Imaging Biomarkers For Alzheimer’s Disease

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**ALZHEIMER’S DISEASE**

Dementia is a growing epidemic and Alzheimer’s disease (AD) represents 60-80% of cases.

The problems:

- No cure
- No pathogenesis
- No diagnosis

Definitive diagnosis is made postmortem by the demonstration of sufficient amount of AD molecular hallmarks of pathology.

New revised diagnostic guidelines propose the introduction of biomarkers to support AD clinical diagnosis.

Disease-changing treatments are likely to be more effective before this phase, when the damage caused by the neurodegeneration can be reversible.

**IMAGING BIOMARKERS**

Biomarkers are parameters that can be reliably measured in vivo and reflect specific features of disease-related pathophysiological processes.

- Pathological processes that begin prior to the stage of clinical AD.
- Indicate the presence, absence or risk of later developing a disease.

There’s no parameter that fully meets this criterion:

- Meanwhile, the use of biomarkers helps to exclude other dementia or conditions with AD-like symptoms.
- The new diagnostic guidelines classify them as biomarkers for neurodegeneration and for β-amyloid abnormalities.
- Although these abnormalities can occur during normal aging or in other dementias, they have specific patterns of changes for AD.
- Combinations of biomarkers are being investigated to improve diagnosis accuracy for AD.

Biomarkers recommend by the new guidelines for diagnosis:

**BIOMARKERS FOR AD**

- Cerebrospinal TAU
- Structural MRI
- FDG-PET

**STRUCTURAL IMAGING - CT and MRI techniques**

- MEASURE OF BRAIN ATROPHY
- CT and MRI are applied as standard workup for AD diagnosis and drug trials to:
  - Rule out other conditions, such as tumours or strokes.
  - Calculate the rate of brain atrophy.
- Brain atrophy is related to the magnitude of neuronal loss, extent of NFT and disease progression.

2 different approaches:

Whole-brain ROI measures:

- Earlier affection
  - Hippocampal atrophy is the gold standard but also MTL, EC and other structures are affected.
- No automated methods available

**FUNCTIONAL IMAGING - fMRI and FDG-PET techniques**

- FMRI is a non-invasive technique (no radiation is used) that detect changes in blood flow associated to brain activity.
- Data can be obtained by task-free and task-based fMRI.

Findings:

- Decrease in neural activity in prefrontal regions, supramarginal gyrus and MTL in AD; in MCI subjects findings are less consistent.
- β-amyloid deposition in posterior cingulate and precuneus rim.

**MOLECULAR IMAGING - PIB-PET technique**

- PET is the most studied radioligand for β-amyloid deposition but 18F-tracers are more likely to be integrated into clinical setting due to their longer half life.

- High PIB retention observed in 50% of MCI patients, CN subjects at risk (ApoE4 carriers) and some older CN patients.

- The 2015 ADNI publication described 157 CN, 105 MCI, 58 HCP, 110 AD subjects and 108 patients with negative PIB-PET scans.

- The CN group showed increased uptake of PIB in precuneus and parietal regions.

- The PIB-negative (left) subjects were positive (middle) and from AD patient (right).

**REFERENCES**

1. © 2005 BrightFocus Foundation
2. Z. © 2005 UCAM, Institute Alzheimer