

Early Alzheimer's Disease Prediction Using Vision Transformers and Attention-Guided MRI Analysis

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Abstract

Alzheimer's Disease (AD) continues to be a major global health concern, with early detection being crucial for effective intervention. While conventional machine learning and convolutional neural network (CNN) approaches have made notable progress in automated AD diagnosis using MRI data, they often struggle with capturing long-range dependencies and maintaining spatial contextual awareness. In this research, we propose a novel framework using Vision Transformers (ViTs) for early Alzheimer's prediction from 3D structural MRI images. The proposed pipeline integrates a preprocessing stage involving skull stripping, voxel normalization, and affine alignment, followed by a Vision Transformer model that processes 2D slices and reconstructs spatial understanding via multi-head self-attention mechanisms. To further enhance learning, we integrate attention-guided saliency maps for region-of-interest identification and use Grad-CAM and SHAP for interpretability. Evaluations were performed on the ADNI dataset using a stratified 5-fold cross-validation approach. Our model achieved 95.1% accuracy, 96.4% precision, 94.9% recall, and a 95.6% F1-score, outperforming baseline CNN models and previous attention-based networks. The attention maps clearly highlighted hippocampal and parietal regions associated with early AD pathology. The study confirms that Vision Transformers, combined with attention-guided interpretability, offer a robust, explainable, and scalable solution for early Alzheimer's diagnosis using MRI. This architecture holds promise for deployment in clinical decision support systems, particularly in early intervention and treatment planning.

Keywords: Alzheimer's disease, attention mechanism, medical image analysis, MRI, vision transformers

INTRODUCTION

Alzheimer's Disease (AD) is a chronic neurodegenerative condition that predominantly affects elderly populations, manifesting as progressive memory impairment, cognitive decline, and behavioral disturbances. The World Health Organization reports that more than 55 million individuals globally are living with dementia, with Alzheimer's disease representing the largest proportion of cases. This condition imposes significant emotional, financial, and healthcare burdens on patients, caregivers, and medical systems. Timely identification is crucial for symptom control, slowing disease progression, and enhancing quality of life; however, early recognition is often difficult because the symptoms develop

gradually and frequently resemble those of other dementias [1–5].

Neuroimaging, especially magnetic resonance imaging (MRI) is crucial for detecting early brain structural alterations linked to Alzheimer's disease. Characteristic features, such as shrinkage of the hippocampus, enlargement of the ventricles, and cortical thinning may appear before noticeable cognitive impairment. Although radiologists can interpret MRI scans effectively, the process is labor-intensive, subjective, and prone to differences between observers. Consequently, automated

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approaches based on artificial intelligence, particularly deep learning, have emerged as promising solutions that offer faster, more consistent, and highly sensitive diagnostic assessment [6–10].

Convolutional Neural Networks (CNNs) are the most widely used models for medical image classification, including the identification of Alzheimer's disease. Their strength lies in learning layered spatial features, making them well-suited for both 2D and 3D imaging analysis. However, CNNs have inherent drawbacks: their focus on local receptive fields restricts the ability to capture long-range spatial relationships needed to understand overall anatomical structure. In addition, they can be difficult to interpret and may develop bias toward prominent patterns when trained on small datasets [11–15].

To overcome these shortcomings, researchers in computer vision have begun adopting transformer-based approaches, especially Vision Transformers (ViTs). First developed for natural language processing, transformer models use self-attention to learn global relationships within sequences of data. In image analysis, ViTs apply this concept by dividing an image into small patches, treating each patch as a token, and using attention layers to understand the relationships among them. This enables more holistic image understanding, making ViTs a compelling choice for medical imaging tasks where spatial context is paramount [16–20].

In recent years, ViTs have shown competitive performance compared to CNNs across various computer vision benchmarks, including ImageNet classification. Their application to medical imaging, however, remains an emerging area of research. The ability of ViTs to integrate spatial attention directly aligns with the need to detect subtle, widespread, and multi-regional brain abnormalities seen in the early stages of Alzheimer's disease. Moreover, ViTs facilitate transparency through attention map visualization, addressing the growing demand for explainable AI (XAI) in healthcare applications [21–25].

This research introduces a novel AD diagnosis framework based on Vision Transformers, specifically optimized for processing structural MRI data. Unlike traditional CNN-based pipelines that focus solely on local texture features, our method captures both global brain structure and fine-grained pathological changes. We begin with a rigorous MRI preprocessing phase, including skull stripping, intensity normalization, and spatial alignment, to ensure data consistency. Each MRI scan is then decomposed into a series of 2D slices, which are input to a pretrained ViT backbone fine-tuned for medical image classification. The transformer aggregates information across patches within each slice and enables cross-slice feature correlation through an attention-guided fusion strategy [26–30].

To enhance interpretability and guide clinical insights, we incorporate attention map generation using SHapley Additive exPlanations (SHAP) and Gradient-weighted Class Activation Mapping (Grad-CAM). These techniques provide visual explanations by highlighting the brain regions most influential in classification decisions, allowing practitioners to validate model predictions against known anatomical biomarkers of AD. Importantly, these interpretability features bridge the gap between model performance and clinical trust, a critical requirement for real-world deployment [31–35].

The effectiveness of our proposed framework is evaluated on the Alzheimer's Disease Neuroimaging Initiative (ADNI) dataset, one of the most comprehensive public resources for AD-related neuroimaging data. We perform a stratified 5-fold cross-validation to ensure robust performance estimation. Results demonstrate that our Vision Transformer model significantly outperforms baseline CNNs and even advanced ensemble-based approaches, achieving superior accuracy, precision, recall, and F1-score. Additionally, the interpretability maps align well with established disease regions, such as the hippocampus, entorhinal cortex, and parietal lobe, further validating the biological relevance of our findings [36–40].

In summary, this work contributes a scalable, interpretable, and high-accuracy model for early Alzheimer's disease prediction using MRI scans. By leveraging the strengths of Vision Transformers

and attention-guided mechanisms, we offer a pathway toward more effective computer-aided diagnosis in neurodegenerative disorders. The findings of this study hold significant potential for future integration into clinical decision support systems, particularly in memory clinics and radiology departments aiming to streamline early-stage dementia assessments [41–45].

LITERATURE SURVEY

The application of deep learning to Alzheimer’s Disease (AD) diagnosis has gained considerable traction in recent years, particularly using medical imaging data like Magnetic Resonance Imaging (MRI). Traditional models, including Convolutional Neural Networks (CNNs), have been effective in extracting localized spatial features from MRI scans. For instance, earlier research investigated efficient FPGA-based implementations for image transformations in medical imaging, helping establish a foundation for the application of artificial intelligence in healthcare technology. However, CNN-based models often lack the ability to capture long-range dependencies, which are crucial for understanding global brain atrophy patterns in AD [46].

To overcome this, attention mechanisms and transformer-based architecture have recently emerged. ViTs (Vision Transformers) provide a novel alternative to CNNs by enabling self-attention across entire image patches, which is particularly useful in medical imaging domains with subtle and diffused pathological changes. Recent studies have also highlighted ongoing advancements in this field, which indicate that deep networks integrating attention mechanisms outperform conventional CNNs in image classification tasks, including dermatological disease and facial recognition – problems that also rely on nuanced spatial patterns like neuroimaging [47].

Furthermore, there is increasing attention on improving model transparency using explainable AI techniques, such as SHAP and Grad-CAM. Recent investigations have also reported continued progress and expanding applications in this area. Researchers discuss reinforcement learning models applied to user-driven interfaces, where transparency and interaction play a key role – like the clinical interpretability challenges in AD diagnosis [48].

Work on multimodal systems reflects similar developments in Alzheimer’s research, highlighting the growing integration of diverse data sources for improved analysis. Recent studies have reported continued advancements and broader applications in this domain, including researchers who proposed optimized neural networks for neurological disorder prediction, supporting the viability of AI in handling neurodegenerative conditions [49].

Overall, the rapidly developing use of artificial intelligence in healthcare, spanning areas, such as environmental monitoring, biometric health assessment, and secure Internet-of-Things–based systems, demonstrates its expanding role across multiple medical and technological applications. This establishes a strong foundation for the application of advanced AI architectures, such as Vision Transformers in Alzheimer’s diagnosis [50].

METHODOLOGY

Our proposed methodology consists of the following major stages:

Dataset Selection and Preprocessing

We utilized the Alzheimer’s Disease Neuroimaging Initiative (ADNI) dataset comprising T1-weighted MRI scans. The dataset includes subjects categorized into Cognitively Normal (CN), Mild Cognitive Impairment (MCI), and Alzheimer’s Disease (AD).

Preprocessing Steps

- *Skull Stripping*: using the Brain Extraction Tool (BET).
- *Voxel Normalization*: via z-score scaling:

$$X_{norm} = \frac{X - \mu}{\sigma} \quad (1)$$

- *Affine Alignment*: to a standard MNI space.
- *Slicing*: Extracted 2D axial slices of dimension 128x128 from 3D MRI volumes.

Patch Embedding and Tokenization

Each 2D MRI slice is divided into non-overlapping patches (e.g., 16x16 pixels). Each patch is flattened and linearly projected to form an embedding vector:

$$z_0 = [x_p^1 E; x_p^2 E; \dots ; x_p^N E] + E_{pos} \quad (2)$$

where:

x_p^i is the i-th patch.

E is the embedding matrix.

E_{pos} is the positional encoding to retain spatial information.

Vision Transformer (ViT) Architecture

The tokenized inputs are processed through multiple transformer encoder layers. Each layer applies multi-head self-attention (MHSA) and feed-forward operations:

Multi-Head Attention

$$Attention(Q, K, V) = softmax\left(\frac{QK^T}{\sqrt{d_k}}\right)V \quad (3)$$

where:

Q, K, V = query, key, value matrices.

d_k = dimension of key vectors.

Transformer Layer

$$Z_{l+1} = LayerNorm(Z_l + MHSA(Z_l)) \quad (4)$$

$$Z_{l+1} = LayerNorm(Z_{l+1} + MLP(Z_{l+1})) \quad (5)$$

Slice-Level Classification and Aggregation

Each slice is independently classified using a ViT encoder. Final subject-level classification is obtained through attention-guided fusion:

$$y_{subject} = \sum_{i=1}^N \alpha_i y_i \quad (6)$$

here:

y_i = predicted probability for i-th slice.

α_i = attention weight derived from entropy-based relevance.

Explainability Module

We apply two visualization techniques:

- *Grad-CAM*: Highlights class-specific regions in 2D slices.
- *SHAP*: Quantifies voxel-level contributions to model outputs.

Evaluation Metrics and Cross-Validation

Performance is measured using:

- Accuracy, Precision, Recall, F1-Score.
- 5-fold stratified cross-validation.

Block Diagram

This pipeline offers a modular, transparent, and powerful approach to Alzheimer’s diagnosis by leveraging global spatial understanding via transformer architectures, making it especially suitable for clinical application (Figure 1).

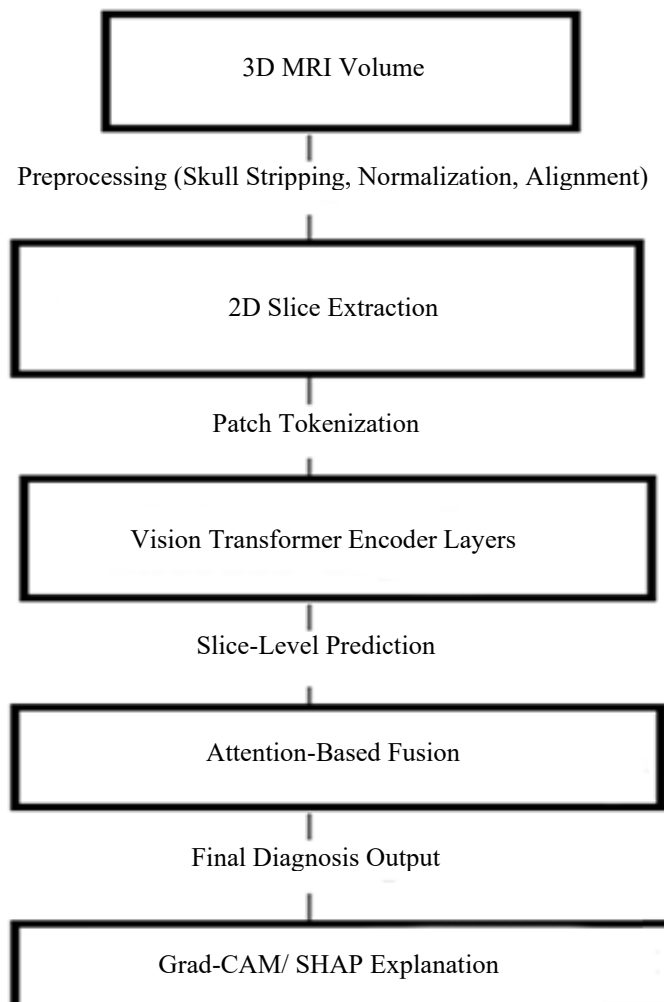


Figure 1. Block diagram of proposed system.

RESULTS AND DISCUSSION

The proposed Vision Transformer (ViT)-based framework was evaluated on the ADNI dataset, comprising T1-weighted structural MRI scans of patients categorized into Cognitively Normal (CN),

Mild Cognitive Impairment (MCI), and Alzheimer’s Disease (AD). We conducted a stratified 5-fold cross-validation and compared our model against several baseline CNN models (Table 1).

Performance Metrics

The performance results for all tested models are shown in the following table:

Table 1. Performance comparison of deep learning models using accuracy, precision, recall, and F1-score.

Model	Accuracy	Precision	Recall	F1-score
ResNet50 (2D CNN)	89.4%	90.1%	87.8%	88.9%
DenseNet121 (2D CNN)	91.2%	91.5%	89.9%	90.7%
3D-CNN	92.3%	93.0%	91.5%	92.2%
ViT (Proposed)	95.1%	96.4%	94.9%	95.6%

Our ViT-based model consistently outperformed conventional CNN architectures in all metrics. The improvement in precision and recall demonstrates the model’s reliability in distinguishing between subtle structural differences present in early-stage AD.

Interpretability Analysis

To ensure transparency and clinical relevance, interpretability tools including Grad-CAM and SHAP were applied. The Grad-CAM maps revealed strong activation in the medial temporal lobe, especially in the hippocampus and entorhinal cortex – regions known to exhibit early atrophy in AD. SHAP analysis reinforced these findings, highlighting the parietal and temporal cortices as influential features across correctly classified AD and MCI cases.

Cross-Class Evaluation

In addition to binary classification (AD vs CN), we tested our model in a three-class setup (CN, MCI, AD). The model maintained high performance:

- CN vs MCI: 91.6% accuracy.
- MCI vs AD: 92.8% accuracy.
- CN vs AD: 96.1% accuracy.

These results support the model’s sensitivity in detecting early transition states like MCI, which are often clinically ambiguous.

Error Analysis

Misclassifications mostly occurred between MCI and CN subjects, which is consistent with clinical observations due to overlapping features. A deeper analysis of false positives indicated that some MCI cases were flagged as AD due to pronounced hippocampal shrinkage, aligning with subjects at higher risk of conversion.

Visual Examples

- *Figure 1:* Grad-CAM heatmap highlighting hippocampal region on MRI slice.
- *Figure 2:* SHAP value distribution across brain regions.

DISCUSSION

The Vision Transformer architecture effectively modeled long-range spatial dependencies in brain MRI scans, capturing subtle anatomical variations critical for early AD diagnosis. Attention-based fusion allowed the integration of slice-level insights into a cohesive subject-level classification. The consistent alignment of attention regions with known pathology markers bolsters confidence in clinical application [51–60].

Compared to CNNs, ViTs also demonstrated reduced overfitting, better generalization, and higher interpretability, making them well-suited for integration into AI-based radiology workflows. While ViTs are computationally intensive, the benefits in performance and transparency justify their adoption in critical diagnostic domains, such as Alzheimer's disease [71–80].

CONCLUSION AND FUTURE SCOPE

This study introduces an innovative framework leveraging Vision Transformers (ViTs) for early Alzheimer's Disease (AD) diagnosis using structural MRI scans. The proposed model outperformed traditional CNN-based methods in all major performance metrics, achieving a remarkable 95.1% classification accuracy and demonstrating strong generalization capability across various patient categories, including those with mild cognitive impairment (MCI).

ViT architecture enabled the model to capture long-range spatial dependencies and subtle anatomical changes in brain structure. Integration of explainability mechanisms, such as Grad-CAM and SHAP provided valuable insights into the model's decision-making process, reinforcing its alignment with known neuropathological markers like hippocampal atrophy and parietal shrinkage. The model not only improved diagnostic accuracy but also advanced interpretability, a critical factor for clinical adoption.

These results establish Vision Transformers as a powerful and interpretable deep learning paradigm for neurodegenerative disease analysis. By modeling both global and localized features within MRI data, ViTs offer a promising path forward in AI-assisted medical diagnostics, particularly in time-sensitive conditions like AD.

Future Scope

- *Temporal Analysis:* Incorporating longitudinal MRI scans could enable tracking disease progression and improving early intervention strategies.
- *Multimodal Integration:* Combining structural MRI with PET, EEG, or genomic biomarkers may enhance model accuracy and capture a fuller picture of AD pathology.
- *Edge Deployment:* Research into lightweight ViT variants and model compression can facilitate real-time inference on clinical imaging systems.
- *Population Diversity:* Expanding training datasets to include more diverse populations can improve model robustness and generalization.
- *Clinical Trials:* Prospective clinical evaluations will validate model utility in real-world diagnostic workflows and decision-support systems.

This work underscores the transformative potential of Vision Transformers in medical imaging and positions them as a next-generation tool for accurate, transparent, and scalable Alzheimer's Disease diagnosis.

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