Mathematical Methods and Models in Biosciences
June 15–20, 2025, Sofia, Bulgaria
https://biomath.math.bas.bg/biomath/index.php/bmcs

Non-invasive, Fast, Comprehensive & Interpretable Characterization of Alzheimer's Disease Patients

Albert Guvenis[1], Ramin Rasi[1], Albert Guvenis[1]

[1]Bogazici University, Istanbul, Türkiye
guvenis@boun.edu.tr

The comprehensive, accurate, interpretable and sensitive characterization of Alzheimer's disease is an important currently investigated research area that will impact the formulation of effective personalized therapies. This project aimed to achieve a fast, non-invasive characterization of AD patients using a single FDG PET study and machine learning. Specifically, we investigated the early detection of AD, prediction of its stages, amyloid positivity, tau tangles and presence of ApoE4 genotype in a unified work for the first time. We employed the Radiomics technique, which involves extracting numerous quantitative features from images beyond human visual perception. This allows for the identification of subtle patterns and variations in metabolic activity within brain regions affected by AD. FDG PET images were obtained from the ADNI online database. We utilized both similarity measures and regional radiomics features to detect AD, determine its stages, and predict biomarkers. Feature selection was performed to improve model performance, interpretability, and computational efficiency. Machine learning algorithms were evaluated for optimal performance in each case.

Both similarity and radiomics methods achieved an AUC greater than 0.95 in discriminating between healthy and AD patients. A significant correlation was found between the similarity index and the MMSE score. AUC values greater than 0.85 were obtained for discriminating between mild cognitive impairment (MCI) and healthy patients, as well as between AD and MCI patients. APOE4 genotype and amyloid positivity were also predicted using a small number of radiomics features with an AUC larger than 0.90. Key regions were identified based on feature importance analysis as hippocampus, entorhinal cortex, inferior parietal, isthmus cingulate and amygdala. Initial work on Tau positivity yielded a promising accuracy of AUC=0.76.

The overall identified imaging biomarkers are expected to be valuable for both researchers and clinicians by providing new insights into disease mechanisms and guiding clinical interventions through monitoring disease progression and treatment responses. Future research will focus on predicting other

biological biomarkers from FDG PET images and investigating the response to therapeutic interventions. This work has been partially supported by the Bogazici University Research Fund (project code 19774). We are also indebted to the Alzheimer's Disease Neuroimaging Initiative (ADNI) for supplying us the necessary data.

Keywords: Alzheimer's disease, FDG PET, amyloid positivity, APOE4, tau tangles, machine learning precision medicine