

**Initial Public Comments for  
PET and Other Neuroimaging Devices for Suspected Dementia CAG-00088R  
Comment Period March 15-31, 2004**

**Comment #1:**

Submitter: Steve Flitman, MD

Organization:

Date: 5/2/04 5:45 PM

Comment:

I am a neurologist specializing in AD in the Phoenix area, and to my knowledge the only one. I see 1500 patients annually with Alzheimer's and related disorders. I do not use FDG-PET routinely, but I feel it can be beneficial in exactly the way that has been requested by UCLA: to distinguish other forms of dementia from AD. This happens to be a big problem when it comes to illnesses like Pick's disease (rare) and Lewy Body disease (probably very common, but hard to diagnose except clinically). In such cases, FDG-PET has proven invaluable because no other objective tests exist. Thanks for all your hard work.

**Comment #2:**

Submitter: Anand Kumar, MD

Organization: President, American Association for Geriatric Psychiatry

Date: 4/15/04

Comment:

The following is a response to the recent CMS-NIA questions on the use of PET in the diagnosis of Alzheimer Disease. I represented the American Association for Geriatric Psychiatry at this meeting. I hope this information is useful in determining the utility of FDG PET in a dementia work up.

Q: What minimal services must be performed and documented as pre-requisites for ordering a PET scan?

A: A complete dementia work up that includes a comprehensive medical exam that includes a neurological exam, a psychiatric exam, relevant laboratory testing and a neuropsychological battery (may be a condensed battery). A structural scan (CT/MRI) has also come to represent the standard of care in a dementia work up. In special circumstances, a PET FDG may provide more information than an MRI/CT scan, but that needs to be considered on an individual basis.

Q: Is a medical history alone sufficient to ascertain six months of cognitive decline or is actual observation by a clinician necessary to assess and document a decline over such a period prior to ordering a PET

scan?

A: When an informed/reliable care giver is available, collateral information is often adequate to document 6 months of decline. When reliable collateral sources are not available, actual observation may be needed.

Q: What qualifications must a practitioner have to be considered "experienced in the diagnosis and assessment of dementia"?

A: THIS IS A VERY IMPORTANT ISSUE - PHYSICIANS TRAINED IN GERIATRICS ARE CRITICAL IN THIS REGARD. THIS INCLUDES, GERIATRIC INTERNISTS, GERIATRIC PSYCHIATRISTS AND NEUROLOGISTS WITH TRAINING IN THE AREA OF COGNITIVE DISORDERS. FAMILY PRACTITIONERS WITH INTEREST/EXPERTISE IN GERIATRICS WILL ALSO QUALIFY. PLEASE NOTE THAT GENERAL INTERNISTS, NEUROLOGISTS AND PSYCHIATRISTS MAY NOT HAVE SUFFICIENT EXPERTISE FOR A HIGH QUALITY WORK UP. ADEQUATE TRAINING IN GERIATRICS IS CRITICAL.

Q: What type of facility or setting is likely to offer the knowledgeable and experienced interdisciplinary staff needed to conduct a comprehensive assessment and render an accurate clinical diagnosis of dementia? Can a minimum set of facility criteria be identified that provide assurance that a comprehensive assessment will be performed? What set of skills and professions must be assembled on the interdisciplinary team?

A: The precise setting is less critical than the qualifications/background of the physician. A broad spectrum of facilities ranging from academic medical centers to private physician offices will qualify provided the physician has the expertise and background needed for a dementia assessment. It is important to get a comprehensive geriatric assessment with interdisciplinary input before making a final clinical diagnosis.

Q: A comprehensive workup utilizing the NINCDS-ADRDA criteria for clinical diagnosis of Alzheimer's disease qualifies the likelihood of Alzheimer's disease as "definite," "probable," "possible," or "uncertain". Should PET be ordered only when the comprehensive assessment results in an uncertain diagnosis?

A: YES. PET scans should be reserved for cases where the diagnosis remains unclear after a complete dementia work up (see response to question 1) and the physician is convinced that a metabolic map of the brain. i.e an FDG PET scan will be of considerable benefit in making a precise diagnosis. An additional requirement might be that a PET facilitated diagnosis will alter the management of a particular case. A PET scan should NOT be part of a routine dementia work up. It is far too expensive for that.

Q: What are the key differential diagnoses among neurodegenerative causes of dementia (e.g., frontotemporal dementia vs. AD) that PET could reasonably be expected to help clarify after an experienced clinician or team has completed an assessment? What are those clinical situations for which other imaging or other tests would be better indicated (e.g., distinguishing AD from mixed AD- multi-infarct dementia)?

A: An MRI scan with a good history and neurologic/medical exam may better than a PET scan in assessing vascular burden and thereby distinguishing AD from MID. A comprehensive psychiatric exam is necessary in order to distinguish clinically between AD and depression in the elderly (which can also have cognitive correlates). Once again, the role of PET in the differential diagnosis cannot/should not be decided a priori. It needs to be determined on a case by case basis.

Q: What are the minimal educational requirements for staff performing and interpreting the PET scans? How should test performance and interpretation be standardized? What accreditation requirements must facilities performing PET scans for AD meet?

A: This will vary. A nuclear medicine physician/Radiologist with expertise in this area or a physician with geriatric experience (see response to question 3) who has received special training (work shop etc.) in reading PET scans in the elderly may have the required expertise. No such formal training/certification mechanism is in place and setting one up is likely to be cumbersome.

**Comment #3:**

Submitter: Arthur Kowell, MD, Ph.D.

Organization: David Geffen School of Medicine, UCLA

Date: March 31, 2004

Comment:

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- 1) performance and documentation of a standard comprehensive medical history and physical examination, including documented neurological examination,
- 2) assessment of mental status and activities of daily living,
- 3) laboratory tests – serum electrolyte (Na<sup>+</sup>, K<sup>+</sup>, Cl<sup>-</sup>, CO<sub>2</sub>), BUN, Cr, glucose, ALT and TSH determinations; CBC, including Hct, MCV and MCHC,
- 4) structural neuroimaging (CT or MRI)

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Minimal sufficient documentation of decline is constituted by one of the following:

- 1) actual longitudinal observation by a clinician over a period extending at least six months,
- 2) a history obtained and deemed reliable by clinician, from interviewing patient and/or close contact(s) of patient, which documents progressive decline over a period of at least six months preceding the time of clinician's evaluation,
- 3) a combination of the above, amounting in total to at least six months of decline documentable by the summed periods of time represented by 1) and 2)

\* What qualifications must a practitioner have to be considered "experienced in the diagnosis and assessment of dementia"?

Acceptable qualifications are:

- 1) Board-eligibility or Board-certification in Neurology, Psychiatry, Internal Medicine or Family Practice, as experience in making this diagnosis is an integral part of the training for each of these specialties, or
- 2) Physicians with other specialty training may be appropriate referrers, if they can document that in the normal course of their professional activity they are called upon to make this kind of assessment concerning dementia (e.g., have records showing that patients are referred to them for that evaluation, or that patients present to the physician for the purpose of being evaluated for cognitive/behavioral complaints)

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Acceptable types of facilities:

- 1) General hospital,
- 2) Psychiatric hospital,
- 3) Outpatient clinics of physicians qualified by criteria described

above

The professional(s) carrying out the required comprehensive assessment must reflect the following set of skills:

- 1) trained in evaluation of dementia, including conducting a medical history and physical examination, neurological examination, assessment of mental status and activities of daily living – as occurs in the professional training of neurologists, psychiatrists, internists and family practice physicians,
- 2) trained and licensed to order and interpret the results of laboratory and neuroradiology tests outlined above.

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PET should be ordered only when the comprehensive assessment does not result in a “definite” diagnosis. It is clear from the primary peer-reviewed literature that the presence of Alzheimer’s disease is “uncertain” in many patients who meet NINCDS-ADRDA criteria of “possible AD” or “probable AD.” For example, in the one peer-reviewed article to examine clinical diagnostic accuracy for evaluation of early dementia, presenting data that met the American Academy of Neurology designation of “Class I” quality of evidence<sup>1</sup>, among all patients who were subsequently proven by autopsy to NOT have AD, 45% of those patients actually met NINCDS-ADRDA criteria for “probable AD”<sup>2</sup> -- and the specificity of “possible AD” was even lower.

\* What are the key differential diagnoses among neurodegenerative causes of dementia (e.g., frontotemporal dementia vs. AD) that PET could reasonably be expected to help clarify after an experienced clinician or team has completed an assessment? What are those clinical situations for which other imaging or other tests would be better indicated (e.g., distinguishing AD from mixed AD- multi-infarct dementia)?

Key differential diagnoses which PET will help clarify after assessment by an experienced clinician or team are:

- 1) AD vs. Frontotemporal dementia,
- 2) Frontotemporal dementia vs. Dementia with Lewy bodies,
- 3) AD vs. non-neurodegenerative causes of progressive dementia,
- 4) Frontotemporal dementia vs. non-neurodegenerative causes of progressive dementia,
- 5) Dementia with Lewy bodies vs. non-neurodegenerative causes of progressive dementia

Differential diagnoses for which other methods of distinguishing are more suitable are:

- 1) AD, Frontotemporal, or other neurodegenerative dementia vs. untreated depression,
- 2) AD, Frontotemporal, or other neurodegenerative dementia vs. untreated substance abuse or adverse effects of other pharmacologic agents,
- 3) AD, Frontotemporal, or other neurodegenerative dementia vs. untreated thyroid disease,
- 4) AD, Frontotemporal, or other neurodegenerative dementia vs. untreated nutrient deficiency

\* What are the minimal educational requirements for staff performing and interpreting the PET scans? How should test performance and interpretation be standardized? What accreditation requirements must facilities performing PET scans for AD meet?

Minimal educational/certification requirements for staff performing the PET scans:

Certified Nuclear Medicine Technologist (CNMT)

Minimal educational/certification requirements for staff interpreting the PET scans include at least one of the following:

- 1) American Board of Nuclear Medicine (ABNM) certification,
- 2) American Board of Radiology (ABR) certification, with ABR special certification in Nuclear Medicine,
- 3) Neurologist, psychiatrist, or radiologist with current eligibility to bill CMS for interpretation of brain CT or MRI, plus documentable specific training in interpretation of brain PET scans

For all kinds of Nuclear Medicine tests, professional guidelines for performance and interpretation of diagnostic studies are often issued (e.g, by the Society for Nuclear Medicine), but there is no official specialty-wide standardization requirements for performance of any Nuclear Medicine study – nor should there be, as performance standards are tailored to the specific conditions and equipment present at each site, and it is ultimately the responsibility of each facility and physician to assure performance and interpretive quality, and maintain professional accreditations.

**Comment #4:**

Submitter: Everett Gayle, MD

Organization: Radiology Associates

Date: March 31, 2004

Comment:

I work with the Radiology Associates group in Corpus Christi, Texas as their PET medical director. We have evaluated several patients in their fifties with cognitive dysfunction sent by neurologists worrisome for early Alzheimer's Disease. One was a classic case and another had frontotemporal dementia. Both had similar presentations but PET established very different treatment options based on the underlying process.

Many of your questions are clinically based outside of our imaging expertise. However, we are heartened by your call for public input and therefore offer our two cents.

The referral for PET should come from a Neurologist who is experienced in diagnosing dementia and has performed the necessary H&P, neurological exams and mental status testing, etc. A minimum of a head CT should also be performed prior to PET AD brain imaging, but a brain MRI would be desirable. A neurologist's direct observation of cognitive decline for six months seems excessive. He should be able to trust a referring colleague's medical history alone and not further delay potential diagnosis and drug therapy. I believe the neurologist's office alone should be able to request AD PET brain studies rather than an interdisciplinary team. The standard should not be excessively high which will deny care to many who need help particularly in smaller communities. A local family practice doctor or physician's assistant should not order these tests, but a full work-up for dementia by a neurologist should suffice. Would the neurologist require additional certification to allow him to order PET brain studies for AD? I again think that is excessive, as their training alone should qualify them as the gatekeeper.

PET brains for AD should be available for any category of NINCDS-ADRDA other than definite if the neurologist desires additional confirmation to justify use of AD pharmaceuticals.

The key diagnoses would include Alzheimer's disease, frontotemporal dementia, dementia with Lewy bodies, mild cognitive impairment and depression. Other dementias have movement disorders that should be distinguishing at H&P by the neurologist including Huntington's disease, progressive supranuclear palsy and corticobasal degeneration.

Cerebrovascular disease should be identified at the time of anatomic imaging (CT or MRI). Mixed forms would be more difficult to tease out. If the other mixed disease does not have good treatment available, one would question the utility of aggressive pursuit of an Alzheimer's diagnosis. AD can be distinguished from frontotemporal dementia and depression at PET imaging. Mild cognitive impairment should have a normal brain pattern at PET as well. I do not have adequate knowledge of the PET findings of dementia with Lewy bodies.

The staff performing the PET scans should be trained and certified as PET techs. Interpreting staff should be Nuclear Medicine or Radiology board certified physicians with PET training. Additional web based CME could be

required for interpreters to ensure adequate knowledge of PET dementia differentials in order to receive CMS payment. This should be sufficient in my view.

**Comment #5:**

Submitter: Michael Reitermann  
Organization: Siemens Medical Solutions USA, Inc.  
Date: March 31, 2004  
Comment:

Thank you very much for the posted questions. Please see my answers:

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\* What type of facility or setting is likely to offer the knowledgeable and experienced interdisciplinary staff needed to conduct a comprehensive assessment and render an accurate clinical diagnosis of dementia? Can a minimum set of facility criteria be identified that provide assurance that a comprehensive assessment will be performed? What set of skills and professions must be assembled on the interdisciplinary team?

Acceptable types of facilities:

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quality of evidence<sup>1</sup>, among all patients who were subsequently proven by autopsy to NOT have AD, 45% of those patients actually met NINCDS-ADRDA criteria for "probable AD"<sup>2</sup> -- and the specificity of "possible AD" was even lower.

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**Comment #6:**

Submitter: Javier Villanueva-Meyer, MD

Organization: River Oaks Imaging

Date: March 31, 2004

Comment:

- What are the minimal educational requirements for staff performing and interpreting the PET scans? How should test performance and interpretation be standardized? What accreditation requirements must facilities performing PET scans for AD meet?

-The physician interpreting studies probably oversees the clinical facility and is key for proper performance and reading of the scans. He/she should be American Board of Nuclear Medicine Certified, or American Board of Radiology with a Fellowship in PET. Alternatively you may have radiologists interested in reading brain PET scan, I suggest a minimum of 20 hours of brain PET CMEs and reading 10 supervised cases. These CME requirements are not too difficult to obtain. The diagnosis rendered can be critical for patient management therefore I suggest minimum training and experience standards as described above.

-Regarding equipment, most dedicated full ring BGO, LSO or GSO crystal PET scanner provide good images. Imaging doses should range from 5 to 10 mCi F18DG. Recent accreditation programs from the ICANL -Intersocietal Commission for the Accreditation of Nuclear Medicine Laboratories (ICANL, [www.icanl.org](http://www.icanl.org)) or the American College of Radiology (ACR, [www.acr.org](http://www.acr.org)) are available for PET. They may be useful in continuous quality improvement tool. The first 6 questions address selection criteria for performing the study, I'll try to be simple here

-a minimum of 6 months cognitive decline must be documented by preferentially a board certified neurologist.

-In the uncertain category FDG PET imaging is very valuable for diagnosis

-In the probable or possible categories it has diagnostic value also, as a significant number of patient do not have AD

-In the definite category it has value to monitor changes as a response to therapy. These occur slow and you could limit studies to no closer than 6 months apart.

I believe PET in AD disease diagnosis will benefit patients, families and caregivers.

**Comment #7:**

Submitter: Jeffrey Cummings, MD

Organization: David Geffen School of Medicine, UCLA

Date: March 31, 2004

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Small, Gary, M.D., Parlow-Solomon Professor on Aging, Professor of

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Ostheimer, Berwick, Team Leader, Nuclear Medicine, Gulfport Memorial Hospital

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2. Lim A, Tsuang D, Kukull W, et al. Clinico-neuropathological correlation of Alzheimer's disease in a community-based case series. J Am Geriatr Soc. 1999; 47:564-569.

**Comment #8:**

Submitter: Soo Borson, MD

Organization: University of Washington Dementia Care Clinic & Alzheimer's Disease Research Center Satellite

Date: March 31, 2004

Comment:

What minimal services must be performed and documented as pre-requisites for ordering a PET scan?

1) Completion and documentation of a standard comprehensive medical history and physical examination, including documented neurological examination. The history should include information from a knowledgeable informant about the patient's cognitive and functional abilities and changes over time.

2) Evaluation of mental status using accepted cognitive screening instruments, neurobehavioral symptoms, and measures of activities of daily living.

Formal neuropsychological batteries should have been considered and the clinical decision-making process as to whether such testing is indicated should be documented in the medical record.

3) Screening laboratory tests to search for systemic factors that may modify clinical presentation. These include a comprehensive metabolic panel (electrolytes, liver and kidney screens, blood sugar, calcium), thyroid screen (free T4 and TSH), and CBC, including Hct, MCV and MCHC.

4) Structural neuroimaging (MRI preferred).

5) Family history of dementing diseases should be asked about, though negative response is much less useful than positive.

Is a medical history alone sufficient to ascertain six months of cognitive decline or is actual observation by a clinician necessary to assess and document a decline over such a period prior to ordering a PET scan?

Minimal sufficient documentation of decline is constituted by one of the following:

1) Actual longitudinal observation by a clinician over a period extending at least six months. This is often impractical for specialists, who are consulted when a cognitive problem is already suspected or obvious, and not helpful for primary care physicians, as they miss 40-75% of demented individuals.

2) A cognitive history, based on a direct interview of the patient and a knowledgeable informant, usually a family member. These interviews must document progressive decline over the six months prior to the clinical examination. (This would exclude, e.g., sudden declines 5 years ago in connection with a major cardiovascular event without any subsequent decline).

What qualifications must a practitioner have to be considered "experienced in the diagnosis and assessment of dementia"?

Acceptable qualifications include:

1) Board-eligibility or Board-certification in Neurology, Psychiatry, Internal Medicine or Family Practice, with documented experience in making this diagnosis, or subspecialty fellowship training and board eligibility or certification in Geriatrics (geriatric psychiatry, geriatric medicine or family practice).

2) Geriatric nurse practitioners may qualify.

What type of facility or setting is likely to offer the knowledgeable and experienced interdisciplinary staff needed to conduct a comprehensive assessment and give an accurate clinical diagnosis of dementia? Can a minimum set of facility criteria be identified that provide assurance that a comprehensive assessment will be performed? What set of skills and professions must be assembled on the interdisciplinary team?

Acceptable types of facilities can include general hospitals, neuropsychiatric hospitals, and certain clinics operated by clinicians who meet the provider criteria specified earlier.

Preferred would be settings known for expertise in dementia as demonstrated by the qualifications of the professionals who conduct the evaluations:

1) Documented training in evaluation of dementia, including conducting a medical history and physical examination, neurological examination, assessment of mental status and activities of daily living - as occurs in the professional training of neurologists, psychiatrists, internists and family practice physicians, as well as certain nurse practitioners and physician assistants working closely with one of these.

2) Documented training and licensing to order and interpret the results of the requisite dementia workup studies.

Should PET be ordered only when the comprehensive assessment results in an uncertain diagnosis?

No. PET should be ordered when the comprehensive assessment does not result in a "definite" diagnosis. The NINCDS-ADRDA and all other diagnostic criterion sets that currently exist lack sufficient specificity. That is, they would classify many patients as having "AD" who in fact have other dementias that follow a slowly progressive downhill course.

PET imaging could make a powerful contribution to the knowledge required to revise these criteria for greater specificity during life.

What are the key differential diagnoses among neurodegenerative causes of dementia (e.g., frontotemporal dementia vs. AD) that PET could reasonably be expected to help clarify after an experienced clinician or team has completed an assessment? What are those clinical situations for which other imaging or other tests would be better indicated (e.g., distinguishing AD from mixed AD- multi-infarct dementia)?

Key differential diagnoses which PET will help clarify after assessment by an experienced clinician or team are:

- 1) AD vs. Frontotemporal dementia.
- 2) Frontotemporal dementia vs. Dementia with Lewy bodies.
- 3) AD vs. non-neurodegenerative causes of progressive dementia.
- 4) Frontotemporal dementia vs. non-neurodegenerative causes of progressive dementia.
- 5) Dementia with Lewy bodies vs. non-neurodegenerative causes of progressive dementia.
- 6) AD vs Dementia with Lewy bodies.
- 7) AD vs microvascular multi-infarct dementia.
- 8) Dementia with Lewy bodies vs microvascular multi-infarct dementia

What are the minimal educational requirements for staff performing and interpreting the PET scans? How should test performance and interpretation be standardized? What accreditation requirements must facilities performing PET scans for AD meet?

1) Minimal educational/certification requirements for staff performing PET scans: Acquisition of training as a Certified Nuclear Medicine Technologist.

2) Minimal educational/certification requirements for staff interpreting the PET scans include at least one of the following:

- 1) American Board of Nuclear Medicine (ABNM) certification,
- 2) American Board of Radiology (ABR) certification, with ABR special certification in Nuclear Medicine and experience in brain studies,
- 3) Neurologist, psychiatrist, or radiologist with current eligibility to bill CMS for interpretation of brain CT or MRI, plus documentable specific training in interpretation of brain PET scans

**Comment #9:**

Submitter: Kenneth Sakauye, MD  
Organization: Louisiana State Health Sciences Center  
Date: March 31, 2004  
Comment:

I want to express my support for coverage by CMS for PET scans for early diagnosis of Alzheimer's Disease. I feel the evidence is strong that PET changes are more sensitive than existing tests for early diagnosis, when patients are still in a phase that is currently labeled mild cognitive impairment or have an uncertain diagnosis. The importance of early diagnosis is becoming more and more important in deciding about preventive treatment to slow further decline, as well as stopping unnecessary treatment or labeling of patients as having AD prematurely (which is stigmatizing for the patient and sometimes has legal implications).

What minimal services must be performed?

I feel evidence of a comprehensive history and medical examination that includes assessment of mental status and activities of daily living, course of changes, a documented neurological examination (not necessarily by a neurologist), and laboratory tests. In addition, structural imaging should be done as a prerequisite for PET (MRI or CT scan) and the diagnosis is still uncertain.

Is a six month observation by a clinician necessary prior to ordering a PET scan?

No. I believe that a history that is deemed reliable by the clinician, which documents progressive decline over a period of at least six months preceding the time of the clinician's evaluation, and a comprehensive medical evaluation that confirms a possible AD diagnosis by NINCDS-ADRDA criteria would be sufficient.

What Qualifications must a practitioner have?

Since cost is driving a way to restrict access to those whose diagnosis is still in doubt after a thorough examination, I think the requirement for a referring doctor should be someone who is Board certified in Neurology or Psychiatry. The rationale is that these patients will have been referred to a specialist for help since the diagnosis is equivocal.

What type of facility or setting is likely to offer the knowledgeable and experienced interdisciplinary staff needed to conduct a comprehensive assessment? Can a minimum set of skills and professions be assembled? I think a certification process should be created for facilities requesting use of PET for AD. Certification would insure that a person administering and interpreting the PET results is certified by the American Board of Nuclear Medicine (ABNM) or the American Board of Radiology (ABR), with special certification in nuclear medicine to interpret the PET scan, and that there is a multidisciplinary team led by a Board Certified Neurologist or Psychiatrist (preferably with Board Certification in Geriatric Psychiatry).

What are the key differential diagnoses?

PET should help the experienced clinician or team differentiate between Alzheimer's Dementia, Frontotemporal dementia, Dementia with Lewy bodies, and non-neurodegenerative causes of progressive dementia.

**Comment #10:**

Submitter: Stan Boling  
Organization: Alzheimer's Association  
Date: March, 30, 2004  
Comment:

I am responding from two different perspectives:

1) as President of the Board of Directors of the East Tennessee Chapter of the Alzheimer's Association

2) as Vice President of senior services for an integrated health care provider in East Tennessee

As to what qualification must a practitioner have to be considered experienced in the diagnosis and assessment of dementia:

An MD with a board certification in neurology, gerontology or gero-psychiatry should be able to order the PET scan as part of their assessment and accurate diagnosis under consultation with a trained and qualified radiologist.

What type of facility or setting is likely to offer the knowledgeable and experienced, interdisciplinary staff needed to conduct a comprehensive assessment and render an accurate clinical diagnosis of dementia:

- \* Geriatric inpatient psychiatric facility or adult psychiatric facility
- \* Specialty physician's private practice including psychiatry and gerontology
- \* Geriatric outpatient assessment programs which have board certified geriatric psychiatry or gerontology.
- \* Inpatient hospital or SNF with proper consultation with outreach behavioral professionals/neurology
- \* Day Hospital programs or structured outpatient with assessment by qualified MDs as noted above

Should PET be ordered only when the comprehensive assessment results in an uncertain diagnosis:



The comprehensive assessment for progressive cognitive impairment, especially in the mild to moderate stages, may remain inconclusive as related to the ultimate diagnosis.

It is essential to differentiate the diagnosis from other causes as soon as possible in light of new pharmaceutical treatments. Even waiting 6 months to observe a decline in cognition is too long to wait to start a combined drug regimen. "Save the Brain" means timely intervention.

Early and specific diagnosis coupled with early intervention reduces the amount of money CMS will have to pay as a result of early institutionalization and dependence on long-term care and community service agency support. This savings should easily offset the expense of one PET scan.

It might be essential to limit the number of PET scans to one in a life-time except for clearly documented exceptions which are pre-authorized. For instance, if a PET scan should be negative for Alzheimer's changes in an early stage, but progressive dementia and otherwise clinical picture of Alzheimer's continues to manifest.

**Comment #11:**

Submitter: Joy Szilagyi

Organization: Sparrow Hospital

Date: March 30, 2004

Comment:

On behalf of Sparrow Hospital and Drs. Annette White and Michael Ouimette I am responding to the questions open for public input for Medicare Coverage for PET for Alzheimer's.

1) What minimal services must be performed and documented as pre-requisites for ordering a PET scan?

Response: Patient should be evaluated by a neurologist. Appropriate laboratory studies and CT or MRI.

2) Is medical history alone sufficient to ascertain six months of cognitive decline or is actual observation by a clinician necessary to assess and document a decline over such a period prior to ordering a PET scan?

Response: Medical history, after appropriate work-up as above.

3) What qualifications must a practitioner have to be considered "experienced in the diagnosis and assessment of dementia"?

Response: Neurology or Psychiatry

4) What type of facility or setting is likely to offer the knowledgeable and experienced interdisciplinary staff needed to conduct a comprehensive assessment and render an accurate clinical diagnosis of dementia? Can a minimum set of facility criteria be identified that provide assurance that a comprehensive assessment will be performed? What set of skills and professions must be assembled on the interdisciplinary?

Response: See above responses.

5) A comprehensive workup utilizing the NINCDS-ADRDA criteria for clinical diagnosis of Alzheimer's disease qualifies the likelihood of Alzheimer's disease as "definite," "probable," "possible," or "uncertain". Should PET be ordered only when the comprehensive assessment results in an uncertain diagnosis?

Response: No. PET should be used in the diagnosis of Alzheimer's disease anytime another explanation for dementia has not been found.

6) What are the key differential diagnoses among neurodegenerative causes of dementia (e.g., frontotemporal dementia vs. AD) that PET could reasonably be expected to help clarify after an experienced clinician or team has completed an assessment? What are those clinical situations for which other imaging or other tests would be indicated (e.g., distinguishing AD from mixed AD- multi-infarct dementia)?

Response: Depression (psychiatry evaluation), Organic syndromes (lab tests), Multi-Infarct (CT or MRI), Dementia

7) What are the minimal educational requirements for staff performing and interpreting the PET scans? How should test performance and interpretation be standardized? What accreditation requirements must facilities performing PET scans for AD meet?

Response: Staff performing the scan should be registered in Nuclear Medicine with either the Nuclear Medicine Technology Certification Board (NMTCB) or the American Registry of Radiologic Technologists (ARRT). Physicians interpreting the scans should hold certification with the American Board of Nuclear Medicine, certification by American Board of Diagnostic Radiology or 200 hours of classroom and laboratory physics (radiopharmaceutical handling, application and safety) including hands-on training, 500 hours supervised training under a licensed user including specific training, and 6 months in a Nuclear Medicine Training program approved by ACGME. (PET interpreter has to be a licensed user).

**Comment #12:**

Submitter: Landis Griffeth, MD, Ph.D.  
Organization: Baylor University Medical Center  
Date: March 29, 2004  
Comment:

Responses to questions raised on CMS website for public input regarding PET in the evaluation of dementia

\* What minimal services must be performed and documented as pre-requisites for ordering a PET scan?

I would suggest minimal “pre-PET” prerequisites include a thorough clinical evaluation by a physician skilled in the assessment of patients with dementia, including:

Thorough history and physical examination, specifically targeted toward determination of the presence of clinically significant memory impairment and exclusion of other possible etiologies,

Routine mental status testing,

Assessment of functional status,

Routine laboratory tests (CBC, routine serum chemistries, thyroid function tests, hepatic function tests, and other tests, such as serum B-12 level, as suggested by other findings),

Routine anatomic imaging (CT or, preferably, MRI, if not contraindicated).

\* Is a medical history alone sufficient to ascertain six months of cognitive decline or is actual observation by a clinician necessary to assess and document a decline over such a period prior to ordering a PET scan?

I believe that this should be left to the discretion of the clinician. While actual observation by a clinician for a period of six months may be preferable, there are many cases in which this is impossible (patients and clinicians relocate, clinicians at academic centers rotate off service, etc.). I would suggest that, in many cases, the clinician can obtain ample historical data from the patient, family members, other health-care providers familiar with the patient, caretakers, and others. In others, if this information is not deemed conclusive, follow-up by the clinician for six months seems a reasonable requirement. In some cases, especially if the situation is complicated by other possible causes of dementia, those causes should be addressed and the clinician MAY need six months of observation AFTER correction of such problems, - again, at the discretion of the clinician.

\* What qualifications must a practitioner have to be considered "experienced in the diagnosis and assessment of dementia"?

I would concur with the following qualifications, which have been proposed by others:

- 1) Board-eligibility or Board-certification in Neurology, Psychiatry, Internal Medicine or Family Practice, as experience in making this diagnosis is an integral part of the training for each of these specialties, or
- 2) Physicians with other specialty training may be appropriate referrers, if they can document that in the normal course of their professional activity they are called upon to make this kind of assessment concerning dementia (e.g., have records showing that patients are referred to them for that evaluation, or that patients present to the physician for the purpose of being evaluated for cognitive/behavioral complaints).

\* What type of facility or setting is likely to offer the knowledgeable and experienced interdisciplinary staff needed to conduct a comprehensive assessment and render an accurate clinical diagnosis of dementia? Can a minimum set of facility criteria be identified that provide assurance that a comprehensive assessment will be performed? What set of skills and professions must be assembled on the interdisciplinary team?

In general, I do not believe that a type of qualified facility or a minimum set of facility criteria can or should be identified. I believe that it is inappropriate to dictate to a referring clinician who meets the criteria outline above exactly what types of personnel he/she should maintain on his/her staff to evaluate and manage dementia patients. It is clear that these patients can be managed appropriately in a number of settings. While a large tertiary-care medical center with a dedicated "Dementia Clinic" may be an ideal to which we could aspire, this is not a practical requirement. These patients can be managed in hospitals, hospital clinics, hospitals and clinics limited to psychiatric or mentally impaired patients, or in individual physician offices. Further, I believe the interpretation of the term "multidisciplinary team" is potentially restrictive. While there may be a number of health care professionals involved in the patient's care, depending on the setting, the only absolutely essential members of such a team would include the clinician (as outlined above) and imaging physicians adequately trained and licensed to provide skilled interpretation of the pertinent imaging studies (CT, MRI, and PET).

\* A comprehensive workup utilizing the NINCDS-ADRDA criteria for clinical diagnosis of Alzheimer's disease qualifies the likelihood of Alzheimer's disease as "definite," "probable," "possible," or "uncertain". Should PET be ordered only when the comprehensive assessment results in an uncertain diagnosis?

This would be unnecessarily restrictive. I believe PET can be justified in any patient in whom comprehensive assessment does not result in a "definitely AD" diagnosis. Neither PET nor

clinical assessment offers either 100% sensitivity or 100% specificity. Thus, as with almost every other situation in clinical medicine, the ultimate management of the patient should be determined based on Bayesian analysis of both pre-test likelihood and test (PET) result. While it is true that, in many cases, PET may offer little additional information, or may provide conflicting results, and the patients who are probably most likely to benefit from PET reside in the “uncertain” category, the clinician should be allowed to combine the results of PET with clinical assessment to determine the most likely diagnosis in any patient not classified as “definite.”

\* What are the key differential diagnoses among neurodegenerative causes of dementia (e.g., frontotemporal dementia vs. AD) that PET could reasonably be expected to help clarify after an experienced clinician or team has completed an assessment? What are those clinical situations for which other imaging or other tests would be better indicated (e.g., distinguishing AD from mixed AD- multi-infarct dementia)?

Key differential diagnoses that PET will help clarify after assessment by an experienced clinician or team are:

- 1) AD vs. Frontotemporal dementia,
- 2) Frontotemporal dementia vs. Dementia with Lewy bodies,
- 3) AD vs. non-neurodegenerative causes of progressive dementia,
- 4) Frontotemporal dementia vs. non-neurodegenerative causes of progressive dementia,
- 5) Dementia with Lewy bodies vs. non-neurodegenerative causes of progressive dementia

Differential diagnoses for which other methods of distinguishing are more suitable are:

- 1) AD, Frontotemporal, or other neurodegenerative dementia vs. untreated depression,
- 2) AD, Frontotemporal, or other neurodegenerative dementia vs. untreated substance abuse or adverse effects of other pharmacologic agents,
- 3) AD, Frontotemporal, or other neurodegenerative dementia vs. untreated thyroid disease,
- 4) AD, Frontotemporal, or other neurodegenerative dementia vs. untreated nutrient deficiency.

\* What are the minimal educational requirements for staff performing and interpreting the PET scans? How should test performance and interpretation be standardized? What accreditation requirements must facilities performing PET scans for AD meet?

Minimal educational/certification requirements for staff performing the PET scans:

Certification as a Certified Nuclear Medicine Technologist (CNMT) and appropriate state licensing.

Minimal educational/certification requirements for staff interpreting the PET scans include at least one of the following:

- 1) American Board of Nuclear Medicine (ABNM) certification,
- 2) American Board of Radiology (ABR) certification, with ABR special certification in Nuclear Medicine,
- 3) American Board of Radiology (ABR) certification, with documented training in PET,
- 4) Appropriate state licensing.

There are no official standardization requirements for performance and interpretation of PET studies or any other types of Nuclear Medicine studies. This is appropriate, as each site and physician can and should tailor methodology to suit the available equipment, the patient's condition, the anticipated findings, and, in some cases, personal preference among various accepted methods. Professional guidelines for performance and interpretation of diagnostic studies are often issued (e.g., by the Society of Nuclear Medicine and by the American College of Radiology), but these guidelines are not mandatory, nor do they include all accepted methods of performing various studies. Moreover, these guidelines can only be updated with practical frequency; thus, the responsibility for decisions regarding such procedures should be left to the interpreting physician. Similarly, various professional bodies, such as the Society of Nuclear Medicine and the American College of Radiology, offer accreditation programs for Nuclear Medicine departments, but such accreditation is optional and should be left to the discretion of the interpreting physician.

**Comment #13:**

Submitter: Murray Grossman, MD, EdD

Organization: University of Pennsylvania School of Medicine

Date: March 26, 2004

Comment:

\* What minimal services must be performed and documented as pre-requisites for ordering a PET scan?

Minimal services required are:

performance and documentation of a standard comprehensive medical history and physical examination, including documented neurological examination,

assessment of mental status and activities of daily living,  
laboratory tests – serum electrolyte (Na<sup>+</sup>, K<sup>+</sup>, Cl<sup>-</sup>, CO<sub>2</sub>), BUN, Cr, glucose, ALT and TSH  
determinations; CBC, including Hct, MCV and MCHC,  
structural neuroimaging (CT or MRI)

\* Is a medical history alone sufficient to ascertain six months of cognitive decline or is actual observation by a clinician necessary to assess and document a decline over such a period prior to ordering a PET scan?

Minimal sufficient documentation of decline is constituted by one of the following:  
actual longitudinal observation by a clinician over a period extending at least six months,  
a history obtained and deemed reliable by clinician, from interviewing patient and/or close contact(s) of patient, which documents progressive decline over a period of at least six months preceding the time of clinician's evaluation,  
a combination of the above, amounting in total to at least six months of decline documentable by the summed periods of time represented by 1) and 2)

\* What qualifications must a practitioner have to be considered "experienced in the diagnosis and assessment of dementia"?

Acceptable qualifications are:

Board-eligibility or Board-certification in Neurology, Psychiatry, Internal Medicine or Family Practice, as experience in making this diagnosis is an integral part of the training for each of these specialties, or

Physicians with other specialty training may be appropriate referrers, if they can document that in the normal course of their professional activity they are called upon to make this kind of assessment concerning dementia (e.g., have records showing that patients are referred to them for that evaluation, or that patients present to the physician for the purpose of being evaluated for cognitive/behavioral complaints)

\* What type of facility or setting is likely to offer the knowledgeable and experienced interdisciplinary staff needed to conduct a comprehensive assessment and render an accurate clinical diagnosis of dementia? Can a minimum set of facility criteria be identified that provide assurance that a comprehensive assessment will be performed? What set of skills and professions must be assembled on the interdisciplinary team?

Acceptable types of facilities:

General hospital,

Psychiatric hospital,

Outpatient clinics of physicians qualified by criteria described above

The professional(s) carrying out the required comprehensive assessment must reflect the following set of skills:

trained in evaluation of dementia, including conducting a medical history and physical examination, neurological examination, assessment of mental status and activities of daily living – as occurs in the professional training of neurologists, psychiatrists, internists and family practice physicians, trained and licensed to order and interpret the results of laboratory and neuroradiology tests outlined above.

\* A comprehensive workup utilizing the NINCDS-ADRDA criteria for clinical diagnosis of Alzheimer's disease qualifies the likelihood of Alzheimer's disease as "definite," "probable," "possible," or "uncertain". Should PET be ordered only when the comprehensive assessment results in an uncertain diagnosis?

PET should be ordered only when the comprehensive assessment does not result in a “definite” diagnosis. It is clear from the primary peer-reviewed literature that the presence of Alzheimer’s disease is “uncertain” in many patients who meet NINCDS-ADRDA criteria of “possible AD” or “probable AD.” For example, in the one peer-reviewed article to examine clinical diagnostic accuracy for evaluation of early dementia, presenting data that met the American Academy of Neurology designation of “Class I” quality of evidence<sup>1</sup>, among all patients who were subsequently proven by autopsy to NOT have AD, 45% of those patients actually met NINCDS-ADRDA criteria for “probable AD”<sup>2</sup> -- and the specificity of “possible AD” was even lower.

\* What are the key differential diagnoses among neurodegenerative causes of dementia (e.g., frontotemporal dementia vs. AD) that PET could reasonably be expected to help clarify after an experienced clinician or team has completed an assessment? What are those clinical situations for which other imaging or other tests would be better indicated (e.g., distinguishing AD from mixed AD- multi-infarct dementia)?

Key differential diagnoses which PET will help clarify after assessment by an experienced clinician or team are:

AD vs. Frontotemporal dementia,  
Frontotemporal dementia vs. Dementia with Lewy bodies,  
AD vs. non-neurodegenerative causes of progressive dementia,  
Frontotemporal dementia vs. non-neurodegenerative causes of progressive dementia,  
Dementia with Lewy bodies vs. non-neurodegenerative causes of progressive dementia

Differential diagnoses for which other methods of distinguishing are more suitable are:

AD, Frontotemporal, or other neurodegenerative dementia vs. untreated depression,  
AD, Frontotemporal, or other neurodegenerative dementia vs. untreated substance abuse or adverse effects of other pharmacologic agents,  
AD, Frontotemporal, or other neurodegenerative dementia vs. untreated thyroid disease,  
AD, Frontotemporal, or other neurodegenerative dementia vs. untreated nutrient deficiency

\* What are the minimal educational requirements for staff performing and interpreting the PET



scans? How should test performance and interpretation be standardized? What accreditation requirements must facilities performing PET scans for AD meet?

Minimal educational/certification requirements for staff performing the PET scans:  
Certified Nuclear Medicine Technologist (CNMT)

Minimal educational/certification requirements for staff interpreting the PET scans include at least one of the following:

American Board of Nuclear Medicine (ABNM) certification,  
American Board of Radiology (ABR) certification, with ABR special certification in Nuclear Medicine,  
Neurologist, psychiatrist, or radiologist with documentable specific training in interpretation of brain PET scans

For all kinds of Nuclear Medicine tests, professional guidelines for performance and interpretation of diagnostic studies are often issued (e.g, by the Society for Nuclear Medicine), but there is no official specialty-wide standardization requirements for performance of any Nuclear Medicine study – nor should there be, as performance standards are tailored to the specific conditions and equipment present at each site, and it is ultimately the responsibility of each facility and physician to assure performance and interpretive quality, and maintain professional accreditations.

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## References:

1. Knopman DS, DeKosky ST, Cummings JL, et al. Practice parameter: diagnosis of dementia (an evidence-based review). Report of the Quality Standards Subcommittee of the American Academy of Neurology. *Neurology*. 2001; 56:1143-1153.
2. Lim A, Tsuang D, Kukull W, et al. Clinico-neuropathological correlation of Alzheimer's disease in a community-based case series. *J Am Geriatr Soc*. 1999; 47:564-569.

## Comment #14:

Submitter: Robert G. Britain  
Organization: National Electrical Manufacturers Association  
Date: March 26, 2004  
Comment:

What minimal services must be performed and documented as pre-requisites for ordering a PET scan ?

RESPONSE:

The following minimal services must be performed and documented:

- Chief complaint
- Family and medical history (including recent and remote issues related to chief complaint)
- Physical examination, including neurological and cognitive assessment
- Interview with significant others related to chief complaint

Is a medical history alone sufficient to ascertain six months of cognitive decline or is actual observation by a clinician necessary to assess and Document a decline over such a period prior to ordering a PET scan ?

RESPONSE:

Relevant questions answered by a significant other on behavior changes over the past 6 months vs. prior 12 months would be acceptable. It is important that specific behavior be documented or a clear but consistent pattern of change is described. Also relevant would be a query of the patient on the issues discussed to determine whether they have a rational explanation for their actions.

What qualifications must a practitioner have to be considered “experienced in the diagnosis and assessment of dementia” ?

RESPONSE:

Experience in the correct diagnosis of patients with the various forms of neurodegenerative disease types is essential. The presence of a correct diagnosis would be based on measured clinical outcomes to include improved well-being and quality of life of the patient, and objective assessment of the input from significant others on either improvement or evidence of no further cognitive decline of the patient. Examples of types of board certified practitioners could include:

- Psychiatrists
- Neurologists
- Internists with specialization in geriatric medicine

(Note: conducting a comprehensive assessment will require the application of various clinical skills. See response to Question 4.)

What type of facility or setting is likely to offer the knowledgeable and experienced interdisciplinary staff needed to conduct a comprehensive assessment and render an accurate clinical diagnosis of dementia ? Can a minimum set of facility criteria be identified that provide assurance that a

comprehensive assessment will be performed ? What set of skills and professions must be assembled on the interdisciplinary team ?

RESPONSE:

There are a number of acceptable models of facilities which are likely to offer the kind of staff needed to conduct a comprehensive assessment and render an accurate clinical diagnosis of dementia. Examples could include: psychiatric hospitals, geriatric assessment centers, or a general hospital which contained the appropriate specialized personnel, as set forth below.

The minimum composition of skills would include the following:

-Internal medicine specialist with experience and background to rule out metabolic or organic causes for the dementia and clinical assessment background to obtain accurate and relevant family and medical histories and to conduct a thorough physical as well as neurological examination.

-Psychologist/Psychiatrist with experience and background sufficient to differentiate neurological from psychotic or neurotic disorders.

-Social worker to assess family issues which might be relevant to differentiate patient-specific dementia vs. family dysfunction or environmental causes for medical visit.

-Diagnostic imaging specialists (PET, MRI, CT) with background and experience in neurological diagnostic imaging with specific expertise for various dementias.

A more sophisticated model might include a neurologist with special expertise in the differential diagnosis of various dementias. The importance of the team would be to establish the presence of a dementia, narrow the type and look to PET to add specificity to the diagnosis.

A comprehensive workup utilizing the NINCDS-ADRDA criteria for clinical diagnosis of Alzheimer's disease qualifies the likelihood of Alzheimer's disease as "definite," "probable," "possible," or "uncertain." Should PET be ordered only when the comprehensive assessment results in an uncertain diagnosis ?

RESPONSE:

A PET scan should be ordered if a comprehensive assessment results in an uncertain diagnosis. PET is important to differentiate between various dementias and in particular to define the presence or absence of Alzheimer's disease. Also, however, PET can quantify the extent of the disease based on the particular segments and severity of disease within each segment. The severity of the disease process provides important prognostic information and is essential in monitoring the progress of the disease over time. Simply saying one has the disease is not

enough. Severity and prognosis are essential to appropriate treatment and to give realistic expectations to the patient and family members on outcomes.

What are the key differential diagnoses among neurodegenerative causes of dementia (e.g. frontotemporal dementia vs. AD) that PET could reasonably be expected to help clarify after an experienced clinician or team has completed an assessment? What are those clinical situations for which other imaging or other tests would be better indicated (e.g. distinguishing AD from mixed AD-multi-infarct dementia)?

RESPONSE:

PET has significant capabilities in making differential diagnoses among a number of different neurodegenerative causes of dementia. It is very useful in differentiating between AD vs. vascular dementia, AD vs. Dementia with Lewy Bodies and AD vs. Parkinson's disease, to cite a few examples.

PET scans reveal specific patterns of symmetric decreased perfusion with a clear pattern of progression depending upon the intensity of uptake and which lobes are involved. It is far and away the most specific in terms of showing the presence of AD and severity of disease, and therefore allows for greater accuracy in measurement of a patient's prognosis. It is also useful to quantify progression of the disease as a serial monitoring methodology. MRI has the ability to identify changes by monitoring atrophy changes, and may be useful in assessment of pre-clinical neurological changes, but lacks the sensitivity and specificity of PET. Further, greater expertise and knowledge of neuroanatomy are required for MRI than is the case for PET.

What are the minimal educational requirements for staff performing and interpreting the PET scans? How should test performance and interpretation be standardized? What accreditation requirements must facilities performing PET scans for AD meet?

RESPONSE:

PET requirements must include the appropriate performance and acquisition of the study. This requires a competent technologist familiar with the protocol for injection, patient positioning, acquisition parameters and processing of image data. The physician must be trained in anatomical PET interpretation, and in certain cases (although rare) correlation of the PET images with either CT or MRI. Physicians should be board certified and technologists should also have received specific training and certification. Test performance and interpretation, and accreditation of facilities should be standardized according to specific, appropriate medical society clinical guidelines, practice protocols, and established accreditation programs, respectively.

A preceptorship program of one week in PET imaging for neurodegenerative disorders with emphasis on AD would be suggested for a PET specialist experienced in oncology PET applications. It does not seem realistic to require certification for AD since most AD studies

would be done in oncology centers. However, a specialty training program of one week should be required and perhaps the training site should offer a standardized curriculum with an assessment examination at the completion of training.

**Comment #15:**

Submitter: Kevin Berger, MD & E. James Potchen, MD  
Organization: Michigan State University  
Date: March 25, 2004  
Comment:

*What are the minimal educational requirements for staff performing and interpreting the PET scans?*

Physicians, clinicians, and technologists at Michigan State University strongly endorse the “Statements from the PET-CT Consensus Conference” of July 31, 2002 in New Orleans, LA regarding Fusion Imaging: A New Type of Technologist For a New Type of Technology. As more institutions move from PET to PET-CT scanning equipment, the personnel qualified to operate this equipment should be clarified. It is highly likely that most brain PET exams done to diagnosis Alzheimer’s Disease will be done on fusion PET-CT equipment. Therefore, qualification standards of personnel operating this equipment need to be appropriately described. Consensus Statement No. 1 states “Any registered radiographer with the credential R.T. (R), registered radiation therapist the credential R.T. (T), or registered nuclear medicine technologist with the credentials R.T. (N) or CNMT may operate PET-CT equipment after obtaining appropriate additional education or training and demonstrating competency. Because so few technologists are credentialed in both radiography and nuclear medicine, and even fewer are credentialed in CT and nuclear medicine, conference participants did not believe it would be reasonable to demand dual certification for operators of PET-CT equipment at this point. To do so would limit patient access to this valuable technology. Instead, they recommended that multiple pathways be created to educate or train registered nuclear medicine technologists, radiographer, and radiation therapists to operate PET-CT equipment.”

To restrict operation of PET-CT scanning equipment to only CNMT or only ARRT qualified personnel would limit patient access and unfairly restrict otherwise qualified personnel. Additional certification requirements beyond either CNMT or ARRT should wait until additional PET-CT certification pathways for additional qualification is widely available to personnel from BOTH CNMT and ARRT.

Furthermore, it is not the mission of CMS to specify which professional categories and their competence are required to read or refer these patients. This is defined in the practice of medicine which is outside the regulatory scope of CMS, and there is no justifiable precedent for CMS to create or enforce such standards selectively.

**Comment #16:**

Submitter: James Frost, MD, Ph.D.  
Organization:

Date: March 25, 2004  
Comment:

\* What minimal services must be performed and documented as pre-requisites for ordering a PET scan?

H&P; mental status; lab tests; CT or MR.

\* Is a medical history alone sufficient to ascertain six months of cognitive decline or is actual observation by a clinician necessary to assess and document a decline over such a period prior to ordering a PET scan?

Either MD observation for at least 6 months or by reliable surrogate such as close family member.

\* What qualifications must a practitioner have to be considered "experienced in the diagnosis and assessment of dementia"?

MD trained in Medicine, Psychiatry, Neurology, etc. Normal medical training should be adequate for detecting symptoms possible due to dementia.

\* What type of facility or setting is likely to offer the knowledgeable and experienced interdisciplinary staff needed to conduct a comprehensive assessment and render an accurate clinical diagnosis of dementia? Can a minimum set of facility criteria be identified that provide assurance that a comprehensive assessment will be performed? What set of skills and professions must be assembled on the interdisciplinary team?

No special facility needed. An interdisciplinary team normally not require to initiate and complete dementia work up, in most cases. A consult to a psychiatrist or neurologist would normally be done prior to PET.

\* A comprehensive workup utilizing the NINCDS-ADRDA criteria for clinical diagnosis of Alzheimer's disease qualifies the likelihood of Alzheimer's disease as "definite," "probable," "possible," or "uncertain". Should PET be ordered only when the comprehensive assessment results in an uncertain diagnosis?

If the NINCDS-ADRDA criteria show definite AD or other dementia then PET is not needed, other than to monitor progression or treatment response. Many cases are uncertain, in which case PET would be indicated.

\* What are the key differential diagnoses among neurodegenerative causes of dementia (e.g., frontotemporal dementia vs. AD) that PET could reasonably be expected to help clarify after an experienced clinician or team has completed an assessment? What are those clinical situations for which other imaging or other tests would be better indicated (e.g., distinguishing AD from mixed AD-multi-infarct dementia)?

PET excellent for diagnosis and differential diagnosis for AD, frontotemporal dementia, Lewy body disease, etc. Depression, substance abuse, metabolic diseases and other disorders possibly confused with dementia would not benefit by PET at this time.

\* What are the minimal educational requirements for staff performing and interpreting the PET scans? How should test performance and interpretation be standardized? What accreditation requirements must facilities performing PET scans for AD meet?

Board certified in Nuclear Medicine or Radiology.

**Comment #17:**

Submitter: Terri Blomker, BS  
Organization: PETNET Pharmaceutical, Inc.  
Date: March 25, 2004  
Comment:

Medicare Coverage• Questions for Public Input on PET for Alzheimer's

- 1) What minimal services must be performed and documented as prerequisites for ordering a PET scan?
  - Must rule out organic causes and drug interactions
  - Must perform cognitive tests
  - Perform labs, MRI and neuropsych testing
  
- 2) Is a medical history alone sufficient to ascertain six months of cognitive decline or is actual observation by a clinician necessary to assess and document a decline over such a period prior to ordering a PET scan?
  - this depends on the patient, their support system, their insurance

coverage and their physician.

3) What qualifications must a practitioner have to be considered 'experienced in the diagnosis and assessment of dementia'?

- any physician should be able to screen their patient, then send to a specialist with experience with Alzheimer's Disease and the differential diagnoses

4) What type of facility or setting is likely to offer the knowledgeable and experienced interdisciplinary staff needed to conduct a comprehensive assessment and render an accurate clinical diagnosis of dementia? Can a minimum set of facility criteria be identified that provide assurance that a comprehensive assessment will be performed? What set of skills and professions must be assembled on the interdisciplinary team?

- any tertiary center with an interdisciplinary team including neuro, psych and neuropsych support and a good relationship with interpreting physicians. The minimal criteria should be set by organizations such as the AAN.

5) A comprehensive workup utilizing the NINCDS-ADRDA criteria for clinical diagnosis of Alzheimer's Disease qualifies the likelihood of Alzheimer's disease as "definite", "probable", "possible", or "uncertain". Should PET be ordered only when the comprehensive assessment results in an uncertain diagnosis?

- a PET should be ordered for any 'uncertain' or 'possible'.
- A PET should be ordered for any 'probable' if the patient is likely to respond to Aricept treatment to slow the progress of the disease.

6) What are the key differential diagnoses among neurodegenerative causes of dementia (e.g., frontotemporal dementia vs. AD) that PET could reasonably be expected to help clarify after an experienced clinician or team has completed an assessment? What are those clinical situations for which other imaging or other tests would be better indicated (e.g., distinguishing AD from mixed AD-multi-infarct dementia)?

- the key differential diagnoses are multi-infarct dementia, fronto-temporal dementia, Parkinson's dementia, hydrocephalus and tumors.
- All the above should have either other tests or imaging to obtain the differential diagnosis.

7) What are the minimal educational requirements for staff performing and interpreting the PET scans? How should test performance and interpretation be standardized? What accreditation requirements must facilities performing PET scans for AD meet?

- minimum of CNMT or ARRT(N)
- physician should have NM fellowship with intensive PET training or dedicated PET fellowship.



- Accreditation requirements should be established by SNM, AMI, ACR or AAN.

**Comment #18:**

Submitter: James W. Dean, MD

Organization: University of Texas-Southwestern Center/Parkland Hospital

Date: March 24, 2004

Comment:

As a practicing neurologist in Tulsa, Oklahoma, I can tell you that patient's and families everywhere (even in rural America, ie. Oklahoma) are being left in limbo daily for months/year(s) by the limitations we currently have in diagnosing with adequate confidence patients' dementia problems as due (or not due) to Alzheimer's. The history/exam/MRI or CT/lab data currently employed by all clinicians primary care or specialist (usually neurologists/occasionally psychiatrists) are simply inadequate in many instances to provide a timely diagnosis of this awful disease so that patients and families can make the most of available treatments, research drug study opportunities, and most importantly, their time together to enjoy one another as well as plan and arrange for the inevitable future that both the patient and family will face.

Watchful waiting is not helpful, and in essentially every case, harmful and regrettable when the fact is that if it's Alzheimer's, hoping it's not won't change the fact when it becomes clinically/radiologically (MRI/CT) obvious that it is, it's often too late for the patient to meaningfully participate in the needed decision making and life/family planning issues always at hand. Or worse, there is no family to assist in the situation!

I implore you to look favorably on Dr Michael Phelps' request to approve Medicare reimbursement for FDG-18 PET (Positron Emission Tomography) in cases that meet the criteria the UCLA Dept. of Molecular and Medical Pharmacology has recommended with perhaps the additional provisional requirement that only a board certified neurologist be allowed to order the exam during a period of time (? 18-24 months) in which CMS could track the appropriateness/cost effectiveness/prudence with which this somewhat expensive neurodiagnostic exam is utilized.

I'm sure you

agree having reviewed the accumulating evidence (studies/literature) that it is obvious that the current state of FDG-18 PET technology is such that it is ready to be employed to "rule in or rule out" Alzheimer's with far superior accuracy (in the 95% range) to current methods and in fact when using current methods allows us a wonderful complement that no doubt will save money and tears over the 'long haul' of each patient's/family's journey with Alzheimer's.

**Comment #19**

Submitter: Jeffrey Cummings, MD

Organization: UCLA, David Geffen School of Medicine

Date: March 24, 2004

Comment:

\* What minimal services must be performed and documented as pre-requisites for ordering a PET scan?

Minimal services required are:

- 1) performance and documentation of a standard comprehensive medical history and physical examination, including documented neurological examination,
- 2) assessment of mental status and activities of daily living,
- 3) laboratory tests – serum electrolyte (Na<sup>+</sup>, K<sup>+</sup>, Cl<sup>-</sup>, CO<sub>2</sub>), BUN, Cr, glucose, ALT and TSH determinations; CBC, including Hct, MCV and MCHC,
- 4) structural neuroimaging (CT or MRI)

\* Is a medical history alone sufficient to ascertain six months of cognitive decline or is actual observation by a clinician necessary to assess and document a decline over such a period prior to ordering a PET scan?

Minimal sufficient documentation of decline is constituted by one of the following:

- 1) actual longitudinal observation by a clinician over a period extending at least six months,
- 2) a history obtained and deemed reliable by clinician, from interviewing patient and/or close contact(s) of patient, which documents progressive decline over a period of at least six months preceding the time of clinician's evaluation,
- 3) a combination of the above, amounting in total to at least six months of decline documentable by the summed periods of time represented by 1) and 2)

\* What qualifications must a practitioner have to be considered "experienced in the diagnosis and assessment of dementia"?

Acceptable qualifications are:

- 1) Board-eligibility or Board-certification in Neurology, Psychiatry, Internal Medicine or Family Practice, as experience in making this diagnosis is an integral part of the training for each of these specialties, or
- 2) Physicians with other specialty training may be appropriate referrers, if they can document that in the normal course of their professional activity they are called upon to make this kind of assessment concerning dementia (e.g., have records showing that patients are referred to them for that evaluation, or that patients present to the physician for the purpose of being evaluated for cognitive/behavioral complaints)

\* What type of facility or setting is likely to offer the knowledgeable and experienced interdisciplinary staff needed to conduct a comprehensive assessment and render an accurate clinical diagnosis of dementia? Can a minimum set of facility criteria be identified that provide

assurance that a comprehensive assessment will be performed? What set of skills and professions must be assembled on the interdisciplinary team?

Acceptable types of facilities:

- 1) General hospital,
- 2) Psychiatric hospital,
- 3) Outpatient clinics of physicians qualified by criteria described above

The professional(s) carrying out the required comprehensive assessment must reflect the following set of skills:

- 1) trained in evaluation of dementia, including conducting a medical history and physical examination, neurological examination, assessment of mental status and activities of daily living – as occurs in the professional training of neurologists, psychiatrists, internists and family practice physicians,
- 2) trained and licensed to order and interpret the results of laboratory and neuroradiology tests outlined above.

\* A comprehensive workup utilizing the NINCDS-ADRDA criteria for clinical diagnosis of Alzheimer's disease qualifies the likelihood of Alzheimer's disease as "definite," "probable," "possible," or "uncertain". Should PET be ordered only when the comprehensive assessment results in an uncertain diagnosis?

PET should be ordered only when the comprehensive assessment does not result in a “definite” diagnosis. It is clear from the primary peer-reviewed literature that the presence of Alzheimer’s disease is “uncertain” in many patients who meet NINCDS-ADRDA criteria of “possible AD” or “probable AD.” For example, in the one peer-reviewed article to examine clinical diagnostic accuracy for evaluation of early dementia, presenting data that met the American Academy of Neurology designation of “Class I” quality of evidence<sup>1</sup>, among all patients who were subsequently proven by autopsy to NOT have AD, 45% of those patients actually met NINCDS-ADRDA criteria for “probable AD”<sup>2</sup> -- and the specificity of “possible AD” was even lower.

\* What are the key differential diagnoses among neurodegenerative causes of dementia (e.g., frontotemporal dementia vs. AD) that PET could reasonably be expected to help clarify after an experienced clinician or team has completed an assessment? What are those clinical situations for which other imaging or other tests would be better indicated (e.g., distinguishing AD from mixed AD- multi-infarct dementia)?

Key differential diagnoses which PET will help clarify after assessment by an experienced clinician or team are:

- 1) AD vs. Frontotemporal dementia,
- 2) Frontotemporal dementia vs. Dementia with Lewy bodies,
- 3) AD vs. non-neurodegenerative causes of progressive dementia,
- 4) Frontotemporal dementia vs. non-neurodegenerative causes of progressive dementia,
- 5) Dementia with Lewy bodies vs. non-neurodegenerative causes of progressive dementia

Differential diagnoses for which other methods of distinguishing are more suitable are:

- 1) AD, Frontotemporal, or other neurodegenerative dementia vs. untreated depression,
- 2) AD, Frontotemporal, or other neurodegenerative dementia vs. untreated substance abuse or adverse effects of other pharmacologic agents,
- 3) AD, Frontotemporal, or other neurodegenerative dementia vs. untreated thyroid disease,
- 4) AD, Frontotemporal, or other neurodegenerative dementia vs. untreated nutrient deficiency

\* What are the minimal educational requirements for staff performing and interpreting the PET scans? How should test performance and interpretation be standardized? What accreditation requirements must facilities performing PET scans for AD meet?

Minimal educational/certification requirements for staff performing the PET scans:  
Certified Nuclear Medicine Technologist (CNMT)

Minimal educational/certification requirements for staff interpreting the PET scans include at least one of the following:

- 1) American Board of Nuclear Medicine (ABNM) certification,
- 2) American Board of Radiology (ABR) certification, with ABR special certification in Nuclear Medicine,
- 3) Neurologist, psychiatrist, or radiologist with current eligibility to bill CMS for interpretation of brain CT or MRI, plus documentable specific training in interpretation of brain PET scans

For all kinds of Nuclear Medicine tests, professional guidelines for performance and interpretation of diagnostic studies are often issued (e.g, by the Society for Nuclear Medicine), but there is no official specialty-wide standardization requirements for performance of any Nuclear Medicine study – nor should there be, as performance standards are tailored to the specific conditions and equipment present at each site, and it is ultimately the responsibility of each facility and physician to assure performance and interpretive quality, and maintain professional accreditations.

Sincerely,

Cummings, Jeffrey, M.D., Augustus S. Rose Professor, Departments of Neurology, and Psychiatry and Biobehavioral Sciences, Director, UCLA Alzheimer's Disease Center, David Geffen School of Medicine, University of California, Los Angeles; Co-Chairman, American Academy of Neurology Practice Parameter Committee on Dementia; President, Alzheimer's Association, Los Angeles, San Bernardino & Riverside Chapter.

Small, Gary, M.D., Parlow-Solomon Professor on Aging, Professor of Psychiatry and Biobehavioral Sciences, Director, UCLA Center on Aging, David Geffen School of Medicine, University of California, Los Angeles; Member, American Academy of Neurology Practice Parameter Committee on Dementia.

Silverman, Daniel, M.D., Ph.D., Assistant Professor, Department of Molecular and Medical Pharmacology, Head, Section of Neuroimaging, David Geffen School of Medicine, University of California, Los Angeles.

Coleman, Edward, M.D., Professor and Vice Chairman, Department of Radiology, Duke School of Medicine.

Chodosh, Joshua, M.D., Associate Professor, Division of Geriatrics, Department of Medicine, David Geffen School of Medicine, University of California, Los Angeles.

Phelps, Michael, Ph.D., Norton Simon Professor, Chairman, Molecular and Medical Pharmacology, Director, Institute for Molecular Medicine, David Geffen School of Medicine, University of California, Los Angeles.

Fowler, Joanna Ph.D, Senior Chemist, Director Brookhaven PET Program, Brookhaven National Laboratory, Upton, NY

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**References:**

1. Knopman DS, DeKosky ST, Cummings JL, et al. Practice parameter: diagnosis of dementia (an evidence-based review). Report of the Quality Standards Subcommittee of the American Academy of Neurology. *Neurology*. 2001; 56:1143-1153.
2. Lim A, Tsuang D, Kukull W, et al. Clinico-neuropathological correlation of Alzheimer's disease in a community-based case series. *J Am Geriatr Soc*. 1999; 47:564-569.

**Comment #20:**

Submitter: Jack Retzlaff  
Organization:  
Date: March 24, 2004  
Comment:

Before I provide my comments on the questions, I want to provide a general comment. In the past, given the fact that viable effective treatments for AD were not available, I was not a proponent of diagnostic exams that simply added cost to the treatment. Now that effective treatments are being uncovered, early diagnosis is critical to the management of this disease. If a definitive diagnosis can be made at an early date, and treatment started earlier, the short and mid term costs of caring for the AD patient will certainly decrease. PET is one of the definitive tools that can, should and must be used in this battle and should be reimbursed.

The medical history and cognitive evaluation of the patient done by a licensed physician should suffice for minimal pre-requisites needed to order a PET scan to confirm the diagnosis.

A medical history of 6 months of cognitive decline must be considered acceptable to order a PET scan. Additional evaluations may do nothing more than delay the onset of treatment.

The qualifications of the practitioner should be broad enough to include the family physician who will in most instances have the most complete profile of the patient.

The acceptable facility should be able to offer the PET scan and provide the "reading" of the scan "on-site". The PET scan should be read by a board-certified radiologist. The facility should be equipped with an existing Nuclear Medicine department and should meet JCAHO certification.

The PET scans should be ordered and reimbursed anytime the comprehensive results are anything but definite.

The site should also offer CT, MRI and Nuclear Medicine exam capabilities to help differentiate between AD and other medical conditions that may present much in the same manner as AD.

The PET staff educational requirements should meet the individual state standards for nuclear medicine examinations.

The radiologist must be board certified. The facility should meet JCAHO certifications.

My interest in this disease is directly related to family history. Both my family and my wife's family have been impacted by AD. If early diagnosis leads to early treatment that can prolong the onset of severe dementia, the costs associated with PET exams as a definitive diagnostic tool will be insignificant in the end.

I fully support the efforts to have PET scans approved for reimbursement through CMS.

**Comment #21:**

Submitter: Carmen Burtea

Organization: University of Mons-Hainaut, Belgium

Date: March 24, 2004

Comment:

Unfortunately, I do not have the appropriate qualification and experience to answer to the questions. I am a biologist researcher and I am working in molecular targeting of atherosclerosis by MRI contrast agents. My personal belief is that a practitioner experience cannot be measured in time units, but in number of AD cases is treating per year

I do not think that a PET scan alone can discriminate between AD and other neurodegenerative diseases. A specific contrast agent that targets receptors/molecules over-expressed in AD (i.e. beta-amyloid protein)

could be helpful. The advantage of PET vs. MRI is that it can detect low concentrations of contrast agent.

The minimal educational requirements for staff performing and interpreting the PET scan is not necessarily MD. A medical technician/nurse with a long experience and interest could perform this task. However, the physician's supervision is prerequisite.

**Comment #22:**

Submitter: Wei Chen, MD, PhD

Organization: Southern California Permanente Medical Group

Date: March 23, 2004

Comment:

\* What minimal services must be performed and documented as pre-requisites for ordering a PET scan?

Minimal services required are:

- 1) performance and documentation of a standard comprehensive medical history and physical examination, including documented neurological examination,
- 2) assessment of mental status and activities of daily living,
- 3) laboratory tests – serum electrolyte (Na<sup>+</sup>, K<sup>+</sup>, Cl<sup>-</sup>, CO<sub>2</sub>), BUN, Cr, glucose, ALT and TSH determinations; CBC, including Hct, MCV and MCHC,
- 4) structural neuroimaging (CT or MRI)

\* Is a medical history alone sufficient to ascertain six months of cognitive decline or is actual observation by a clinician necessary to assess and document a decline over such a period prior to ordering a PET scan?

Minimal sufficient documentation of decline is constituted by one of the following:

- 1) actual longitudinal observation by a clinician over a period extending at least six months,
- 2) a history obtained and deemed reliable by clinician, from interviewing patient and/or close contact(s) of patient, which documents progressive decline over a period of at least six months preceding the time of clinician's evaluation,
- 3) a combination of the above, amounting in total to at least six months of decline documentable by the summed periods of time represented by 1) and 2)

\* What qualifications must a practitioner have to be considered "experienced in the diagnosis and assessment of dementia"?

Acceptable qualifications are:

- 1) Board-eligibility or Board-certification in Neurology, Psychiatry, Internal Medicine or Family Practice, as experience in making this diagnosis is an integral part of the training for

each of these specialties, or

- 2) Physicians with other specialty training may be appropriate referrers, if they can document that in the normal course of their professional activity they are called upon to make this kind of assessment concerning dementia (e.g., have records showing that patients are referred to them for that evaluation, or that patients present to the physician for the purpose of being evaluated for cognitive/behavioral complaints)

\* What type of facility or setting is likely to offer the knowledgeable and experienced interdisciplinary staff needed to conduct a comprehensive assessment and render an accurate clinical diagnosis of dementia? Can a minimum set of facility criteria be identified that provide assurance that a comprehensive assessment will be performed? What set of skills and professions must be assembled on the interdisciplinary team?

Acceptable types of facilities:

- 1) General hospital,
- 2) Psychiatric hospital,
- 3) Outpatient clinics of physicians qualified by criteria described above

The professional(s) carrying out the required comprehensive assessment must reflect the following set of skills:

- 1) trained in evaluation of dementia, including conducting a medical history and physical examination, neurological examination, assessment of mental status and activities of daily living – as occurs in the professional training of neurologists, psychiatrists, internists and family practice physicians,
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for which other imaging or other tests would be better indicated (e.g., distinguishing AD from mixed AD- multi-infarct dementia)?

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- 1) AD vs. Frontotemporal dementia,
- 2) Frontotemporal dementia vs. Dementia with Lewy bodies,
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- 4) Frontotemporal dementia vs. non-neurodegenerative causes of progressive dementia,
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- 1) AD, Frontotemporal, or other neurodegenerative dementia vs. untreated depression,
- 2) AD, Frontotemporal, or other neurodegenerative dementia vs. untreated substance abuse or adverse effects of other pharmacologic agents,
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- 3) Neurologist, psychiatrist, or radiologist with current eligibility to bill CMS for interpretation of brain CT or MRI, plus documentable specific training in interpretation of brain PET scans

For all kinds of Nuclear Medicine tests, professional guidelines for performance and interpretation of diagnostic studies are often issued (e.g, by the Society for Nuclear Medicine), but there is no official specialty-wide standardization requirements for performance of any Nuclear Medicine study – nor should there be, as performance standards are tailored to the specific conditions and equipment present at each site, and it is ultimately the responsibility of each facility and physician to assure performance and interpretive quality, and maintain professional accreditations.

References:

1. Knopman DS, DeKosky ST, Cummings JL, et al. Practice parameter: diagnosis of dementia (an evidence-based review). Report of the Quality Standards Subcommittee of the American Academy of Neurology. *Neurology*. 2001; 56:1143-1153.

2. Lim A, Tsuang D, Kukull W, et al. Clinico-neuropathological correlation of Alzheimer's disease in a community-based case series. *J Am Geriatr Soc.* 1999; 47:564-569.

**Comment #23:**

Submitter: Gary W. Small, MD

Organization: UCLA Center on Aging

Date: March 23, 2004

Comment:

\* What minimal services must be performed and documented as pre-requisites for ordering a PET scan?

Minimal services required are:

- 5) performance and documentation of a standard comprehensive medical history and physical examination, including documented neurological examination,
- 6) assessment of mental status and activities of daily living,
- 7) laboratory tests – serum electrolyte (Na<sup>+</sup>, K<sup>+</sup>, Cl<sup>-</sup>, CO<sub>2</sub>), BUN, Cr, glucose, ALT and TSH determinations; CBC, including Hct, MCV and MCHC,
- 8) structural neuroimaging (CT or MRI)

\* Is a medical history alone sufficient to ascertain six months of cognitive decline or is actual observation by a clinician necessary to assess and document a decline over such a period prior to ordering a PET scan?

Minimal sufficient documentation of decline is constituted by one of the following:

- 4) actual longitudinal observation by a clinician over a period extending at least six months,
- 5) a history obtained and deemed reliable by clinician, from interviewing patient and/or close contact(s) of patient, which documents progressive decline over a period of at least six months preceding the time of clinician's evaluation,
- 6) a combination of the above, amounting in total to at least six months of decline documentable by the summed periods of time represented by 1) and 2)

\* What qualifications must a practitioner have to be considered "experienced in the diagnosis and assessment of dementia"?

Acceptable qualifications are:

- 3) Board-eligibility or Board-certification in Neurology, Psychiatry, Internal Medicine or Family Practice, as experience in making this diagnosis is an integral part of the training for each of these specialties, or
- 4) Physicians with other specialty training may be appropriate referrers, if they can document that in the normal course of their professional activity they are called upon to make this kind of assessment concerning dementia (e.g., have records showing that patients are referred to them for that evaluation, or that patients present to the physician for the purpose of being

evaluated for cognitive/behavioral complaints)

\* What type of facility or setting is likely to offer the knowledgeable and experienced interdisciplinary staff needed to conduct a comprehensive assessment and render an accurate clinical diagnosis of dementia? Can a minimum set of facility criteria be identified that provide assurance that a comprehensive assessment will be performed? What set of skills and professions must be assembled on the interdisciplinary team?

Acceptable types of facilities:

- 4) General hospital,
- 5) Psychiatric hospital,
- 6) Outpatient clinics of physicians qualified by criteria described above

The professional(s) carrying out the required comprehensive assessment must reflect the following set of skills:

- 3) trained in evaluation of dementia, including conducting a medical history and physical examination, neurological examination, assessment of mental status and activities of daily living – as occurs in the professional training of neurologists, psychiatrists, internists and family practice physicians,
- 4) trained and licensed to order and interpret the results of laboratory and neuroradiology tests outlined above.

\* A comprehensive workup utilizing the NINCDS-ADRDA criteria for clinical diagnosis of Alzheimer's disease qualifies the likelihood of Alzheimer's disease as "definite," "probable," "possible," or "uncertain". Should PET be ordered only when the comprehensive assessment results in an uncertain diagnosis?

PET should be ordered only when the comprehensive assessment does not result in a “definite” diagnosis. It is clear from the primary peer-reviewed literature that the presence of Alzheimer’s disease is “uncertain” in many patients who meet NINCDS-ADRDA criteria of “possible AD” or “probable AD.” For example, in the one peer-reviewed article to examine clinical diagnostic accuracy for evaluation of early dementia, presenting data that met the American Academy of Neurology designation of “Class I” quality of evidence<sup>1</sup>, among all patients who were subsequently proven by autopsy to NOT have AD, 45% of those patients actually met NINCDS-ADRDA criteria for “probable AD”<sup>2</sup> -- and the specificity of “possible AD” was even lower.

\* What are the key differential diagnoses among neurodegenerative causes of dementia (e.g., frontotemporal dementia vs. AD) that PET could reasonably be expected to help clarify after an experienced clinician or team has completed an assessment? What are those clinical situations for which other imaging or other tests would be better indicated (e.g., distinguishing AD from mixed AD- multi-infarct dementia)?

Key differential diagnoses which PET will help clarify after assessment by an experienced

clinician or team are:

- 6) AD vs. Frontotemporal dementia,
- 7) Frontotemporal dementia vs. Dementia with Lewy bodies,
- 8) AD vs. non-neurodegenerative causes of progressive dementia,
- 9) Frontotemporal dementia vs. non-neurodegenerative causes of progressive dementia,
- 10) Dementia with Lewy bodies vs. non-neurodegenerative causes of progressive dementia

Differential diagnoses for which other methods of distinguishing are more suitable are:

- 5) AD, Frontotemporal, or other neurodegenerative dementia vs. untreated depression,
- 6) AD, Frontotemporal, or other neurodegenerative dementia vs. untreated substance abuse or adverse effects of other pharmacologic agents,
- 7) AD, Frontotemporal, or other neurodegenerative dementia vs. untreated thyroid disease,
- 8) AD, Frontotemporal, or other neurodegenerative dementia vs. untreated nutrient deficiency

\* What are the minimal educational requirements for staff performing and interpreting the PET scans? How should test performance and interpretation be standardized? What accreditation requirements must facilities performing PET scans for AD meet?

Minimal educational/certification requirements for staff performing the PET scans:

Certified Nuclear Medicine Technologist (CNMT)

Minimal educational/certification requirements for staff interpreting the PET scans include at least one of the following:

- 4) American Board of Nuclear Medicine (ABNM) certification,
- 5) American Board of Radiology (ABR) certification, with ABR special certification in Nuclear Medicine,
- 6) Neurologist, psychiatrist, or radiologist with current eligibility to bill CMS for interpretation of brain CT or MRI, plus documentable specific training in interpretation of brain PET scans

For all kinds of Nuclear Medicine tests, professional guidelines for performance and interpretation of diagnostic studies are often issued (e.g. by the Society for Nuclear Medicine), but there is no official specialty-wide standardization requirements for performance of any Nuclear Medicine study – nor should there be, as performance standards are tailored to the specific conditions and equipment present at each site, and it is ultimately the responsibility of each facility and physician to assure performance and interpretive quality, and maintain professional accreditations.

Cummings, Jeffrey, M.D., Augustus S. Rose Professor, Departments of Neurology, and Psychiatry and Biobehavioral Sciences, Director, UCLA Alzheimer's Disease Center, David Geffen School of Medicine, University of California, Los Angeles; Co-Chairman, American Academy of Neurology Practice Parameter Committee on Dementia; President, Alzheimer's Association, Los Angeles, San Bernardino & Riverside Chapter.

Small, Gary, M.D., Parlow-Solomon Professor on Aging, Professor of Psychiatry and Biobehavioral Sciences, Director, UCLA Center on Aging, David Geffen School of Medicine, University of California, Los Angeles; Member, American Academy of

Neurology Practice Parameter Committee on Dementia.

Silverman, Daniel, M.D., Ph.D., Assistant Professor, Department of Molecular and Medical Pharmacology, Head, Section of Neuroimaging, David Geffen School of Medicine, University of California, Los Angeles.

Coleman, Edward, M.D., Professor and Vice Chairman, Department of Radiology, Duke School of Medicine.

Chodosh, Joshua, M.D., Associate Professor, Division of Geriatrics, Department of Medicine, David Geffen School of Medicine, University of California, Los Angeles.

Phelps, Michael, Ph.D., Norton Simon Professor, Chairman, Molecular and Medical Pharmacology, Director, Institute for Molecular Medicine, David Geffen School of Medicine, University of California, Los Angeles.

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**References:**

1. Knopman DS, DeKosky ST, Cummings JL, et al. Practice parameter: diagnosis of dementia (an evidence-based review). Report of the Quality Standards Subcommittee of the American Academy of Neurology. *Neurology*. 2001; 56:1143-1153.
2. Lim A, Tsuang D, Kukull W, et al. Clinico-neuropathological correlation of Alzheimer's disease in a community-based case series. *J Am Geriatr Soc*. 1999; 47:564-569.

**Comment #24:**

Submitter: Corissa Wise  
Organization:  
Date: March 22, 2004  
Comment:

I am writing to request that PET be approved for Alzheimer's. This test is the only definitive way to positively diagnose ALZ. If individuals can be accurately diagnosed, we can treat them with appropriate medications.

**Comment #25:**

Submitter: Christopher Kirk, MD  
Organization: Mid-Valley IPA  
Date: March 15, 2004  
Comment:

I would focus on 2 main topics in considering this issue:

1. Is there solid scientific evidence demonstrating that PET scan can actually & reliably differentiate AD from the neuroanatomical changes associated with other forms of dementia? If not, the decision process need go no further.
2. Are there specific examples of existing therapies that would be tried or withheld based on the PET findings? Current therapies, such as Aricept, are recommended based on a clinical diagnosis using a standardized measurement tool (such as an MMSE, etc.) In order to be clinically valuable, the PET scan findings would need to dictate a treatment decision that would be significantly different than the one based on current "technology".
3. However passionate, pleas for coverage from reputable organizations are not scientific data.

**Comment #26:**

Submitter: Paul Tuite, MD

Organization: University of Minnesota Department of Neurology

Date: March 16, 2004

Comment:

From my review of the literature and use of FDG PET scanning, I believe that it is useful in evaluating patients.

Specifically, the following conditions may be differentiated based on scanning:

Frontotemporal dementia

Corticobasal degeneration

Lewy body dementia

Progressive supranuclear palsy

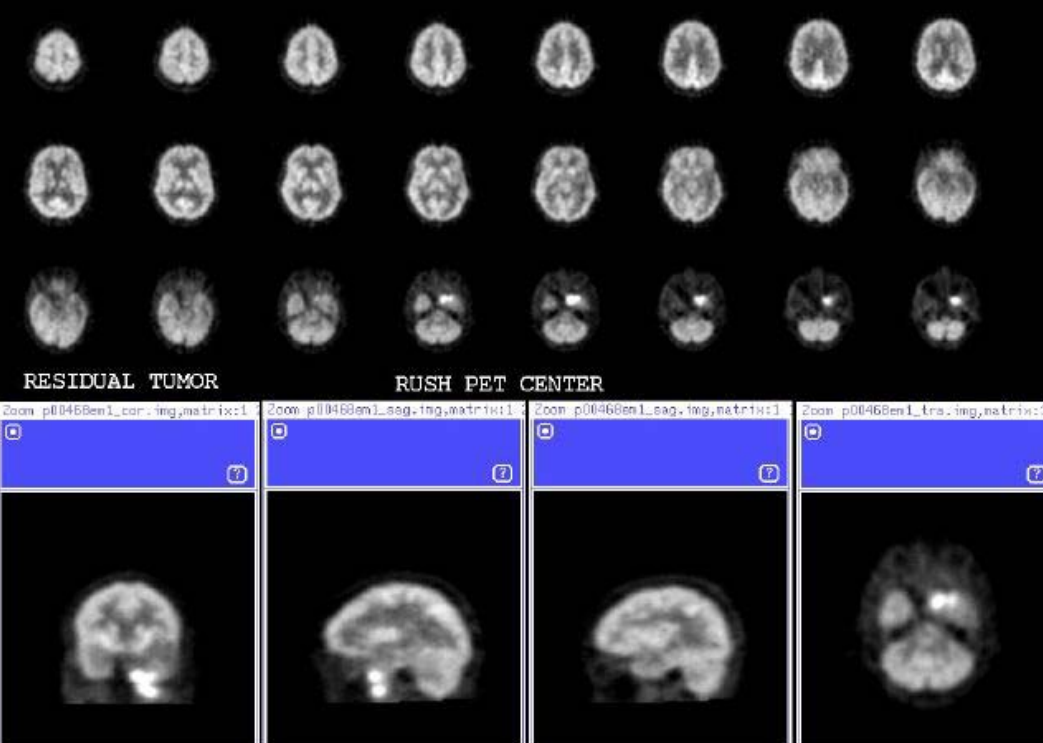
Primary progressive aphasia

Possibly vascular dementia

I have attached a powerpoint file with images for use and would be happy to provide review articles, etc.

# FDG PET Scanning Dementia Syndromes

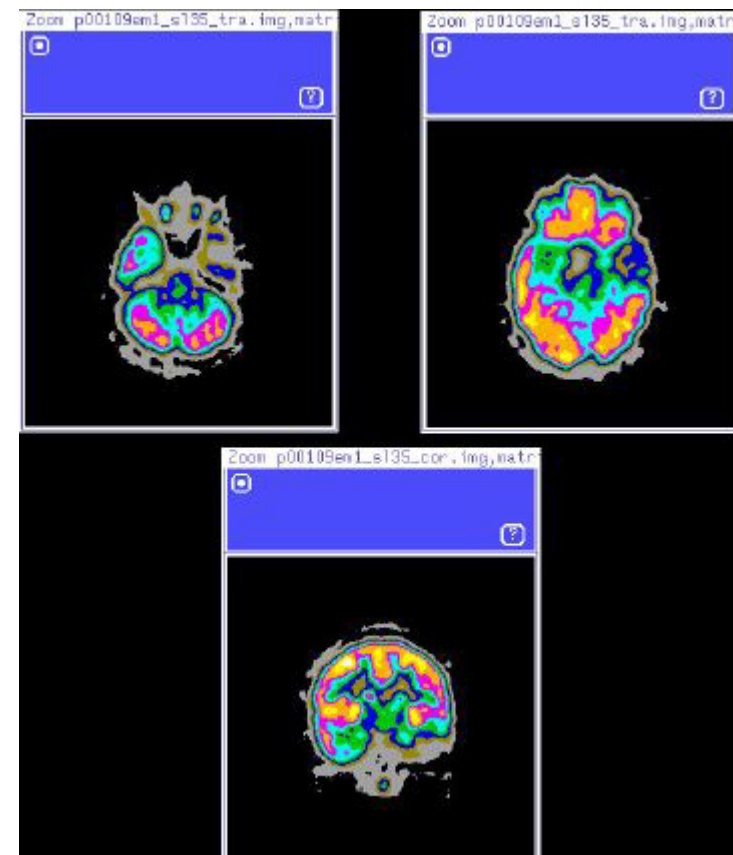
Paul Tuite, MD  
University of Minnesota



**Tumor: Left Temporal Lobe**

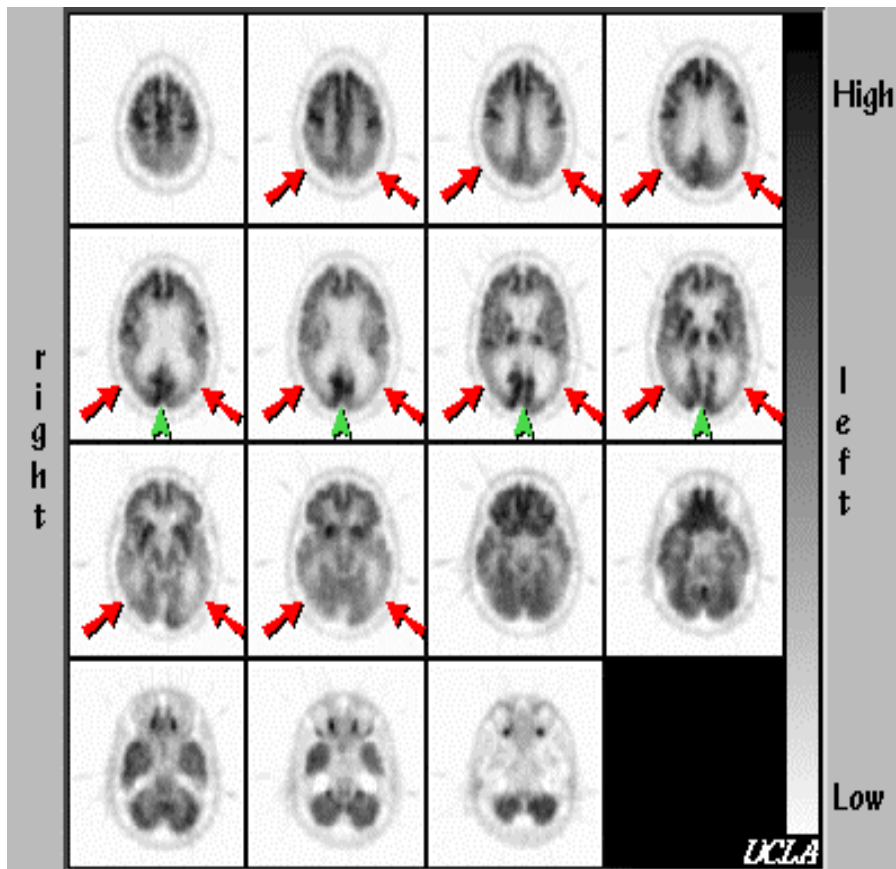
[geocities.com/HotSprings/Villa/8162/mypet.html](http://geocities.com/HotSprings/Villa/8162/mypet.html)

**Epilepsy Interictal,  
Left Temporal Lobe**

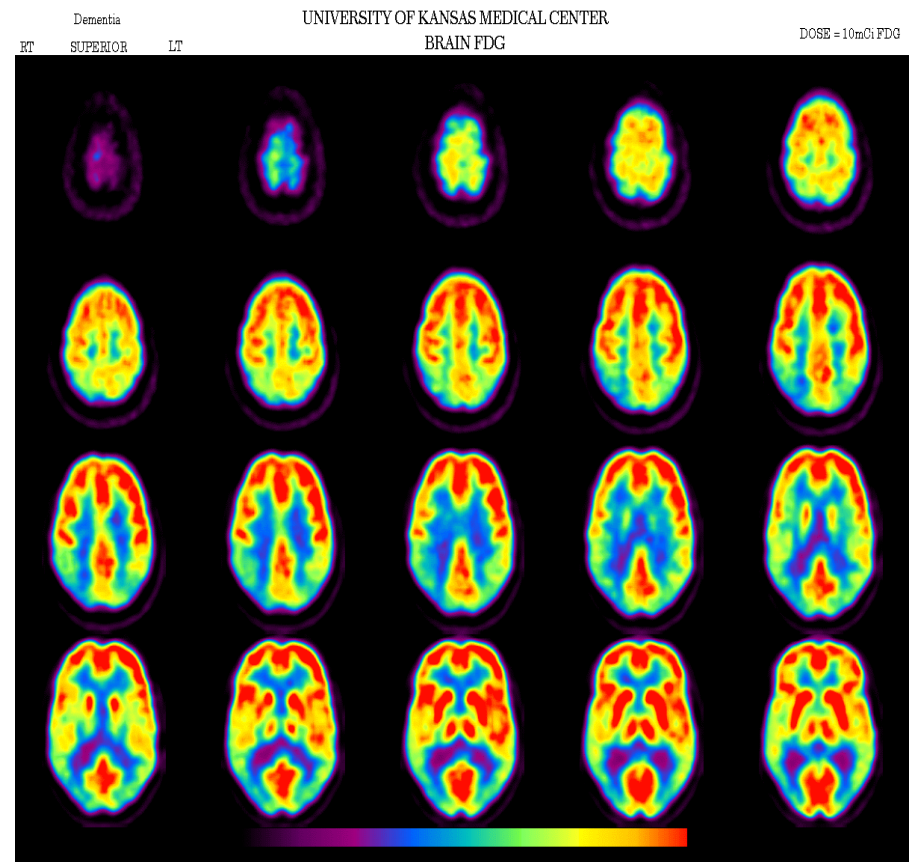




# Alzheimer's disease (AD)

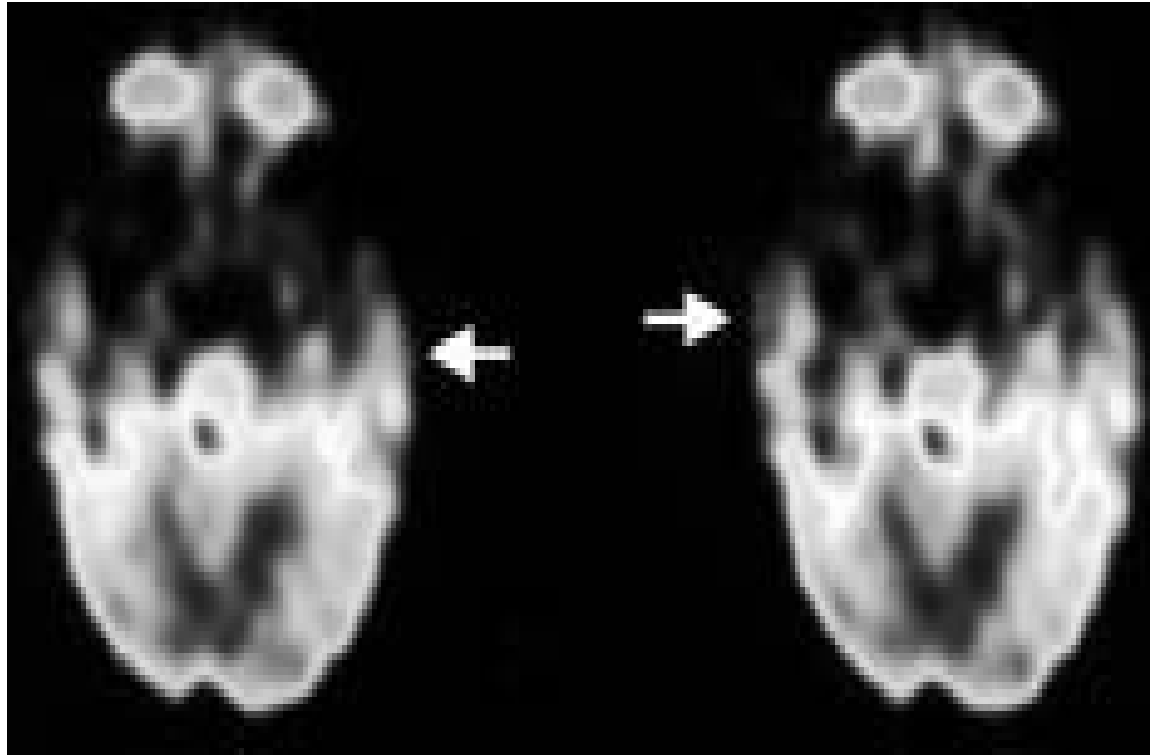


UCLA



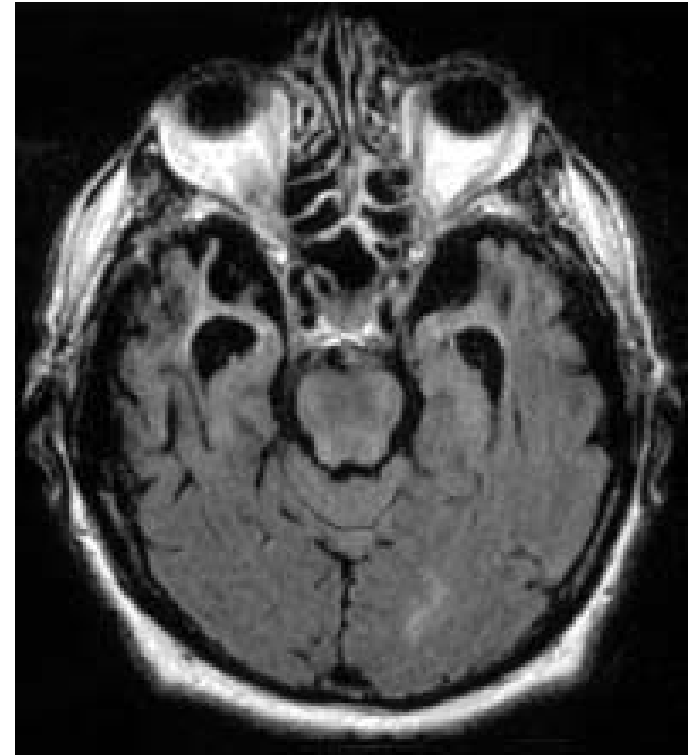
U Kansas

# Frontotemporal Dementia (FTD)



FDG PET:

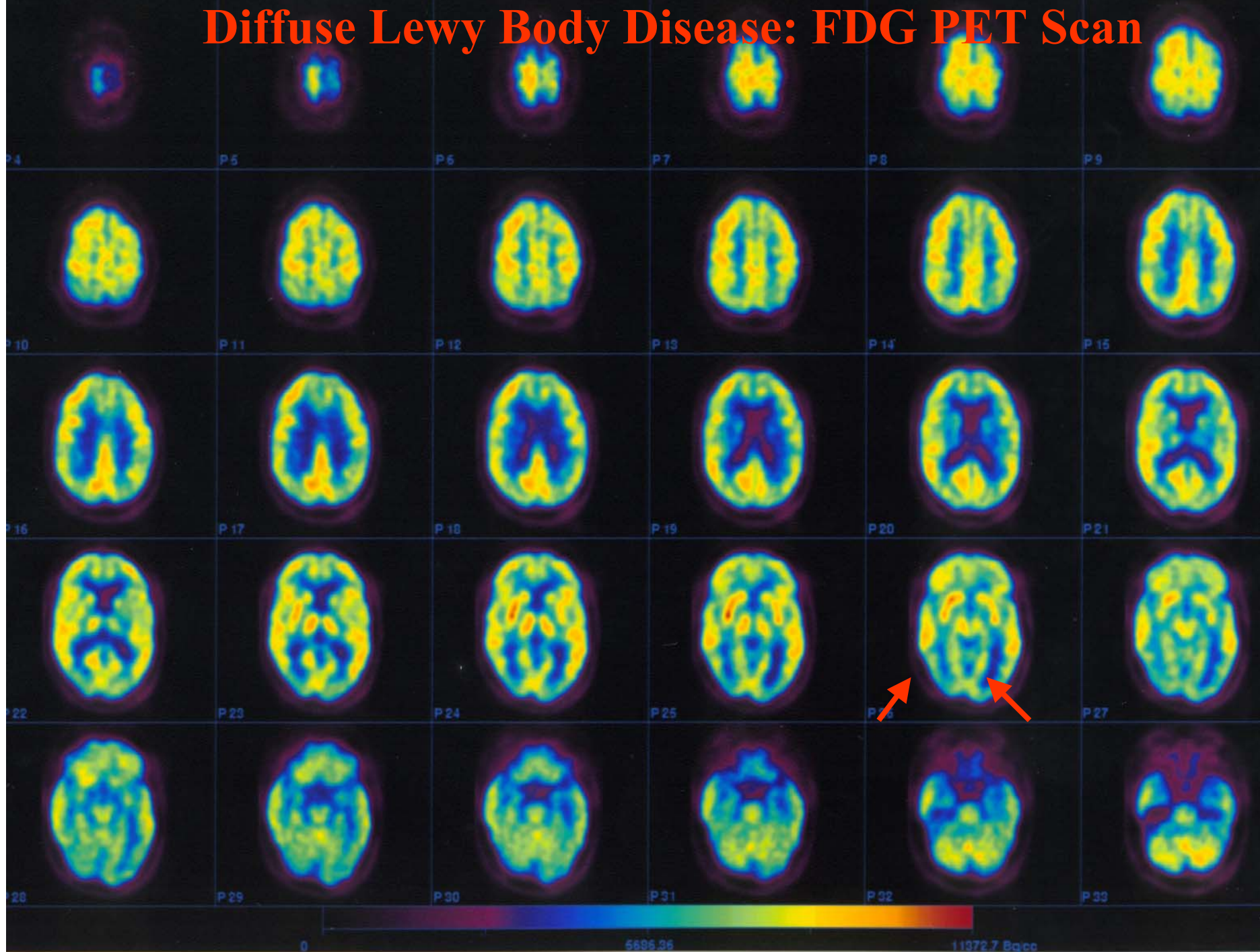
Temporal Lobe Hypometabolism



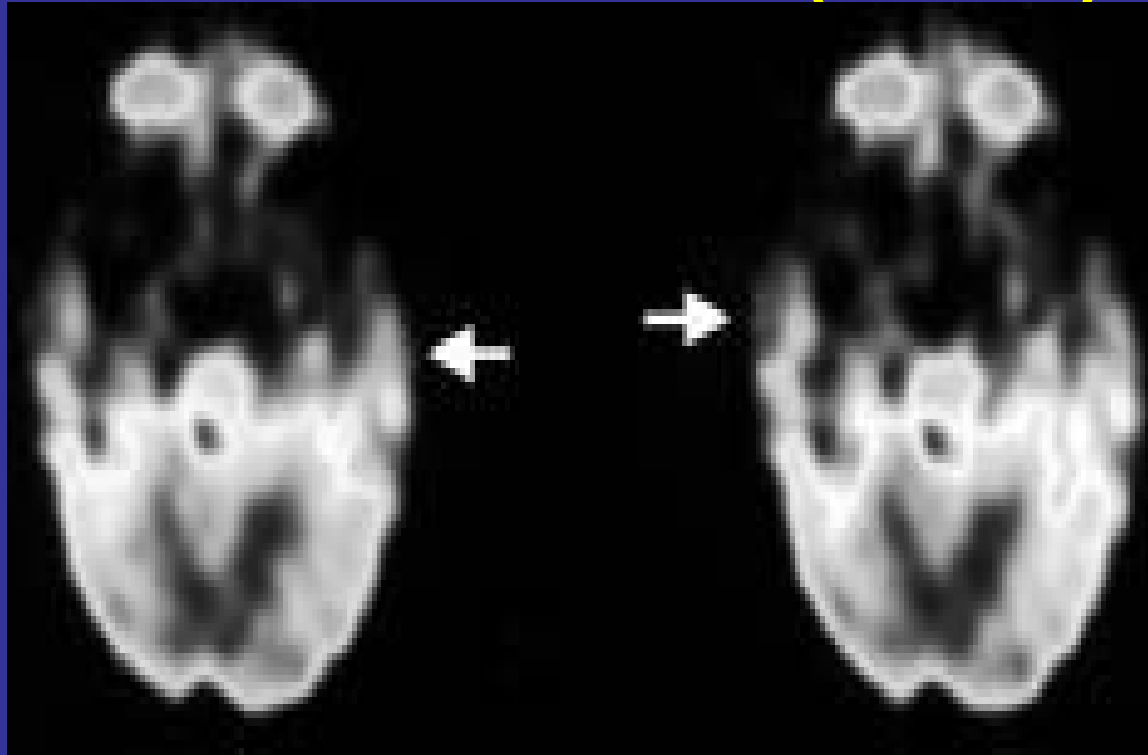
Brain MRI:

Ant Temp Atrophy

# Diffuse Lewy Body Disease: FDG PET Scan

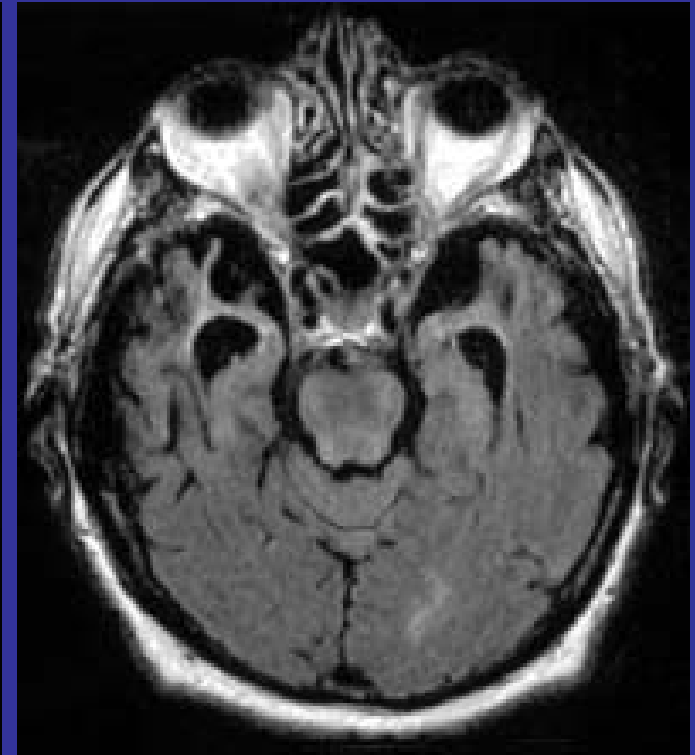


# Frontotemporal Dementia (FTD)



FDG PET:

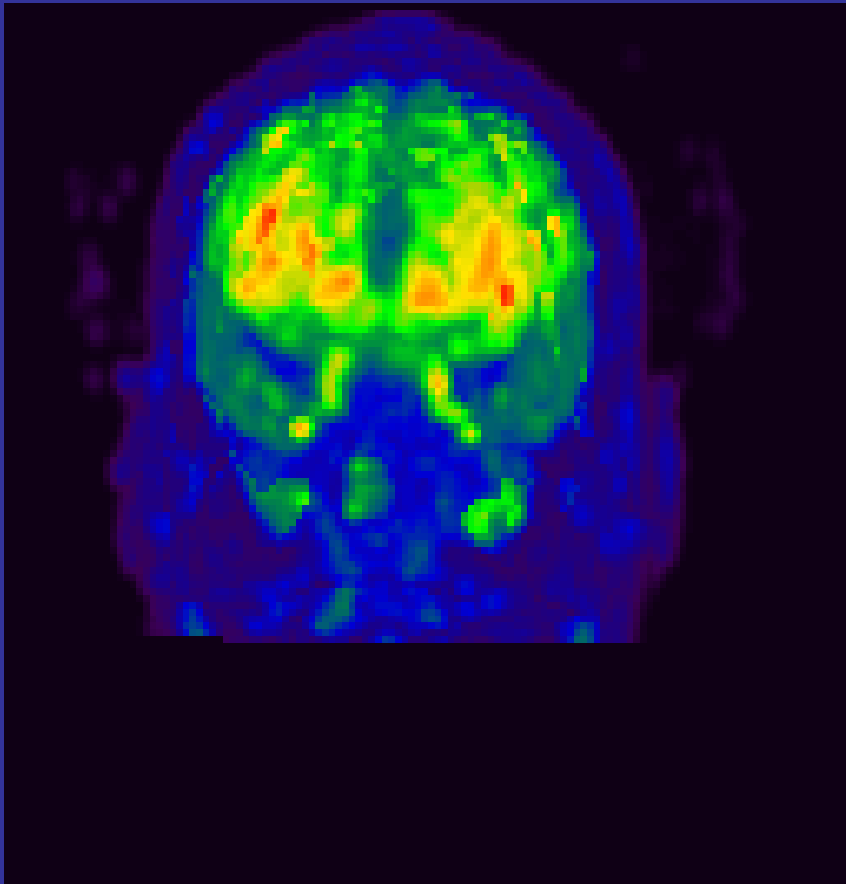
Temporal Lobe Hypometabolism



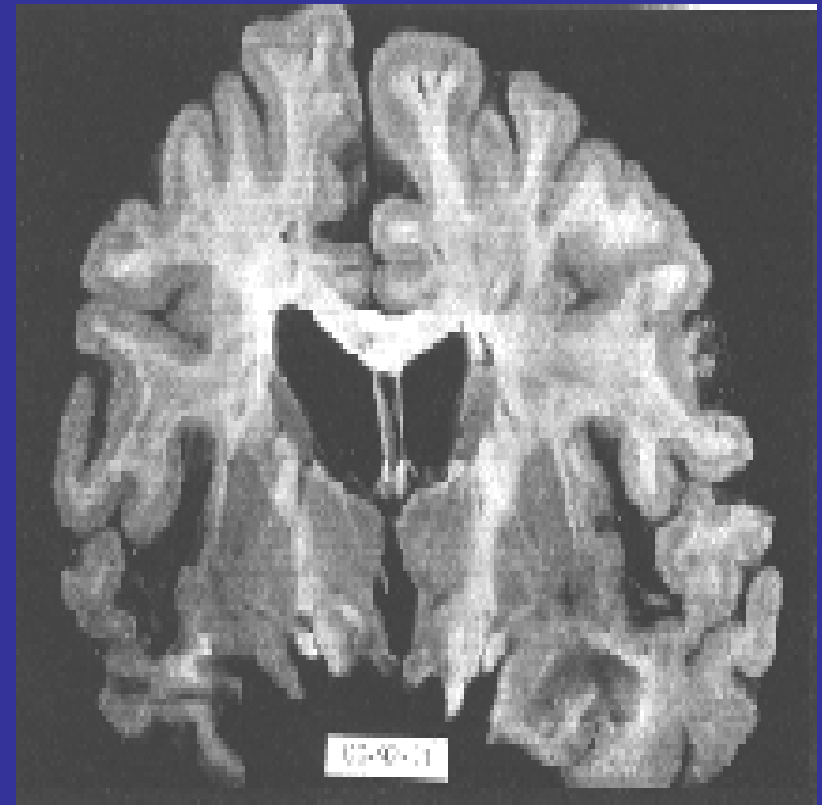
Brain MRI:

Ant Temp Atrophy

# Pick's Disease



U of Iowa



Wash U

# Primary Progressive Aphasia Progressive Non-Fluent Aphasia

**<sup>99</sup>Tc-HMPAO SPECT:**

Decreased uptake in the left temporal and posterior parietal lobes.

Uptake in the right hemisphere and both thalami is within normal limits



**Comment #27:**

Submitter: Robert L. Meredith, MD

Organization:

Date: March 22, 2004

Comment:

I am a nuclear medicine physician who performs PET at 500 bed community hospital in Wisconsin. While I can not answer all the questions listed below related to PET and Alzheimer's disease I do feel I am qualified to comment on at least some of the issues raised below.

a..

b.. What minimal services must be performed and documented as pre-requisites for ordering a PET scan?

It would seem to me that this question is best left to neurologists. As they are the ones who will likely be most involved in determining when a study would be ordered. From my perspective as a Nuclear Medicine specialist I would rely on their opinion of when a study would be appropriate.

It would seem to me that a diagnosis of dementia either by skill testing or clinical judgment would be the minimum pre-requisites. While a CT scan may be beneficial to rule out infarct related dementia, beyond this readily available test the quality of PET for differentiation of brain abnormalities is unmatched.

a.. Is a medical history alone sufficient to ascertain six months of cognitive decline or is actual observation by a clinician necessary to assess and document a decline over such a period prior to ordering a PET scan?

It seems to me that history alone is sufficient. Information would come from sources such as the patient's family and family physician which would be nearly as valid as actual observation in most cases, as these are the people most aware of the changes in the patient's mental state. As the medications currently available to treat AD are for early cases it seems that a long prerequisite period of evaluation would be harmful to the patient.

a.. What qualifications must a practitioner have to be considered "experienced in the diagnosis and assessment of dementia"?

I can not answer this question for clinicians, but for PET practitioners anyone sufficiently knowledgeable about PET should be able to acquire the necessary skills readily if they are not already familiar with AD changes by PET. Personally I would like to see evaluation of PET scans limited to people who have residency training in PET or board certified in Nuclear Medicine rather than the proliferation of radiologists trained in two day weekend courses and video courses. My partner and I were both residency trained in PET and have seen several brain PET scans for various diseases. Speaking personally I would return to my place of training at the University of Wisconsin to review brain PET studies before I would take on the diagnosis of

AD by PET, although it is a relatively straight forward diagnosis by PET. Persons specifically trained in PET are more likely to have dedication to the future of the modality needed for more complex studies such as evaluation of the brain.

a.. What type of facility or setting is likely to offer the knowledgeable and experienced interdisciplinary staff needed to conduct a comprehensive assessment and render an accurate clinical diagnosis of dementia? Can a minimum set of facility criteria be identified that provide assurance that a comprehensive assessment will be performed? What set of skills and professions must be assembled on the interdisciplinary team?

Our facility has a dedicated full ring PET with two board certified nuclear medicine physicians. We will be getting a PET/CT unit in approximately two months. We are approved for 500 beds at our hospital and have a staff of six certified nuclear medicine technologists. I am positive we have the technical expertise and equipment necessary for evaluation of AD by PET. We have neurologists and psychiatrists on staff, but again, as I am not a clinician I can not speak to the clinical side of the equation.

a.. A comprehensive workup utilizing the NINCDS-ADRDA criteria for clinical diagnosis of Alzheimer's disease qualifies the likelihood of Alzheimer's disease as "definite," "probable," "possible," or "uncertain". Should PET be ordered only when the comprehensive assessment results in an uncertain diagnosis?

"Possible" and "probable" would likely benefit by PET evaluation beyond just using PET for "uncertain" cases as it would provide a more definite diagnosis and provide some measurement of the severity of the disease. If it is "definitely" AD it is likely advanced and PET probably would not offer any significant clinical benefit that I am aware of, but again I can not fully speak to the clinical side of the disease.

a.. What are the key differential diagnoses among neurodegenerative causes of dementia (e.g., frontotemporal dementia vs. AD) that PET could reasonably be expected to help clarify after an experienced clinician or team has completed an assessment? What are those clinical situations for which other imaging or other tests would be better indicated (e.g., distinguishing AD from mixed AD- multi-infarct dementia)?

CT may be beneficial to evaluate multi-infarct dementia. The narrow focus of my specialty makes it difficult for me to comment on other types of imaging.

a.. What are the minimal educational requirements for staff performing and interpreting the PET scans? How should test performance and interpretation be standardized? What accreditation requirements must facilities performing PET scans for AD meet?

I think I spoke to this to some degree above. Personally I have mixed feelings about the proliferation of PET readers nationwide who have a bare minimum of training. It does put a valuable modality into the community and for the most part PET scans are relatively straight forward, but a two day or one week course does not likely provide the background and experience necessary to truly understand the limitations and abilities of the modality and will likely lead to decreased precision and accuracy with PET over time as it has with general nuclear



medicine. JCHO and NRC licensure are probably sufficient facility accreditation. I would prefer board certification in nuclear medicine for interpreting of PET. I am sure the Nuclear Medicine community and Society of Nuclear Medicine would be willing to help in setting up test performance and interpretation standards.

**Comment #28:**

Submitter: Julie Mann Bullen

Organization:

Date: March 22, 2004

Comment:

As a PET technologist, I see everyday the importance and impact PET imaging has on people's lives. I would like to add my name to your list in favor of implementing and reimbursing PET imaging in defining Alzheimer's/dementia dx. Diagnosing and staging such a disabling condition seems imperative when dealing with life decisions, life quality, and hopefully expanding medical knowledge in treating this disease. I support the use and reimbursement of PET imaging in the diagnosis, treatment and management of Alzheimer's and dementia disease.

**Comment #29:**

Submitter: Guiyun Wu, MD

Organization: Cleveland Clinic Foundation

Date: March 17, 2004

Comment:

The accurate diagnosis of Alzheimer's is important for the reason that medication can delayed the symptom manifestation and buy some good quality life for the patient. Clinical assessment alone is not enough to make a diagnosis most of the time. For the early stage or preclinical stage, PET seems the only tool to make the diagnosis. PET can detect abnormality before clinical manifestation, which is the best time to start medical management to delay the symptom development. It is also cost effective. The earlier the test is done, the less likely patient will receive the unnecessary tests. I think it helpful the patient be evaluated by neurologist first to exclude some other etiology including depression, cerebral vascular disease, etc. But if the internist have good clinical indication, go straight to have the PET might be more cost effective to avoid unnecessary tests. To interpret the PET do need some experience. But with nuclear medicine training will usually be enough.

**Comment #30:**

Submitter: Scott L. Lucas

Organization:

Date: March 18, 2004

Comment:

PLEASE HELP ENCOURAGE COVERAGE OF ALZHEIMER'S AS AN INDICATION FOR A PET SCAN. PET TECHNOLOGY IS A WONDERFUL TECHNOLOGY WHICH IS OF GREAT VALUE THOUGH IT IS RESTRICTED FROM HELPING PATIENTS BY THE SLOW ACTION OF THE GOVERNMENT. NOT JUST FOR ALZHEIMERS BUT FOR SEVERAL TYPES OF CANCER WHICH AFFLICT MANY AMERICANS WHO ARE HURT BY THOSE RESTRICTIONS IN PAYMENT COVERAGE. AND AS YOU KNOW THE PRIVATE INSURANCE COMPANIES OFTEN TAKE THEIR LEAD FROM MEDICARE. HELPING PET TECHNOLOGY THRIVE WOULD BE A GREAT SERVICE TO MANY PATIENTS WHO ALREADY FACE HORRIFYING DISEASE AND HUGE MEDICAL BILLS

**Comment #31:**

Submitter: Hussein M. Abdel-Dayem, MD

Organization: New York Medical College

Date: March 18,2004

Comment:

I am writing in favour of the request submitted by UCLA for the revision of the previous decision made by CMS regarding the coverage for use of F-18 FDG for the diagnosis of early dementia. The published data supports that the specific pattern and the sensitivity of the test will lead to the early start of treatment if the diagnosis is based only on the current psychometric tests. The early start of treatment will decrease the nursing home care period, increase the productivity of the candidates may be for few years and eventually will result in financial savings for CMS and social benefits for the patients and their families.

I hope that a favourable decision will be agreed to in the coming review.

Thank you for your services;

**Comment #32:**

Submitter: Joseph Castronuovo, MD

Organization:

Date: March 18, 2004

Comment:

As a nuclear medicine physician with 20 plus years experience in the field, I know there is an underutilized nuclear study that has been validated in

this group of patients. In most cases a Cerebral SPECT will provide adequate confirmatory diagnostic information if properly performed and interpreted by a qualified physician. This type of procedure can be performed in most nuclear medicine departments or outpatient nuclear medicine facilities. The sensitivity of this test is less than that of PET for very early or mild cases and PET scan is probably most indicated in this latter group of Alzheimer patients.

**Comment #33:**

Submitter: Edwin Holmes, MD

Organization:

Date: March 18, 2004

Comment:

PET should be approved for Alzheimer's as it is the most accurate non invasive diagnostic method and will save money by appropriate patients being treated earlier reducing clinic visits, repeats of other tests which add no value, reduced use of other meds which are only symptomatic in nature and have depressive side effects, longer time functioning in society and less time in expensive care centers. Over all money will be saved and better care will be given.

**Comment #34:**

Submitter: George W. Privett, MD

Organization:

Date: March 18, 2004

Comment:

This is to voice my comment about the need for a reimbursement for an excellent diagnostic test for Alzheimer's Disease (AD). As a neurologist and neuro-imager, I know that it is very frustrating to treat patients with dementia. While the differential diagnosis of dementia is Alzheimer's dementia (AD), non-Alzheimer's dementia or pseudo-dementia. It is even more frustrating to have to play guessing games and jump through many expensive diagnostic hoops to try to arrive at a diagnosis, while all the while knowing that there is an excellent noninvasive diagnostic test for AD, i.e., PET, which is not covered by Medicare.

While there may not be an entirely satisfactory treatment for AD, there are certainly some treatments which seem to slow the progress of the disease and many other possible treatments are on the horizon. However, there are other reasons than treatment, that make a definite diagnosis important. Those reasons include:

Ruling in or out other treatable causes of dementia;  
Being able to plan one's life;  
Being able to make informed decisions about future care before the dementia makes planning impossible;  
Being able to seek out and join drug treatment clinical trials AD based on a firm diagnosis.

Please record my support for the adding of dementia as a reimbursable diagnosis for reimbursement for PET.

**Comment #35:**

Submitter: James W. Fletcher, MD  
Organization: Indiana/Purdue University at Indianapolis  
Date: March 18, 2004  
Comment:

We are currently reviewing the evidence. We request public input on operational issues that might arise should the evidence support the request.

\* What minimal services must be performed and documented as pre-requisites for ordering a PET scan?

I would agree with the pre-requisite criteria submitted by UCLA in their request: the patient should have undergone a comprehensive H & P including neurological examination, common screening tests for other causes of dementia and possibly anatomic imaging with CT or MRI (if indicated e.g. high likelihood for MID) and there is still no explanation for the decline in cognition or there has been no treatment of reversible causes of dementia that have restored the patient to normal state of cognition.

\* Is a medical history alone sufficient to ascertain six months of cognitive decline or is actual observation by a clinician necessary to assess and document a decline over such a period prior to ordering a PET scan?

A medical history of six months of decline in combination with the criteria above would be sufficient and actual observation by a clinician over a six month interval would not be required.

\* What qualifications must a practitioner have to be considered "experienced in the diagnosis and assessment of dementia"?  
Fully licensed to practice medicine without restriction and capable of performing a thorough neurological examination and mental status examination. I do not believe that certification in Neurology is required.

\* What type of facility or setting is likely to offer the

knowledgeable and experienced interdisciplinary staff needed to conduct a comprehensive assessment and render an accurate clinical diagnosis of dementia? Can a minimum set of facility criteria be identified that provide assurance that a comprehensive assessment will be performed? What set of skills and professions must be assembled on the interdisciplinary team?

Generally a multidisciplinary setting that includes expertise in application of the criteria noted below (NINCDS-ADRDA) for clinical diagnosis of AD as well as expertise in diagnostic imaging with special emphasis on performance and interpretation of high-quality FDG-PET imaging studies of the brain. This would typically involve expertise in neurology, diagnostic imaging including nuclear medicine for metabolic imaging and radiology for structural imaging and laboratory facilities for performance of appropriate screening tests.

\* A comprehensive workup utilizing the NINCDS-ADRDA criteria for clinical diagnosis of Alzheimer's disease qualifies the likelihood of Alzheimer's disease as "definite," "probable," "possible," or "uncertain". Should PET be ordered only when the comprehensive assessment results in an uncertain diagnosis?

There would generally still be no explanation for cognitive decline under any of the likelihood scenarios noted above with the exception of "definite." I would favor not using or coupling these criteria or likelihood levels with the consideration to perform PET. I would prefer the language in my first paragraph response noted above.

\* What are the key differential diagnoses among neurodegenerative causes of dementia (e.g., frontotemporal dementia vs. AD) that PET could reasonably be expected to help clarify after an experienced clinician or team has completed an assessment? What are those clinical situations for which other imaging or other tests would be better indicated (e.g., distinguishing AD from mixed AD- multi-infarct dementia)?

As the pattern of FDG distribution is very unique in AD compared to other progressive neurodegenerative diseases FDG-PET would be useful in all circumstances that fit the scenario indicated above that is indicated in my response to the first paragraph. It is beyond the scope of this response to develop a comprehensive reply, but a matrix that considered major health factors for a given patient and associated required testing could be developed similar to a practice guideline.

\* What are the minimal educational requirements for staff performing and interpreting the PET scans? How should test performance and interpretation be standardized? What accreditation requirements must facilities performing PET scans for AD meet?

The determination of minimal educational requirements for staff performing and interpreting PET scans should be left to the professional organizations that educate, train and certify in this area (e.g. ABNM,

ABR, NMTCB, ARRT, etc.). I do not believe that you want to get into setting criteria for competency or proficiency in the medical professional arena. Standardization of performance and interpretation are also the responsibility of the professional organizations just mentioned. Accreditation requirements for PET imaging centers are in evolution and while certain criteria exist, there is no general agreement on these requirements. I do not believe that accreditation of a facility should necessarily be linked to ability to perform a diagnostically acceptable PET scan and subsequently be reimbursed for that procedure.

**Comment #36:**

Submitter: James H. Timmons, MD, Ph.D.

Organization: Radiology Consultants

Date: March 18, 2004

Comment:

Services to perform - suggest evaluation by Board Certified Neurologist, assessment of ADL by clinical social worker in association with caregiver, MRI of brain. Consider neuropsychological testing as a prerequisite (I would defer to those with more knowledge of sensitivity and specificity of this test battery)

In this unique situation, history given by the patient on two occasions does constitute observation and documentation of decline by a physician. History obtained entirely from caregivers would not necessarily be reliable.

Qualifications for diagnosis and assessment for dementia- Board Certified Neurologist. Probably Board Certified Psychiatrist. Possibly Psychologists specializing in neuropsychiatric testing.

Minimum facility criteria should be availability of one of above with interest in dementia plus clinical social worker and experienced radiologist. (If you want to avoid self-referral problems, have the MRI component done by a radiologist. The examining physician has a conflict of interest if they are also ordering and interpreting the MRI. This could affect both the MRI and the history/physical examination interpretation, resulting in increased expense to CME for MRI examinations.)

I believe PET is reasonable for possible or uncertain diagnosis. Possible is not much help if you have to make a therapeutic decision on that basis. Probable is adequate for therapeutic decisions. "Definite" is never achieved in medicine, NINCDS-ADRDA criteria notwithstanding. This category should be "highly probable".

Prominent competing diagnoses are multi-infarct and Lewy body dementia. The patterns are generally quite distinct.

PET should be interpreted by Nuclear Medicine Physician, Radiologist with Special Competence in Nuclear Medicine, or Radiologist with experience equivalent to Special Competence in Nuclear Medicine. Facilities should have either PET-CT capability, or CT/PET, MR/PET fusion capability and a technologist trained in performing the fusion. A controlled environment for injection and a standard protocol for the injection period are mandatory, since brain activation during the immediate post-injection period can definitely create false positive and false negative results. Suggest that the standards of the Brain Imaging Council of the Society of Nuclear Medicine be consulted and an appropriate set of standards be developed from this source, since most of the experienced functional brain imagers have served on this council. To avoid costs resulting solely from the conflict of interest inherent in self-referral, I would again stress that the person interpreting the PET imaging should not be the person performing the clinical examination and managing the patient.

With regard to initial credentials and credentials maintenance, I would suggest a experience in interpreting at least thirty functional brain scanning images of some type (not necessarily PET) under supervision by an experienced functional imager and a requirement for a minimum of 10 hours PET continuing medical education and 10 hours of continuing medical education (CME) in dementia prior to initial credentialing, with a requirement of 15 hours CME in each area every 3 years thereafter. The initial CME requirement should be waived for those graduating from an accredited program in nuclear medicine or radiology who have had rotations in functional imaging in the three years prior to beginning interpretation of brain PET. This approach is similar to the ones adopted for MQSA qualification for breast imaging, ACR accreditation for imaging facilities, and ICVL accreditation for vascular laboratories.

Thanks for the opportunity to respond.

**Comment #38:**

Submitter: Eric K. Fitzcharles, MD

Organization:

Date: March 19, 2004

Comment:

I would like to submit input regarding the use of PET scanning for Alzheimer's diagnosis.

Specifically, since I am a board certified radiologist who regularly reads PET scans, I would like to comment on the last question posed by CMS, regarding the performance and interpretation of PET scans.

The American College of Radiology has an existing program for PET accreditation, including requirements for those performing and interpreting PET scans. While this program is most likely useful in promoting quality, I'm not clear on what percentage of PET imaging centers elect to pursue this type of accreditation, most likely due to a variety of demands including the time and money involved. Furthermore, once a decision is made to pursue accreditation, it may take years to meet the requirements. For example, ACR PET accreditation requires a brain PET interpreter to have read at least 30 brain PET scans in the last three years. Since brain PET is not a frequently ordered exam, many centers may not have enough volume to meet such a requirement even if they would like to. I believe that especially in the case of a newly emerging PET application such as Alzheimer's dementia, it is reasonable to allow the trained physicians who interpret PET scans to maintain standards of quality on their own volition and supervision, as this is already an integral part of their background and training. This will allow the qualified physician base to become quickly involved in Alzheimer's-PET imaging and bring this service to the public in an efficient manner.

**Comment #39:**

Submitter: Mary DeMaio

Organization:

Date: March 19, 2004

Comment:

We are currently reviewing the evidence. We request public input on operational issues that might arise should the evidence support the request.

\* What minimal services must be performed and documented as



pre-requisites for ordering a PET scan?

Physical exam, cognitive test

\* Is a medical history alone sufficient to ascertain six months of cognitive decline or is actual observation by a clinician necessary to assess and document a decline over such a period prior to ordering a PET scan?

Actual observation

What qualifications must a practitioner have to be considered "experienced in the diagnosis and assessment of dementia"?

I think a primary care doctor sees many of these patients & can make decision

\* A comprehensive workup utilizing the NINCDS-ADRDA criteria for clinical diagnosis of Alzheimer's disease qualifies the likelihood of Alzheimer's disease as "definite," "probable," "possible," or "uncertain". Should PET be ordered only when the comprehensive assessment results in an uncertain diagnosis?

No. My reading suggests that only PET can definitely determine Alzheimer's.

\* What are the minimal educational requirements for staff performing and interpreting the PET scans? How should test performance and interpretation be standardized? What accreditation requirements must facilities performing PET scans for AD meet?

Individuals with experience in interpretation of neurology PET

**Comment #40:**

Submitter: Russell H. Swerdlow, MD

Organization: University of Virginia Health System

Date: March 19, 2004

Comment:

There are now dozens of peer-reviewed manuscripts demonstrating PET and SPECT can contribute to the etiologic diagnosis of persons with cognitive disorders. As for my personal perspective, I am a dementia subspecialist neurologist. For the past 8 years I have served as one of Virginia's two tertiary referral neurologists regarding matters of cognitive decline (University of Virginia Memory Disorders Clinic). In my experience, PET and SPECT can be helpful when used to confirm or refute cerebral lesion localization as deduced via history, neurologic exam, and/or cognitive assessment.

To address the some of the question posed, I do not use PET/SPECT to "make a diagnosis". I use it as a tool for corroborating or refuting complicated clinical hypotheses that I've already posited based on history/exam/neuropsych/structural neuroimaging data. When all data point towards a clear differential diagnosis and provide a clear indication of the most likely diagnosis on the differential list, PET/SPECT is not required. IN THE REAL WORLD, though, sometimes historical/exam/neuropsych/structural imaging data are not concordant in suggesting

a particular diagnosis or particular cerebral localization. In these cases (probably 5% of those cases seen at the University of Virginia's Tertiary referral Memory Disorders Clinic), functional neuroimaging can contribute substantially to generating the most appropriate diagnosis.

At the very least, dementia subspecialty neurologists seeing patients within the context of tertiary referral memory disorders clinics should be allowed to decide whether or not PET/SPECT is reasonable in the evaluation of the dementia patients they are evaluating.

**Comment #41:**

Submitter: Puneet Chandak, MD

Organization: PET-CT and Nuclear Medicine Imaging of San Jose

Date: March 21, 2004

Comment:

I could not get to the Web-pages suggested in the email to PET\_Mail list that I could fill out, however, I strongly support the utilization of PET in Alzheimer's Disease.

**Comment #42:**

Submitter: Jeff Ervin

Organization:

Date: March 22, 2004

Comment:

a.. What minimal services must be performed and documented as pre-requisites for ordering a PET scan? EEG AND COGNITIVE ASSESSMENT BY A NEUROLOGIST

a.. Is a medical history alone sufficient to ascertain six months of cognitive decline or is actual observation by a clinician necessary to assess and document a decline over such a period prior to ordering a PET scan? THE DECLINE SHOULD BE TRACKED BY A CLINICIAN WITH SERIAL COGNITIVE TESTING OR THROUGH A COLLECTION OF MEDICALLY DOCUMENTED SOURCES

a.. What qualifications must a practitioner have to be considered "experienced in the diagnosis and assessment of dementia"? SHOULD HAVE A CLINICAL BACKGROUND IN NEUROLOGY OR PSCHIATRY

a.. What type of facility or setting is likely to offer the knowledgeable and experienced interdisciplinary staff needed to conduct a comprehensive assessment and render an accurate clinical diagnosis of dementia? Can a minimum set of facility criteria be identified that provide assurance that a comprehensive assessment will be performed? What set of skills and professions

must be assembled on the interdisciplinary team? A NEUROLOGIST OR PSYCHIATRIST SHOULD BE ABLE TO RENDER AN ACCURATE ASSESSMENT USING WHATEVER ANCILLARY STAFF THEY HAVE IN THEIR INDIVIDUAL OFFICES AS LONG AS THEIR EEG EQUIPMENT IS UP TO CODE.

a.. A comprehensive workup utilizing the NINCDS-ADRDA criteria for clinical diagnosis of Alzheimer's disease qualifies the likelihood of Alzheimer's disease as "definite," "probable," "possible," or "uncertain". Should PET be ordered only when the comprehensive assessment results in an uncertain diagnosis? IF PET CAN HELP DELINEATE A "POSSIBLE" OR "PROBABLE" LIKELIHOOD OF ALZHEIMER'S THEN IT SHOULD BE USED TO PROVIDE EARLY DIAGNOSIS AND TREATMENT

a.. What are the key differential diagnoses among neurodegenerative causes of dementia (e.g., frontotemporal dementia vs. AD) that PET could reasonably be expected to help clarify after an experienced clinician or team has completed an assessment? What are those clinical situations for which other imaging or other tests would be better indicated (e.g., distinguishing AD from mixed AD- multi-infarct dementia)? AD VS: CORICOBASAL DEGENERATION, HUNTINGTON'S DISEASE, MULTIPLE SYSTEM ATROPHY, SPINOCEREBELLAR DEGENERATION, NORMAL AGING, AND DLB. IF CLINICALLY INDICATED, TESTING FOR INFARCT RELATED DEMENTIA SHOULD BE ACCOMPLISHED BEFOREHAND WITH CT OR MRI.

a.. What are the minimal educational requirements for staff performing and interpreting the PET scans? How should test performance and interpretation be standardized? What accreditation requirements must facilities performing PET scans for AD meet? PET SCANS SHOULD BE PERFORMED AND CURRENTLY CAN ONLY BE LEGALLY PERFORMED BY CERTIFIED NUCLEAR MEDICINE TECHNOLOGISTS. INTERPRETATION AND PROTOCOLS SHOULD BE ESTABLISHED BY A COLLABORATION OF MULTIPLE RESEARCH FACILITIES AND THEIR NUCLEAR MEDICINE PHYSICIANS. FACILITIES SHOULD HAVE EXPERIENCED RADIOLOGISTS AND/OR NUCLEAR MEDICINE PHYSICIANS AVAILABLE FOR INTERPRETATION AND SHOULD HAVE A RADIOACTIVE MATERIALS LICENSE TO ALLOW FOR PET AGENTS TO BE ADMINISTERED.

**Comment #43:**

Submitter: Wes Thompson

Organizatin: Ray County Memorial Hospital

Date: March 22, 2004

Comment:

I am the Director of Radiology@ Ray County Memorial Hospital. We recently added PET to our list of services, and we happen to be adjacent to a skilled nursing facility/retirement home, that cares for 30 Alzheimer's patients. We added PET not as a revenue producer, but as a service to our

rural community. A service that allows patients to receive care in their home town, with caregivers they know and trust. Although the PET scanner is to be used for cancer DX/staging, I hope CMS reconsiders their stance on the coverage for Alzheimer's. My reasons are simple:

If you were diagnosed today with Alzheimer's, wouldn't you inform your family about the way you wished to be cared for prior to losing the ability to convey your wishes? Don't you think it would ease a family's conscience to know that their loved one said " when the time comes that i no longer recognize my family, or need constant care, its ok to put me in a facility that can handle my needs"?

Consider the ability to arrange financially, ahead of symptoms, for long term care when needed. As opposed to family members having to weigh their hearts vs. their bank accounts.

What of the many patients who suffer from dementia that is mistaken for Alzheimer's, and subsequently treated for a disease they do not have. How many millions of dollars are being wasted on unnecessary treatment, and what of the side effects of the unnecessary drugs being given.

We have the ability to correctly diagnose this disease,save on drug costs, allow time between diagnosis and onset of symptoms to be spent productively, to assist in financial planning, and to appropriately care for our patients. The problem remains the same, technology arrives faster than reimbursement issues are settled. Unfortunately this debate has far outlasted the acceptable time for resolution. Again, we are not providing the service to improve our bottom line, we provide the service to allow greater access to care. The continued denial of reimbursement for accurate Alzheimer's diagnosis, is an excellent example of our industry's greatest issue"how much care is our elderly population entitled to". In my opinion they are entitled to the best care available, care that improves quality of life, care that may be expensive, but care they have earned. I hope that when I reach my golden years that these issues will have been resolved, I have 30 more years before retirement, unfortunately it seems to take longer. I would be happy to provide you any statistical/financial info that would help in your decision.

**Comment #44:**

Submitter: Joanna Fowler, Ph.D.

Organization: Brookhaven National Laboratory

Date: March 24, 2004

Comment:

\* What minimal services must be performed and documented as pre-requisites for ordering a PET scan?

Minimal services required are:

- 9) performance and documentation of a standard comprehensive medical history and physical examination, including documented neurological examination,
- 10) assessment of mental status and activities of daily living,
- 11) laboratory tests – serum electrolyte (Na<sup>+</sup>, K<sup>+</sup>, Cl<sup>-</sup>, CO<sub>2</sub>), BUN, Cr, glucose, ALT and TSH determinations; CBC, including Hct, MCV and MCHC,
- 12) structural neuroimaging (CT or MRI)

\* Is a medical history alone sufficient to ascertain six months of cognitive decline or is actual observation by a clinician necessary to assess and document a decline over such a period prior to ordering a PET scan?

Minimal sufficient documentation of decline is constituted by one of the following:

- 7) actual longitudinal observation by a clinician over a period extending at least six months,
- 8) a history obtained and deemed reliable by clinician, from interviewing patient and/or close contact(s) of patient, which documents progressive decline over a period of at least six months preceding the time of clinician's evaluation,
- 9) a combination of the above, amounting in total to at least six months of decline documentable by the summed periods of time represented by 1) and 2)

\* What qualifications must a practitioner have to be considered "experienced in the diagnosis and assessment of dementia"?

Acceptable qualifications are:

- 5) Board-eligibility or Board-certification in Neurology, Psychiatry, Internal Medicine or Family Practice, as experience in making this diagnosis is an integral part of the training for each of these specialties, or
- 6) Physicians with other specialty training may be appropriate referrers, if they can document that in the normal course of their professional activity they are called upon to make this kind of assessment concerning dementia (e.g., have records showing that patients are referred to them for that evaluation, or that patients present to the physician for the purpose of being evaluated for cognitive/behavioral complaints)

\* What type of facility or setting is likely to offer the knowledgeable and experienced interdisciplinary staff needed to conduct a comprehensive assessment and render an accurate clinical diagnosis of dementia? Can a minimum set of facility criteria be identified that provide assurance that a comprehensive assessment will be performed? What set of skills and professions must be assembled on the interdisciplinary team?

Acceptable types of facilities:

- 7) General hospital,
- 8) Psychiatric hospital,
- 9) Outpatient clinics of physicians qualified by criteria described above

The professional(s) carrying out the required comprehensive assessment must reflect the following set of skills:

- 5) trained in evaluation of dementia, including conducting a medical history and physical examination, neurological examination, assessment of mental status and activities of daily living – as occurs in the professional training of neurologists, psychiatrists, internists and family practice physicians,
- 6) trained and licensed to order and interpret the results of laboratory and neuroradiology tests outlined above.

\* A comprehensive workup utilizing the NINCDS-ADRDA criteria for clinical diagnosis of Alzheimer's disease qualifies the likelihood of Alzheimer's disease as "definite," "probable," "possible," or "uncertain". Should PET be ordered only when the comprehensive assessment results in an uncertain diagnosis?

PET should be ordered only when the comprehensive assessment does not result in a “definite” diagnosis. It is clear from the primary peer-reviewed literature that the presence of Alzheimer’s disease is “uncertain” in many patients who meet NINCDS-ADRDA criteria of “possible AD” or “probable AD.” For example, in the one peer-reviewed article to examine clinical diagnostic accuracy for evaluation of early dementia, presenting data that met the American Academy of Neurology designation of “Class I” quality of evidence<sup>1</sup>, among all patients who were subsequently proven by autopsy to NOT have AD, 45% of those patients actually met NINCDS-ADRDA criteria for “probable AD”<sup>2</sup> -- and the specificity of “possible AD” was even lower.

\* What are the key differential diagnoses among neurodegenerative causes of dementia (e.g., frontotemporal dementia vs. AD) that PET could reasonably be expected to help clarify after an experienced clinician or team has completed an assessment? What are those clinical situations for which other imaging or other tests would be better indicated (e.g., distinguishing AD from mixed AD- multi-infarct dementia)?

Key differential diagnoses which PET will help clarify after assessment by an experienced clinician or team are:

- 11) AD vs. Frontotemporal dementia,
- 12) Frontotemporal dementia vs. Dementia with Lewy bodies,
- 13) AD vs. non-neurodegenerative causes of progressive dementia,
- 14) Frontotemporal dementia vs. non-neurodegenerative causes of progressive dementia,
- 15) Dementia with Lewy bodies vs. non-neurodegenerative causes of progressive dementia

Differential diagnoses for which other methods of distinguishing are more suitable are:

- 9) AD, Frontotemporal, or other neurodegenerative dementia vs. untreated depression,
- 10) AD, Frontotemporal, or other neurodegenerative dementia vs. untreated substance abuse or adverse effects of other pharmacologic agents,
- 11) AD, Frontotemporal, or other neurodegenerative dementia vs. untreated thyroid disease,
- 12) AD, Frontotemporal, or other neurodegenerative dementia vs. untreated nutrient deficiency

\* What are the minimal educational requirements for staff performing and interpreting the PET scans? How should test performance and interpretation be standardized? What accreditation requirements must facilities performing PET scans for AD meet?

Minimal educational/certification requirements for staff performing the PET scans:  
Certified Nuclear Medicine Technologist (CNMT)

Minimal educational/certification requirements for staff interpreting the PET scans include at least one of the following:

- 7) American Board of Nuclear Medicine (ABNM) certification,
- 8) American Board of Radiology (ABR) certification, with ABR special certification in Nuclear Medicine,
- 9) Neurologist, psychiatrist, or radiologist with current eligibility to bill CMS for interpretation of brain CT or MRI, plus documentable specific training in interpretation of brain PET scans

For all kinds of Nuclear Medicine tests, professional guidelines for performance and interpretation of diagnostic studies are often issued (e.g. by the Society for Nuclear Medicine), but there is no official specialty-wide standardization requirements for performance of any Nuclear Medicine study – nor should there be, as performance standards are tailored to the specific conditions and equipment present at each site, and it is ultimately the responsibility of each facility and physician to assure performance and interpretive quality, and maintain professional accreditations.

Sincerely,

Cummings, Jeffrey, M.D., Augustus S. Rose Professor, Departments of Neurology, and Psychiatry and Biobehavioral Sciences, Director, UCLA Alzheimer's Disease Center, David Geffen School of Medicine, University of California, Los Angeles; Co-Chairman, American Academy of Neurology Practice Parameter Committee on Dementia; President, Alzheimer's Association, Los Angeles, San Bernardino & Riverside Chapter.

Small, Gary, M.D., Parlow-Solomon Professor on Aging, Professor of Psychiatry and Biobehavioral Sciences, Director, UCLA Center on Aging, David Geffen School of Medicine, University of California, Los Angeles; Member, American Academy of Neurology Practice Parameter Committee on Dementia.

Silverman, Daniel, M.D., Ph.D., Assistant Professor, Department of Molecular and Medical Pharmacology, Head, Section of Neuroimaging, David Geffen School of Medicine, University of California, Los Angeles.

Coleman, Edward, M.D., Professor and Vice Chairman, Department of Radiology, Duke

School of Medicine.

Chodosh, Joshua, M.D., Associate Professor, Division of Geriatrics, Department of Medicine, David Geffen School of Medicine, University of California, Los Angeles.

Phelps, Michael, Ph.D., Norton Simon Professor, Chairman, Molecular and Medical Pharmacology, Director, Institute for Molecular Medicine, David Geffen School of Medicine, University of California, Los Angeles.

Fowler, Joanna Ph.D, Senior Chemist, Director Brookhaven PET Program, Brookhaven National Laboratory, Upton, NY

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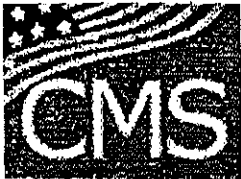
**References:**

1. Knopman DS, DeKosky ST, Cummings JL, et al. Practice parameter: diagnosis of dementia (an evidence-based review). Report of the Quality Standards Subcommittee of the American Academy of Neurology. *Neurology*. 2001; 56:1143-1153.
2. Lim A, Tsuang D, Kukull W, et al. Clinico-neuropathological correlation of Alzheimer's disease in a community-based case series. *J Am Geriatr Soc*. 1999; 47:564-569.

**Comment #45**

Submitter: Dr. Joel Bolen  
Organization: Integrated Magnetic Imaging  
Date: March 31, 2004  
Comment:





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## Medicare Coverage ~ Questions for Public Input on PET for Alzheimer's

CMS is requesting input from the public regarding questions we have developed after reviewing the NCD request and the Alzheimer's Association statement. All comments received will be made public and will not be kept confidential. Responses requested by March 31, 2004.



After reviewing the questions, please send responses to Samantha Richardson at [srichardson@cms.hhs.gov](mailto:srichardson@cms.hhs.gov).

### Questions on the use of PET scans in diagnosing Alzheimer's disease (AD)

CMS has opened an NCD in response to a request for coverage for a PET scan when:

- It is difficult to distinguish patients with AD from those with other causes of symptoms confounding the diagnosis of dementia; or
- To assist with the diagnosis of early dementia in beneficiaries for whom the differential diagnosis includes one or more kinds of neurodegenerative disease.

In addition, we have correspondence from the Alzheimer's Association that recommends coverage in the following circumstances:

- a. Dementia diagnosis, or cause for progressive cognitive impairment, remains uncertain after a physician experienced in the diagnosis and assessment of dementia has conducted a comprehensive clinical evaluation. The evaluation should include review of the medical history, physical and neurological examinations, mental status testing, assessment of activities of daily living, laboratory tests, and structural imaging (MRI or CT); and
- b. The information available through PET reasonably is expected to help clarify the diagnosis and/or help guide future treatment.

We are currently reviewing the evidence. We request public input on operational issues that might arise should the evidence support the request.

1  
2

- What minimal services must be performed and documented as pre-requisites for ordering a PET scan? *H+P, MMSE, appropriate lab + MRI brain*
- Is a medical history alone sufficient to ascertain six months of cognitive *medical history is sufficient*

decline or is actual observation by a clinician necessary to assess and document a decline over such a period prior to ordering a PET scan?

- 3) • What qualifications must a practitioner have to be considered "experienced in the diagnosis and assessment of dementia"? *geriatrician, neurologist, geriatric psychiatrist*
- 4) • What type of facility or setting is likely to offer the knowledgeable and experienced interdisciplinary staff needed to conduct a comprehensive assessment and render an accurate clinical diagnosis of dementia? Can a minimum set of facility criteria be identified that provide assurance that a comprehensive assessment will be performed? What set of skills and professions must be assembled on the interdisciplinary team?
- 5) • A comprehensive workup utilizing the NINCDS-ADRDA criteria for clinical diagnosis of Alzheimer's disease qualifies the likelihood of Alzheimer's disease as "definite," "probable," "possible," or "uncertain". Should PET be ordered only when the comprehensive assessment results in an uncertain diagnosis? *MD, social worker, occupational therapist*
- 6) • What are the key differential diagnoses among neurodegenerative causes of dementia (e.g., frontotemporal dementia vs. AD) that PET could reasonably be expected to help clarify after an experienced clinician or team has completed an assessment? What are those clinical situations for which other imaging or other tests would be better - *uncertain, possible, + mild cognitive impairment* - *MRI for vascular dementia* indicated (e.g., distinguishing AD from mixed AD- multi-infarct dementia)? *AD, Lewy Body, frontotemporal, PICKS*
- 7) • What are the minimal educational requirements for staff performing and interpreting the PET scans? How should test performance and interpretation be standardized? What accreditation requirements must facilities performing PET scans for AD meet? *radiologist experienced in PET*

FDG Positron Emission Tomography and other neuroimaging devices for suspected Dementia



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March 22, 2004

Centers for Medicare and Medicaid Services  
 7500 Security Boulevard  
 Baltimore, Maryland 21244-1850

RE: QUESTIONS FOR PUBLIC INPUT ON PET FOR ALZHEIMER'S DISEASE

To Whom It May Concern,

I am quite surprised, as a neurologist, that on April 14, 2003 CMS released a decision memorandum stating that it would retain the previous non-coverage decision of PET for Alzheimer's disease. PET is proven to be an incredible tool in assisting the physician to make a diagnosis of Alzheimer's disease.

I know in my practice each year I see several hundred patients who complain of significant memory problems, and routine diagnostic testing is inconclusive. The typical dementia workup, in a patient where I feel that there is a possibility of senile dementia of the Alzheimer's type, includes: MRI scan of the brain with and without contrast, EEG, chem. profile, thyroid screen, B12, RPR, mini-mental status exam, and a detailed neurological exam.

During the detailed neurological exam, a medical history is done to determine the level of insight this patient has lost and the level of cognitive decline over a period of six months or longer. Many of these patients return from their workup, and their workup is entirely normal, and then I wish I had a diagnostic test that would be helpful in this patient class. PET is a perfect study because it is very objective.

PET has been clearly shown to aid in the diagnosis of Alzheimer's disease in over 85% of patients. It has also been shown that if the diagnosis is made early by PET, then with appropriate therapy we can delay huge caregiver costs, and that PET more than pays for itself with early diagnosis, early treatment, and delayed progression to 24 hour caregiver or institutional cost.

I really think a PET should be ordered any time a patient is suspected of having Alzheimer's disease. The cost of the Alzheimer's drugs are expensive, and now there are two medications that we are using together: Aricept and Namenda, both of which are expensive. PET will clearly aid in this diagnosis. We are no longer doing brain biopsies for Alzheimer's disease, and this is the next best thing.

I don't think that you can reliably at the bedside differentiate between many cases of frontotemporal dementia, multiinfarct dementia, Alzheimer's disease, or pseudodementia, in some cases, without PET.

With regard to qualifications a practitioner must have to be considered "experienced in the diagnosis and assessment of dementia", I think it may be reasonable, since PET is an expensive diagnostic tool, to require that this study only be ordered through a neurologist, neurosurgeon, or internal medicine physician who has expertise in geriatric medicine.

Medicare simply cannot continue to not cover PET as a diagnostic service because it is a wonderful tool. I would be happy to answer any questions by phone at any time.

Sincerely,

Caudill Miller, M.D.  
 PCM/tbh