Parkinson's disease (PD) is a brain disorder that leads to motor symptoms, such as shaking (tremors) and difficulty with walking, movement, and coordination. Patients with PD may also experience non-motor symptoms, such as changes in mood or cognition, sleep disturbance, and loss of the sense of smell. PD is a progressive and neurodegenerative disorder.

PD is the second most common neurodegenerative disorder after Alzheimer's disease. According to the Parkinson's Foundation, nearly one million people in the US will be living with Parkinson's disease (PD) this year. This number is expected to rise to 1.2 million by 2030. This is more than the
combined number of people diagnosed with multiple sclerosis, muscular dystrophy and Lou Gehrig's disease (or Amyotrophic Lateral Sclerosis, ALS).

- Approximately 90,000 Americans are diagnosed with PD each year.
- More than 10 million people worldwide are living with PD.
- Incidence of Parkinson's disease increases with age, but an estimated four percent of people with PD are diagnosed before age 50.
- Men are 1.5 times more likely to have Parkinson's disease than women.

A major finding in individuals with PD is the loss of dopamine-producing neurons that normally send signals that coordinate muscle movement, balance, and gait. As a result, the common motor symptoms of the disorder are:

- tremor, or trembling in hands, arms, legs, or chin
- rigidity, or stiffness
- slowness of movement and impaired balance and coordination

The symptoms develop on one side of the body in most patients, and later in the disease, affects the other side. The disease most often develops after age 50 and symptoms vary from patient to patient.

PD is the most common among a group of movement disorders called Parkinsonian syndromes, all of which have similar symptoms. Studies of brain tissues of persons with PD have shown typical microscopic findings of so-called Lewy bodies, which are made up of clumps of a protein called alpha synuclein. This is called typical or idiopathic PD. Lewy bodies are generally not present in the persons with atypical Parkinsonian syndrome, except for progressive supranuclear palsy, (PSP), in whom the symptoms may be caused by other types of neurodegeneration, side-effects of drugs, toxins, or strokes.

With no known cure for the disease, the goal of treatment through medication is to control symptoms. Patients may be prescribed L-DOPA, a drug that can be converted in the brain to dopamine. In some cases, surgery may be appropriate for patients whose disease no longer responds well to drugs. A therapy called deep brain stimulation (DBS) has now been approved by the US Food and Drug Administration. In DBS, electrodes are implanted in the brain and connected to a small electrical device.

**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) 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 the abnormality, 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:
• assess the function of nerves or brain tissue that use dopamine or other neurotransmitters that have become abnormal in PD
• make an accurate diagnosis, early in the disease, even before motor symptoms occur as images pick up changes in the brain as much as 5-10 years before typical motor problems manifest
• 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 on the image
• 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

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 and die off. 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. Two common clinically used molecular imaging technologies are positron emission tomography (PET) and single-photon emission computed tomography (SPECT).

**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.

**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 $^{18}$F-fluorodeoxyglucose (FDG), a compound derived from a simple sugar and a small amount of radioactive fluorine.

Once the 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 radiotracer is distributed in the area of the body being studied.

PET and SPECT scanners are most often combined with 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 kinds 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 or SPECT/CT study is able to provide detail on both the anatomy and the function of organs and tissues. This is accomplished by superimposing the precise location of abnormal metabolic activity (from PET or SPECT) against the detailed anatomic image (from CT).

**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. 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 far outweigh the potential risks.

**What molecular imaging technologies are used for Parkinson's disease?**
Because multiple neurological disorders mimic Parkinson's disease and there can be overlaps in multiple conditions, the disease can be difficult to diagnose. Scanning with SPECT and with the FDA-approved radiotracer $^{123}$iodoamphetamine injection (also called DaTscan) may allow for earlier and more accurate diagnosis of Parkinson's disease. A scan using DaTscan is able to detect dopamine transporters (DaTs), which are markers for the nerve cells which become impaired and die off. The distribution of DaTs is abnormal in patients with Parkinsonian syndromes but normal in patients with other conditions, such as essential tremor and Alzheimer's disease. Furthermore, DaTscan may be used to differentiate dementia with Lewy bodies from other types of dementia, such as
Alzheimer’s disease. In the US, the approved indication is to help differentiate essential tremor from tremor due to Parkinsonian syndromes.

PET scanning with the radiotracer fluorine-18-dihydroxyphenylalanine (F-18-DOPA) is a marker of dopamine activity of those same nerve cells as DaTs. By revealing a dopamine deficiency, F-18-DOPA PET scanning is used to help diagnose Parkinson’s disease and distinguish it from other neurological conditions. PET with F-18-DOPA has also been used to measure the effectiveness of dopamine-producing stem cell transplantation. F-18 DOPA is used in clinical trials and recently received FDA-approval.

What are the advantages of SPECT and PET for the brain?

- Dopamine SPECT or PET scans allow direct assessment of the activity of dopamine-producing neurons in the brain and will assist the clinician in making a differential diagnosis between Parkinson’s disease (where there is a decrease in brain dopamine-producing nerve cells) and essential tremor (where these scans are normal)
- PET allows metabolic activity to be directly visualized, not inferred
- SPECT or PET studies allow abnormal brain function to be detected before structural changes resulting from brain cell death can be seen on CT or MRI
- PET is highly useful in detecting specific types of dementia, such as Alzheimer’s disease and Pick’s disease, a type of frontotemporal dementia

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

While molecular imaging technologies such as SPECT PET are helping patients today, future research may have a role for SPECT or PET brain imaging to:

- monitor the progression of Parkinson’s disease
- assess patient response to drug, stem cell, or gene therapies that contribute to the development of targeted drugs and therapies for Parkinson’s disease
- make a very early diagnosis of Parkinson’s disease before the clinical emergence of symptoms to optimize the use of future therapies which will be focused on modifying the course of disease, preserving neurons and slowing down or stopping the progression of symptoms

Is molecular neuroimaging covered by insurance?

Check with your insurance company for specific information on your plan. Not all procedures described herein are covered by every insurance plan.
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.

The material presented in this pamphlet 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.