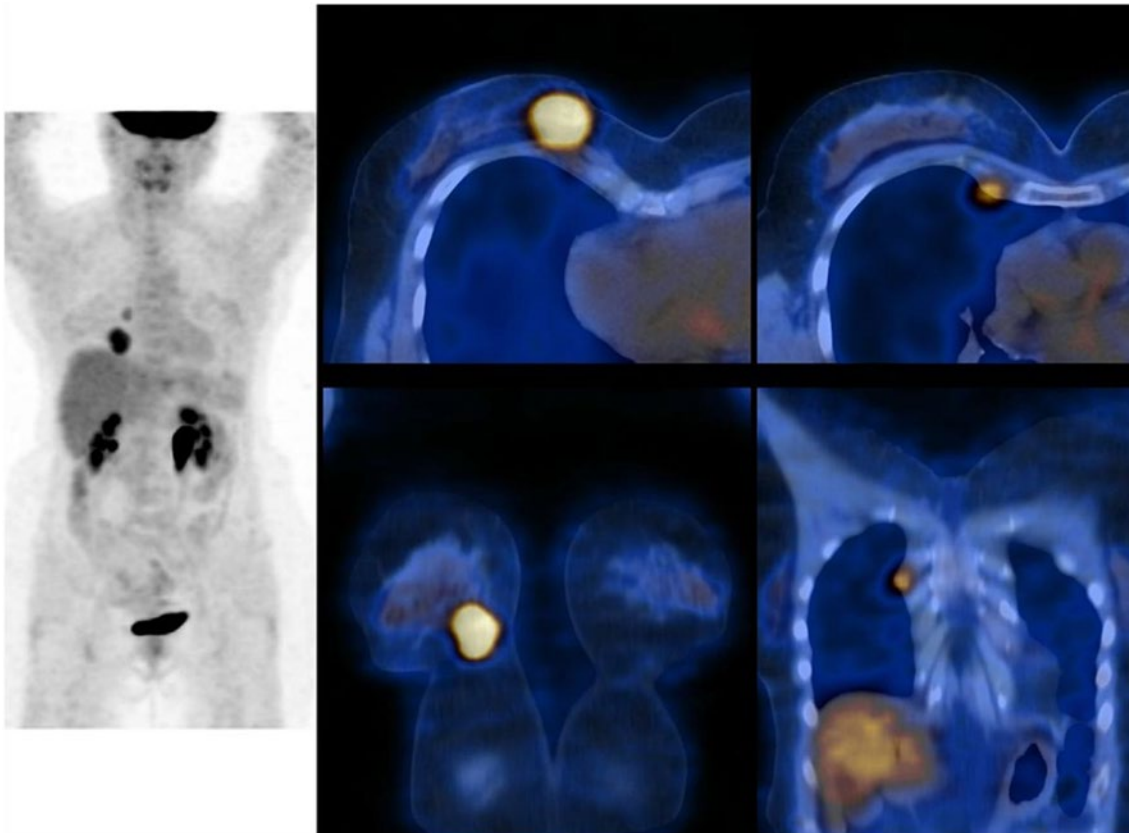


Figure 1. Invasive ductal carcinoma of right breast initially classified as T4cN0M0 (on basis of clinical examination, mammography, breast MRI, breast and axilla ultrasound, chest and abdominal CT scans, and bone scanning) in 63-y-old woman. PET/CT shows large breast tumor infiltrating skin and pectoral muscle (T4c) and depicts FDG-avid internal mammary node (final classification: T4cN2bM0). *Reprinted with permission from Groheux D J et al. JNM February 2016, 57 (Supplement 1) 17S-26S.*

While FDG is the most common radiotracer used for PET of breast cancer, newer radiotracers can target specific molecules within breast cancers, for example, FES, which targets the estrogen receptor (Figure 2). Knowledge of receptor status – whether a breast cancer has receptors for estrogen, progesterone, and/or human epidermal growth factor receptor 2 (HER2) – is critical for determining treatment options. Receptor-targeted PET allows for non-invasive evaluation of receptor status and the likelihood that a tumor will respond to receptor-targeted therapy.

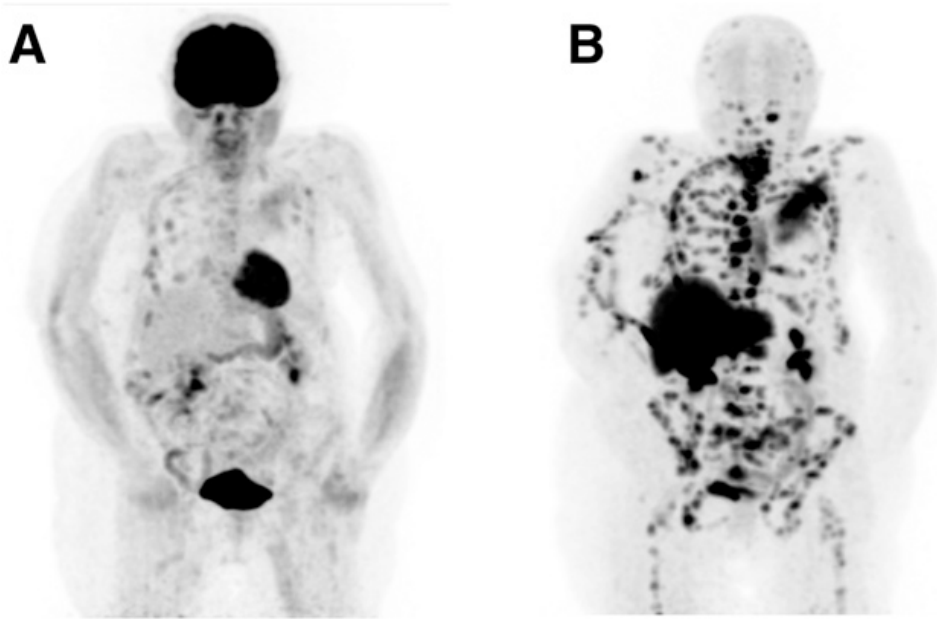


Figure 2. Patient had ER+, human epidermal growth factor receptor (HER2)–, T2N0M0 lobular carcinoma of left breast, which was treated with neoadjuvant chemotherapy, surgery, adjuvant chemotherapy, radiation therapy, and (for 5 y) tamoxifen hormone therapy. Eight years after total treatment completion (chemotherapy, surgery, radiation, and tamoxifen), vertebral fractures of T10 and T12 emerged, and cancer antigen 15-3 level was 3,500 U/mL (reference value 25 U/mL). (A) FDG PET/CT study showing that some lesions were barely seen with FDG. (B) FES PET/CT study 1 d after FDG PET/CT study, showing that all lesions expressed estrogen receptors and that accumulation of FES was higher than that of FDG, probably because of lobular histology. Patient was subsequently treated with aromatase inhibitor (exemestane), resulting in lesion stabilization and cancer antigen 15-3 reduction to 150 U/mL 2 y after beginning treatment. (Courtesy of Zionexa.) *Reprinted with permission from Grabher BJ JNMT 2020; 48:191–201.*

[PET/CT](#) is a combination of PET and [computed tomography \(CT\)](#) that provides both anatomical and functional information in a single examination. The combination of the two imaging techniques—called [co-registration](#), [fusion imaging](#) or [hybrid imaging](#)—allows information from each scan to be viewed in a single set of images. This is accomplished by superimposing the precise location of functional activity (from PET) against detailed anatomic image (from CT). PET/MRI, a combination of PET and magnetic resonance imaging (MRI), is a newer technology that is less widely available. Like PET/CT, PET/MRI provides both anatomical and functional information in a single examination (Figure 3). However, MRI provides better soft tissue contrast and has no additional radiation compared with PET/CT.

Scans are reviewed and interpreted by a nuclear medicine physician or radiologist.

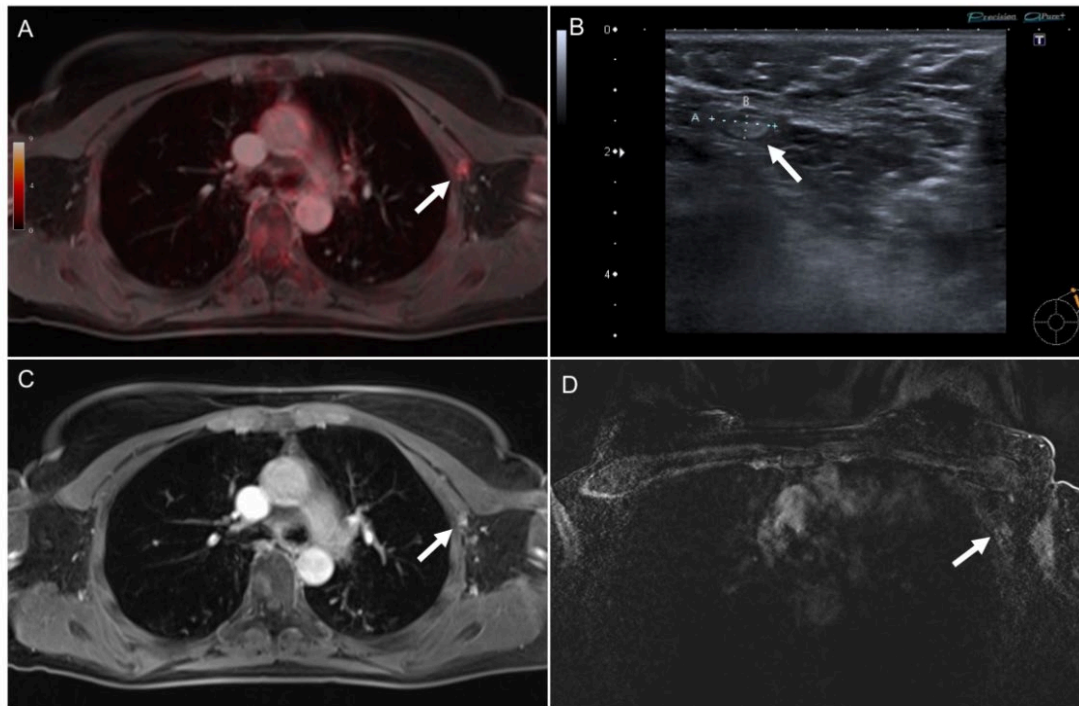


Figure 3. Pathologically confirmed axillary lymph node metastasis that was correctly identified in FDG PET/MRI (A) because of its tracer uptake above the background (SUVmax 4.7). This lymph node was rated false negative in axillary sonography (B), thoracic MRI (C), and breast MRI (D). *Reprinted with permission from Morawitz J et al. JNM May 2021; DOI: <https://doi.org/10.2967/jnumed.121.262009>.*

What is the radiation dose from molecular imaging?

We are exposed to daily low levels of radiation simply by living on Earth. This is called background radiation, which amounts to an average of 3 mSv (a unit describing radiation absorbed by the body) per year. Radiation dose from a whole-body PET/CT can range from 10 mSv to 25 mSv depending on what type of CT performed alongside the PET. This is equivalent to approximately 3-8 years of background radiation from simply living on Earth. The radiation dose of MBI is 6.5 mSv to 8 mSv. The radiation dose of lymphoscintigraphy is less than 1 mSv.

Further information about nuclear medicine and radiation safety can be found on [this factsheet](#).

Are molecular imaging procedures covered by insurance?

Most PET/CT studies for breast cancer are covered by Medicare and Medicaid. Major insurance companies and health maintenance organizations also provide coverage for PET/CT studies for breast cancer. Patients should check with their insurance companies for specific information on their health plan's coverage and payment policies.

What is the future of molecular imaging and breast cancer?

Molecular imaging is a major driver of personalized medicine. New and emerging molecular imaging technologies will continue to improve on the:

- Characterization of the biologic features of breast cancer tumors
- Selection of a treatment course that is tailored to an individual patient's tumor characteristics
- Prediction of treatment outcome
- Determination of effectiveness of treatments earlier in the treatment course, such as HER2-directed therapy without chemotherapy in patients with HER2+ tumors ¹³


Additional resources

SNMMI offers additional factsheets and resources on the following procedures:

- [Lymphoscintigraphy](#)
- [Sentinel node biopsy](#)
- [Molecular breast imaging](#)
- [Appropriate Use Criteria for bone scintigraphy in prostate and breast cancer](#)

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About SNMMI

The Society of Nuclear Medicine (SNMMI) is an international scientific and medical organization dedicated to raising public awareness about nuclear and molecular imaging and therapy and how they can help provide patients with the best health care possible. With more than 18,000 members, SNMMI has been a leader in unifying, advancing and optimizing nuclear medicine and molecular imaging since 1954.

The material presented in this pamphlet is for informational purposes only and is not intended as a substitute for discussions between you and your physician. Be sure to consult with your physician or the nuclear medicine department where the treatment will be performed if you want more information about this or other nuclear medicine procedures.

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