Molecular Imaging and the Brain

Molecular imaging technologies are playing an important role in neuroimaging, a branch of medical imaging, by providing a "window" into the living brain. Where computed tomography (CT) and conventional magnetic resonance (MR) imaging provide important structural and anatomic information on the brain, molecular imaging (MI) technologies allow scientists to visualize and measure brain function.

Researchers are using MI to gain a better understanding of the brain and develop treatments for diseases and disorders including:

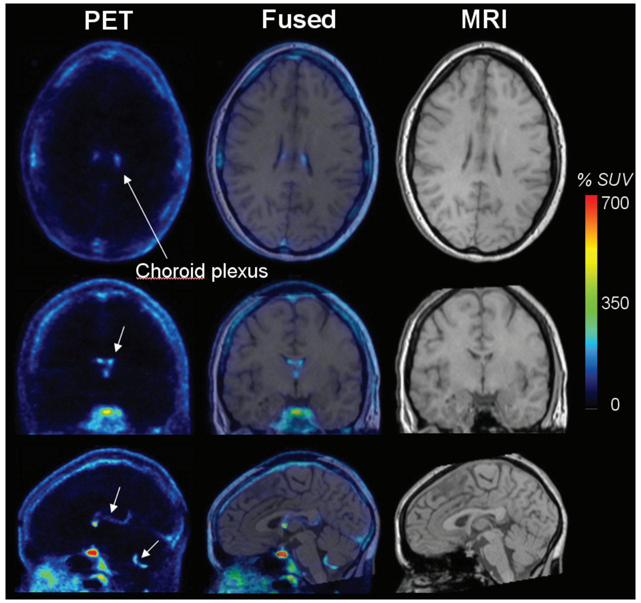
- brain tumors
- brain trauma
- stroke and transient ischemic attack (TIA)
- neurodegenerative diseases, such as Parkinson's disease, amyotrophic lateral sclerosis (ALS), multiple sclerosis, Huntington's disease, Alzheimer's disease and other forms of dementia
- epilepsy and other seizure disorders
- mental illnesses such as schizophrenia
- developmental disorders such as attention deficit disorder and autism spectrum disorders
- drug and alcohol addiction

Using MI technologies, research is underway to:

- understand relationships between specific areas of the brain and the functions they perform
- locate areas of the brain affected by neurological disorders
- develop new strategies to treat brain disorders
- develop new drugs and therapies
- find ways to identify individuals who may be at risk for brain disorders
- optimize patient care

What is molecular imaging, and how does it help people with brain disorders?

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, 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 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 normal areas. Similarly, the heart muscle cells that are affected stop contracting and 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 or 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. 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 in neuroimaging?

Positron emission tomography (PET) and single-photon emission-computed tomography (SPECT) are the most commonly used molecular imaging technologies for the brain.

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.

Because brain cells affected by dementia are less active, they consume, or metabolize less glucose than normal cells and will appear less bright on PET scans. Researchers are exploring the use of additional neuroimaging probes, including FDDNP and PiB, which bind to the abnormal plaques and tangles associated with Alzheimer's disease and allow them to be visualized on a PET scan.

In addition to dementia, PET scanning is used to diagnose other brain disorders that cause changes in metabolism and blood flow. For example, an area of decreased glucose metabolism may indicate the source of epilepsy. Decreased oxygen use and blood flow may indicate a stroke and abnormal patterns of glucose metabolism, and an accumulation of amino acid may signal the presence of a brain tumor.

How is PET performed?

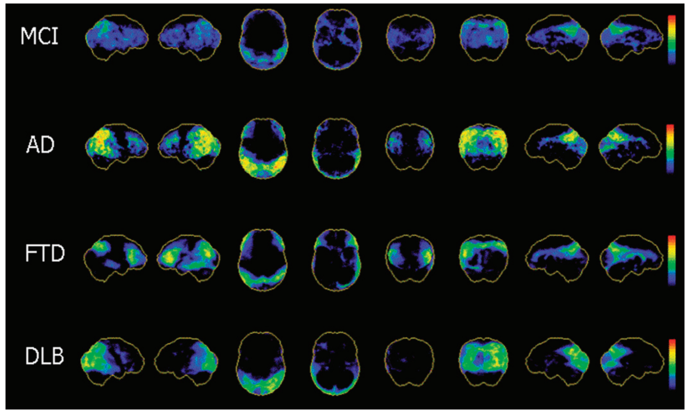
The procedure begins with an intravenous injection of a radiotracer, such as FDG, which usually takes between 30 and 60 minutes to distribute throughout the body. The patient is then placed in the PET scanner, where special detectors are used to create a three-dimensional image of the FDG distribution.

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 is SPECT?

A SPECT scan uses a gamma camera that rotates around the patient to detect a radiotracer in the body. Working with a computer, SPECT creates three-dimensional images of the area being studied. SPECT may also be combined with CT for greater accuracy.

Like PET, SPECT also can be used to differentiate different disease processes that produce dementia, and it is increasingly used for this purpose. SPECT also plays an important role in epilepsy imaging and the surgical treatment of severe epilepsy.



What are the advantages of molecular imaging for people with brain disorders?

- Molecular imaging allows metabolic activity to be directly visualized, not inferred. PET studies allow abnormal brain function to be detected before structural changes resulting from brain cell death can be seen on CT or MR imaging.
- PET scans are able to detect the early onset of neurological disorders such as Alzheimer's disease and are highly useful in detecting specific types of dementia, such as Alzheimer's disease and frontotemporal dementia, e.g., Pick's disease.
- PET and SPECT are highly accurate methods of pinpointing areas of the brain causing epileptic seizures and for evaluating surgery as a treatment option.
- Molecular imaging is very useful for guiding the management of brain tumors. Physicians use PET and SPECT studies to determine the extent of the disease, define the degree of malignancy and detect cancer recurrences.

Is molecular imaging covered by insurance?

Medicare and private insurance companies cover the cost of many molecular imaging technologies. Check with your insurance company for specific information on your plan.

What is role of molecular imaging in dementing disease?

- FDG-PET can help distinguish Alzheimer's disease from frontotemporal dementia
- SPECT dopamine imaging can identify dopaminergic deficiency in dementia with Lewy bodies and Parkinson's disease with dementia
- Amyloid PET can determine whether or not clinically significant amyloid pathology is present

What is the future of molecular imaging and neuroimaging?

Important research underway includes the National Institute on Aging's Alzheimer's Disease Neuroimaging Initiative (ADNI), which is following hundreds of cognitively healthy individuals and others with mild cognitive impairment (MCI) and early Alzheimer's disease (AD) over at least five years. Participants will undergo annual MRI and PET scans so that researchers can assess changes both in the normal aging brain and in individuals with MCI and AD.

By correlating these images with other test results from the study's participants, such as cognitive evaluations and fluid and urine samples, researchers hope to identify valuable biomarkers of the disease process.

While molecular imaging technologies are now moving into clinical practice and helping physicians to diagnose AD more accurately, there are other areas that will require more research, such as using PET to:

- Identify individuals who are at high risk of developing Alzheimer's disease
- Monitor the progress of the disease
- Assess patient response to drug treatment
- Contribute to the development of targeted drugs and therapies for dementia and Alzheimer's disease

About SNM

The Society of Nuclear Medicine (SNM) 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 17,000 members, SNM has been a leader in unifying, advancing and optimizing nuclear medicine and molecular imaging since 1954.

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