First guidelines for brain amyloid imaging in Alzheimer's released

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Only recently has it become possible to create high-quality images of the brain plaques characteristic of Alzheimer's disease in living people through positron emission tomography (PET). Even so, questions remain about what can be learned from these PET images and which people should have this test.

To provide guidance for physicians, individuals and families affected by Alzheimer's, and the public, the Society of Nuclear Medicine and Molecular Imaging (SNMMI) and the Alzheimer's Association have jointly published the first criteria for the appropriate use of this imaging technology to aid in the diagnosis of people with suspected Alzheimer's disease. The criteria were published online today as an article "in press" by *Alzheimer's & Dementia: The Journal of the Alzheimer's Association* and "ahead of print" in The *Journal of Nuclear Medicine*.

"Our primary goal is to provide healthcare practitioners with the information and options available to provide patients with the best possible diagnosis and care in a cost effective manner," said Maria Carrillo, Ph.D., Alzheimer's Association vice president of Medical and Scientific Relations.

Appropriate Use Criteria (AUC) for Brain Amyloid Imaging with PET in Alzheimer's

While elevated beta amyloid plaques are one of the defining pathologic

features of Alzheimer's, many elderly people with normal cognition also have elevated levels of these plaques, as do people with conditions other than Alzheimer's dementia. Therefore, the potential clinical use of amyloid PET requires careful consideration so that its proper role may be identified.

To develop the new criteria, the Alzheimer's Association and SNMMI assembled an Amyloid Imaging Taskforce (AIT) consisting of dementia and imaging experts to review the scientific literature and develop consensus recommendations for the clinical use of this promising new technology.

The AIT concluded that amyloid imaging could potentially be helpful in the diagnosis of people with cognitive impairment when considered along with other clinical information, and when performed according to standardized protocols by trained staff. In addition, they emphasized that the decision whether or not to order amyloid imaging should be made only after a comprehensive evaluation by a physician experienced in the assessment and diagnosis of cognitive impairment and dementia, and only if the presence or absence of amyloid would increase certainty in the diagnosis and alter the treatment plan.

According to the AIT, appropriate candidates for amyloid PET imaging include:

- Those who complain of persistent or progressive unexplained memory problems or confusion and who demonstrate impairments using standard tests of cognition and memory.
- Individuals meeting tests for possible Alzheimer's, but who are unusual in their clinical presentation.
- Individuals with progressive dementia and atypically early age of onset (before age 65).

Inappropriate candidates for amyloid PET imaging include:

- Those who are age 65 or older and meet standard definitions and tests for Alzheimer's, since a positive PET scan would provide little added value.
- Asymptomatic people or those with a cognitive complaint but no clinical confirmation of impairment.

Amyloid PET imaging is also inappropriate:

- As a means of determining the severity of dementia.
- When requested solely based on a family history of dementia or presence of other risk factors for Alzheimer's, such as the ApoE-e4 gene.
- As a substitute for genetic testing for mutations that cause Alzheimer's.
- For non-medical reasons, such as insurance, legal or employment decisions.

"As amyloid imaging becomes more prevalent in clinical settings, medical professionals must understand how to appropriately utilize the test," said Frederic H. Fahey, D.Sc., SNMMI president. "Neurology and dementia experts should order the test only when appropriately indicated, and nuclear medicine and molecular imaging professionals must ensure they have been adequately trained to interpret the results of the scan. Working together, we hope that the information garnered from amyloid PET imaging will aid in diagnosis and play a pivotal role in the development of new treatments for Alzheimer's."

The taskforce acknowledged that the healthcare provider makes the ultimate judgment regarding the care of each patient. The AIT sought to

assist this process and identified the following general sequence of events for the use of amyloid PET according to the new criteria:

1. Evaluation by a dementia expert to assess the need for diagnostic testing, possibly to include amyloid PET if the AUC are met.
2. Referral to a qualified provider of amyloid PET services.
3. Performance, interpretation and reporting of the amyloid PET scan according to established standards.
4. Incorporation of the PET result into the clinical assessment process.
5. Disclosure of the PET result by the clinician to the patient and caregivers, along with discussion of the result and its management consequences.

Although identifying potential benefits, the AIT concluded that amyloid PET results will not constitute and is not equivalent to a clinical diagnosis of Alzheimer's disease dementia. They said that imaging is only one tool among many that clinicians should use judiciously to manage patients, and that amyloid PET imaging does not substitute for a careful history and examination.

"Because both dementia care and amyloid PET technology are in active development, these new appropriate use criteria will require periodic reassessment and updating," Carrillo said.

PET Amyloid Imaging in Alzheimer's – An Overview

PET uses radiopharmaceuticals (radioactive drugs) to produce three-dimensional functional images of the brain or other body part. In amyloid PET imaging, the radiopharmaceutical is introduced into the body by injection into a vein and binds specifically to the amyloid protein, enabling visualization of areas in the brain where amyloid has

clumped together into plaques. One of the new PET compounds was approved for general use by the U.S. Food and Drug Administration in April 2012.

- If a person with dementia does not have amyloid buildup in their brain, then the cause of the dementia is very likely to be something other than Alzheimer's disease. Other causes of dementia include: strokes, thyroid problems, drug interactions, chronic alcoholism, and vitamin deficiencies.
- If an amyloid imaging PET scan shows that a person with memory impairment has amyloid buildup in their brain, this increases the likelihood that the memory impairment is caused by Alzheimer's disease, but it remains a likelihood, not a certainty.
- If a person without memory complaints or impairment has amyloid buildup, it does not necessarily mean that they will develop Alzheimer's. Many people have amyloid in their brains but are cognitively normal. More research is needed to understand the significance of amyloid plaques in this population.

Amyloid imaging is not covered by insurance at this time, and costs for the scan are "out of pocket." While costs of amyloid PET are not yet established, and PET costs in general can vary depending upon location, other PET scans are known to cost between $1,000 and $3,000, or more. Nonetheless, the AIT concluded that the proven sensitivity and specificity of the new radiopharmaceuticals for brain amyloid and the known association between brain beta amyloid deposition and Alzheimer 's suggest these new radiopharmaceuticals could potentially be helpful in the workup and diagnosis of patients with cognitive impairment.

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