

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 2004–2006, the National Cancer Institute estimate that one in six men will be diagnosed with cancer of the prostate during their lifetime and one in 35 will die from the disease.

The American Cancer Society estimated that approximately 192,280 new cases of prostate cancer were diagnosed in the United States and 27,360 men died of the disease in 2009.

When detected early, prostate cancer has more than a 90 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 cancers?

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 prostate cancer?

Molecular imaging technologies most commonly used to diagnose and guide the treatment of prostate cancer include a bone scan, the prostate-specific membrane antigen (PSMA) study and positron emission tomography (PET) scanning and PET in conjunction with computer-aided tomography (CT).

What is a bone scan and how is it performed?

A bone scan is a diagnostic imaging test used to determine whether cancer has spread beyond the prostate. 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 an imaging device. The resulting two-dimensional or three-dimensional images can reveal various processes such as bony fractures, infection, inflammation and changes secondary to presence of cancer cells.

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

A PSMA study, also called a ProstaScint® scan, is an imaging test to locate and determine the extent of prostate cancer. PSMA studies are performed on newly diagnosed prostate cancer patients to determine if the disease has spread to pelvic

lymph nodes. The study is also performed on patients who have had their prostate gland removed (prostatectomy) and have an increase in prostate-specific antigen (PSA) blood levels.

The study involves a special molecule called a monoclonal antibody developed in a laboratory and designed to bind to the prostate-specific membrane antigen on cancer cells. This antibody is paired with a radioactive material called Indium-111 that can be detected by a gamma camera. When injected into the patient's bloodstream, the radioactive antibody, called a radiotracer, travels and attaches to cancer cells. The gamma camera then produces three-dimensional images of the tumor and its location inside the body.

How is a PSMA study performed?

This study is performed over as many as three days. On the first day, the patient first receives an intravenous (IV) injection of the radioactive antibody. Imaging is performed in two sessions, separated by 24 or more hours. Each imaging session will last between two and four hours. The camera rotates around the patient, who remains still.

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

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 FDG 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.

A radiotracer called choline is currently used for PET studies of the prostate.



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 performed?

The procedure begins with an intravenous (IV) injection of a radiotracer, such as FDG, which usually takes between 30 and 60 minutes to distribute throughout the body. The patient is then placed in the PET scanner where special detectors are used to create a three dimensional image of the FDG 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 are the advantages of PET for people with prostate cancer?

- PET is able to identify fast-growing, aggressive tumors. In addition, a PET scan may be used in place of a bone scan to painlessly determine whether prostate cancer has spread to the bone
- PSMA 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, unlike 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
- 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 monitor patient response to treatment of advanced-stage prostate cancer

Is molecular imaging covered by insurance?

Medicare and private insurance companies cover the cost of most PET-CT scans. 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 studies or PET 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?

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 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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Society of Nuclear Medicine and Molecular Imaging
1850 Samuel Morse Drive
Reston, VA 20190
www.snmmi.org
www.discovermi.org