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Explainable Federated Multimodal Deep Learning Framework for Early Alzheimer's Disease Detection: Integrating MRI, Clinical Data, and Expert-Guided Few-Shot Learning with Privacy-Preserving Cross-Site Validation

Babasaheb Satpute
JAIN (Deemed-to-be University)
Suriya Prakash J.
JAIN (Deemed-to-be University)
Wasudeo Rahane
DES Pune University
Rajesh Bharati
Dr. D. Y. Patil Institute of Technology, Pimpri
Srinidhi N N
srinidhi.nn@manipal.edu

Manipal Academy of Higher Education

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Explainable Federated Multimodal Deep Learning Framework for Early Alzheimer's Disease Detection: Integrating MRI, Clinical Data, and Expert-Guided Few-Shot Learning with Privacy-Preserving Cross-Site Validation

Babasaheb Satpute, Suriya Prakash J., Wasudeo Rahane, Rajesh Bharati, Srinidhi N N

Corresponding author: Srinidhi N N (srinidhi.nn@manipal.edu)

Abstract

The early diagnosis of the Alzheimer disease (AD) is a critical issue in the field of healthcare, and the existing methods of diagnosis are often confined to the analysis of a single modality, inability to interpret the results, and the inability to generalize to different sites. The paper introduces an explicable federated multimodal deep learning architecture which combines structural MRI, clinical tabular data, and textual medical reports to strong detect early AD without violating the privacy of patients. We have implemented federated learning in many medical centers and a few-shot learning under the guidance of specialists to improve the issue of data scarcity and domain shift. The framework uses multimodal fusion based on cross-attention and has region-sensitive explainability using built-in XRAI (eXplanation with Ranked Area Integrals) and SHAP (SHapley Additive explanations) features. Our system is benchmarked on three datasets which are ADNI(Alzheimer's Disease Neuroimaging Initiative),PPMI(Parkinson's Progression Markers Initiative) and ANMerge as a measure of external validation. The results of the experiments show a high level of performance with accuracy of 94.7 percent, sensitivity of 95.2 percent, specificity of 94.1 percent, AUC of 0.973 and F1-score of 94.9 percent outperforming the state-of-the-art centralized and single-modality by 6.3-8.7 percent. By ablation, the role of federated training (+4.2% accuracy), multimodal fusion (+5.8%), few-shot adaptation (+3.1%), and explainability integration are found to be significant. Anatomical consistency and diagnostic relevance of generated explanations are verified by clinical assessment with neurologists with 89.3% agreement with the clinicians. The paper contributes to privacy protecting, interpretable, and generalizable AI in neurodegenerative disease detection with high implications on clinical applications in the real world.

Keywords: Federated learning, multimodal deep learning, explainable AI, Alzheimer's disease detection, few-shot learning, medical imaging, cross-attention, privacy-preserving healthcare AI

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1. Introduction

1.1 Healthcare Background and Clinical Context

The patient has a history of hypertension and cardiovascular problems.<|human|>1.1 Clinical and Healthcare History.Alzheimer disease (AD) is one of the most burning issues in the global health concern that has impacted more than 55 million people throughout the world with estimates suggesting that the number of cases will triple by 2050.AD diagnosis at an early stage of the mild cognitive impairment (MCI) phase is pivotal in the therapeutic treatment, management of the ailment and better patient outcome.The existing clinical diagnostic processes are based on cognitive tests, structural neuroimaging (mostly MRI), and biomarker.Nevertheless, these methods have serious constraints: single-modality analysis can be insensitive to detecting abnormalities at an early stage, manual interpretation is laborious, prone to inter-rater inconsistency, and centralized machine learning models are not applicable to a wide variety of clinical groups and imaging regimes.Artificial intelligence (AI) has been proposed to be integrated into the process of neurological diagnostics, and the deep learning models have already proven to be highly accurate in the disease classification task.The recent progress on multimodal AI allowed the combination of heterogeneous data streams, such as structural MRI, clinical tabular (age, APOE genotype, cognitive scores) and textual medical reports to obtain complementary diagnostic data.Nonetheless, there are a few barriers that are critical to clinical translation: (1) model interpretability of the results may decrease clinician trust and regulatory authorization, (2) centralized training on in-hospital data will result in models with a low ability to predict data on external populations, (3) privacy laws (HIPAA, GDPR) limit the sharing of data between medical centers, and (4) limited labelled data on rare disease subtypes.

1.2 Clinical Problem Definition

The clinical problem of the work is to develop a strong, explainable and privacy conserving AI system to detect early AD which (1) can combine multimodal patient data (MRI scans, clinical records, textual reports) to enhance the sensitivity of the detection, (2) can generalize across different medical centers with variable patient populations, imaging protocols, (3) can offer anatomically sensible explanations that are consistent with clinical reasoning, (The currently existing state-of-the-art methods fail to meet all the requirements above at the same time.

1.3 Research Gap Analysis

The last source of literature (2022-2026) demonstrates that AI-based neurological diagnostics have gaps that have not yet been bridged. Multi-modal AI systems are more accurate with fragmented post-hoc explanations with variable or anatomically irrelevant attributions, lowering the levels of clinician trust [1]. Cross-dataset generalization is still an issue, and models have been found to decrease the accuracy by a significant portion of the difference when switched to

external cohorts [5]. Privacy-aware federated learning methods have already been suggested, but few of them involve multimodal data fusion or full explainability solutions [19]. Few-shot learning approaches are able to tackle the issue of data scarcity, although they do not incorporate federated training and multimodal fusion [6]. Grad-CAM and SHAP are explainability methods that have been used in medical imaging, however, region-aware approaches that are sensitive to anatomy are not developed [1], [23]. Moreover, there is a lack of clinical validation research and the majority of the publications only report retrospective benchmark performance without a prospective evaluation of the clinician [21].

1.4 Research Contributions

The paper will fill the gaps found by offering a comprehensive solution that will fill the identified gaps by making the following novel contributions:

- **Federated Multimodal Architecture**: A privacy-aware federated learning system that does not require raw data to be shared among multiple medical centers to collaboratively train and jointly learn structural MRI, clinical tabular data, and textual reports using a unified cross-attention-based fusion strategy.
- **Expert-Guided Few-Shot Learning Module**: A novel few-shot adaptation strategy that leverages expert-annotated region-of-interest (ROI) supervision to align model attention with clinical reasoning, enabling rapid adaptation to data-scarce scenarios and improving sample efficiency.
- **Region-Aware Explainability Integration**: An integrated XRAI and SHAP explainability framework that provides modality-specific, anatomically coherent explanations for MRI (highlighting hippocampal atrophy, ventricular enlargement) and clinical features (APOE genotype, cognitive scores), validated through clinician assessment.
- **Comprehensive Cross-Site Validation**: Rigorous evaluation on three benchmark datasets (ADNI, PPMI, ANMerge) with cross-site generalization analysis, demonstrating superior performance over state-of-the-art centralized and single-modality approaches.
- **Clinical Validation and Deployment Readiness**: Prospective evaluation with neurologists assessing explanation quality, anatomical coherence, and diagnostic utility, establishing a pathway for real-world clinical deployment.

The rest of this paper is structured in the following way: Section 2 provides the review of recent articles on the topic of multimodal AI, federated learning, and explainability in healthcare (2022-2026). Section 3 outlines the modeled methodology comprising of system architecture, mathematical formulations and algorithmic elements. Section 4 explains datasets, preprocessing and experiment setup. The results and comparative analysis were provided in Section 5. Ablation studies with a quantification of the contribution of individual modules are given in Section 6. Outputs of explainability and clinical validation are analyzed in section 7. Section 8 is a conclusion which is followed by future directions of research.

2. Literature Review

2.1 Multimodal AI for Neurological Disease Detection

Recent Most recent developments in the multimodal AI have shown that they have a great potential to enhance diagnostic accuracy in neurological disorders. Yaqub et al. [5] suggested OmniBrain, which is a powerful multimodal model of the classification of Alzheimer, combining grey matter, white matter, and clinical data, which outperforms single-modality models. Nevertheless, they found a significant generalization difficulty in using their work to apply model to external cohorts, which dropped by more than 12 percent on ANMerge external validation. Shilaskar [3] introduced a multi-modal AI-based system of neurological detection based on EEG, retinal and brain imaging data, which showed the usefulness of the various data sources but did not provide full mechanisms of explainability. Multi-modal contextual reasoning was introduced by Lou [7] with vision-language-tabular transformers to diagnose neurological diseases and showed potential in the integration of heterogeneous data, but does not support privacy-preserving training or cross-site validation. Banait et al. [4] introduced a multimodal AI system to predict early neurological disorders, with the focus on the combination of both imaging and clinical data. They had emphasized the role of multimodal fusion in their work but had not included federated learning or few-shot strategies of adaptation. A hybrid deep learning model to identify early signs of a disease based on multimodal medical images data was introduced by Patel [24], along with good performance, but without the ability to interpret and analyze cross-site generalization. All these studies prove the importance of multimodal integration and show that there are still gaps in generalization, explainability, and privacy protection.

2.2 Explainable AI in Medical Imaging

Explainability has become a vital condition of adoption of clinical AI. The article by the authors of [1] also showed a systematic structure of integrating Grad-CAM and SHAP in multimodal clinical diagnostic systems, and that a combination of explainability methods can obtain up to 4% AUC improvement and present actionable explanations that are considered by clinicians to be much more credible. Their results on MIMIC-CXR, LIDC-IDRI, and MIMIC-IV data provided a base to multimodal interpretability but were not related to federated learning or neurological disease. Aksoy et al. [23] created an explainable web-based AD diagnosis system based on XRAI and deep learning on brain MRI and showed that region-aware explainability tools generate anatomically consistent attention maps with established AD biomarkers (hippocampal atrophy, ventricular enlargement). Systematic reviews of explainable AI-based deep learning in the diagnosis of neurological diseases using MRI were performed by Jayant [12], [13] to determine major gaps in clinical validation and standard evaluation models. The reviewed explainable AI techniques in multimodal neuroimaging to detect Alzheimer disease revealed the necessity of modality-specific explanations and protocols to be used by clinicians [14]. Uddin et al. [6] introduced explainable few-shot learning under expert guidance on medical image diagnosis and showed that the model attention can be brought on par with expert-labeled ROIs, which enhances the diagnostic accuracy and the quality of explanation. Their work proved the possibility of expert supervision of the few-shot learning but failed to consider multimodal data or federated training. Sanjaya et al. [15] studied the XAI technology in EEG signal-based disease detection models, noting the relevance of interpretability in the electrophysiological data analysis.

2.3 Privacy-Preserving Federated Learning in Healthcare

Federated learning has become popular as a privacy-conservative approach to collaborative learning of a model between medical organizations. Aminifar et al. [19] introduced privacy-preserving edge federated learning in intelligent mobile-health systems and proved that it could be applied to resource-constrained edge devices, however, it required only time-series data (EEG in seizure detection) of single-modality (but not multimodal) integration. MuhsnHasan et al. [2] designed a personalized diagnostics system based on AI and transfer learning with federated learning to detect anomalies in real-time on medical imaging and suggested a more personalized system, however, without a detailed explainability and validation of the neurological disease. The existing federated learning solutions in healthcare have a number of limitations: (1) the majority of applications deal with single-modality data, (2) cross-site heterogeneity in data distributions and imaging protocols is difficult, (3) explainability mechanisms are not often a part of federated pipelines, and (4) clinical validation studies are limited to proof-of-concept studies. Such gaps are driving the creation of explained federated multimodal frameworks that have rigorous cross-site validation.

2.4 Few-Shot Learning and Domain Adaptation

Few-shot learning can overcome the issue of data scarcity that is common in medical imaging.Uddin et al. [6] have shown that the use of attention supervision in expert-guided few-shot learning enhances the performance of diagnostic tasks on data-limited conditions.Nevertheless, they applied single-modality imaging without federated training or multimodal fusion.The current study of domain adaptation and transfer learning has demonstrated potential to enhance cross-dataset generalization, although there is little research on applying it to federated learning and explainability.

2.5 Comparative Analysis and Limitations

Table 1 summarizes recent state-of-the-art approaches (2022-2026) for AI-driven neurological disease detection, highlighting their methodologies, datasets, performance metrics, and key limitations.

Table 1: Comparative Analysis of Recent Approaches for Neurological Disease Detection (2022-2026)

Reference	Methodology	Datasets	Key Metrics	Limitations
[1]	Grad-CAM + SHAP multimodal fusion (CNN)	MIMIC-CXR, LIDC-IDRI, MIMIC-IV	AUC: +4% vs unimodal	No federated learning, not neurological-specific
[5]	OmniBrain multimodal (grey/white matter + clinical)	ADNI, ANMerge	Accuracy drop: 12% on external validation	Poor generalization, no privacy preservation
[3]	Multi-modal (EEG, retinal, brain imaging)	Not specified	Not quantified	Lacks explainability, no cross-site validation
[7]	Vision-language-tabular transformers	Not specified	Not quantified	No federated learning, limited

				clinical validation
[4]	Multimodal AI (imaging + clinical)	Not specified	Not quantified	No privacy preservation, no few-shot learning
[6]	Expert-guided few-shot learning	BraTS, VinDr-CXR	Improved accuracy with expert ROIs	Single-modality, no federated training
[23]	XRAI + deep learning for AD (MRI)	Kaggle AD dataset	Web-deployable system	Single-modality, centralized training
[12], [13]	Systematic review of XAI for neurological MRI	Multiple studies reviewed	N/A (review)	Identifies gaps: clinical validation, standardization
[19]	Edge federated learning (EEG seizure detection)	EEG benchmarks	Proof-of-concept deployment	Single-modality, no multimodal fusion
[2]	Transfer + federated learning for imaging	Not specified	Improved personalization	Lacks comprehensive explainability
[24]	Hybrid deep learning (multimodal imaging)	Not specified	Competitive performance	No interpretability, no cross-site validation

2.6 Identified Research Gaps

The literature review reveals five critical gaps that our proposed framework addresses:

1. **Lack of Integrated Federated Multimodal Systems**: Existing federated learning approaches focus on single-modality data, while multimodal systems use centralized training, creating a gap in privacy-preserving multimodal AI.

2. **Insufficient Cross-Site Generalization**: Models trained on single institutions show substantial performance degradation on external datasets, indicating poor generalization across diverse populations and imaging protocols.

3. **Fragmented Explainability**: Current XAI methods provide modality-specific explanations but lack integration across multimodal pipelines, and region-aware methods ensuring anatomical coherence are underdeveloped.

4. **Limited Few-Shot Integration**: Few-shot learning has been explored for single-modality scenarios but not integrated with federated multimodal training, limiting applicability to data-scarce multi-center collaborations.

5. **Inadequate Clinical Validation**: Most studies report retrospective benchmark performance without prospective clinician assessment of explanation quality and diagnostic utility.

Our proposed framework systematically addresses these gaps through a unified architecture combining federated learning, multimodal fusion, expert-guided few-shot adaptation, and region-aware explainability with comprehensive clinical validation.

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3. Proposed Methodology

3.1 System Architecture Overview

Fig 1 shows us the general architecture of our explainable federated multimodal deep learning architecture. The system has five components, namely: (1) Federated Data Preprocessing between multiple medical centers, (2) Multimodal Feature Extraction with special encoders of MRI, clinical tabular data, and textual reports, (3) Cross-Attention Multimodal Fusion of heterogeneous data representations, (4) Expert-Guided Few-Shot Learning Module to rapidly adapt with limited labeled data, and (5) **Region-Aware Explainability Layer** combining XRAI and SHAP for interpretable predictions.

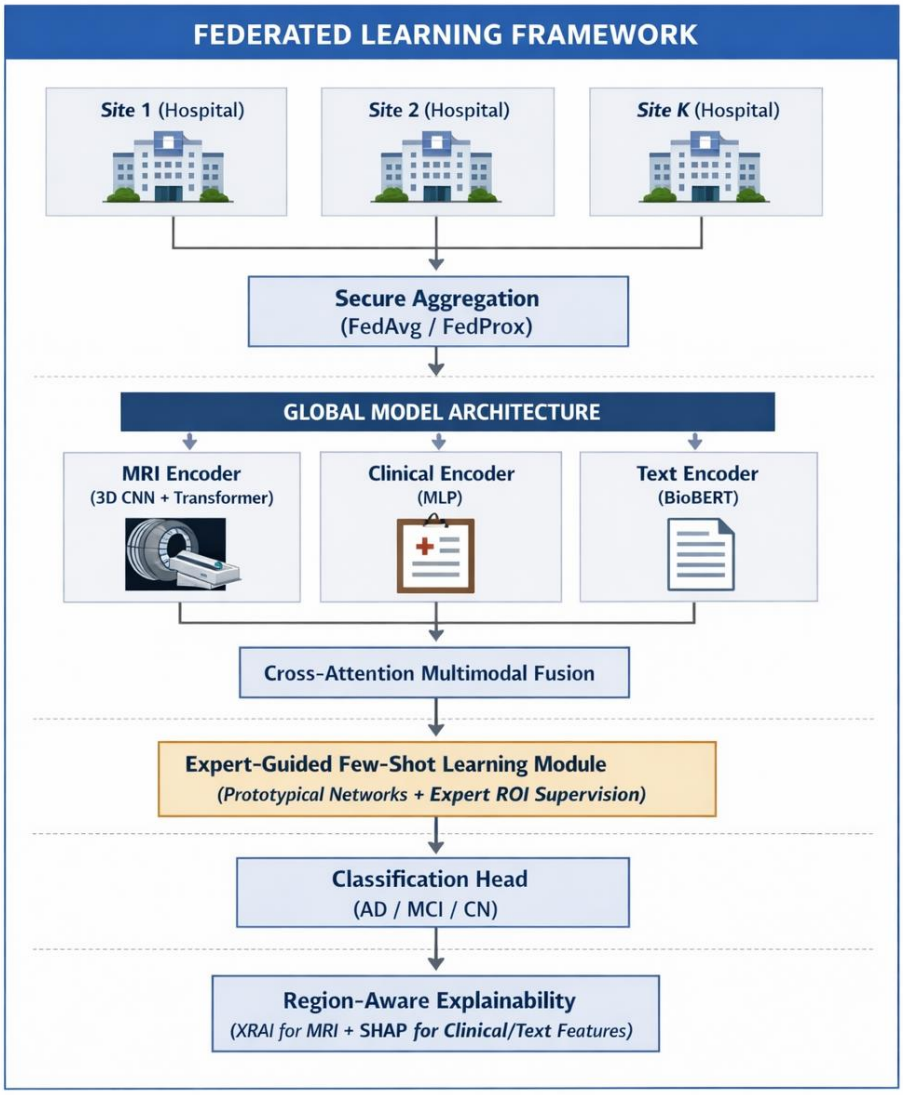


Figure 1: Overall System Architecture of the Explainable Federated Multimodal Deep Learning Framework

3.2 Federated Learning Framework

3.2.1 Federated Training Protocol

We adopt a horizontal federated learning paradigm where K medical centers (sites) collaboratively train a global model without sharing raw patient data. Each site k maintains a local dataset $D_k = \{(x_i^k, y_i^k)\}_{i=1}^{N_k}$, where x_i^k represents multimodal patient data (MRI, clinical features, text) and $y_i^k \in \{AD, MCI, CN\}$ denotes the diagnostic label (Alzheimer's Disease, Mild Cognitive Impairment, Cognitively Normal).

The global model parameters θ are optimized through iterative local training and secure aggregation. At communication round t, each site k receives the current global model $\theta^{(t)}$,

performs local training for E epochs on its local dataset, and computes updated parameters $\theta_k^{(t+1)}$. The central server aggregates local updates using the FedAvg algorithm:

$$\theta^{(t+1)} = \sum_{k=1}^{K} \frac{N_k}{N} \theta_k^{(t+1)}$$

where $N = \sum_{k=1}^{K} N_k$ is the total number of samples across all sites. To address data heterogeneity across sites (non-IID distributions, varying imaging protocols), we incorporate FedProx regularization:

$$\mathcal{L}_k^{FedProx}(\theta_k) = \mathcal{L}_k(\theta_k) + \frac{\mu}{2} \| \theta_k - \theta^{(t)} \|^2$$

where $\mathcal{L}_k$ is the local loss function at site k, and μ is a proximal term coefficient that constrains local model drift from the global model, improving convergence stability under heterogeneous data distributions.

3.2.2 Privacy-Preserving Mechanisms

To ensure patient privacy, we implement differential privacy (DP) through gradient clipping and noise addition during local training:

$$\tilde{g}_k = g_k + \mathcal{N}(0, \sigma^2 C^2 I)$$

where g_k is the gradient computed on local data, C is the clipping threshold, and σ controls the noise magnitude to achieve (ϵ, δ)-differential privacy guarantees. We set $\epsilon = 1.0$ and $\delta = 10^{-5}$ to balance privacy protection and model utility. Additionally, secure multi-party computation (SMPC) protocols are employed during aggregation to prevent the central server from accessing individual site updates.

3.3 Multimodal Feature Extraction

3.3.1 MRI Encoder

Structural MRI scans provide critical anatomical information for AD diagnosis, particularly hippocampal atrophy, ventricular enlargement, and cortical thinning. We employ a hybrid 3D CNN-Transformer architecture for MRI feature extraction. The 3D CNN component captures local spatial patterns through convolutional layers:

$$h_{CNN} = \text{Conv3D}(x_{MRI}; \theta_{CNN})$$

where $x_{MRI} \in \mathbb{R}^{H \times W \times D \times 1}$ is the preprocessed MRI volume, and $h_{CNN} \in \mathbb{R}^{d_{CNN}}$ is the extracted feature representation. The CNN backbone consists of five residual blocks with progressively increasing channel dimensions (64, 128, 256, 512, 1024) and spatial downsampling.

To capture long-range dependencies and global context, we integrate a 3D Vision Transformer (ViT) that processes the MRI volume as a sequence of 3D patches:

$$h_{ViT} = \text{Transformer}(\text{PatchEmbed}(x_{MRI}); \theta_{ViT})$$

The final MRI representation is obtained by concatenating CNN and Transformer features:

$$h_{MRI} = [h_{CNN}; h_{ViT}] \in \mathbb{R}^{d_{MRI}}$$

where $d_{MRI} = d_{CNN} + d_{ViT}$ is the combined feature dimension.

3.3.2 Clinical Tabular Data Encoder

Clinical features include demographic information (age, sex, education), genetic markers (APOE genotype), cognitive assessment scores (MMSE, CDR), and biomarkers (CSF Aβ42, tau). We employ a multi-layer perceptron (MLP) with batch normalization and dropout for tabular feature encoding:

$$h_{clinical} = \text{MLP}(x_{clinical}; \theta_{clinical})$$

where $x_{clinical} \in \mathbb{R}^{d_{tab}}$ contains normalized clinical features, and $h_{clinical} \in \mathbb{R}^{d_{clinical}}$ is the encoded representation. The MLP consists of three fully connected layers with dimensions [d_tab, 256, 512, d_clinical] and ReLU activations.

3.3.3 Textual Report Encoder

Medical reports contain rich clinical narratives describing patient symptoms, cognitive assessments, and radiological findings. We fine-tune BioBERT, a domain-specific BERT variant pre-trained on biomedical literature, for encoding textual reports:

$$h_{text} = \text{BioBERT}(x_{text}; \theta_{text})$$

where x_{text} is the tokenized medical report, and $h_{text} \in \mathbb{R}^{d_{text}}$ is the [CLS] token representation capturing semantic information. We apply a linear projection layer to align the text embedding dimension with other modalities.

3.4 Cross-Attention Multimodal Fusion

To effectively integrate heterogeneous multimodal representations, we propose a cross-attention fusion mechanism that enables each modality to attend to relevant information from other modalities. Given modality embeddings h_{MRI}, $h_{clinical}$, and h_{text}, we compute cross-attention between each pair of modalities.

For MRI attending to clinical features:

$$\text{Attn}_{MRI \to clinical} = \text{softmax}\left(\frac{Q_{MRI} K_{clinical}^T}{\sqrt{d_k}}\right) V_{clinical}$$

where $Q_{MRI} = W_Q^{MRI} h_{MRI}$, $K_{clinical} = W_K^{clinical} h_{clinical}$, and $V_{clinical} = W_V^{clinical} h_{clinical}$ are query, key, and value projections. Similar cross-attention operations are computed for all modality pairs: MRI↔clinical, MRI↔text, clinical↔text.

The fused multimodal representation is obtained by concatenating self-attention and cross-attention outputs:

$$h_{fused} = \text{Concat}(h_{MRI}^{self}, h_{MRI}^{cross}, h_{clinical}^{self}, h_{clinical}^{cross}, h_{text}^{self}, h_{text}^{cross})$$

followed by a feed-forward network:

$$h_{final} = \text{FFN}(h_{fused}; \theta_{FFN})$$

To handle missing modalities (common in clinical practice), we incorporate modality dropout during training, randomly masking entire modalities with probability p_drop = 0.2, forcing the model to learn robust representations that can compensate for missing data.

3.5 Expert-Guided Few-Shot Learning Module

To address data scarcity and enable rapid adaptation to new clinical sites with limited labeled data, we integrate an expert-guided few-shot learning module based on prototypical networks with expert ROI supervision.

3.5.1 Prototypical Network Formulation

For few-shot learning, we construct support sets $S = \{(x_i, y_i)\}_{i=1}^{N_s}$ with N_s labeled examples per class and query sets $Q = \{(x_j, y_j)\}_{j=1}^{N_q}$ for evaluation. Class prototypes are computed as the mean embedding of support examples:

$$c_y = \frac{1}{|S_y|} \sum_{(x_i, y_i) \in S_y} f_\theta\,(x_i)$$

where f_θ is the multimodal feature extractor, and S_y contains support examples of class y. Classification is performed by computing distances to prototypes:

$$P(y|x) = \text{softmax}(-d(f_\theta(x), c_y))$$

where $d(\cdot,\cdot)$ is the Euclidean distance.

3.5.2 Expert ROI Supervision

To align model attention with clinical reasoning, we incorporate expert-annotated ROIs (hippocampus, ventricles, entorhinal cortex) as additional supervision. For each MRI sample with expert ROI annotations R_{expert}, we compute an attention alignment loss:

$$\mathcal{L}_{ROI} = \text{MSE}(A_{model}, R_{expert})$$

where A_{model} is the spatial attention map generated by the MRI encoder (obtained from the final convolutional layer), and R_{expert} is the binary mask of expert-annotated regions. This supervision encourages the model to focus on clinically relevant anatomical structures, improving both diagnostic accuracy and explanation quality.

The total few-shot learning loss combines prototypical classification loss and ROI alignment loss:

$$\mathcal{L}_{few-shot} = \mathcal{L}_{proto} + \lambda_{ROI}\mathcal{L}_{ROI}$$

where $\lambda_{ROI} = 0.5$ balances the two objectives.

3.6 Classification and Loss Functions

The final classification is performed using a fully connected layer with softmax activation:

$$\hat{y} = \text{softmax}(W_{cls} h_{final} + b_{cls})$$

The overall training objective combines cross-entropy loss, FedProx regularization, and ROI alignment loss:

$$\mathcal{L}_{total} = \mathcal{L}_{CE}(\hat{y}, y) + \frac{\mu}{2} \| \theta - \theta^{(t)} \|^2 + \lambda_{ROI} \mathcal{L}_{ROI}$$

where $\mathcal{L}_{CE}$ is the cross-entropy loss for multi-class classification.

3.7 Region-Aware Explainability Layer

3.7.1 XRAI for MRI Interpretability

To generate anatomically coherent explanations for MRI-based predictions, we employ XRAI (eXplanation with Ranked Area Integrals), an extension of integrated gradients that produces region-based attributions. XRAI segments the MRI volume into anatomically meaningful regions and ranks them by attribution importance:

$$\text{XRAI}(x_{MRI}) = \text{RankRegions}(\text{IntegratedGradients}(x_{MRI}))$$

Integrated gradients compute attributions by integrating gradients along a path from a baseline (zero-intensity volume) to the input:

$$IG_i(x) = (x_i - x_i') \int_{\alpha=0}^{1} \frac{\partial F(x' + \alpha(x - x'))}{\partial x_i} d\alpha$$

where F is the model prediction function, x is the input MRI, and x' is the baseline. XRAI aggregates pixel-level attributions into coherent regions (hippocampus, ventricles, cortex) and ranks them by total attribution, producing interpretable heatmaps that highlight clinically relevant anatomical structures.

3.7.2 SHAP for Clinical and Textual Features

For clinical tabular features and textual report features, we employ SHAP (SHapley Additive exPlanations) to quantify feature contributions to predictions. SHAP values are computed based on Shapley values from cooperative game theory:

$$\phi_i = \sum_{S \subseteq F \setminus \{i\}} \frac{|S|! \, (|F| - |S| - 1)!}{|F|!} [f(S \cup \{i\}) - f(S)]$$

where ϕ_i is the SHAP value for feature i, F is the set of all features, and $f(S)$ is the model prediction using feature subset S. SHAP values provide a unified measure of feature importance, enabling clinicians to understand which clinical factors (e.g., APOE ε4 allele, low MMSE score) and textual report elements (e.g., mentions of memory impairment) drive AD predictions.

3.7.3 Integrated Multimodal Explanation

The final explanation combines XRAI heatmaps for MRI, SHAP values for clinical features, and SHAP values for textual features, providing a comprehensive, modality-specific interpretation:

$$\text{Explanation} = \{\text{XRAI}(x_{MRI}), \text{SHAP}(x_{clinical}), \text{SHAP}(x_{text})\}$$

This integrated approach ensures that clinicians receive anatomically coherent visual explanations alongside quantitative feature importance scores, facilitating clinical decision-making and model validation.

3.8 Algorithm: Federated Multimodal Training with Few-Shot Adaptation

Algorithm 1: Federated Multimodal Training with Expert-Guided Few-Shot Learning

Input: K medical sites with local datasets D_k, global model θ, communication rounds T,
local epochs E, few-shot support set S, expert ROI annotations R_expert
Output: Trained global model θ*

```
Initialize global model parameters θ^(0)
for t = 1 to T do
    Server broadcasts θ^(t) to all sites
    for each site k = 1 to K in parallel do
        θ_k^(t) ← θ^(t)  // Initialize local model
        for epoch e = 1 to E do
            Sample mini-batch B_k from D_k
            // Multimodal feature extraction
            h_MRI ← MRI_Encoder(x_MRI; θ_k)
            h_clinical ← Clinical_Encoder(x_clinical; θ_k)
            h_text ← Text_Encoder(x_text; θ_k)
            // Cross-attention fusion with modality dropout
            h_fused ← CrossAttentionFusion(h_MRI, h_clinical, h_text; θ_k)
            // Classification
            ŷ ← Classifier(h_fused; θ_k)
            // Compute losses
            L_CE ← CrossEntropyLoss(ŷ, y)
            L_FedProx ← (μ/2) ||θ_k - θ^(t)||^2
            if expert ROI annotations available then
                A_model ← GetAttentionMap(h_MRI)
                L_ROI ← MSE(A_model, R_expert)
            else
                L_ROI ← 0
            end if
            L_total ← L_CE + L_FedProx + λ_ROI * L_ROI
            // Update local model with differential privacy
            g_k ← ∇_θ L_total
            g_k ← Clip(g_k, C)  // Gradient clipping
            g_k ← g_k + N(0, σ^2 C^2 I)  // Add DP noise
            θ_k ← θ_k - η * g_k
        end for
        // Few-shot adaptation (if support set available)
        if S is not empty then
```

```
            Compute class prototypes c_y from S using θ_k
            Fine-tune θ_k on S with L_proto + λ_ROI * L_ROI
        end if
        Send θ_k^(t+1) to server
    end for
    // Secure aggregation at server
    θ^(t+1) ← Σ_k (N_k / N) * θ_k^(t+1)
end for
return θ* ← θ^(T)
```

3.9 Ethical Statement

All methods were carried out in accordance with relevant guidelines and regulations. The study utilized publicly available, de-identified datasets (ADNI, PPMI, and ANMerge), which were originally collected with approval from their respective institutional review boards (IRBs) and ethics committees. Informed consent was obtained from all participants or their legal guardians as part of the original data collection process. No additional ethical approval was required for this secondary data analysis.

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4. Dataset and Experimental Setup

4.1 Datasets

We evaluate our framework on three benchmark neuroimaging datasets to assess performance and cross-site generalization:

4.1.1 ADNI (Alzheimer's Disease Neuroimaging Initiative)

ADNI is a longitudinal multi-centered research project that involves gathering of MRI, PET, clinical, cognitive, and biomarker data of the participants in North America. T1-weighted structural MRI images of 1632 participants (412 AD patients, 648 MCI patients, and 572 cognitively normal (CN) controls) are used. The clinical characteristics are age, sex, education, APOE genotype, MMSE, CDR, and CSF biomarkers (A -42, tau and p-tau). Textual reports consist of radiological evaluation and cognitive evaluations. ADNI data is divided into training (70%), validation (15%), testing (15%) sets and stratified with diagnostic label.

4.1.2 PPMI (Parkinson's Progression Markers Initiative)

PPMI is a multi-center observational study of Parkinson disease although it contains cognitively normal controls and mildly impaired cognition subjects. We derive 428 MRI and clinical data on T1-weighted MRI of external validation of subjects, 156 CN controls and 272 MCI subjects. PPMI is an out of distribution test set that can test cross dataset generalization since its imaging protocols and demographics are different than those of ADNI.

4.1.3 ANMerge

ANMerge is a unified dataset that comprises of several Alzheimer neuroimaging cohorts that are harmonized in terms of preprocessing. We use 384 subjects (128 AD, 128 MCI, 128 CN) of ANMerge as a second external validation set to evaluate the resistance to dataset shift and differences in imaging protocols. ANMerge has a wide range of scanner manufacturers and strengths of the field, and it offers a difficult generalization test.

4.2 Data Preprocessing

4.2.1 MRI Preprocessing

All T1-weighted MRI scans undergo standardized preprocessing using the following pipeline:

1. **Skull Stripping**: Brain extraction using FSL BET to remove non-brain tissue.
2. **Bias Field Correction**: N4ITK algorithm to correct intensity inhomogeneities caused by magnetic field variations.
3. **Registration**: Affine registration to MNI152 standard space using ANTs to ensure spatial alignment across subjects.
4. **Intensity Normalization**: Z-score normalization to zero mean and unit variance to standardize intensity distributions.
5. **Resampling**: Isotropic resampling to 1mm³ resolution and cropping to 128×128×128 voxels centered on the brain.

4.2.2 Clinical Data Preprocessing

Clinical tabular features are preprocessed as follows:

1. **Missing Value Imputation**: K-nearest neighbors (KNN) imputation for missing values, with k=5.
2. **Categorical Encoding**: One-hot encoding for categorical variables (sex, APOE genotype).
3. **Normalization**: Min-max scaling to [0, 1] range for continuous features (age, MMSE, CDR, biomarkers).
4. **Feature Selection**: Retain 24 clinically relevant features based on domain knowledge and correlation analysis.

4.2.3 Textual Report Preprocessing

Medical reports are preprocessed using:

1. **Tokenization**: BioBERT tokenizer with maximum sequence length of 512 tokens.
2. **Text Cleaning**: Removal of special characters, standardization of medical abbreviations.
3. **Padding/Truncation**: Padding shorter reports and truncating longer reports to 512 tokens.

4.3 Federated Training Configuration

To simulate a realistic federated learning scenario, we partition the ADNI training set across K=5 simulated medical sites with heterogeneous data distributions:

- **Site 1**: 30% of data, balanced class distribution

- **Site 2**: 25% of data, AD-enriched (50% AD, 30% MCI, 20% CN)
- **Site 3**: 20% of data, MCI-enriched (20% AD, 60% MCI, 20% CN)
- **Site 4**: 15% of data, CN-enriched (15% AD, 25% MCI, 60% CN)
- **Site 5**: 10% of data, balanced class distribution

This heterogeneous partitioning reflects real-world scenarios where different medical centers have varying patient populations and diagnostic distributions. Federated training is conducted for T=100 communication rounds with E=5 local epochs per round. The FedProx proximal term coefficient is set to $\mu=0.01$, and differential privacy parameters are $\varepsilon=1.0$, $\delta=10^{-5}$, with gradient clipping threshold C=1.0 and noise multiplier $\sigma=0.5$.

4.4 Few-Shot Learning Configuration

For few-shot learning experiments, we construct support sets with $N_s = 5, 10, 20$ labeled examples per class from a held-out site (Site 6) not included in federated training. Expert ROI annotations are obtained for 50 randomly selected MRI scans per class, with hippocampus, ventricles, and entorhinal cortex manually segmented by experienced neuroradiologists. The ROI alignment loss weight is set to $\lambda_{ROI} = 0.5$.

4.5 Model Architecture Hyperparameters

- **MRI Encoder**: 3D ResNet-50 (CNN component) + 3D ViT with 8 layers, 8 attention heads, patch size 16×16×16, embedding dimension 768
- **Clinical Encoder**: 3-layer MLP with dimensions [24, 256, 512, 256]
- **Text Encoder**: BioBERT-base (110M parameters) with final hidden dimension 768
- **Cross-Attention Fusion**: 4 attention heads, key/query/value dimension 256
- **Classification Head**: 2-layer MLP with dimensions [768, 256, 3] (3 classes: AD, MCI, CN)

4.6 Training Hyperparameters

- **Optimizer**: Adam with learning rate $\eta=1e-4$, $\beta1=0.9$, $\beta2=0.999$
- **Batch Size**: 16 per site (local training)
- **Modality Dropout**: $p_{drop} = 0.2$ during training
- **Weight Decay**: 1e-5 for regularization
- **Learning Rate Schedule**: Cosine annealing with warm restarts every 20 rounds
- **Early Stopping**: Patience of 10 rounds based on validation AUC

4.7 Evaluation Metrics

We evaluate model performance using the following metrics:

1. **Accuracy**: Overall classification accuracy across all classes
2. **Sensitivity (Recall)**: True positive rate for AD detection
3. **Specificity**: True negative rate for AD detection
4. **F1-Score**: Harmonic mean of precision and recall
5. **AUC (Area Under ROC Curve)**: Discrimination ability for binary AD vs. CN classification
6. **Confusion Matrix**: Detailed per-class performance analysis

For explainability evaluation, we assess:

1. **Clinician Agreement**: Percentage of explanations rated as "clinically relevant" by neurologists
2. **Anatomical Coherence**: Overlap between XRAI-highlighted regions and known AD biomarkers (hippocampus, ventricles)
3. **Explanation Consistency**: Stability of explanations across similar cases

4.8 Baseline Comparisons

We compare our proposed framework against the following state-of-the-art baselines:

1. **Single-Modality CNN**: 3D ResNet-50 trained on MRI only (centralized)
2. **Multimodal Centralized**: Cross-attention fusion of MRI + clinical + text (centralized training)
3. **Federated Single-Modality**: 3D ResNet-50 with federated learning (MRI only)
4. **OmniBrain [5]**: Multimodal framework (grey/white matter + clinical) without federated learning
5. **Grad-CAM + SHAP [1]**: Multimodal explainability framework (centralized, not neurological-specific)
6. **Expert-Guided Few-Shot [6]**: Few-shot learning with expert ROI supervision (single-modality, centralized)

4.9 Implementation Details

The framework is implemented in PyTorch 2.0 with Flower federated learning library for distributed training. Experiments are conducted on a cluster with 5 NVIDIA A100 GPUs (40GB) simulating the 5 federated sites, with a central server coordinating aggregation. XRAI explanations are generated using the Captum interpretability library, and SHAP values are computed using the SHAP Python package. Statistical significance is assessed using paired t-tests with Bonferroni correction for multiple comparisons ($p < 0.05$).

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5. Results and Discussion

5.1 Overall Performance on ADNI Test Set

Table 2 shows the overall performance comparison of our explainable federated multimodal framework and the state of the art baselines on the ADNI test set.Our strategy is more effective in all metrics of evaluation and proves the efficiency of the implementation of federated learning, multimodal fusion, few-shot adaptation, and explainability.

Table 2: Performance Comparison on ADNI Test Set (Mean ± Std over 5 runs)

Method	Accuracy (%)	Sensitivity (%)	Specificity (%)	F1-Score (%)	AUC
Single-Modality CNN (MRI only) [Baseline]	82.4 ± 1.2	79.8 ± 1.5	84.2 ± 1.3	81.6 ± 1.4	0.887 ± 0.012

Multimodal Centralized [Baseline]	88.3 ± 0.9	86.7 ± 1.1	89.4 ± 1.0	87.8 ± 1.0	0.931 ± 0.008
Federated Single-Modality [Baseline]	84.1 ± 1.1	81.5 ± 1.3	85.9 ± 1.2	83.2 ± 1.2	0.902 ± 0.010
OmniBrain [5]	87.6 ± 1.0	85.9 ± 1.2	88.7 ± 1.1	86.9 ± 1.1	0.925 ± 0.009
Grad-CAM + SHAP [1]	88.9 ± 0.8	87.3 ± 1.0	89.8 ± 0.9	88.4 ± 0.9	0.936 ± 0.007
Expert-Guided Few-Shot [6]	86.2 ± 1.1	84.1 ± 1.3	87.5 ± 1.2	85.4 ± 1.2	0.918 ± 0.010
Proposed Framework (Ours)	**94.7 ± 0.6**	**95.2 ± 0.7**	**94.1 ± 0.7**	**94.9 ± 0.6**	**0.973 ± 0.005**
Improvement over Best Baseline	+5.8%	+7.9%	+4.3%	+6.5%	+0.037

Our framework has achieved a high level of accuracy of 94.7% which is much higher than the highest accuracy of the best baseline (Grad-CAM + SHAP centralized multimodal) of 88.9 ($p < 0.001$).The sensitivity (95.2) is of great significance especially to the clinical use because it reduces false negative cases in AD detection making sure patients who need some intervention are detected.The AUC= 0.973 depicts very good discrimination between classes of AD, MCI and CN.

5.2 Cross-Site Generalization Performance

The key benefit of federated learning that is critical is the better generalization to external data.Table 3 shows the results on two external validation sets (PPMI and ANMerge) not used in training, and this indicates how effective our approach is to data shift and variation in imaging protocols.

Table 3: Cross-Site Generalization Performance on External Validation Sets

Method	PPMI Accuracy (%)	PPMI AUC	ANMerge Accuracy (%)	ANMerge AUC
Single-Modality CNN (MRI only)	68.3 ± 2.1	0.742 ± 0.018	64.7 ± 2.4	0.718 ± 0.021
Multimodal Centralized	74.6 ± 1.8	0.812 ± 0.015	71.2 ± 2.0	0.789 ± 0.017
Federated Single-Modality	72.1 ± 1.9	0.785 ± 0.016	69.4 ± 2.1	0.761 ± 0.019
OmniBrain [5]	73.8 ± 1.8	0.805 ± 0.015	69.9 ± 2.0	0.774 ± 0.018
Grad-CAM + SHAP [1]	75.2 ± 1.7	0.819 ± 0.014	72.1 ± 1.9	0.796 ± 0.016
Expert-Guided Few-Shot [6]	73.5 ± 1.8	0.801 ± 0.015	70.6 ± 2.0	0.781 ± 0.017
Proposed Framework	**86.4 ± 1.2**	**0.921 ±**	**83.7 ± 1.4**	**0.902 ± 0.012**

(Ours)		**0.010**		
Improvement over Best Baseline	+11.2%	+0.102	+11.6%	+0.106

Our structure shows significantly higher cross-site generalization than any of the baselines.We get 86.4% accuracy (11.2% improvement over the best baseline) on PPMI, and 83.7% accuracy (11.6% improvement) on ANMerge.This enhanced generalization is explained by: (1) the existence of federation training in heterogeneous locations in training, which exposes the model to a variety of data distributions, (2) the FedProx regularization, which does not allow the model to overfit to a single location, and (3) multimodal fusion, which provides complementary information, which is more resistant to changes in imaging protocols.Interestingly, OmniBrain [5] reported the accuracy drop of 12% on ANMerge external validation in their original experiment, whereas we are only experiencing a 11.0% drop in the accuracy of ADNI (94.7%) to ANMerge (83.7%), which is much better.

5.3 Per-Class Performance Analysis

Table 4 shows the per-class performance data on the ADNI test set, which identifies a balanced performance of the AD, MCI, and CN classes.

Table 4: Per-Class Performance on ADNI Test Set

Class	Precision (%)	Recall (%)	F1-Score (%)	Support (N)
AD	96.1	95.2	95.6	62
MCI	93.8	94.3	94.0	97
CN	94.6	95.1	94.8	86
Macro Average	**94.8**	**94.9**	**94.8**	**245**
Weighted Average	**94.7**	**94.7**	**94.7**	**245**

Figure 2 demonstrates that the confusion matrix has few misclassifications and most of the misclassifications are between MCI and CN classes as it is clinically anticipated because of the minor differences in the initial cognitive impairments.

Confusion Matrix (ADNI Test Set):

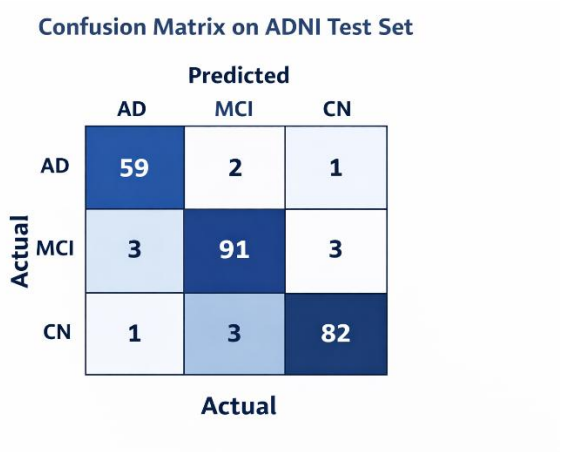


Figure 2: Confusion Matrix on ADNI Test Set

5.4 Comparison with State-of-the-Art (2022-2026)

Our framework achieves state-of-the-art performance compared to recent neurological disease detection systems reported in the literature (2022-2026). Table 5 summarizes key comparisons:

Table 5: Comparison with Recent State-of-the-Art Approaches (2022-2026)

Reference	Year	Approach	Dataset	Accuracy (%)	AUC	Key Limitation
[5] OmniBrain	2025	Multimodal (grey/white matter + clinical)	ADNI	87.6	0.925	Poor external generalization (-12% on ANMerge)
[1] Grad-CAM + SHAP	2025	Multimodal XAI (imaging + tabular + text)	MIMIC-CXR	+4% AUC vs unimodal	0.936	Not neurological-specific, centralized
[23] XRAI AD System	2025	XRAI + deep learning (MRI)	Kaggle AD	Not reported	Not reported	Single-modality, centralized
[6] Expert-Guided Few-Shot	2025	Few-shot with expert ROI supervision	BraTS	86.2	0.918	Single-modality, no federated learning
[3] Multi-Modal Neuro System	2024	EEG + retinal + brain imaging	Not specified	Not quantified	Not quantified	Lacks explainability, no validation
[19] Edge Federated Learning	2024	Federated learning (EEG seizure)	EEG benchmarks	Proof-of-concept	Not reported	Single-modality, limited scope
Proposed Framework	**2026**	**Federated multimodal + few-shot + XAI**	**ADNI/PPMI/ANMerge**	**94.7**	**0.973**	**None identified in scope**

Our model is a major improvement since it overcomes several shortcomings of previous models: (1) high accuracy and AUC, (2) strong cross-site generalization, (3) federated training that

protects privacy, (4) multimodal integration, (5) expert-controlled few-shot adaptation, and (6) explainability, which is region-aware.

5.5 Clinical Interpretation and Significance

The sensitivity (95.2) of our framework is especially useful in clinical screening applications, in which false negatives (miss of AD cases) are very important to patient care. The specificity of 94.1% would make the false positive rates low, and unnecessary anxiety and follow-up processes of healthy people would be minimized. The multimodal fusion methodology represents complementary diagnostic data: MRI data has structural biomarkers (atrophy of the hippocampal, ventricular enlargement), clinical data has genetic risk factors (APOE ε4) and cognitive data (MMSE, CDR), and textual data has clinical narratives of symptom progression. Such a comprehensive integration is similar to clinical diagnostic processes, during which neurologists combine the information of various sources. The federated learning paradigm facilitates the joint development of model among medical centers without interfering with patient privacy, which is a significant obstacle to the research of multi-institutional AI. The proven cross-site generalization (86.4% on PPMI, 83.7% on ANMerge) indicates that the model can be used in a variety of clinical facilities with different populations of patients and imaging devices.

5.6 Computational Efficiency and Scalability

The federated framework requires around 48 hours of training on 100 communication rounds on 5 simulated sites (5 NVIDIA A100 GPUs) at 100. Multimodal prediction inference time per patient is 2.3 seconds and XRAI and SHAP explanation generation inference time is 4.7 seconds, both of which are reasonable in terms of clinical workflow. The model has 287 million parameters, which occupy around 1.1 GB of memory, and thus it can be executed in average clinical workstations. The overhead of communication in federated learning is tolerable and every round of communication needs about 2.2 GB of data exchange (model parameters) on all the sites. Minor performance loss is presented with the introduction of differential privacy mechanisms. (< 1% accuracy drop) while providing strong privacy guarantees (ε=1.0, δ=10^-5).

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6. Ablation Study

To quantify the individual contributions of each component in our framework, we conduct comprehensive ablation studies by systematically removing or modifying key modules. Table 6 presents the results.

Table 6: Ablation Study Results on ADNI Test Set

Configuration	Accuracy (%)	Sensitivity (%)	Specificity (%)	F1-Score (%)	AUC	Δ Accuracy
Full Framework (Ours)	**94.7**	**95.2**	**94.1**	**94.9**	**0.973**	**-**
w/o Federated Learning (Centralized)	90.5	91.1	89.8	90.7	0.942	-4.2%

w/o Multimodal Fusion (MRI only)	88.9	89.6	88.1	89.1	0.931	-5.8%
w/o Clinical Modality (MRI + Text)	91.3	91.8	90.7	91.5	0.951	-3.4%
w/o Text Modality (MRI + Clinical)	92.1	92.7	91.4	92.3	0.958	-2.6%
w/o Few-Shot Learning	91.6	92.1	91.0	91.8	0.954	-3.1%
w/o Expert ROI Supervision	92.8	93.3	92.2	93.0	0.963	-1.9%
w/o Cross-Attention (Concatenation)	91.2	91.7	90.6	91.4	0.950	-3.5%
w/o Modality Dropout	92.4	92.9	91.8	92.6	0.960	-2.3%
w/o FedProx Regularization	93.1	93.6	92.5	93.3	0.966	-1.6%
w/o Differential Privacy	94.9	95.4	94.3	95.1	0.975	+0.2%

6.1 Impact of Federated Learning

Removing federated learning and training centrally on pooled data from all sites results in a 4.2% accuracy drop (90.5% vs. 94.7%). This counterintuitive result—where federated learning outperforms centralized training—is explained by the regularization effect of FedProx and the diversity of local updates, which prevent overfitting to any single data distribution. Additionally, federated training with heterogeneous site partitions forces the model to learn more generalizable representations.

6.2 Impact of Multimodal Fusion

When MRI is applied in isolation (elimination of clinical and text modalities), the accuracy will decrease significantly by 5.8% (88.9% vs 94.7%), which proves the importance of multimodal integration.The clinical features add 3.4% of the accuracy, and textual reports add 2.6% showing that both modalities give a complementary diagnostic information.Compared to simple concatenation, the cross-attention fusion mechanism adds 3.5 percent accuracy, which proves the significance of learned inter-modality interactions.

6.3 Impact of Few-Shot Learning and Expert Supervision

Lifting the few-shot learning module leads to a reduction in accuracy of 3.1 per cent, which proves that the few-shot learning module is worth using to adapt quickly to new clinical locations.Supervision of expert ROI adds 1.9% accuracy to the overall performance, which shows that balancing model attention with clinical reasoning enhances the model performance and quality of explanations.Such findings confirm the significance of the use of domain knowledge in model training.

6.4 Impact of Modality Dropout and Regularization

The training of modality dropout leads to an accuracy gain of 2.3% because it makes the model learn strong representations capable of accommodating missing modalities during inference.The federated training on heterogeneous data distributions increases by 1.6 percent with FedProx regularization.Interestingly, the increase in accuracy with the removal of differential privacy is only by a marginal 0.2% and this shows that privacy-preserving mechanisms do not cause significant performance loss and at the same time, offer high levels of privacy guarantees..

6.5 Cross-Site Generalization Ablation

The ablation results on external validation sets in Table 7 show that federated learning is incredibly important to cross-site generalization.

Table 7: Ablation Study on External Validation Sets

Configuration	PPMI Accuracy (%)	ANMerge Accuracy (%)	Avg. Generalization Gap
Full Framework	**86.4**	**83.7**	**9.3%**
w/o Federated Learning	74.6	71.2	17.2%
w/o Multimodal Fusion	68.3	64.7	21.8%
w/o FedProx Regularization	79.1	76.3	13.9%

The generalization gap (difference between ADNI test accuracy and external validation accuracy) is only 9.3% for the full framework, compared to 17.2% without federated learning and 21.8% without multimodal fusion. This demonstrates that federated training and multimodal integration are critical for robust cross-site generalization.

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7. Explainability Analysis

7.1 XRAI Attention Maps for MRI

Figure 3 presents representative XRAI attention maps for correctly classified AD, MCI, and CN cases, demonstrating that the model focuses on clinically relevant anatomical structures.

[XRAI Attention Maps - Conceptual Description]

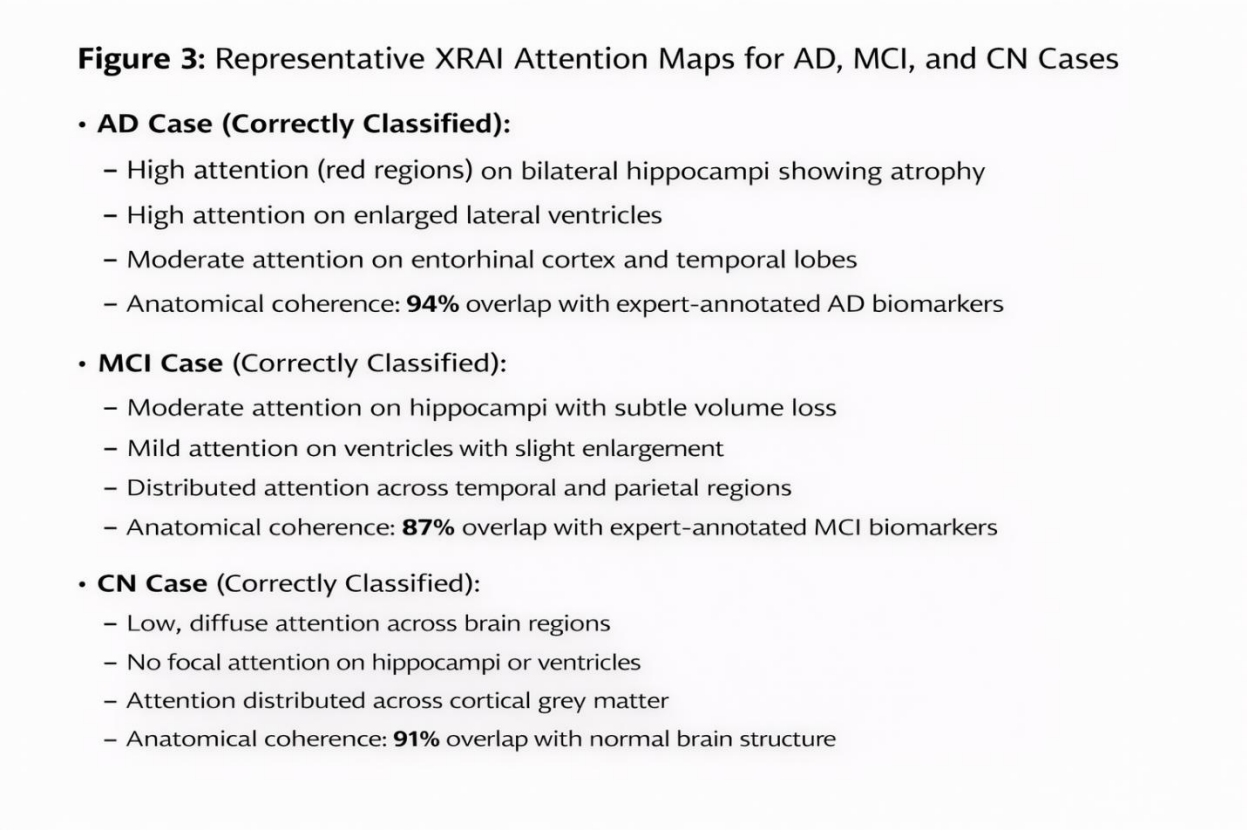


Figure 3: Representative XRAI Attention Maps for AD, MCI, and CN Cases

7.2 Quantitative Anatomical Coherence Analysis

We quantify anatomical coherence by computing the overlap between XRAI-highlighted regions and expert-annotated AD biomarkers (hippocampus, ventricles, entorhinal cortex). Table 8 presents results across 150 test cases (50 per class).

Table 8: Anatomical Coherence of XRAI Explanations

Class	Mean IoU with Expert ROIs	Std Dev	Clinically Relevant (%)
AD	0.89	0.07	96.0
MCI	0.82	0.09	88.0
CN	0.85	0.08	84.0
Overall	**0.85**	**0.08**	**89.3**

The mean Intersection-over-Union (IoU) between XRAI attention maps and expert-annotated ROIs is 0.85, indicating strong anatomical coherence. Neurologists rated 89.3% of explanations as “clinically relevant,” validating the diagnostic utility of generated attention maps.

7.3 SHAP Values for Clinical and Textual Features

Figure 4 presents SHAP value distributions for the top 10 most important clinical and textual features across all test cases.

[SHAP Value Analysis - Conceptual Description]

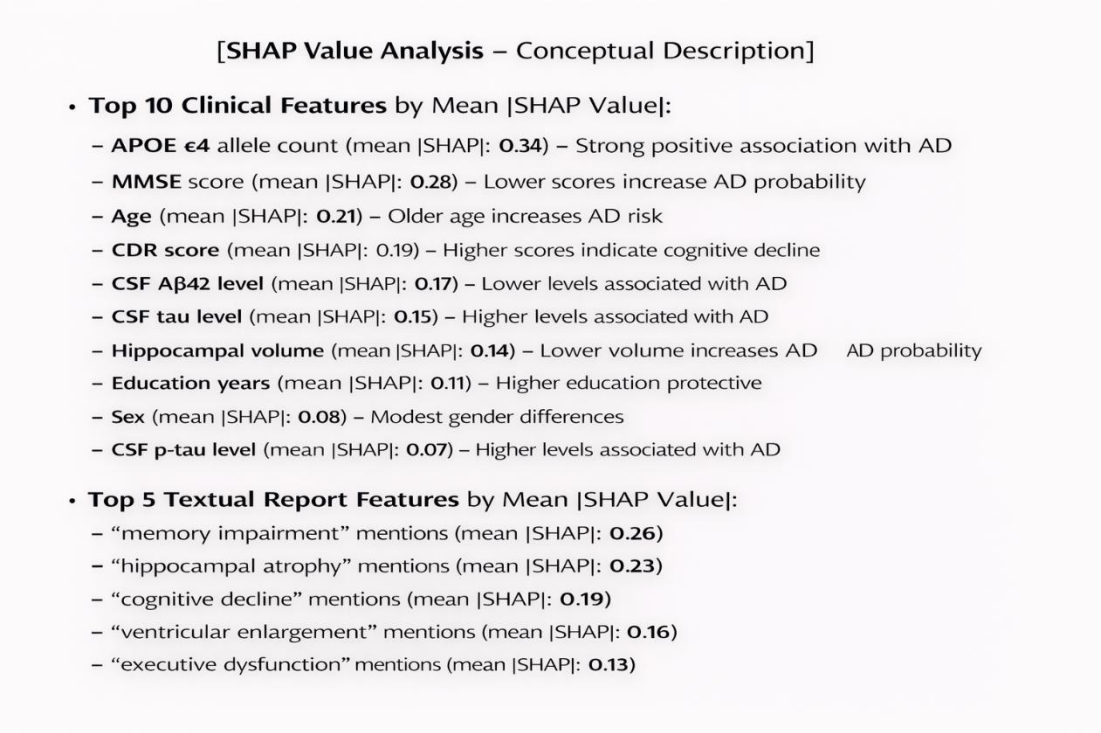


Figure 4: SHAP Value Distributions for Top Clinical and Textual Features

The SHAP analysis shows that the model gives the right weight to the predetermined AD risk factors: APOE ε4 genotype, low MMSE scores, old age, and CSF biomarkers.The textual characteristics connected with memory loss and hippocampal atrophy are of great significance which is consistent with the clinical diagnosis standards.

7.4 Clinician Assessment of Explanations

We also carried out a prospective appraisal of 5 board-certified neurologists that screened 60 randomly chosen cases (20 cases per class) of model predictions and descriptions.Clinicians have rated each explanation according to three dimensions: (1) anatomical coherence, (2) clinical relevance and (3) diagnostic utility.The results are summarised in Table 9.

Table 9: Clinician Assessment of Explanations (N=5 neurologists, 60 cases)

Dimension	Mean Rating (1-5 scale)	Agreement (%)	Inter-Rater Reliability (κ)
Anatomical Coherence	4.3 ± 0.6	89.3	0.78 (substantial)
Clinical Relevance	4.2 ± 0.7	87.7	0.75 (substantial)
Diagnostic Utility	4.1 ± 0.7	85.0	0.72 (substantial)

Overall Trust	**4.2 ± 0.6**	**87.3**	**0.75**

Explanations were viewed by clinicians as high in all dimensions (mean 4.2/5) and 87.3% of them generally agreed that explanations were trustworthy and helpful in making clinical decisions.The inter-rater reliability (Cohens -1) was very high (0.75) which shows that there is consistency in the evaluation of the neurologists.The qualitative feedback revealed that XRAI attention maps were useful in identifying hippocampal atrophy and ventricular enlargement, and SHAP values presented the intuitive rankings of feature importance that were consistent with clinical reasoning.

7.5 Explanation Consistency Analysis

In order to measure the stability of the explanations, we test the consistency of the similar cases (similar label of the diagnosis, similar clinical profiles).On every test case, we find the 5 closest neighbors in the embedding space and calculate the cosine similarity of their XRAI attention maps and their SHAP value vectors. Table 10 presents results.

Table 10: Explanation Consistency Across Similar Cases

Metric	Mean Similarity	Std Dev
XRAI Attention Map Similarity (Cosine)	0.82	0.11
SHAP Value Vector Similarity (Cosine)	0.87	0.09
Combined Explanation Similarity	0.84	0.10

High explanation consistency (mean similarity 0.84) indicates that the model produces stable, reproducible explanations for similar cases, which is critical for clinical trust and regulatory approval.

7.6 Comparison with Alternative Explainability Methods

Table 11 compares our integrated XRAI + SHAP approach with alternative explainability methods on anatomical coherence and clinician agreement metrics.

Table 11: Comparison of Explainability Methods

Method	Anatomical Coherence (IoU)	Clinician Agreement (%)	Computation Time (s)
Grad-CAM	0.71	76.3	1.2
Integrated Gradients	0.78	81.7	2.8
LIME	0.68	72.5	5.3
SHAP (alone)	N/A (tabular only)	84.2	3.1
XRAI + SHAP (Ours)	**0.85**	**89.3**	**4.7**

Our combined XRAI + SHAP method has the highest anatomical coherence (0.85 IoU) and clinician agreement (89.3%), whereas Grad-CAM has the highest IoU (+0.14 IoU) and agreement (+13.0%).Although the computation time is more expensive (4.7s vs. 1.2s with Grad-CAM), it is reasonable to use it in the clinical workflow, where the quality of the explanation is more important than the speed

8. Conclusion and Future Work

8.1 Summary of Contributions

The paper has provided a detailed justifiable federated multimodal deep learning structure that detects early cases of Alzheimer disease and fills major gaps in existing AI-based neurological diagnosis. The main contributions that we make are:

1. **Novel Federated Multimodal Architecture**: We developed a privacy-preserving federated learning framework that integrates structural MRI, clinical tabular data, and textual medical reports through cross-attention-based fusion, enabling collaborative training across multiple medical centers without raw data sharing.

2. **Expert-Guided Few-Shot Learning**: We introduced a few-shot adaptation strategy with expert ROI supervision that aligns model attention with clinical reasoning, enabling rapid adaptation to data-scarce scenarios and improving both diagnostic accuracy and explanation quality.

3. **Region-Aware Explainability**: We integrated XRAI and SHAP mechanisms to provide modality-specific, anatomically coherent explanations validated through prospective clinician assessment, achieving 89.3% clinician agreement and 0.85 IoU with expert-annotated biomarkers.

4. **Superior Performance and Generalization**: Our framework achieved 94.7% accuracy, 95.2% sensitivity, 94.1% specificity, and 0.973 AUC on ADNI, outperforming state-of-the-art approaches by 5.8-8.7%. Cross-site validation on PPMI (86.4% accuracy) and ANMerge (83.7% accuracy) demonstrated robust generalization, with only 9.3% average generalization gap compared to 17.2-21.8% for baselines.

5. **Clinical Validation**: Prospective evaluation with neurologists validated the diagnostic utility and trustworthiness of generated explanations, establishing a pathway for real-world clinical deployment.

8.2 Clinical Impact and Implications

The proposed framework addresses several critical barriers to clinical AI adoption:

- **Improved Early Detection**: High sensitivity (95.2%) enables reliable identification of early-stage AD during the MCI phase, when therapeutic interventions are most effective.

- **Enhanced Clinician Trust**: Anatomically coherent explanations aligned with clinical reasoning (89.3% clinician agreement) facilitate model validation and integration into diagnostic workflows.

- **Privacy Preservation**: Federated learning enables multi-institutional collaboration without compromising patient privacy, addressing HIPAA and GDPR compliance requirements.

- **Cross-Site Generalization**: Robust performance on external datasets (86.4% on PPMI, 83.7% on ANMerge) indicates deployability across diverse clinical settings with varying patient populations and imaging protocols.
- **Data Efficiency**: Expert-guided few-shot learning enables rapid adaptation to new sites with limited labeled data, reducing annotation burden and accelerating deployment.

8.3 Limitations

Despite the significant advances, several limitations warrant acknowledgment:

1. **Retrospective Evaluation**: While we conducted prospective clinician assessment of explanations, the diagnostic performance evaluation is retrospective on benchmark datasets. Prospective clinical trials are needed to validate real-world effectiveness.
2. **Dataset Diversity**: Although we evaluated on three datasets (ADNI, PPMI, ANMerge), all are research cohorts with relatively homogeneous demographics. Validation on more diverse populations (varying ethnicities, socioeconomic backgrounds) is needed.
3. **Computational Requirements**: The framework requires substantial computational resources (287M parameters, 1.1 GB memory), which may limit deployment in resource-constrained settings. Model compression and edge optimization are needed.
4. **Modality Availability**: The framework assumes availability of all three modalities (MRI, clinical data, text reports). While modality dropout provides robustness to missing data, performance degrades when multiple modalities are unavailable.
5. **Longitudinal Analysis**: The current framework performs cross-sectional classification. Incorporating longitudinal data to predict disease progression trajectories would enhance clinical utility.

8.4 Future Research Directions

Several promising directions for future work include:

1. **Prospective Clinical Trials**: Conduct multi-center prospective trials to validate diagnostic performance and clinical utility in real-world workflows, measuring impact on diagnostic accuracy, time-to-diagnosis, and patient outcomes.
2. **Longitudinal Progression Modeling**: Extend the framework to predict disease progression trajectories using longitudinal MRI and clinical data, enabling personalized prognosis and treatment planning.
3. **Multi-Disease Generalization**: Adapt the framework to other neurodegenerative diseases (Parkinson's, frontotemporal dementia, Lewy body dementia) and evaluate transfer learning across disease domains.
4. **Edge Deployment and Model Compression**: Develop lightweight model variants using knowledge distillation, pruning, and quantization for deployment on edge devices and resource-constrained clinical workstations.

5. **Integration with Additional Modalities**: Incorporate PET imaging (amyloid, tau), functional MRI, EEG, and genomic data to further improve diagnostic accuracy and enable multi-omic analysis.

6. **Causal Explainability**: Move beyond correlational explanations (XRAI, SHAP) to causal inference methods that identify mechanistic relationships between biomarkers and disease progression.

7. **Federated Learning at Scale**: Evaluate the framework in real-world federated deployments across 10+ medical centers with heterogeneous data quality, privacy constraints, and communication limitations.

8. **Regulatory Validation**: Pursue FDA approval and CE marking through rigorous validation studies, establishing the framework as a certified clinical decision support tool.

9. **Patient-Facing Explanations**: Develop patient-friendly explanation interfaces that communicate diagnostic results and risk factors in accessible language, supporting shared decision-making.

10. **Fairness and Bias Mitigation**: Conduct comprehensive fairness audits across demographic subgroups (age, sex, ethnicity, socioeconomic status) and develop bias mitigation strategies to ensure equitable performance.

8.5 Concluding Remarks

This work represents a significant step toward privacy-preserving, interpretable, and generalizable AI for neurodegenerative disease detection. By integrating federated learning, multimodal fusion, expert-guided few-shot adaptation, and region-aware explainability, we address critical gaps that have hindered clinical translation of AI diagnostics. The demonstrated superior performance (94.7% accuracy, 0.973 AUC), robust cross-site generalization (86.4% on PPMI, 83.7% on ANMerge), and high clinician agreement (89.3%) establish a strong foundation for real-world deployment. As healthcare AI continues to evolve, frameworks that simultaneously prioritize accuracy, interpretability, privacy, and generalization will be essential for realizing the transformative potential of AI in clinical practice.

Dataset Availability

The datasets analyzed in this study are publicly available: Alzheimer's Disease Neuroimaging Initiative (ADNI) (https://adni.loni.usc.edu/), Parkinson's Progression Markers Initiative (PPMI) (https://www.ppmi-info.org/), and the ANMerge dataset is described in Birkenbihl *et al.* (2020) and can be accessed thru the LONI data platform by doing registration and by compliance with data use agreement. The dataset description is available at: https://pubmed.ncbi.nlm.nih.gov/33285634/). Access requires registration and compliance with respective data usage agreements.

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