

Molecular Imaging and Neuroendocrine Tumors

What are neuroendocrine tumors?

A neuroendocrine tumor (NET) occurs when cells of the body's neuroendocrine system grow in an uncontrolled, abnormal manner.

Neuroendocrine cells have traits similar to nerve cells and to the hormone-producing cells of the endocrine glands. Neuroendocrine cells are located in organs throughout the body and perform specific functions, such as regulating air and blood flow and controlling the speed at which food is moved through the gastrointestinal tract.

NETs are rare and develop most commonly in the lungs, appendix, small intestine, rectum, and pancreas. Many NETs start in the digestive tract, as it has more neuroendocrine cells than any other part of the body. Some tumors grow slowly while others can be very aggressive and spread to other parts of the body (metastasize), most often to the liver or bone.

NETs may secrete higher-than-normal amounts of hormones, which can cause conditions including diabetes, flushing, and diarrhea. Because NET symptoms resemble those of other diseases, such as irritable bowel syndrome (IBS) or Crohn's disease, they are often misdiagnosed. Special blood tests can accurately diagnose these tumors.

There are several types of NET, including carcinoid tumors, islet cell tumors, medullary thyroid carcinomas, pheochromocytomas, and neuroendocrine carcinomas of the skin (Merkel cell cancer).

Treatment depends on the type of tumor and its location, whether it produces excess hormones, how aggressive it is, and whether it has spread. Advances in treatment have improved the length of survival for patients with NETs.

NETs account for only 0.5% of all malignancies. The incidence is approximately 2/100,000, with a female preponderance under the age of 50 years due to appendiceal location. The

main primary sites are the gastrointestinal tract (62–67%) and the lung (22–27%). Presentation with metastatic disease accounts for 12–22%. In the last decades, the incidence has been rising. This might be due to more awareness, improved diagnostic tools, or a change in definition.

How is molecular imaging helping people with NETs?

Molecular imaging has become part of standard care for many types of cancer. By allowing scientists and physicians to see what is happening in the body at a cellular level, molecular imaging provides unique information to assist in the detection, diagnosis, evaluation, treatment, and management of cancer.

Molecular imaging research is advancing and personalizing cancer care by uncovering new information on tumor properties and pathways that enable physicians to better visualize cancer cells within the body—and deliver therapy directly to the cancer. Certain NETs produce an abundance (called overexpression) of a specific cell feature called somatostatin receptors. Molecular imaging technologies use this cell feature to detect cancerous cells throughout the body and as a target for the delivery of therapy.

What is molecular imaging?

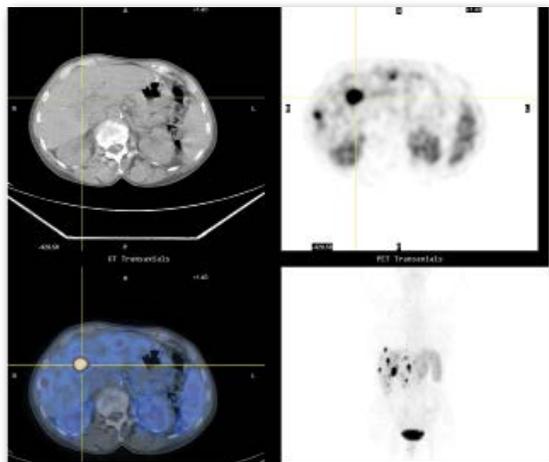
Molecular imaging is a type of medical imaging that provides detailed pictures of what is happening inside the body at the molecular and cellular levels. Where other diagnostic imaging procedures—such as x-rays, computed tomography (CT), and ultrasound—predominantly offer anatomical pictures, molecular 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, 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



⁶⁸Ga-DOTANOC PET/CT scans of 62-y-old woman with multiple hepatic secondary NET lesions (gastrinoma). At follow-up, patient showed partial response (PRRT plus somatostatin analogs).

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- 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 magnetic resonance (MR) 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 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 NETs?

Physicians are using molecular imaging to:

- diagnose and stage: an octreotide scan or Octreoscan™ is an imaging study used to find carcinoids and other types of NETs. The patient is injected with a drug called octreotide—a

synthetic form of the naturally occurring hormone somatostatin—that is chemically bound to the radiotracer indium-111. The radioactive octreotide attaches to tumor cells that have somatostatin receptors and is detected by a special camera that creates pictures showing where the tumor cells are in the body. Approximately 80 percent of NETs can be identified with this study, which is also called somatostatin receptor scintigraphy (SRS).

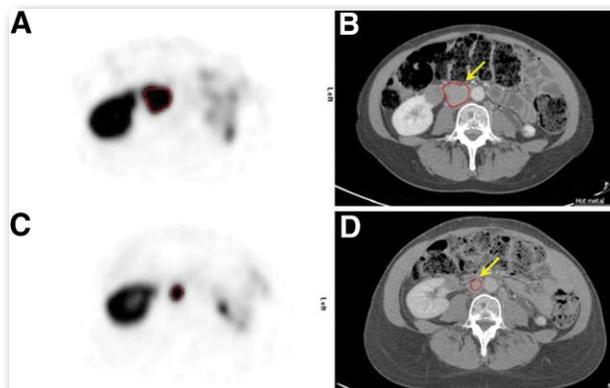
- deliver treatment: molecular radiotherapy (MRT) is a systemically administered, targeted therapy for cancer that delivers radiation at the cellular and molecular levels. In contrast to chemotherapy, wherein all proliferating cells are affected, MRT delivers radiation to only those cells that express cancer markers.

Peptide receptor radionuclide therapy (PRRT) is a highly targeted and effective form of MRT with minimal side effects for treating NETs with an abundance (or overexpression) of somatostatin receptors.

In PRRT, the patient receives an intravenous injection of a drug such as octreotide that is chemically bound to (or radiolabeled with) a radioactive material such as lutetium-177, yttrium-90, or indium-111. The radioactive octreotide attaches to somatostatin receptors on tumor cells, which are destroyed by the radiation.

What are the advantages of molecular imaging technologies for people with NETs?

- They can accurately evaluate the extent of disease.
- They can evaluate somatostatin receptors status prior to PRRT.
- They can provide information complementary to anatomic imaging.



PET (A) and CT (B) slices, compared with posttherapeutic PET (C) and CT (D) slices, showing abdominal lymph node metastasis (arrow) of patient 6. Both SUVmax (−55%) and SUV_T/S (−60%) decreased markedly after PRRT. This patient has been progression-free for 28 months.

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- PRRT may be more effective at the tumor cell level and cause fewer systemic side effects than external beam radiation or systemic chemotherapy.

Are PET and SPECT safe?

Many medical procedures have side effects and risks; the same is true of nuclear medicine diagnostic tests such as PET and SPECT (single photon emission computerized tomography). Each procedure takes a certain amount of radiation to perform appropriately. Used in the right way for the right patient at the right time, nuclear medicine is very safe—the benefits of the procedure very far outweigh the potential risks.

Are molecular imaging technologies covered by insurance?

Check with your insurance company for specific information on your plan.

What is the future of molecular imaging and NETs?

Researchers continue to evaluate different methods of PRRT. A multicenter, randomized, Phase III study comparing treatment with different versions of octreotide in patients with inoperable, progressive, somatostatin receptor–positive mid-gut carcinoid tumors is scheduled to soon begin enrolling patients in the United States.

Novel PET/CT radiopharmaceuticals targeting somatostatin receptors such as Ga-68 DOTATATE and Ga-68 DOTATOC are currently evaluated in the United States to assist in locating NETs for staging and restaging and managing the ongoing care of patients.

Where can I get more information?

To learn more, visit www.snmmi.org or ask your physician.

About SNMMI

The Society of Nuclear Medicine and Molecular Imaging (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 fact sheet 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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