PALZ Alzheimer's Analysis for FDG PET

FDG PET in Alzheimer's Disease

FDG brain PET images address the local glucose metabolism, which can be considered as a proxy for neuronal activity at rest[1]. Therefore, impaired neuronal activity is reflected by a reduced FDG uptake in the affected brain areas. In subjects suffering from Alzheimer's Disease (AD), the reduction is evident as a characteristic pattern and becomes detectable as a significant deviation from normal controls 1 to 2 years before onset of dementia.

PALZ implements a licensed and validated analysis of research FDG brain PET scans particularly targeting Alzheimer's Disease.

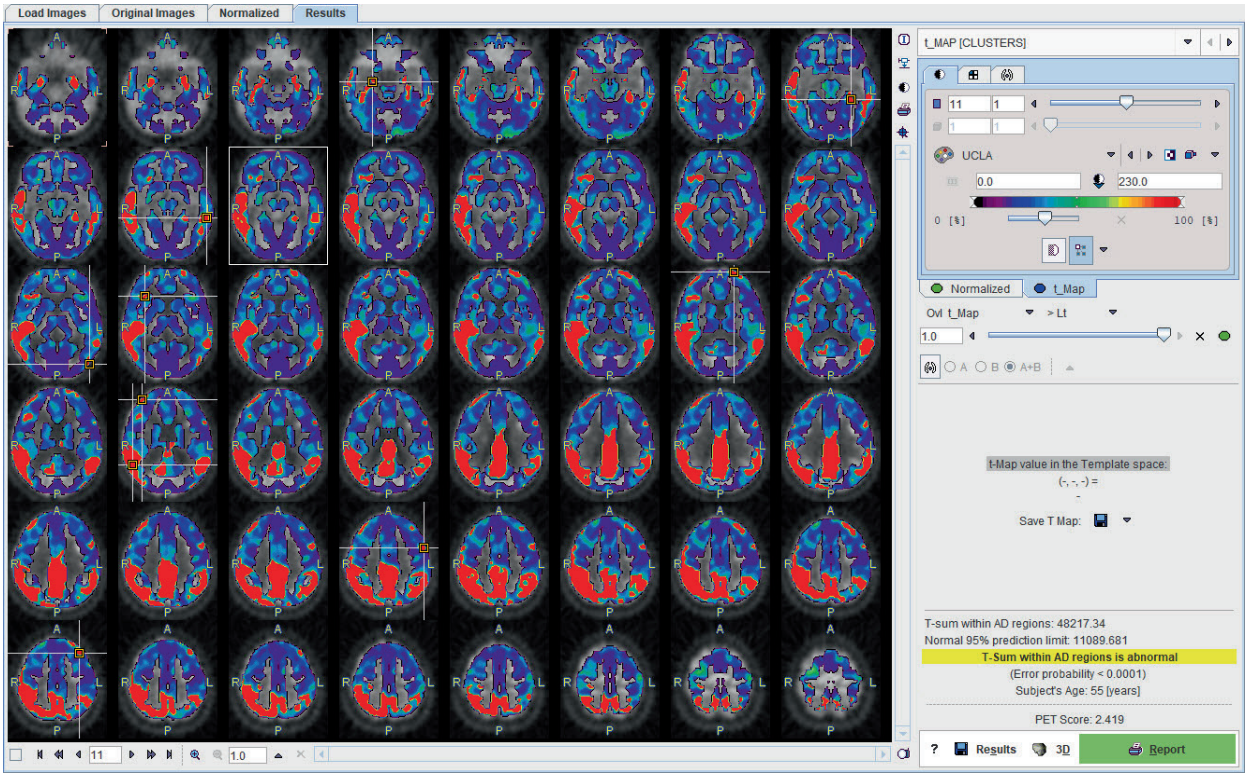
Discrimination from Normal Controls

In a large multi-center trial, it was found that it is possible to discriminate AD subjects from normal controls based on the FDG uptake pattern in the brain[2]. The methodology developed calculates a criterion that states, together with a statistical probability, whether the finding is abnormal. The method has been successfully validated several times[2, 3, 4] with several data sets, and resulted in high sensitivity/specificity outcomes which are somewhat dependent on the sample selection: ADNI (83 % / 78 %), NEST-DD (78 % / 94 %)[3]. In addition, it has recently been shown that the outcome can be transformed into a biomarker for tracking the progression of MCI to AD in clinical trials[2].

Data processing is fully automatic and results in an objective measure of Alzheimer's Disease probability.

Analysis of FDG PET Images with PALZ

PMOD's PALZ tool is a licensed and streamlined implementation of the validated AD discrimination analysis. It is applicable in research contexts to FDG brain PET scans of subjects with symptoms of AD. Data processing is fully automatic and results in an objective discrimination criterion, substantiated by an error probability of abnormality. The numerical out- come is complemented by a visual summary high- lighting the significantly abnormal brain areas. These unique features make it easy to get an overview of hypometabolism. Naturally, all results can be docu- mented in DICOM and exported numerically for dedi- cated statistical analyses.



PALZ user interface illustrating the abnormal outcome of an AD subject.

Requirements

In order to interpret the outcome of a PALZ analysis with regard to a classification as AD, the following requirements must be met:

- The FDG brain PET images are corrected for attenuation and scatter
- The subject has symptoms of AD
- The subject is at least 49 years old

Analysis Procedure

The PALZ tool performs the following analysis steps:

- The subject images are stereotactically normalized and smoothed with a 12-mm Gaussian filter.
- The image values are normalized with reference to an area that is known to have AD-preserved activity.
- The normal image at the subject's age is calculated and the difference to the subject image calculated as a t-map.
- All abnormal t-values within a predefined AD-mask are summed, yielding the AD t-sum. The t-sum is a criterion of scan abnormality with a 95 % prediction limit of 11089.
- The AD t-sum is tested for significance of abnormality.
- The PET Score is calculated from the AD t-sum by: PET Score = $\log_2$(AD t-sum/11089+1).
- A cluster analysis of the t-map is performed, grouping $\geqslant$ 216 contiguous pixels with $p < 0.05$.

Results

The PALZ tool provides the following research results from a discrimination analysis:

- The AD t-sum criterion of scan abnormality together with its statistical error probability.
- The PET Score, an imaging biomarker for monitoring the progression of Mild Cognitive Impairment to Alzheimer's Disease.
- The t-map, representing the deviation from the age-corrected normal uptake.
- A cluster map showing groups of pixels with significantly reduced uptake.
- A summary report which includes the statistical outcome.

Limitations

The PALZ research tool is not a general FDG brain PET analysis tool and thus not suited to searches for non AD-related defects. Any other disease that affects the associated brain areas may also lead to a significantly abnormal result.

References

[1] Herholz K., Westwood S., Haense K., Dunn G. Evaluation of a Calibrated 18F-FDG PET Score as a Biomarker for Progression in Alzheimer Disease and Mild Cognitive Impairment. J Nucl Med 2011; 52:1218–1226.

[2] K. Herholz, E. Salmon, D. Perani, et al., Discrimination between Alzheimer Dementia and Controls by Automated Analysis of Multicenter FDG PET. Neuroimage 2002; 17(1): 302–316.

[3] Haense C, Herholz K, Jagust WJ, Heiss WD. Performance of FDG PET for detection of Alzheimer's disease in two independent multicentre samples (NEST-DD and ADNI). Dement Geriatr Cogn Disord. 2009; 28(3): 259–66.

[4] Caroli A, Prestia A, Chen K, Ayutyanont N, Landau SM, Madison CM, Haense C, Herholz K, Nobili F, Reiman EM, Jagust WJ, Frisoni GB. Summary Metrics to Assess Alzheimer Disease-Related Hypometabolic Pattern with 18F-FDG PET: Head-to-Head Comparison. J Nucl Med. 2012; 53(4): 592–600.