Is PET/CT imaging really helpful in diagnosing Alzheimer's Disease?

Yes it is!
Is the Clinical Diagnosis good enough?

Clinical Diagnosis vs. Neuropathology (gold standard)

- Sensitivity 71% & Specificity 71% for probable Alzheimer’s (> 600 pts)

- ~ 40% of pts with a clinical diagnosis of “No Alzheimer’s” had detectable levels of AD histopathology

U.S. Alzheimer Disease Centers 2005-2010

Alzheimer’s - Guidelines

National Institute on Aging Alzheimer’s Association criteria

• Include **Biomarkers** for the pathophysiological process of AD
• **Biomarkers** increase the certainty that the basis of the dementia syndrome is the AD pathophysiological process

International Working Group -2 criteria

Specific Clinical Phenotype
+ In-vivo evidence of AD pathology

*Alzheimer’s & Dementia 2011*  
*Lancet Neurology 2014*
Alzheimer’s Disease

- Amyloid β Plaques
  - Tau Neurofibrillary tangles
  - Neuroinflammation
  - Neuronal Injury
FDG-PET

- Neuronal Injury
- **↓↓↓** Synaptic Density & Function

**↓** Glu Metabolism

**←** Disease Severity

Topographical Biologic Marker

Neuronal Degeneration/Injury Marker

2. Alzheimer's & Dementia 2011
Alzheimer’s Dementia  FDG-PET
Advanced Alzheimer’s FDG-PET
FDG-PET the evidence

Case-control Studies

*Sensitivity & Specificity >90-95%*

Prospective Study

~ 100 pts with suspected early-onset dementia/ follow-up 5-6 y (ref. std)

*Sensitivity 78% & Specificity 81%

Pre-test probability: 48%  
FDG-PET (+)  
Post-test probability: 79%

1. Mosconi et al, *JNM 2008*
2. Panegyres et al, *BMC Neurol 2009*
FDG-PET in Differential Diagnosis

AD vs. FrontoTemporal D  Specificity >90%
AD vs. DLB    Sensitivity: 90% & Specificity: 80%

Bohnen et al, JNM 2012
Amyloid β Imaging

\[^{11}\text{C}\]-PIB (Pittsburgh Compound-B)

Thioflavin-T (histopathologic dye) derivative
Crosses blood-brain-barrier
High Affinity for Amyloid β

\[
\begin{align*}
\text{thioflavin-T} \\
\xrightarrow{\text{Autoradiography}} \\
[N\text{-methyl-}^{11}\text{C}]\text{PIB}
\end{align*}
\]

PIB uptake in cortex of AD patients

Klunk et al, Ann Neurol 2004
PET with $[^{11}\text{C}]$-PIB (Pittsburgh Compound-B)

25 patients: 16 AD & 9 controls

Significantly higher PIB retention in frontal (x2) parietal (x1,7) temporal & occipital (x1,5) cortex in AD patients compared with controls

Negative associations of PIB with FDG uptake.

Klunk et al, Ann Neurol 2004
Use of Florbetapir-PET for Imaging β-Amyloid Pathology

59 pts
Mean age: 78-80 y
MMSE: 21-22

Amyloid-PET 2 years → death-autopsy

Uptake correlates with Amyloid β burden

36/39 (+) for Aβ
Sensitivity 93%

20/20 (-) for Aβ
Specificity 100%

Clark et al, JAMA 2011
Clark et al, Lancet Neurol 2012
## Amyloid-PET tracers

<table>
<thead>
<tr>
<th>Tracer</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Florbetabir</td>
<td>90%</td>
<td>81%</td>
</tr>
<tr>
<td>Florbetaben</td>
<td>89%</td>
<td>89%</td>
</tr>
<tr>
<td>Flutemetamol</td>
<td>95%</td>
<td>87%</td>
</tr>
</tbody>
</table>

**Morris et al, Eur J Nucl Med 2015**
Prognostic Value of Amyloid-PET

Prospective multicentre study

Florbetapir-PET

69 Normal controls
52 MCI
31 probable AD

3 years

significant deterioration of ADAS-cog in $\alpha$β+

Alzheimer’s Disease Assessment Scale (ADAS-cog)

Doraiswamy et al, *Molecular Psychiatry* 2014

Suspected Non-AD Pathophysiology

SNAP

+ Aβ
+ Neurodegeneration
Amyloid associates with age in normal subjects

Jansen et al, *JAMA* 2015
The antibody aducanumab reduces \( \text{A}\beta \) plaques in Alzheimer’s disease

**PRIME study**

165 patients
double-blind placebo controlled phase 1b randomized trial
 Persistent or progressive unexplained MCI

 Core clinical criteria for “possible AD” are satisfied but there is an unclear clinical or mixed presentation

 Progressive dementia with atypically early age of onset (<65 y)
The INcremental DIagnostic Value of Amyloid PET with Florbetapir (INDIA-FBP) Study

Multicenter study in 18 centers in Northern Italy
228 consecutive adults with cognitive impairment

- Diagnostic change in 1/3 of patients

- Acetylcholinesterase inhibitors and memantine were introduced in 61 (65.6%) pts with (+) scan results

Boccardi et al, JAMA Neurology 2016
Society of Nuclear Medicine Mol Imaging
Image of the year 2016

Amyloid Plaques

$^{11}$C-PiB PET

Tau Fibrillary Tangles

$^{18}$F-AV1451 PET

Neuronal Dysfunction

$^{18}$F-FDG PET
A Negative Florbetapir Scan:
- sparse to no neuritic plaques
- inconsistent with a neuropathological diagnosis of AD
- reduces the likelihood that a patient’s cognitive impairment is due to AD

A Positive Florbetapir Scan:
- moderate to frequent amyloid neuritic plaques
- may be observed in older people with normal cognition and in patients with various neurologic conditions, including AD
FDA approved PET Amyloid tracers
Alzheimer’s Dementia $^{99m}$Tc-HMPAO SPECT