Molecular Imaging and Alzheimer’s Disease

Alzheimer’s disease (AD) is an irreversible, progressive brain disease that slowly destroys memory and thinking skills and, eventually, the ability to carry out the simplest tasks of daily living. Although treatment can help manage its symptoms, there is no cure for AD. The Alzheimer’s Association estimates that more than five million people are currently living with the disorder.

AD begins deep in the brain where healthy neurons begin to work less efficiently and eventually die. This process gradually spreads to the brain’s learning and memory center—the hippocampus—and other areas of the brain, which also begin to shrink. At the same time, beta-amyloid plaques and neurofibrillary tangles begin to spread throughout the brain. Scientists believe these brain changes begin 10-20 years before the signs or symptoms of the disease appear.

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 level. Where other diagnostic imaging procedures—such as x-rays, computed tomography (CT), magnetic resonance (MR) imaging 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 otherwise require more invasive procedures such as biopsy or surgery
• identify disease in its earliest stages and determine the exact location of a disease, 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
• select the most effective therapy based on the unique biologic characteristics of the patient and the molecular properties of a disease
• assess disease progression

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 diseases that cause 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 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. 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 Alzheimer’s disease?

Diagnosis of AD is currently a long process that may include a detailed patient history, physical and neurological exams, laboratory tests and a lengthy process of eliminating other possible causes of mental decline. Although experienced expert practitioners can diagnose the disease with up to 90 percent accuracy, a definitive diagnosis of AD is still only possible by autopsy following a patient’s death.

Molecular imaging technologies are now moving into clinical practice and helping physicians to diagnosis AD more accurately. In addition, researchers are exploring how positron emission tomography (PET) can more accurately and effectively manage patients with the disease. Early diagnosis will be critical in future therapeutic approaches.
What is PET?

PET is a molecular imaging technique involving 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 indicate that a high level of chemical activity or metabolism is occurring there, thus there may be a “bright” area on the scan. Areas of low metabolic activity appear less intense, less “bright.” 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, such as Pittsburgh compound B (PiB) and F-18 florbetapir (which has received FDA approval), that bind to the abnormal plaques associated with AD and allow them to be visualized on a PET scan.

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, who shares the results with the patient’s physician.

What are the advantages of PET for the brain?

- PET allows metabolic activity to be directly visualized.
- PET studies allow abnormal brain function to be detected before structural changes resulting from brain cell death can be seen on CT or MR images.
- PET is highly useful in detecting specific types of dementia, such as AD and frontotemporal dementia. In these disorders, early brain damage is too spread out, or diffuse, and may not impact brain volume or structure that is identifiable on routine CT or MR.

Is PET safe?

Many medical procedures have side effects and risks; the same is true of nuclear medicine diagnostic tests such as PET. 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.

Is PET covered by insurance?

Insurance companies will cover the cost of most PET scans; however, coverage for PET scans that measure brain amyloid plaques is not yet available. Check with your insurance company for specific information on your plan.

What is SPECT?

In single-photon emission-computed tomography (SPECT), a gamma camera 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 is the role of molecular imaging in neurodegenerative disease?

- FDG-PET can help distinguish AD from frontotemporal dementia.
- SPECT dopamine imaging can identify dopaminergic deficiency in Parkinson’s disease and related syndromes.
- Amyloid PET can determine whether or not clinically significant amyloid pathology is present in the brain.

What is the future of molecular imaging and Alzheimer’s disease?

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 AD over at least five years. Participants will undergo annual MR and PET scans so that researchers can assess changes in both the normal aging brain and in individuals with MCI and AD to better understand when and where in the brain degeneration occurs.

By correlating these images with other test results from the study’s participants, such as cognitive function tests and fluid samples, researchers hope to identify valuable biomarkers of the disease process. Researchers hope that this study and future initiatives using the ADNI database will create imaging and biomarker standards for measuring the success of potential treatments.
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 AD
• 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
• gain a better understanding of dementing disease, including its causes and progression

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 19,000 members, SNMMI has been a leader in unifying, advancing and optimizing nuclear medicine and molecular imaging since 1954.

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