

## Review Article Artificial Intelligence in Disease Diagnosis

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### I. INTRODUCTION

Alzheimer's disease (AD) is the most common cause of dementia in the elderly. This disease can mainly lead to impairment of higher intellectual; function, with alterations in mood and behavior. Later, progressive disorientation, , memory loss and aphasia.

Grossly the brain shows a variable degree of cortical atrophy marked by widening of the cerebral sulci that is pronounced in the frontal, parietal and the temporal lobes. With significant cortical atrophy this leads to compensatory ventricular enlargement secondary to loss of brain parenchyma and reduced brain volume. Structures of the medial temporal lobe that includes hippocampus, entorhinal cortex and amygdala. The major microscopic abnormalities of AD which form the basic histological diagnosis are neuritic plaques and neurofibrillary tangles.

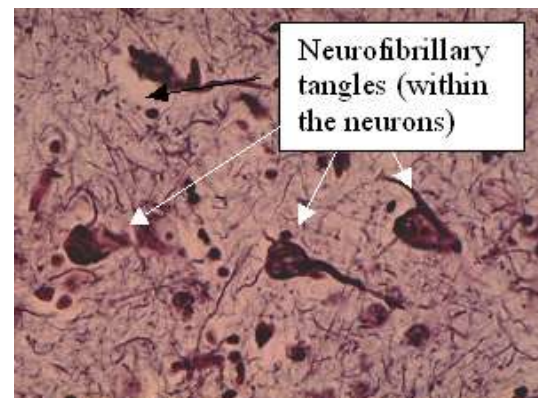
Neurotic plaques are extracellular structures that consist predominantly of insoluble deposits of Beta amyloid protein ( $A\beta$ ); hence the alternative name, amyloid plaques. However, there are also many other proteins associated with plaques, including apoE, components of the complement cascade and cytokines. The plaque core is surrounded by dystrophic neurites and reactive astroglia and microglia.

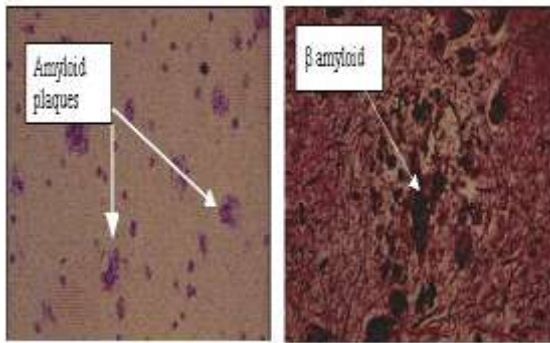
Neurofibrillary tangles associated with AD are intracellular collections of hyperphosphorylated tubulin-associated unit (tau) protein. There is autopsy evidence to suggest that tau pathology is present prior to  $A\beta$  plaques, below clinically detectable levels, and that tau pathology may be exacerbated rather than production-driven by  $A\beta$  plaques .

Positron emission tomography (PET) scans, which measure the levels of specific molecules, like glucose, in the brain, have been investigated as one tool to help diagnose Alzheimer's disease before the symptoms become severe. Glucose is the primary source of fuel for brain cells, and the more active a cell is, the more glucose it uses. As brain cells become diseased and die, they use less and, eventually, no glucose.

Other types of PET scans look for proteins specifically related to Alzheimer's disease, but glucose PET scans are much more common

and cheaper, especially in smaller health care facilities and developing countries, because they're also used for cancer staging. Radiologists have used these scans to try to detect Alzheimer's by looking for reduced glucose levels across the brain, especially in the frontal and parietal lobes of the brain. However, because the disease is a slow progressive disorder, the changes in glucose are very subtle and so difficult to spot with the naked eye.





**Fluorine - 18 - FDG PET**

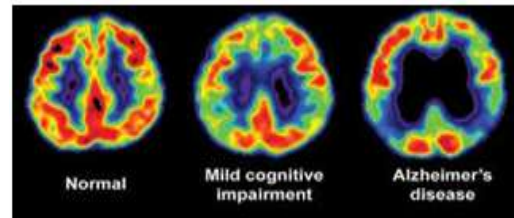
FDG-PET is extensively and increasingly used to support the clinical diagnosis in the examination of patients with suspected neurodegenerative disorders, especially AD. It reflects both cumulative loss of neuropil, loss of synapse, and functional impairment of the neurons. Lower FDG-PET was regarded as a signal of neuronal hypometabolism due to neurodegeneration and was labeled as “N” biomarkers as the research framework defined. However, a recent study showed it reflects the consumption of glucose by astrocytes, rather than by neurons. Moreover, there is a literature that has demonstrated that diminished FDG brain uptake by PET might be a biomarker tracking vascular, more precise, blood-brain barrier (BBB) transport, abnormality. Based upon this hypothesis, an analysis was conducted in the Alzheimer’s Disease Neuroimaging Initiative (ADNI) prospective clinical cohort to explore the necessity and feasibility of making FDG-PET function as a separate biomarker, which is independent from “N” biomarker and labeled as “F” representing FDG hypometabolism in A+T+ individuals. This refinement enables an independent identification of non-specific neurodegenerative biomarkers to be independent, leading to a more precise understanding of the biological underpinnings of brain aging.

The different biomarkers used in the FDG PET imaging are A, T, N. This is a descriptive system for categorizing multidomain biomarker findings at the individual person level. The biomarkers (A,T,N) have respective meanings.

The A biomarker is the  $\beta$ - Amyloid Marker, T biomarker is the value of tau PET biomarker & N biomarker of neurodegeneration or neuroinjury. Each biomarker category is rated as positive or negative. (A+/T+/N-) or (A+/T-/N-). The (A+/T+/N-) system includes the new modality tau PET. It is agonistic to Alzheimer’s Disease diagnosis.

The 3 binary Biomarkers include

- Biomass of fibrillary A $\beta$  deposition are high ligand retention on amyloid PET/ low CSFA $\beta_{42}$ .
- Biomarkers of tau pathology / elevated CSFA $\beta_{42}$ .
- Biomarkers of AD/Neurodegeneration.



**FED NEUROIMAGING**

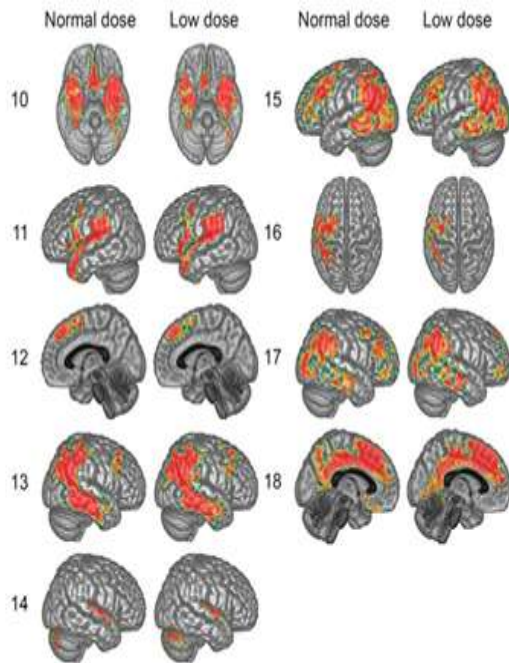
### 3D SSP Z score maps

Diagnostic accuracy can be improved by constructing 3D SSP Z-score maps, showing patterns of significant deficits. During FDG-PET, the subject receives a moderate but not insignificant dose of ionizing radiation, and a dose reduction with retained image quality is desirable. With lower dose, repeated examinations can become a useful tool for monitoring disease progress and potential effects of disease-modifying interventions. The aim of this study was to evaluate Z-maps created from low-dose and normal-dose FDG-PET of the brain, with quantitative and qualitative methods.

### Diagnostic methods

The patients who had received diagnosis of neurodegeneration dementia disease (FDG/AD) are enrolled. The diagnosis imply that all patients had neurodegenerative disease with assumed or previously proven regional hypometabolism on FDG-PET. All patients undergo 2 FDG/ FET/ CTSCAN.

First A routine scan with (Normal dose ND) with an injected dose of 3MBq/Kg FDG. The Second Scan with (Low Dose LD) with an injected dose of 0.75 MBq/Kg FDG. Then the 3 DSSP images showing Z scores from both normal dose and lower dose are checked using Batch analysis.



### Arterial Spine Labeling (Asl)

ASL MRI utilizes magnetically labeled blood water as an endogenous tracer for quantification of brain perfusion. Unlike other measures of CBF, such as <sup>15</sup>O-PET, there is no requirement for an exogenous tracer or exposure to ionizing radiation. After a region of flowing blood is magnetized, the resulting tissue perfusion produces local change to tissue magnetization, which can be measured with a standard MRI imaging sequence and compared to an unlabelled “control” image. Similar to PET ligands, the tracer decays at a fixed rate, but in ASL the decay is determined by T1 relaxation. Accordingly, CBF can be calculated from a knowledge of the brain magnetization with and without arterial labeling and assumptions about the labeling efficiency and T1 relaxation time. In human ASL, the transit time from the labeling location to the imaging location

must also be considered in the data acquisition and modeling.

There are various strategies for carrying out arterial labeling and for sampling and modeling the resulting changes in brain magnetization. All of these methods ultimately allow CBF quantification in MRI independent physiologic units (e.g. mL/100 g/min), facilitating comparisons across sites and scanning sessions. This particular feature offers an advantage over the more commonly applied blood oxygen level dependent (BOLD) fMRI, which is susceptible to baseline drift across longer time scales and produces increased intersubject variability. Further, this capability makes ASL MRI particularly suitable for measuring drug effects over varying intervals.

Although ASL-MRI technology has been available for human use for over a decade, numerous advances in data acquisition and analysis, as well as the greater availability of 3T MRI, have resulted in improvements in signal-to-noise (SNR) and reliability of the methodology. Currently, several different variants of ASL MRI are widely used and have been applied to neurodegenerative populations. Continuous ASL (CASL) involves the continuous labeling of blood water as it passes through a labeling plane while pulsed ASL (PASL) uses short RF pulses to selectively label blood and tissue. Pseudocontinuous ASL (pCASL) represents a hybrid of these approaches in which many short pulses simulate the continuous labeling of CASL. Continuous inversion allows labeling throughout the cardiac cycle, greatly reducing cardiac noise. More recent developments with 3D sequences such as fast spin echo, as opposed to the echoplanar imaging most frequently employed, allow for background suppression of static tissue water, increasing the sensitivity to CBF. This sequence is now also available commercially on some platforms.

