

PET Scans for Alzheimer's Disease

A View of Hope

Among the greatest hardships for the 4.5 million Americans afflicted with Alzheimer's disease and for their families are the unknowns prior to establishing a clinical diagnosis and the uncertainties about what to expect once a diagnosis has been confirmed. Recent advances in the area of neuroimaging, in PET (positron

emission tomography) imaging in particular, may however help to shed some light on Alzheimer's by offering hope of an earlier, more accurate diagnosis, as well as a way to monitor the progression of the illness and the benefits of treatment.

The Centers for Medicare and Medicaid Services (CMS) currently has approved reimbursement for a limited group of Medicare beneficiaries for PET scans. (See sidebar for specific indications.) Some private insurers also cover PET for Alzheimer's on a case-by-case basis.

IMAGING ALZHEIMER'S WITH PET

Traditionally, physicians have relied upon medical history, physical examination, neuropsychological evaluation, and interviews with family members and friends to detect Alzheimer's. But because Alzheimer's symptoms may resemble those of other neuropsychiatric disorders, reaching an early, accurate diagnosis and selecting appropriate treatment can be difficult. Previously, the only way to confirm an Alzheimer's diagnosis was through a brain biopsy or autopsy.

PET imaging enables physicians to visualize Alzheimer's disease by identifying rather characteristic patterns of regional brain hypometabolism in some patients. Unlike CT and MRI scans, which show physical structures, PET scans reveal the body's metabolic or chemical activity. For Alzheimer's, the ability to view changes in metabolic activity is critical, since early in the disease, structural changes are too minute to be seen on MRI or CT scans.

Before undergoing a PET scan, patients receive an injection containing a radiolabeled tracer in such a tiny quantity that it has no clinical side effects. For suspected Alzheimer's, individuals receive a tracer known as FDG, which contains radiolabeled glucose. After the injection, the distribution of this compound reflects

brain glucose metabolism. In Alzheimer's disease there is a characteristic pattern of abnormality.

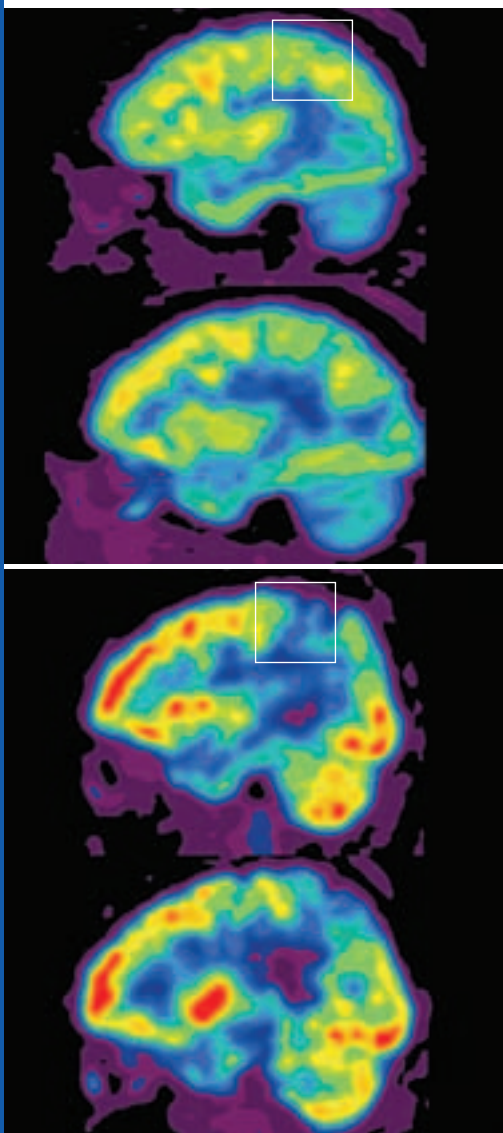
"PET for Alzheimer's has three major potential purposes," says **Ronald L. Van Heertum, MD**, *Professor of Radiology, Columbia University College of Physicians and Surgeons and Director, Columbia Kreitchman PET Center*. "First, it is a noninvasive tool to help establish an early diagnosis. Second, it is useful in determining differential diagnoses—identifying Alzheimer's versus other dementia disorders. Finally, in the future we may use it to evaluate response to therapy—seeing whether a patient is benefiting from a particular medication or treatment."

THE DIAGNOSTIC ROLE OF PET

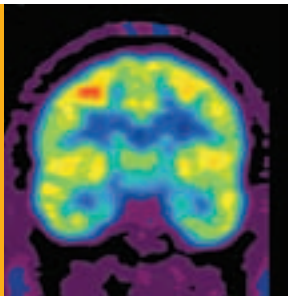
"Alzheimer's can be difficult to diagnose in its initial stages, when individuals have mild cognitive impairments and some memory problems," says **Davangere P. Devanand, MD**, *Professor of Clinical Psychiatry and Neurology, Columbia University College of Physicians and Surgeons*. "When added to other diagnostic techniques, and when read and interpreted by an expert radiologist, PET may help us achieve an earlier diagnosis."

According to **Yaakov Stern, PhD**, *Professor of Clinical Neuropsychology and Director of the Cognitive Neuroscience Division, Gertrude H. Sergievsky Center and the Taub Institute for Research on Alzheimer's Disease and the Aging Brain, Columbia University College of Physicians and Surgeons*, "PET can really have a beneficial role when the differential diagnosis is not clear. For example, when we're not sure if a patient has frontotemporal dementia versus Alzheimer's. If the symptoms are similar and the history is not quite clear, then PET may be able to help point us in the right direction."

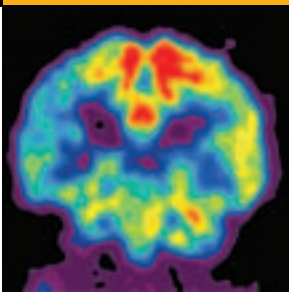
While researchers have yet to find a



The top PET scan shows a healthy brain, while the bottom scan shows Alzheimer's disease. The marked decrease in brain activity in the highlighted portion is consistent with Alzheimer's.



Left: PET scan of a healthy brain.
Below: PET scan of a brain with Alzheimer's disease.



cure for Alzheimer's, there are medications available—such as cholinesterase inhibitors and memantine—that may help to improve or stabilize symptoms for some patients. “We are trying to push the envelope back on making a diagnosis to an earlier point in time, when there is greater likelihood of a treatment response,” says Dr. Van Heertum. “Also, if we can identify the disease earlier, we can hopefully cut down on the number of tests and the associated anxiety and stress for patients and their families. It would be very helpful to be able to establish a diagnosis at a time when patients are still capable of making decisions and can take an active role in planning their own future.”

PET AND ALZHEIMER'S RESEARCH

Further advances in PET for Alzheimer's may be on the horizon. Dr. Stern has spearheaded a novel technique of identifying Alzheimer's disease through covariance patterns—a statistical analysis of relationships between areas of the brain. Using this analytic approach to compare brain PET scans of patients with early and mid-stage Alzheimer's with those of healthy elderly individuals, he and his colleagues found a pattern expressed in all the participants, but to a significantly greater degree in the Alzheimer's patients. In subsequent analysis, working in collaboration with Dr. Devenand, the investigators found that people who showed some cognitive problems and expressed a pattern more like an Alzheimer's patient were more likely to show cognitive change over time. “We think this may be a way to use the PET data to diagnose Alzheimer's disease very, very early,” he says. He and his

colleagues are now conducting additional research to validate these results.

In another study of elderly patients, researchers at the Columbia Kreitchman PET Center are investigating how

much beta amyloid is present in the brain during the early stage of Alzheimer's disease. Excessive amounts of beta amyloid protein in the brain are a classic diagnostic feature of the illness and considered a critical part of the disease process. Using PET, they are comparing brain images of people with normal memory, people with mild cognitive impairment but not Alzheimer's disease, and people with early, mild Alzheimer's. “Measuring beta amyloid may allow physicians to detect Alzheimer's disease much earlier—before patients develop memory deficits,” explains **J. John Mann, MD**, *Professor of Radiology and Psychiatry* at Columbia University College of Physicians and Surgeons. When it is complete, this study will provide a baseline for a second stage of research on drugs designed to reduce levels of beta amyloid in patients with Alzheimer's. These drugs have the potential not only to arrest the progression of the illness but to save some parts of the brain that have not yet been irreversibly damaged.

PET may eventually help to advance the development of new Alzheimer's medications by allowing researchers and physicians to view how the brain responds to treatments. “Since PET gives us the ability to measure very small concentrations of chemicals, it is uniquely suitable for the study of neurotransmitters, enzymes, receptors, and other proteins in the brain,” says Dr. Mann. “By examining these individual components we can understand the impact of diseases

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PET FOR ALZHEIMER'S: MEDICARE COVERAGE

The approved CMS criteria for Medicare coverage of FDG-PET for Alzheimer's include the following:

- Six months of documented cognitive decline from unclear origin
- Comprehensive clinical evaluation by a physician experienced in the diagnosis and assessment of dementia
- Scan performed in an accredited PET facility and the reading of the scan conducted by an expert with substantial experience in interpreting such scans in the presence of dementia
- A SPECT scan or previous FDG-PET scan has not been obtained for the same indication

such as Alzheimer's on the brain, as well as the effect of potential new treatments.”

By improving the ability of researchers to evaluate medications, PET may help reduce the cost associated with developing new therapies while helping to determine optimal doses. “Currently we use animal models to initially test new medications and have to guesstimate on efficacy and dosages levels once we move to clinical trials with people,” Dr. Mann continues. “With PET, we can use a tracer to specifically label our targets, so we will know precisely how much of a given medication is required for the drug to work. And we will be able to do this at a fraction of the cost, in a fraction of the time, and with a fraction of the number of clinical trial patients.”

For more information on PET for Alzheimer's disease, please contact the Columbia Kreitchman PET Center at 212.923.1555.

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