

Molecular Imaging and Prostate Cancer

Prostate cancer is the second leading cause of cancer death in American men, behind only lung cancer. Based on rates from 2012–2014, the National Cancer Institute estimates that one in nine men will be diagnosed with cancer of the prostate during their lifetime and one in 50 will die from the disease.

The American Cancer Society estimates there will be approximately 164,690 new cases of prostate cancer diagnosed in the United States, and 29,430 men will die of the disease in 2018.

When detected early, prostate cancer has more than a 95 percent cure rate. Because treatment is highly individualized, molecular imaging technologies are dramatically improving the ways in which prostate cancer is diagnosed and treated.

Treatment options include surgery to remove the prostate, radiation therapy and chemotherapy. Determining whether the prostate cancer has spread to the lymph nodes or other parts of the body is critical for making accurate decisions on whether and how to treat prostate cancer. In addition to improving the accuracy of prostate cancer diagnosis, molecular imaging tools can provide detailed information about the cancer that help patients and their physicians choose the best treatment option.

What is molecular imaging and how does it help people with prostate 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, the 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. Similarly molecular imaging can detect treatment-induced cellular activity changes earlier than structural changes.

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 very small amount of 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 the imaging agent 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 prostate cancer?

There are several molecular radiotracers commonly used to diagnose and guide the treatment of prostate cancer. These include metabolic radiotracers such as FDG, fluciclovine, and choline as well as structurally specific agents that target the prostate-specific membrane antigen (PSMA). These radiotracers employ positron emission tomography (PET) scanning in conjunction with computer-aided tomography (CT) to identify sites of disease. Additional molecular imaging radiopharmaceuticals used to specifically target prostate cancer bone metastases include sodium fluoride PET and bisphosphonate bone scans.

What is PET?

Positron emission tomography (PET) is an imaging technique that is able to localize and quantify the amount of positron emitting radiotracers that accumulate in the body's tissues and organs. These radiotracers decay by 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 FDG is distributed in the area of the body being studied.

Areas where a large amounts of radiotracers accumulate are called 'hot spots' because they appear more intense than surrounding tissue, and indicate that a high level of chemical targets or metabolism are 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).

FDG PET

FDG PET involves the use of a PET and 18F-Fluorodeoxyglucose (FDG) which is a compound derived from a simple sugar and a small amount of radioactive fluorine. FDG accumulates in tissues that have high levels of metabolic activity, such as the brain. Many cancers, including prostate cancer, accumulate high levels of FDG due to their altered metabolism and rapid cell growth. FDG PET is typically used in patients with known prostate cancer to determine if the disease has spread to pelvic lymph nodes or the skeleton.

Choline PET

Choline PET uses PET and 11C-choline, which like FDG, is a positron emitting radiopharmaceutical. Choline is an essential component of cell membranes and accumulates in tissues with high cellular proliferation. Malignancies, such as prostate cancer, demonstrate increased high choline uptake and incorporation into their cellular membranes. Choline PET is used in patients with prostate cancer previously treated either by surgery (prostatectomy) or radiation therapy, and now have an increase in prostate-specific antigen (PSA) blood levels suggesting recurrent prostate cancer.

Fluciclovine PET

Fluciclovine is a positron emitting amino acid radiotracer that accumulates in prostate cancer cells. Amino acids are essential to cell metabolism and growth, and prostate cancer cells have a much higher nutrient demand compared to normal tissues. Like choline PET, fluciclovine PET is used in patients that have previously been treated for prostate cancer and now have clinical suspicion of recurrent disease and rising PSA blood levels.

What is a Prostate-Specific Membrane Antigen (PSMA) study?

A PSMA study is an imaging test to locate and determine the extent of prostate cancer. PSMA studies may be performed on newly diagnosed prostate cancer patients to determine if the disease has spread to pelvic lymph nodes. The study is also performed on previously treated prostate cancer patients that now have rising PSA blood levels.

A PSMA study involves a PET camera and small molecule positron emitting radiopharmaceutical that binds to the extracellular portion of the prostate-specific membrane antigen. These PSMA PET studies are used in patients with previously treated prostate cancer that now have clinical suspicion of recurrent prostate cancer. There are no small molecule PSMA PET radiopharmaceuticals that are currently FDA approved for prostate cancer imaging in the United States.

How is PET performed?

Depending on the specific radiotracer used for the PET study (FDG, fluciclovine) patients may be asked to fast prior to arriving for the PET study. The procedure begins with an intravenous (IV) injection of the radiotracer followed by a waiting period to allow the radiotracer to distribute throughout the body. The waiting time





required depends on the radiotracer and may either be short (5 minutes for fluciclovine) or longer (60 minutes for FDG). The patient is then placed in the PET scanner, where special detectors are used to create a three-dimensional image radiotracer bio-distribution.

Scans are reviewed and interpreted by a qualified imaging professional such as a nuclear medicine physician or radiologist who shares the results with the patient's physician.

What is a bone scan and how is it performed?

A bone scan is a diagnostic imaging test used to determine whether prostate cancer has spread to the skeleton. A radioactive material called a radiotracer is injected into the patient's bloodstream and accumulates predominantly in the bones where it can be detected by a gamma camera. The resulting two-dimensional or three-dimensional images can reveal various processes such as bony fractures, infection, inflammation and changes secondary to the presence of cancer cells. ¹⁸F-sodium fluoride is a positron emitting radiotracer that uses a PET camera and is similar to a bone scan with better sensitivity for bone metastases.

What are the advantages of molecular imaging for people with prostate cancer?

- Molecular imaging with PET can be used to identify locally recurrent prostate cancer as well as sites of lymph node or skeletal metastatic disease. While a molecular imaging PET scan may be used in place of a bone scan to painlessly determine whether prostate cancer has spread to the bone, it can also be used in conjunction with a bone scan or MRI to increase the accuracy of skeletal disease identification
- PET studies are able to determine the extent of prostate cancer and whether it has spread to the lymph nodes or other parts of the body before traditional imaging technologies such as magnetic resonance imaging (MRI) and computed tomography (CT), which are often unable to detect the spread of prostate cancer cells until later stages when metastases are more pronounced
- Molecular imaging technologies help physicians select the most effective therapy for prostate cancer, taking into account a tumor's unique molecular properties and whether the cancer is localized or diffuse, or spread out
- PET-CT has proven very effective in helping physicians determine sites of prostate cancer lymph node metastases and can be used to monitor patient response to treatment of advanced-stage prostate cancer

How are PET and PSMA studies used for prostate cancer?

Physicians use PET 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

Is molecular imaging covered by insurance?

Medicare and most insurance companies will cover the cost of most PET scans and PSMA studies. Check with your insurance company for specific information on your plan.



What is the future of molecular imaging and prostate cancer?

Developments underway include:

- new imaging agents for PET scanning of the prostate
- Hybrid imaging in which PSMA PET studies are combined with other imaging technologies such as computed tomography (CT) to improve image accuracy and to offer more targeted treatment
- the use of radioimmunotherapy

New molecular imaging techniques that will:

- predict the aggressiveness of a tumor
- predict the outcome of treatment
- detect genetic markers of the disease
- assist physicians in developing even more tailored treatment plans

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 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 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 and optimizing nuclear medicine and molecular imaging since 1954.

The material presented in this pamphlet is for information 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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