Amyloid Imaging for Alzheimer’s Disease
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Since 2011, the US Food and Drug Administration (FDA) has approved three drugs for the imaging of beta-amyloid plaque in the brain. These drugs are florbetaben, florbetapir and flutemetamol (trade names NeuraCeq, Amyvid and Vizamyl, respectively).

Beta-amyloid plaques in the brain are one of the hallmarks of Alzheimer’s disease (AD). Previously, a definitive diagnosis of Alzheimer’s disease required post-mortem autopsy of the brain to evaluate for amyloid plaque using a special stain and a microscope. With these new imaging agents, amyloid plaque in the brain can now be detected non-invasively in live patients with a positron emission tomography/computed tomography (PET/CT) scan.

These drugs are labeled with radioactivity and, when injected intravenously, they bind to amyloid in the brain and the radioactive label allows localization. The radioactivity decreases by half every 2 hours. Given this rapid decay, no special radiation precautions are required. The typical PET/CT scan with these agents delivers approximately the same amount of radiation as 3 years of background radiation.

For example, after florbetapir is injected, it is allowed to circulate for approximately 30 minutes. The patient then lies down in a PET/CT scanner (Figure 1). A CT scan of the head is performed in a few seconds and is followed by a ten-minute PET scan. The radiologist then views the three-dimensional image of the brain as slices. Normal scans will show accumulation of radiolabeled florbetapir only in the white matter (Figure 2), while abnormal scans with significant amounts of amyloid plaque will show radioactivity in the white and gray matter out to the periphery of the brain (Figure 3).

Although approved by the FDA, amyloid imaging for AD was not initially covered by Medicare, and most other health plans also did not provide coverage. One reason for the lack of coverage is concern about the high costs that will be generated by extensive use of this imaging to diagnose AD. Medicare did reconsider coverage after the FDA’s approval of aducanumab, an amyloid-targeted antibody therapy, but ultimately again decided not to cover it (along with not covering aducanumab) outside of an approved clinical trial. Concern has also been expressed that a positive scan does not by itself provide a definitive diagnosis of AD. For example, some cognitively normal older adults will have a positive scan, even though they do not have and may never develop AD. Conversely, a negative scan means that a patient has little or no amyloid plaque at the time of the scan. But, it does not mean that the patient will never develop amyloid plaque in the future.

Still, there are several clinical situations in which amyloid imaging has potential utility. One is when a patient exhibits findings of AD at a younger-than-expected age. A second is to determine if a patient with mild cognitive impairment who does not meet criteria for AD is simply demonstrating normal age-related memory changes or if the patient is in the early stages of AD. The third is when a

TIPS ABOUT AMYLOID IMAGING FOR DIAGNOSIS OF ALZHEIMER’S DISEASE
- A patient with a typical presentation of Alzheimer’s disease (AD) does not usually require amyloid imaging for confirmation of the diagnosis.
- Keep in mind that currently Medicare and most health insurance plans will not pay for amyloid scans. So, only order them if they will change the plan of care and after evaluation of financial issues.
- Consider ordering an amyloid scan if it would be useful to identify the presence of amyloid, and thus confirm or exclude a diagnosis of AD in patients who present with Alzheimer’s-like dementia at a younger-than-expected age, in patients with mild cognitive impairment who do not meet criteria for AD, and in those with an unclear diagnosis.
patient’s differential diagnosis includes conditions such as frontotemporal dementia, primary progressive aphasia, or posterior cortical atrophy/visual-variant AD, and the correct diagnosis is unclear. In these situations, the presence of significant amyloid on PET/CT would suggest that amyloid pathology is causing the patient’s cognitive impairment.

To collect more data on the clinical utility of amyloid imaging, the Centers for Medicare & Medicaid Services (CMS) approved the large phase IV trial, Imaging Dementia—Evidence for Amyloid Scanning (IDEAS) study. (visit the IDEAS study website for more information at https://www.ideas-study.org/Original-Study). IDEAS showed that amyloid PET resulted in a change of diagnosis in 36% of patients and a change in patient management 60% and 64% in MCI and dementia patients respectively. The New Imaging Dementia—Evidence for Amyloid Scanning (New IDEAS) trial builds on the success of the original IDEAS study and strives to enroll a more diverse patient population.

The other potential use of these scans is for research on new AD treatments. To determine the efficacy of such treatments, it will be essential to confirm that research subjects do, in fact, have AD. Detection of amyloid with a PET/CT scan helps to provide that confirmation. In clinical trials, use of amyloid PET has even been extended to identify a cognitively normal population at-risk for development of AD that could be treated to prevent the development of AD. Similarly, when studying therapies targeting amyloid plaque with the intention of slowing the progression of AD, serial scans will assist with the longitudinal assessment of outcomes. Two anti-amyloid antibodies have now been approved by the USFDA based on their ability to decrease brain amyloid burden as measured by serial amyloid PET.

References and Resources
Information about studies presented at the 2017 Alzheimer’s Association International Conference can be found at www.alz.org/AAIC17-Sun-PET-Scan-Release.asp