

Molecular Imaging and Breast Cancer

Breast cancer forms in tissues of the breast—usually in the ducts, tubes that carry milk to the nipple, and lobules, the glands that make milk. It occurs in both men and women, although male breast cancer is rare. According to estimates by the American Cancer Society, more than 279,000 people in the United States will be diagnosed with breast cancer and nearly 42,000 people will die from the disease in 2020. Accurately pinpointing the location of the primary tumor(s) and determining whether the cancer has spread to other parts of the body is critical for determining treatment options for people with breast cancer.

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

Molecular imaging is a type of medical imaging that provides detailed pictures of what is happening inside the body at the molecular and cellular level. Where other diagnostic imaging procedures—such as x-rays, computed tomography (CT) and ultrasound—predominantly offer anatomical pictures, molecular imaging allows physicians to see how the body is functioning and to measure its chemical and biological processes.

Molecular imaging offers unique insights into the human body that enable physicians to personalize patient care. In terms of diagnosis, molecular imaging is able to:

- provide information that is unattainable with other imaging technologies or that would require more invasive procedures such as biopsy or surgery
- identify disease in its earliest stages and determine the exact location of a tumor, often before symptoms occur or abnormalities can be detected with other diagnostic tests

As a tool for evaluating and managing the care of patients, molecular imaging studies help physicians:

- determine the extent or severity of the disease, including whether it has spread elsewhere in the body
- select the most effective therapy based on the unique biologic characteristics of the patient and the molecular properties of a tumor or other disease
- determine a patient's response to specific drugs
- accurately assess the effectiveness of a treatment regimen
- adapt treatment plans quickly in response to changes in cellular activity
- assess disease progression
- identify recurrence of disease and help manage ongoing care

Molecular imaging procedures are noninvasive, safe and painless.

How does molecular imaging work?

When disease occurs, the biochemical activity of cells begins to change. For example, cancer cells multiply at a much faster rate and are more active than normal cells. Brain cells affected by dementia consume less energy than normal brain cells. Heart cells deprived of adequate blood flow begin to die.

As disease progresses, this abnormal cellular activity begins to affect body tissue and structures, causing anatomical changes that may be seen on CT or MRI scans. For example, cancer cells may form a mass or tumor. With the loss of brain cells, overall brain volume may decrease or affected parts of the brain may appear different in density than the normal areas. Similarly, the heart muscle cells that are affected stop contracting and the overall heart function deteriorates.

Molecular imaging excels at detecting the cellular changes that occur early in the course of disease, often well before structural changes can be seen on CT and MR images.

Most molecular imaging procedures involve an imaging device and an imaging agent, or probe. A variety of imaging agents are used to visualize cellular activity, such as the chemical processes involved in metabolism, oxygen use or blood flow. In nuclear medicine, which is a branch of molecular imaging, the imaging agent is a radiotracer, a compound that includes a radioactive atom, or isotope. Other molecular imaging modalities, such as optical imaging and molecular ultrasound, use a variety of different agents. Magnetic resonance (MR) spectroscopy is able to measure chemical levels in the body, without the use of an imaging agent.

Once the imaging agent is introduced into the body, it accumulates in a target organ or attaches to specific cells. The imaging device detects the imaging agent and creates pictures that show how it is distributed in the body. This distribution pattern helps physicians discern how well organs and tissues are functioning.

What molecular imaging technologies are used for breast cancer?

There are currently three molecular imaging technologies used for breast cancer:

- positron emission tomography (PET) scanning and PET in conjunction with computer-aided tomography (CT) scanning (PET-CT)
- molecular image-guided sentinel node biopsy
- breast specific gamma imaging (BSGI)

What is PET?

PET involves the use of an imaging device (PET scanner) and a radiotracer that is injected into the patient's bloodstream. A frequently used PET radiotracer is ¹⁸F-fluorodeoxyglucose (FDG), a compound derived from a simple sugar and a small amount of radioactive fluorine.

Once the FDG radiotracer accumulates in the body's tissues and organs, its natural decay includes emission of tiny particles called positrons that react with electrons in the body. This reaction, known as annihilation, produces energy in the form of a pair of photons. The PET scanner, which is able to detect these photons, creates three-dimensional images that show how the radiotracer is distributed in the area of the body being studied.

Areas where a large amount of FDG accumulates, called 'hot spots' because they appear more intense than surrounding tissue, indicate that a high level of chemical activity or metabolism is occurring there. Areas of low metabolic activity appear less intense and are sometimes referred to as 'cold spots.' Using these images and the information they provide, physicians are able to evaluate how well organs and tissues are working and to detect abnormalities.

PET-CT is a combination of PET and computed tomography (CT) that produces highly detailed views of the body. The combination of two imaging techniques—called co-registration, fusion imaging or hybrid imaging—allows information from two different types of scans to be viewed in a single set of images. CT imaging uses advanced x-ray equipment and in some cases a contrast-enhancing material to produce three dimensional images. A combined PET-CT study is able to provide detail on both the anatomy and function of organs and tissues. This is accomplished by superimposing the precise location of abnormal metabolic activity (from PET) against the detailed anatomic image (from CT).

How is PET used for breast cancer?

Physicians use PET and PET-CT studies to:

- **diagnose and stage:** by determining the exact location of a tumor, the extent or stage of the disease and whether the cancer has spread in the body
- **plan treatment:** by selecting the most effective therapy based on the unique molecular properties of the disease and of the patient's genetic makeup
- **evaluate the effectiveness of treatment:** by determining the patient's response to specific drugs and ongoing therapy. Based on changes in cellular activity observed on PET-CT images, treatment plans can be quickly altered
- **manage ongoing care:** by detecting the recurrence of cancer

What are the advantages of PET studies for breast cancer patients?

PET helps physicians and their patients:

- gain a clear understanding of where and how aggressive the disease is
- select a course of treatment
- determine the effectiveness of treatments after just one cycle of treatment
- eliminate unnecessary surgeries after treatment by distinguishing active tumors from residual masses

What is a sentinel node biopsy and how is it performed?

When breast cancer spreads, cancer cells are often found in the lymph nodes that are located under the arm, called axillary lymph nodes. The lymph nodes in this armpit region drain lymph from the breast and nearby areas. To determine if cancer has spread to a patient's lymph nodes, an axillary lymph node dissection may be performed in addition to removing part or all of the breast. In a dissection, five to thirty nodes are surgically removed so they may be analyzed in a laboratory for evidence of cancer.

A sentinel node biopsy is a relatively new alternative to the axillary lymph node dissection. Molecular imaging is used to identify the first few or sentinel nodes into which a tumor drains. Sentinel nodes that are closest to the tumor are most likely to contain cancer cells if the tumor has metastasized, or (spread). In a sentinel node biopsy, only the sentinel nodes are surgically removed, which reduces complications and side effects, including lymphedema, for the patient.

Prior to surgery to remove part of or the entire breast, a radiotracer that contains radioactive material is injected near the tumor and/or around the nipple. Images may be taken to visualize the radiotracer's pathway as it leaves the breast. The physician makes an incision underneath the arm and passes a hand-held probe over the area to measure levels of



radioactivity; only the lymph nodes that have absorbed the radiotracer are removed. In less than five percent of sentinel node biopsies, the sentinel node cannot be identified and a full axillary dissection is done.

What are the advantages of sentinel node biopsy?

A sentinel lymph node biopsy is:

- highly reliable in detecting cancerous cells
- more accurate than the traditional axillary dissection in assessing whether breast cancer has spread to the lymph nodes
- may be performed on an outpatient basis
- easier for the patient in terms of recuperation

A negative sentinel lymph node indicates a greater than 95 percent chance that the remaining lymph nodes are also cancer-free. Most patients resume regular activities within a few days and incisions generally heal within a few weeks.

What is breast-specific gamma imaging (BSGI)?

Breast-specific gamma imaging is a diagnostic procedure performed as a follow-up study to a mammogram that detects cancer or a mammogram that is inconclusive in its findings. BSGI is used to detect:

- additional lesions missed by mammography and physical exam
- cancers that are difficult to detect using mammography

The procedure involves the use of a radiotracer called Technetium Tc99m_Sestamibi that is injected into the patient's bloodstream and accumulates in malignant tissue. Images acquired with a special gamma camera modified for breast imaging reveal the distribution of the radiotracer, identifying abnormal areas.

What are the advantages of BSGI?

Recent studies have shown that BSGI is able to:

- identify lesions less than one centimeter in diameter that are difficult for mammography to detect
- provide information that helps physicians and patients choose the most appropriate treatment plan

What 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?

There are many new and emerging molecular imaging technologies that may benefit people with breast cancer, including:

- hybrid imaging systems, such as combined PET-MR, may improve accuracy and allow physicians to see how cancer is affecting other systems in the body
- the use of PET imaging biomarkers, such as fluorothymidine (FLT) to show tumor proliferation, and fluoroestrogen (FES) to detect estrogen receptors
- positron emission mammography (PEM)
- radioimmunotherapy (RIT)

What is Positron Emission Mammography (PEM), how does it work, and what are its advantages?

Positron emission mammography (PEM) uses a high-resolution PET scanner designed specifically for breast cancer detection.

PEM works much like PET scanning: the patient is injected with a very small amount of a radiotracer such as ¹⁸F-fluorodeoxyglucose (FDG), which travels through the body and is absorbed by breast tissue. The breast is then imaged with detectors mounted on compression paddles similar to those used in traditional mammography. Working with a computer, the scanner creates three-dimensional images showing the distribution of the radiotracer in the breast.

Specifically, PEM:

- produces much more accurate images of small breast lesions
- may be helpful in pinpointing the exact location of tumors and as a tool for surgical planning
- has a high level of accuracy in correctly identifying tumors, according to recent studies
- may reduce the need for breast biopsy when used in conjunction with other imaging modalities
- may be especially helpful for detecting and determining the size of ductal carcinoma in situ (DCIS), a common type of breast cancer that can be difficult to identify with conventional technologies

What is radioimmunotherapy (RIT)?

Radioimmunotherapy (RIT) is a personalized cancer treatment that combines radiation therapy with the precise targeting ability of immunotherapy, a treatment that mimics cellular activity in the body's immune system.

In a healthy immune system, certain white cells are able to recognize invading organisms, such as bacteria and viruses. The white cell secretes a protein substance called an antibody that identifies a feature of the foreign (or "invading") cell called an antigen. The antibody coats the invading cell, which enables other white cells to destroy it. In immunotherapy, scientists create monoclonal antibodies in a laboratory that are designed to recognize and bind to the antigen of a specific cancer cell. In RIT, the monoclonal antibody is paired with a radioactive material. When injected into the patient's bloodstream, the antibody travels to and binds to the cancer cells, allowing a high dose of radiation to be delivered directly to the tumor.

Several new radioimmunotherapy agents are under development or in clinical trials.



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.

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