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Diagnostic Performance of Vision Transformer (ViT) and SPM12 in Prodromal Alzheimer's Dementia: A Comparative 18F-FDG PET/CT Study.

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ABSTRACT

The vague clinical symptoms in the early stages of prodromal Alzheimer's disease lead to diagnostic difficulties. The aim of this study is to compare the diagnostic performance of a Vision Transformer (ViT)-based deep learning model in interpreting 18F-FDG PET/CT images for prodromal dementia diagnosis with that of a traditional quantitative method, Statistical Parametric Mapping (SPM12), and expert visual assessment. This retrospective study included 3,766 transactional PET images from 73 patients who underwent 18F-FDG PET/CT scans due to suspected prodromal dementia. The performance of the developed ViT model was evaluated on a patient-specific test dataset to ensure its generalizability. The ViT model demonstrated superior diagnostic performance with 98.29% accuracy, 97.69% sensitivity, and 98.88% specificity. In comparison, SPM12 analysis yielded 95.7% accuracy and 82.6% sensitivity, while expert visual assessment yielded 92% accuracy and 91.3% sensitivity. The model's focus on clinically meaningful brain regions was confirmed using Grad-CAM interpretability maps. In conclusion, the ViT-based artificial intelligence model was found to offer significantly higher sensitivity and overall accuracy compared to both SPM12 and expert evaluation in the diagnosis of prodromal dementia. These findings demonstrate that AI-supported systems have significant potential as a powerful, objective, and reliable decision support tool for clinicians in the early and accurate diagnosis of neurodegenerative diseases.

Key words: Prodromal Alzheimer's dementia, 18-FDG, PET/CT, artificial intelligence.

1. INTRODUCTION

Neurodegenerative episodes are becoming an increasingly significant cause of death and a profound social burden with the global aging of the disease (Ward et al., 2025). It is estimated that more than 55 million people worldwide currently live with Alzheimer's disease (AD) or similar neurodegenerative diseases, a number that is expected to increase significantly over the years (Wang et al., 2024). The intermittent prodromal phase is often distinguishable from Mild Cognitive Impairment (MCI) and presents a critical therapeutic window for early intervention. However, clinical analyses at this stage are ambiguous, and mild problems present significant challenges, with conventional clinical assessment methods often rendering them inadequate for definitive diagnosis (Petersen, 1999). Since the underlying pathophysiology, independent progression, and management techniques demonstrate significant differences between these problems, accurately differentiating AD from other types of dementia at this early stage will be of paramount importance.

In recent years, biomarker-based neuroimaging techniques have emerged as key tools for the early and accurate diagnosis of AD. In particular, 18F-fluorodeoxyglucose positron emission tomography/computed tomography (18F-FDG PET/CT) is widely used to identify characteristic cerebral hypometabolism patterns that can help differentiate various dementia syndromes. Despite its benefits, the interpretation of 18F-FDG PET/CT images has some limitations. Often, convergent metabolic features are found among different dementia subtypes, and atypical patterns can be inferred or lead to inconclusive findings. Quantification of 18F-FDG PET/CT data using methods such as Statistical Parametric Mapping (SPM) has been extensively evaluated to improve diagnostic objectivity (Rizzo et al., 2016). This is particularly critical in prodromal dementia, a clinical entity exhibiting a high probability of neurodegenerative disease options; Because at this stage, the effectiveness of visual image interpretation decreases due to the ease of metabolic processing (Brugnolo et al., 2019; Mosconi et al., 2008). The diagnostic patterns of 18F-FDG PET often show clarity in these early stages, and the improved diagnostic support results can provide significant clinical benefit (Mosconi et al., 2008; Smailagic et al., 2015).

Simultaneously, the emergence of artificial intelligence (AI) and deep learning has triggered a boom in medical imaging analysis. Architectures such as Convolutional Neural Networks (CNNs) have demonstrated superior effectiveness in complex tasks such as image indicators, segmentation, and anomaly discrimination (Esteva, 2017; Litjens, 2017). In Alzheimer's and dementia data, AI-based analytical models have consistently reported higher parameters and accuracy rates compared to traditional visual or quantitative replicates (Basaia, 2019; Lu, 2018). Recently, Vision Transformer (ViT) architectures have shown extraordinary promise, with the potential to offer deeper insights into subtle metabolic shifts characteristic of early-stage dementia by capturing long-range relationships (long-range dependencies) across entire images. Unlike traditional CNNs, ViT models are able to more effectively model both local features and global context by dividing ratios into fixed-size patches and utilizing self-attention mechanisms.

However, one of the biggest obstacles in the clinical applications of deep learning models is the lack of transparency in decision-making scopes. Overcoming this "black box" problem and disrupting the model's failure to focus on clinically significant components necessitates interpretability techniques such as Grad-CAM (Gradient-weighted Class Activation Mapping).

Therefore, the primary objective of this study is to highlight the additional diagnostic value of combining traditional parametric mapping with enhanced AI techniques in the assessment of

prodromal dementia using 18F-FDG PET/CT imaging. Specifically, this research analyzes the contribution of digitalization and an advanced ViT-based deep learning model in comparison with classical quantitative analyses (SPM12) and expert visual interpretation. Furthermore, clinical reliability is tested by ensuring the transparency of the model's decision unit with Grad-CAM. By detailing the diagnostic unit of this AI-assisted system, this study aims to illuminate its potential for improving early and accurate diagnosis, particularly in the critical MCI (Multiple Intervention in Dementia) phase, thereby facilitating timely and targeted clinical interventions.

2. MATERIALS AND METHODS

2.1. Patients

The patients with complaints related to prodromal dementia were subjects of this study. The pediatric patients, pregnant or lactating women, and patients without at least 8 months of follow-up were also excluded from the study. 73 patients who underwent 18F-FDG PET/CT between November 2018- December 2023 were included. The physical examination and laboratory results including mini-mental scores of the patients were recorded. The necessary ethical approval was obtained from the Mersin University Ethics Committee and all data were analyzed in accordance with the principles of the Declaration of Helsinki.

2.2. Imaging

The injection of the radiopharmaceutical (minimum 14 MBq, 3.7 MBq/kg 18F FDG) in a dark room and imaging was performed according to the brain imaging guidelines with at least 4 hours of fasting prior to the examination. The scanner was the Biograph mCT 20 PET/CT (Siemens) and imaging with 3 mm slice thickness, 200x200 matrix, with OSEM algorithm reconstruction, two iteration/21 subset and Gauss-filtration and transaxial resolution full with half maximum of 3 mm was performed.

Raw PET images were first normalized using histogram equalization, interpolation, and rescaling techniques. These operations were performed using Python 3.10 software, and the images centered after interpolation were processed into the final format for analysis.

The raw images were scaled using a series of image processing techniques and used to train the artificial intelligence model. Figure 1 shows the raw image, the transformed image, and the interpolated, centered image, respectively.

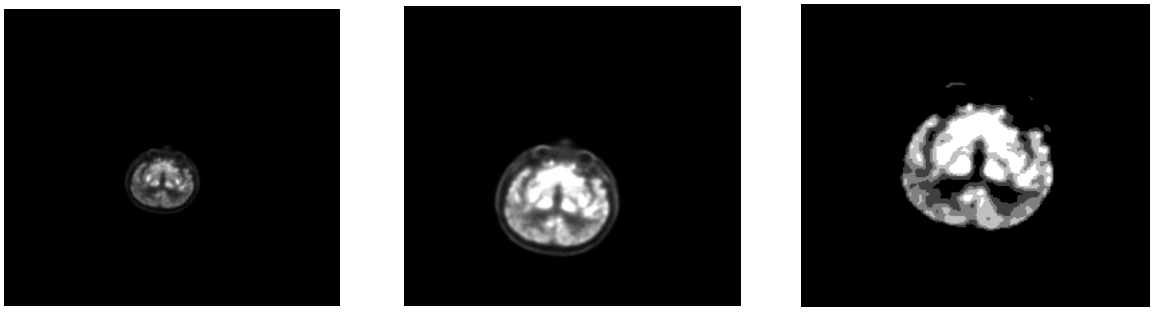


Figure 1. a) Raw image b) Histogram equalized image c) Interpolated image

Retrospective analysis of the datasets was performed for research purposes by a Nuclear Medicine physician who is experienced in the Neurologic studies.

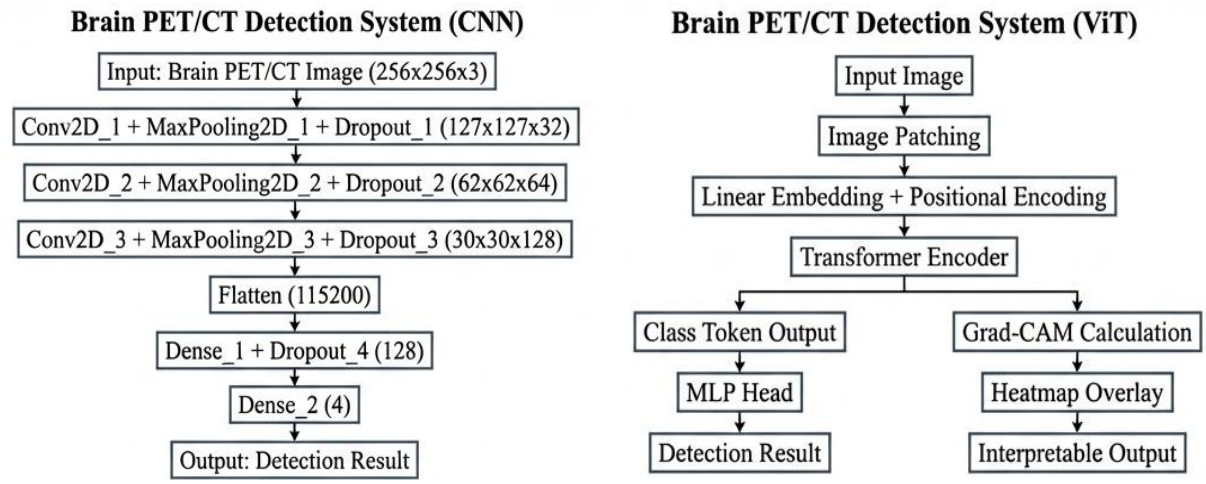
2.3. Development of Deep Learning Architectures

In this study, an innovative deep learning architecture was developed to analyze data obtained from brain PET/CT images. A total of 73 patients and 3,766 pre-processed transaxial PET images were obtained for the study. The dataset was partitioned into training (80%) and test (20%) sets. To ensure the validity of the results and prevent data leakage, this partitioning was performed at the patient level, not at the slice level. This allocation meant that all 2D images from a single subject were assigned to either the training or test subset, and the test set consisted entirely of unseen patients. Consequently, the training set consisted of data from 58 patients, while the test set included 15 patients. This strict separation ensures that the reported performance metrics reflect the model's ability to generalize to new subjects, rather than memorizing patient-specific features. The images were scaled to a size of 256x256 pixels, and normalization processes were applied to enable more effective learning by the model.

Unlike traditional Convolutional Neural Network (CNN)-based approaches used in previous studies, this study adopts the Vision Transformer (ViT) architecture. ViT works by dividing images into small patches of a fixed size (e.g., 16x16 pixels) and embedding these patches linearly. Each patch is treated as a token, and positional information is added to these tokens before feeding them into the Transformer encoder (Azad et al., 2023; Sun et al., 2024). This approach enables the model to capture long-range dependencies and global context in images more effectively (Sun et al., 2024). The ViT architecture demonstrates superior performance in understanding both local features and overall structural relationships, particularly in complex medical images (Hartsock & Rasool, 2024). Dropout layers and L2 regularization were applied to prevent the model from overfitting. ReLU was chosen as the activation function, and softmax was used in the final layer to obtain a multi-class output.

To increase the transparency of the model's decision-making processes and ensure clinical interpretability, Grad-CAM (Gradient-weighted Class Activation Mapping) integration has been implemented. Grad-CAM generates a heatmap that visualizes the image regions on which the model focuses when making a specific classification decision (Selvaraju et al., 2017). This heatmap is created using gradient information obtained from the final layers of the ViT model and highlights critical regions that indicating the model's attention through color intensity (Selvaraju et al., 2017). This allows experts to verify whether the model focuses on clinically important areas in PET/CT images, such as lesions or abnormalities (Selvaraju et al., 2017).

Model training was performed in the Python 3.10 and Visual Studio Code development environment. A 12 GB NVIDIA RTX 3060 GPU was used during the training process, and the model was optimized over 200 iterations. The general architecture of the developed artificial intelligence model is shown in Figure 2.



(a) (b)

Figure 2. Deep learning architectures: a) A baseline CNN Model, b) The proposed model with Grad-CAM interpretability

The performance of the model was evaluated with the following metrics: Accuracy, sensitivity, specificity, positive and negative predictive value (PPV, NPV), F1 Score and ROC Curve. Classification performance was also visually analyzed using the confusion matrix.

2.4. SPM analysis

The quantification of the images was performed by the SPM12 (MATLAB based) software. The patients' glucose metabolism distribution was compared with the normative value in database. The scores of the cerebral regions were obtained. Reference (control) data used for SPM12 analysis were obtained from cognitively normal individuals acquired at the same center and using the same PET/CT scanner as the patient group, in order to eliminate hardware-related bias. In voxel-based analyses, the statistical threshold for identifying significant hypometabolism clusters was set at $p < 0.001$ (uncorrected), and the minimum cluster extent threshold k was accepted as $k > 100$ voxels.

3. RESULTS

In this study, a system for analyzing 18F-FDG PET/CT imaging data for the early diagnosis of prodromal Alzheimer's dementia with artificial intelligence supported deep learning algorithms was developed and evaluated comparatively with the classical quantitative analysis method SPM12. During the training process of the model, the training (accuracy) and loss (loss) values were monitored graphically for a total of 200 iterations, and the learning success of the model increased significantly in this process. The training and test curves obtained confirm that the model exhibits generalizable performance by avoiding over learning. The error and performance results of the model in the training and test set are given in Figure 3.

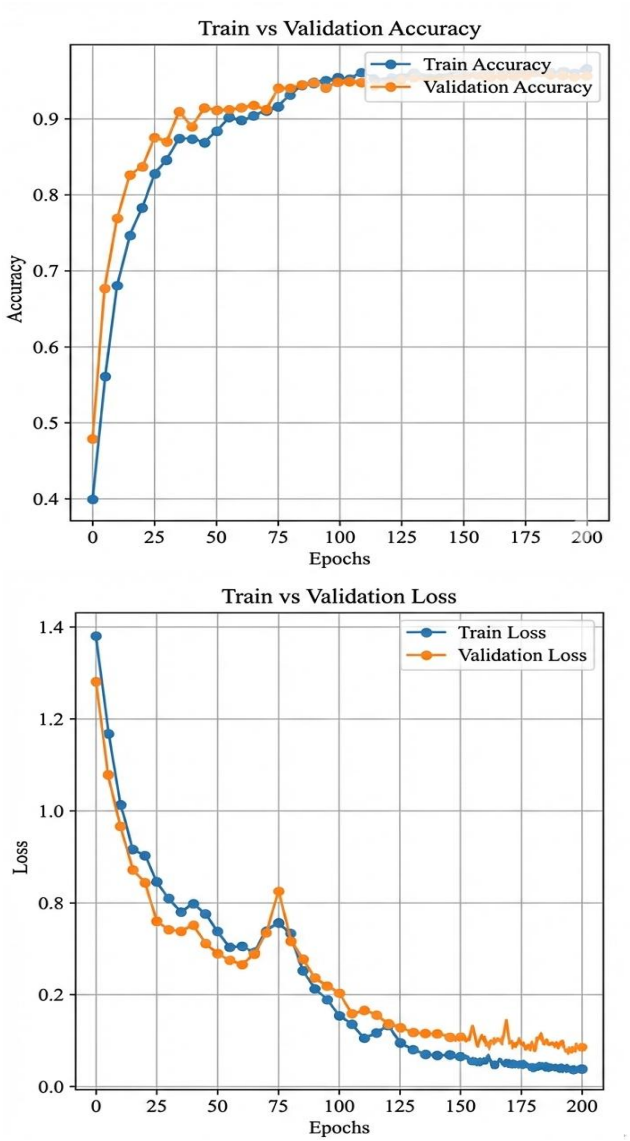


Figure 3. Performance metrics demonstrated by the recommended Deep Learning (ViT) architecture throughout the training process.

Figure 3A shows the change in training and validation accuracy rates over epochs. The parallel rise of both curves indicates that the model's learning capacity is consistent. Figure 3B shows the decrease over time in the cross-entropy loss values calculated for the training and validation sets. The convergence between the training and test curves indicates that the "overfitting" problem in the model is minimized and that the model has high generalization ability.

Figure 4 shows the confusion matrix showing the test results. Here 0: healthy, 1: MCI, 2: FTD, 3: advanced dementia.

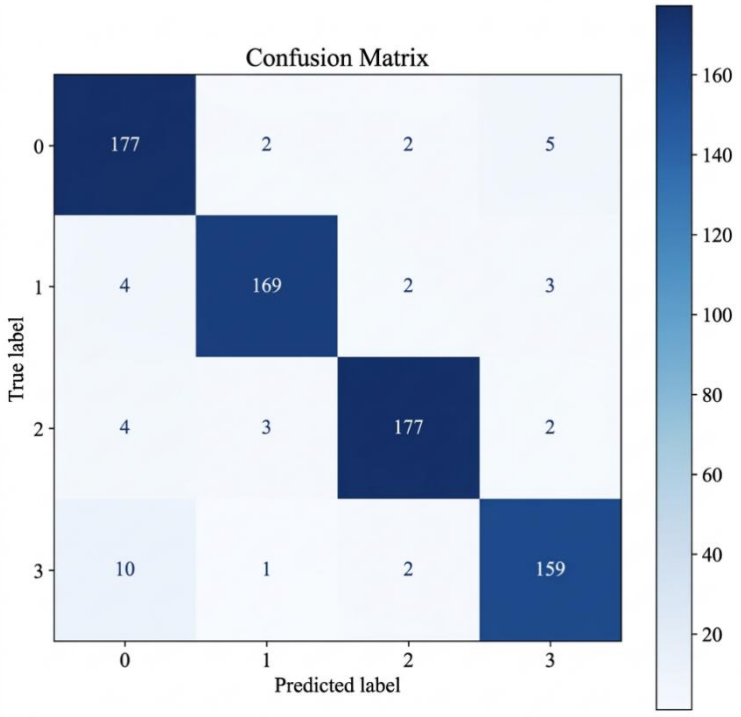


Figure 4. Confusion Matrix showing the classification performance of the Vision Transformer (ViT) model on the test dataset. Labels of the classes are Healthy:0, MCI:1, FTD: 2, AD: 3.

The rows represent the patients' actual clinical diagnoses (true label), while the columns represent the classes predicted by the model (predicted label). The dark-colored cells on the diagonal show the number of patient images correctly identified by the model (True Positive and True Negative). Cells outside the diagonal represent misclassifications (False Positive / False Negative). A high diagonal density in the matrix visually demonstrates the model's high success in distinguishing between classes. Basically, this structure shows the success rate of the model in detecting the test data in each class. 682 of the total 722 test data were correctly classified. The average accuracy rate of the model was calculated as 94.5% and the highest success rate was obtained in the FTD group. High accuracy was also achieved in the classification of healthy individuals, but a relatively higher rate of classification confusion was observed between healthy individuals and the advanced dementia group.

These results show that the model works with high sensitivity, especially in the discrimination of groups of MCI and FTD. In addition, the classifications made by the system on randomly selected test data support the generasibility and reliability of the model. Figure 5 shows the random test data showing the actual values and the values predicted by the model.

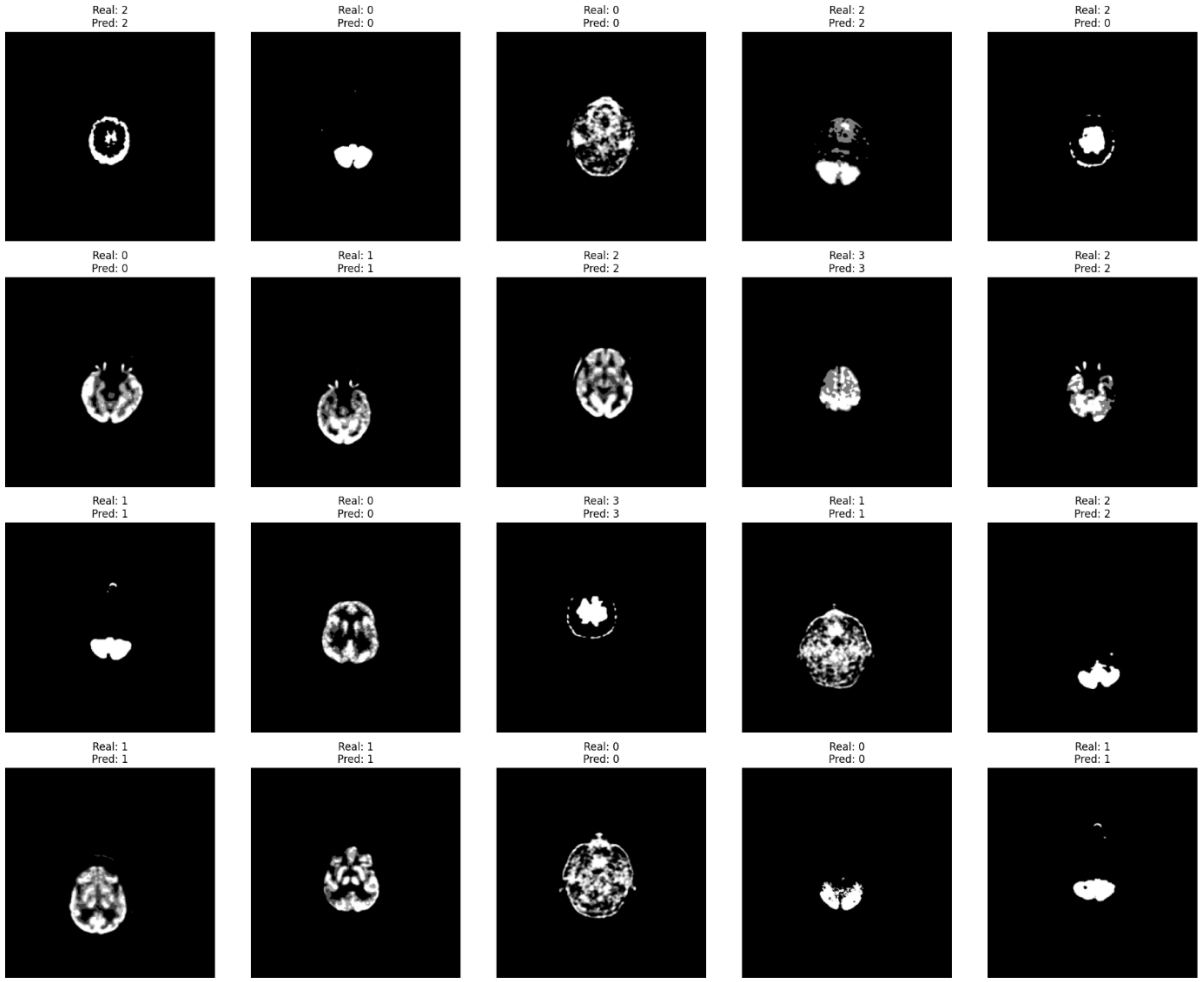


Figure 5. Prediction versus Ground Truth on test data

The success of deep learning models in medical imaging has gained significant momentum, particularly due to the ability of architectures such as Vision Transformer (ViT) to understand complex visual patterns. ViT models effectively capture global and local context by dividing images into fixed-size 'patches' and passing these patches through a series of transformer layers. This approach offers a more comprehensive analysis by modeling long-range dependencies, unlike traditional convolutional networks. However, the transparency of such models' decision-making processes is critically important for clinical applications. In this context, interpretability techniques such as Grad-CAM (Gradient-weighted Class Activation Mapping) from the Class Activation Maps (CAM) family are valuable tools for visualizing which regions of an image the model focuses on when making a classification decision. Grad-CAM uses gradient information from the model's final convolutional layer to create a heatmap highlighting regions important for a specific class. This heatmap allows experts to assess whether the model is looking at clinically meaningful features or misleading artifacts by overlaying the areas of interest as a transparent layer on the original image.

The overall accuracy of the ViT model was calculated as 98.29%, sensitivity as 97.69%, and specificity as 98.88%. The Grad-CAM technique was used for interpretability to ensure that the model's decisions were not based on artifacts and to understand its clinical suitability. Figure 6 shows the model's attention maps, confirming that it focuses on clinically meaningful regions such as the temporoparietal and frontal lobes in correct classifications.



Figure 6. Representative Grad-CAM visualization demonstrating the interpretability of the model. Heatmaps overlaid on PET images show the brain regions the model focuses on for its predictions.

Based on the results of the SPM analysis, the patients (37 M, 36 F, mean 61.42±7.86 years old) included in the study has the mini mental scores of mean 21.73±6.71 and 15.3% of the patients had the anamnesis of family history. According to the clinical decision making the 23 (31.9%) of the patitents had the prodromal dementia while 46 (63.9%) determined to have neurodegenerative disease and 4 patient was normal. Among these patients visual interpretation of the PET results revealed 21/23 determination ratio for prodromal dementia and the diagnostic sensitivity, specificity, accuracy, positive and negative predictive value was 91.3%, 100%, 92%, 100% and 50% respectively and SPM analysis demonstrated concordant results in 19 of these 23 patients with the diagnostic sensitivity, specificity accuracy positive and negative predictive value was 82.6%, 100%, 95.7%, 100% and 42.8% respectively. In the study, the sensitivity of SPM12 was 82.6%, specificity was 100% and overall accuracy was 95.7%, while the sensitivity of the artificial intelligence model was 97.69%, specificity was 98.88% and accuracy was 98.29%.

4. DISCUSSION

FDG PET/CT is a common imaging modality in brain metabolism imaging as well as oncologic imaging. The Nuclear Medicine imaging techniques investigated the metabolic consequences as well as diagnosis and follow-up of many brain pathologies, including dementia. Prodromal dementia is an early phase of other dementia syndromes. The early diagnosis and follow up might lead to normal cognition at this disease stage. Early diagnosis of this disease is possible by means of FDG PET/CT. However, the interpretation of the images is complicated and quantification might benefit from support systems. The statistical parametrical mapping (SPM) analysis which is one of the voxel-based method of quantification and the method of choice in this study is employed. The previous observations about this method demonstrated high accuracy in detecting the patterns of hypometabolism and also in determining patients who would convert to Alzheimer's disease and other dementia syndromes including frontotemporal dementia (Rathore et al., 2017). The ratio of patients who develop Alzheimer's dementia in the prodromal dementia group is 10-15% (Cerami et al., 2014). These patients typically have sclerosis and hypometabolism in medial temporal and hippocampal regions (Petersen et al., 2009). This finding discriminates dementia from normal aging (Jack et al., 2013). 18F FDG PET, especially when combined with SPM analysis, is superior to MRI in determining this finding at an earlier phase (Ewers et al., 2014). The superiority of SPM analysis over 18F FDG PET, with significantly higher sensitivity and specificity (96%, 84% vs 91%, 40%, respectively), was documented in a

previous study (Rabinovici et al., 2011). In contrast, the results in this study showed that visual analysis has similar diagnostic value to SPM analysis. This might be due to the fact that the SPM analysis depends on the cumulative normative data however in this study there were limited number of normal subjects which might be listed as a leading limitation in this study.

Alzheimer's disease typically involves the temporoparietal lobes, precuneus, and posterior cingulate gyrus (Perani et al., 2014). These findings discriminate the disease from other dementia types (frontotemporal, Lewy body) (Perani, 2014). The comparative analysis of 18F FDG PET and SPM analysis revealed the false negativity of 16% and 0%, respectively, which also showed high negative and positive predictive value with additional SPM analysis (Gorno-Tempini et al., 2011). In this analysis we obtained high positive predictive value but limited negative predictive value in both visual and quantitative evaluation. Another comparative study with cerebrospinal fluid findings and 18F FDG PET showed that the most important determinant in Alzheimer's disease is the SPM analysis (Caminiti et al., 2018). The patients with prodromal dementia have mild symptoms and do not have restrictions in daily life (Petersen et al., 2009). 18F FDG PET based SPM analysis might also indicate neurodegeneration in non-amyloid pathologies (Perani et al., 2014). Amyloid imaging by means of PET/CT also can determine early disease (Nordberg, 2009). A recent study has demonstrated that combination of 11C-PiB-PET and SPM analysis by means of 18F FDG PET could determine the prodromal dementia (Iaccarino et al., 2017). Although the aim of this study was to evaluate patients with prodromal dementia, the patient group consisted mostly of degenerative dementia and also included other causes of dementia, such as Frontotemporal dementia. This is another limitation of this study, but it also provides a wide range of disease analysis. There are recent reports demonstrating possible superiority of volumetric based quantification methods instead of voxel-based methods including SPM (Brugnolo et al., 2019).

The artificial intelligence, as expected, provided significantly higher diagnostic accuracy compared to visual interpretation and SPM analysis. Previous studies also presented this observation which are summarized in a recent review (Aljuhani et al., 2024). There are several different methods for artificial intelligence models including deep learning and machine learning (Mirkin & Albensi, 2023). A previous study including deep learning-based method with an MR dataset demonstrated prediction of early and late mild cognitive impairment and AD (Odusami et al., 2021). Another deep learning based method was implemented in an 18F FDG PET dataset, and follow-up results showed sensitivity of 100% and specificity of 82% in AD (ing et al., 2019). A multimodal MR-PET deep neural network study provided classification of the MCI patients who would convert to AD in follow up (Lu et al., 2018). A tailor-made 3D convolutional neural networks accurately determined patients with AD, FTD, or CN and the method outperformed the visual interpretation (Rogeau et al., 2024). The deep learning-based method performed in this analysis had significantly high diagnostic accuracy in determining the individuals with prodromal dementia, as well as with other dementia syndromes (AD and FTD). The significantly high diagnostic accuracy yielded by this modality was also higher compared to the previous similar literature data (Litjens et al., 2017).

In this study, the results obtained by analyzing 18F-FDG PET/CT imaging data with both traditional quantification methods (SPM12) and deep learning-based artificial intelligence models in the diagnosis of prodromal Alzheimer's dementia were comparatively evaluated. The findings revealed that the artificial intelligence-assisted model diagnosed MCI with higher accuracy and sensitivity than conventional methods.

These findings confirm that artificial intelligence-based diagnostic support systems, which have recently appeared in the literature, can make important contributions to clinical decision-making processes.

The MCI stage, in particular, is defined as the most critical period of Alzheimer's disease that is amenable to treatment. However, the uncertainty of symptoms in this stage makes it difficult to classify correctly with traditional diagnostic methods (Petersen, 2004). Studies such as (Mosconi, 2005) reported that 18F-FDG PET imaging is a valuable biomarker for assessing the potential for conversion of MCI to Alzheimer's disease. However, the subjectivity and observer dependence of analyses based solely on visual interpretation reveal the need for more objective and reproducible systems.

At this point, deep learning-based models offer a promising alternative as they are sensitive to patterns that the human eye cannot detect and can analyze high volumes of data in a short time (Alasiry et al., 2025; Esteva, 2017). (Lu, 2018) reported that the multi-model deep learning system they developed to diagnose Alzheimer's disease from FDG PET images performed better than classical methods (Lu, 2018). Similarly, this study showed that the artificial intelligence model offers a high success rate, especially in groups where differential diagnosis is critical, such as FTD and MCI.

One of the main reasons for the success of the model is the preprocessing of the data (histogram equalization, interpolation) and the application of techniques such as dropout and L2 regularization to prevent overfitting. In addition, a deep-layered CNN architecture was trained to enhance performance by providing GPU-assisted fast optimization during training.

However, this study also has some limitations. The sample size was relatively limited and a single-center dataset was used. Another significant limitation of our study is that the reference diagnosis (ground truth) was not confirmed by histopathological evidence or biomarkers such as amyloid PET/cerebrospinal fluid (CSF) analysis. The study primarily based diagnostic confirmation on clinical follow-up and FDG PET imaging findings. Given the ambiguity of symptoms in the prodromal phase and the slow-progressing nature of Alzheimer's disease, the minimum follow-up period of 8 months, established as a criterion in the study, may be relatively short to observe definitive clinical progression or confirm the diagnosis with absolute certainty. Therefore, this limitation of the reference standard (clinical diagnosis) used when evaluating the performance of the artificial intelligence model should be considered. In addition, researchers did not test the model's performance with images acquired at another center or with different devices. This is an issue that should be considered in terms of generalizability. Future studies should be supported by multi-center, prospective data and researchers should test the applicability of the model in real clinical settings.

In line with the results of the study, we can draw the following conclusions:

- Artificial intelligence can contribute to clinical decision-making processes by providing faster, objective and sensitive results compared to traditional imaging analyses.

18F-FDG PET/CT images provide reliable biomarkers in the differential diagnosis of MCI and other types of dementia (Mosconi et al., 2008).

- When deep learning models are trained with sufficient quantity and quality of data, they can be applied to clinical practice (Ting et al., 2019).

In conclusion, this study shows that artificial intelligence-based decision support systems have significant potential in neuroimaging-based dementia diagnosis and that these systems can be integrated into routine clinical applications in the near future.

REFERENCES

Alasiry, A., Shinan, K., Alsadhan, A. A., Alhazmi, H. E., Alanazi, F., Ashraf, M. U., & Muhammad, T. (2025). A novel neuroimaging based early detection framework for alzheimer disease using deep learning. *Scientific Reports*, *15*(1), 23011. https://doi.org/10.1038/s41598-025-05529-5

Aljuhani, M., Ashraf, A., & Edison, P. (2024). Use of Artificial Intelligence in Imaging Dementia. Cells, 13(23), 1965. https://doi.org/10.3390/cells13231965

Azad, R., Kazerouni, A., Heidari, M., Aghdam, E. K., Molaei, A., Jia, Y., Jose, A., Roy, R., & Merhof, D. (2023). Advances in medical image analysis with vision Transformers: A comprehensive review. Medical Image Analysis, 91, 103000. Elsevier BV. https://doi.org/10.1016/j.media.2023.103000

Basaia, S. (2019). Automated classification of Alzheimer's disease and mild cognitive impairment using a single MRI and deep neural networks. NeuroImage:Clinical, 21, 101645.

Brugnolo, A., Carli, F. D., Pagani, M., Morbelli, S., Jonsson, C., Chincarini, A., Frisoni, G. B., Galluzzi, S., Perneczky, R., Drzezga, A., Berckel, B. N. M. van, Ossenkoppele, R., Didic, M., Guedj, É., Arnaldi, D., Massa, F., Grazzini, M., Pardini, M., Mecocci, P., … Nobili, F. (2019). Head-to-Head Comparison among Semi-Quantification Tools of Brain FDG-PET to Aid the Diagnosis of Prodromal Alzheimer's Disease1. Journal of Alzheimer s Disease, 68(1), 383. https://doi.org/10.3233/jad-181022

Caminiti, S. P., et al. (2018). FDG-PET and CSF biomarker accuracy in prediction of conversion to different dementias in a large multicentre MCI cohort. NeuroImage Clinical, 18, 167. https://doi.org/10.1016/j.nicl.2018.01.019

Cerami, C., Rosa, D. P. A., Magnani, G., Santangelo, R., Marcone, A., Cappa, S. F., & Perani, D. (2014). Brain metabolic maps in Mild Cognitive Impairment predict heterogeneity of progression to dementia. Neuroimage Clinical, 7, 187. https://doi.org/10.1016/j.nicl.2014.12.004

Chertkow, H., Feldman, H., Jacova, C., & Massoud, F. (2013). Definitions of dementia and predementia states in Alzheimer's disease and vascular cognitive impairment: consensus from the Canadian conference on diagnosis of dementia. Alzheimer s Research & Therapy, 5. https://doi.org/10.1186/alzrt198

Esteva, A. (2017). Dermatologist-level classification of skin cancer with deep neural networks. Nature, 542(7639), 115.

Ewers, M., Brendel, M., Rizk-Jackson, A., Rominger, A., Bartenstein, P., & Schuff, N. (2014). Reduced FDG-PET brain metabolism and executive function predict clinical progression in elderly healthy subjects. Neuroimage Clin., 4, 45.

Gorno-Tempini, M., et al. (2011). Classification of primary progressive aphasia and its variants. Neurology, 76(11), 1006. https://doi.org/10.1212/wnl.0b013e31821103e6

Hartsock, I., & Rasool, G. (2024). Vision-Language Models for Medical Report Generation and Visual Question Answering: A Review. arXiv (Cornell University). Cornell University. https://doi.org/10.48550/arxiv.2403.02469

Iaccarino, L., et al. (2017). A Cross-Validation of FDG- and Amyloid-PET Biomarkers in Mild Cognitive Impairment for the Risk Prediction to Dementia due to Alzheimer's Disease in a Clinical Setting. Journal of Alzheimer s Disease, 59(2), 603. https://doi.org/10.3233/jad-170158

Ding, Y., Sohn, J. H., Kawczynski, M. G., Trivedi, H., Harnish, R., Jenkins, N. W., Lituiev, D., Copeland, T. P., Aboian, M. S., & Aparici, C. M. (2019). A Deep Learning Model to Predict a Diagnosis of Alzheimer Disease by Using (18)F-FDG PET of the Brain. Radiology, 290, 456.

Jack, C. R., Jr, Wiste, H. J., Weigand, S. D., Knopman, D. S., Lowe, V., & Vemuri, P. (2013). Amyloid-first and neurodegeneration-first profiles characterize incident amyloid PET positivity. Neurology, 81, 1732.

Litjens, Get al. (2017). A survey on deep learning in medical image analysis. Medical Image Analysis, 42, 60. https://doi.org/10.1016/j.media.2017.07.005

Lu, D., et al. (2018). Multimodal and Multiscale Deep Neural Networks for the Early Diagnosis of Alzheimer's Disease using structural MR and FDG-PET images. Scientific Reports, 8(1), 5697. https://doi.org/10.1038/s41598-018-22871-z

Mirkin, S., & Albensi, B. C. (2023). Should artificial intelligence be used in conjunction with Neuroimaging in the diagnosis of Alzheimer's disease? Frontiers in Aging Neuroscience, 15, 1094233. https://doi.org/10.3389/fnagi.2023.1094233

Mosconi, L. (2005). Brain glucose metabolism in the early and specific diagnosis of Alzheimer's disease. European Journal of Nuclear Medicine and Molecular Imaging, 32(4), 486.

Mosconi, L., et al. (2008). Multicenter Standardized 18F-FDG PET Diagnosis of Mild Cognitive Impairment, Alzheimer's Disease, and Other Dementias. Journal of Nuclear Medicine, 49(3), 390. https://doi.org/10.2967/jnumed.107.045385

Nordberg, A. (2009). High PIB Retention in Alzheimer's Disease is an Early Event with Complex Relationship with CSF Biomarkers and Functional Parameters. Current Alzheimer Research, 999(999), 1. https://doi.org/10.2174/1567209198607192050

Odusami, M., Maskeliūnas, R., Damaševičius, R., & Krilavičius, T. (2021). Analysis of Features of Alzheimer's Disease: Detection of Early Stage from Functional Brain Changes in Magnetic Resonance Images Using a Finetuned ResNet18 Network. Diagnostics, 11(6), 1071. https://doi.org/10.3390/diagnostics11061071

Perani, D. (2014). FDG-PET and amyloid-PET imaging. Current Opinion in Neurology, 27(4), 405. https://doi.org/10.1097/wco.0000000000000109

Perani, D., et al. (2014). Validation of an optimized SPM procedure for FDG-PET in dementia diagnosis in a clinical setting. NeuroImage Clinical, 6, 445. https://doi.org/10.1016/j.nicl.2014.10.009

Perani, D., Schillaci, O., Padovani, A., Nobili, F., Iaccarino, L., Rosa, P. A. D., Frisoni, G. B., & Caltagirone, C. (2014). Erratum to "A Survey of FDG- and Amyloid-PET Imaging in Dementia and GRADE Analysis." BioMed Research International, 2014, 1. https://doi.org/10.1155/2014/246586

Petersen, R. C. (1999). Mild cognitive impairment: Clinical characterization and outcome. Archives of Neurology, 56(3), 303.

Petersen, R. C. (2004). Mild cognitive impairment as a diagnostic entity. Journal of Internal Medicine, 256(3), 183. https://doi.org/10.1111/j.1365-2796.2004.01388.x

Petersen, R. C., Roberts, R. O., Knopman, D. S., Boeve, B. F., Geda, Y. E., & Ivnik, R. J. (2009). Mild cognitive impairment: ten years later. Arch. Neurol., 66(12), 1447.

Rabinovici, G. D., et al. (2011). Amyloid vs FDG-PET in the differential diagnosis of AD and FTLD. Neurology, 77(23), 2034. https://doi.org/10.1212/wnl.0b013e31823b9c5e

Rathore, S., Habes, M., Iftikhar, M. A., Shacklett, A., & Davatzikos, C. (2017). A review on neuroimaging-based classification studies and associated feature extraction methods for Alzheimer's disease and its prodromal stages. Neuroimage, 155, 530. https://doi.org/10.1016/j.neuroimage.2017.03.057

Rizzo, G., Copetti, M., Arcuti, S., Martino, D., Fontana, A., & Logroscino, G. (2016). Accuracy of clinical diagnosis of parkinson disease: a systematic review and meta-analysis. Neurology, 86(6), 566.

Rogeau, A., et al. (2024). A 3D convolutional neural network to classify subjects as Alzheimer's disease, frontotemporal dementia or healthy controls using brain 18F-FDG PET. Neuroimage, 288, 120530.

Saif, F. H., Al-Andoli, M. N., & Bejuri, W. M. Y. W. (2024). Explainable AI for Alzheimer Detection: A Review of Current Methods and Applications. Applied Sciences, 14(22), 10121. Multidisciplinary Digital Publishing Institute. https://doi.org/10.3390/app142210121

Selvaraju, R. R., Cogswell, M., Das, A., Vedantam, R., Parikh, D., & Batra, D. (2017). Grad-CAM: Visual Explanations from Deep Networks via Gradient-Based Localization. 618. https://doi.org/10.1109/iccv.2017.74

Smailagic, N., Vacante, M., Hyde, C., Martin, S., Ukoumunne, O. C., & Sachpekidis, C. (2015). 18F-FDG PET for the early diagnosis of Alzheimer's disease dementia and other dementias in people with mild cognitive impairment (MCI). Cochrane Library, 2015(2). Elsevier BV. https://doi.org/10.1002/14651858.cd010632.pub2

Sun, K., et al. (2024). Medical Multimodal Foundation Models in Clinical Diagnosis and Treatment: Applications, Challenges, and Future Directions. arXiv (Cornell University). https://doi.org/10.48550/arxiv.2412.02621

Ting, D. S., Rim, T. H., Choi, Y. S., & Ledsam, J. R. (2019). Deep Learning in Medicine. Are We Ready? Annals of the Academy of Medicine Singapore, 48(1), 1. https://doi.org/10.47102/annals-acadmedsg.v48n1p1

Wang, S., Jiang, Y., Yang, A., Meng, F., & Zhang, J. (2024). The Expanding Burden of Neurodegenerative Diseases: An Unmet Medical and Social Need. Aging and Disease, 16(5), 0. Buck Institute for Research on Aging. https://doi.org/10.14336/ad.2024.1071

Ward, E., et al. (2025). Modeling neurodegeneration in the retina and strategies for developing pan-neurodegenerative therapies. Molecular Neurodegeneration, 20(1). BioMed Central. https://doi.org/10.1186/s13024-025-00858-5