

# A FEDERATED LEARNING APPROACH FOR ROBUST HEART DISEASE RISK SCORING FROM DISTRIBUTED DATA

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## ABSTRACT

Heart disease remains the leading cause of mortality worldwide, with accurate risk stratification being crucial for effective prevention and treatment. However, the development of robust machine learning models for cardiovascular risk prediction is severely hampered by the fragmentation of patient data across multiple healthcare institutions and stringent privacy regulations (e.g., HIPAA, GDPR) that prohibit centralized data sharing. To address this critical challenge, this paper proposes FedCARDIA, a novel federated learning framework with cross-institutional feature fusion for heart disease risk stratification. Unlike conventional federated averaging methods that share model weights which remain vulnerable to inversion attacks FedCARDIA shares only abstract intermediate feature representations from local multi-modal data (longitudinal electronic health records and echocardiogram images). A global classifier is then trained on these aggregated features, enabling collaborative learning without exposing raw patient data. Evaluated on a multi-institutional dataset comprising 12,458 patients from three independent hospitals with non-IID data distributions, FedCARDIA achieves an area under the ROC curve of 0.923 for 5-year cardiovascular risk prediction. This significantly outperforms single-institution local models (AUC: 0.834–0.861) and standard Federated Averaging (AUC: 0.882), while closely approaching the privacy-violating centralized oracle model (AUC: 0.935). The framework maintains robust performance across

heterogeneous institutional data, offering a viable and scalable pathway for privacy-preserving collaborative learning in healthcare without compromising patient confidentiality.

**Keywords** *Federated Learning, Heart Disease Risk Stratification, Privacy-Preserving Machine Learning, Feature Fusion, Multi-Modal Learning, Cardiovascular Informatics.*

## 1. INTRODUCTION

Cardiovascular diseases (CVDs) account for approximately 17.9 million deaths annually, making accurate risk stratification a critical component of preventive cardiology [1]. Traditional risk scores like Framingham have limitations in personalized prediction, leading to increased interest in machine learning (ML) approaches that can leverage complex patterns in electronic health records (EHR) and medical imaging [2]. However, developing robust ML models requires large, diverse datasets that are typically siloed across different healthcare institutions due to privacy concerns, legal restrictions, and data governance policies [3].

Federated Learning (FL) has emerged as a promising paradigm for training ML models across decentralized data sources without exchanging raw data [4]. Instead, participating institutions train models locally and share only model updates with a central server. While standard FL approaches (e.g., Federated Averaging) have been applied to healthcare tasks, they often underperform when data is highly heterogeneous (non-IID) across institutions [5]. Moreover, they typically do not address the challenge of fusing diverse data types (e.g., structured EHR and medical images) in a privacy-preserving manner.

To overcome these limitations, we propose FedCARDIA (Federated Cardiovascular Risk Assessment with Distributed Intelligence Aggregation). Our contributions are:

- A novel federated feature fusion framework that enables cross-institutional learning from both structured EHR data and echocardiogram images while keeping all patient data localized.
- A hybrid deep learning model that combines temporal convolutional networks for EHR sequence processing with convolutional neural networks for image feature extraction.
- A personalized aggregation strategy that accounts for inter-institutional data heterogeneity, improving model

performance compared to standard federated averaging.

- Comprehensive evaluation on a multi-institutional dataset demonstrating superior performance while maintaining privacy guarantees.

### 1.1 Problem Statement

Despite the demonstrated potential of machine learning for cardiovascular risk prediction, the development of accurate, generalizable models is fundamentally constrained by two interrelated challenges. First, patient data is inherently fragmented across healthcare institutions due to privacy regulations (e.g., HIPAA, GDPR), legal liability concerns, and competitive pressures, creating data silos that prevent the aggregation of diverse, large-scale datasets necessary for robust model training. Second, conventional federated learning approaches particularly Federated Averaging suffer from significant performance degradation when applied to non-IID (non-identically and independently distributed) data, which is the norm in healthcare settings where patient populations, clinical practices, and data recording protocols vary substantially across institutions. Furthermore, existing FL frameworks are not designed for multi-modal data fusion (e.g., combining time-series EHR with medical images), and the common practice of sharing model weights or gradients remains susceptible to inversion attacks that can reconstruct sensitive patient information.

- Therefore, there exists a critical need for a federated learning framework that can: (1) enable collaborative training across institutions with heterogeneous, non-IID data distributions; (2) effectively fuse multiple clinical data modalities (temporal and imaging) without centralizing raw data; (3) provide stronger privacy guarantees than weight-sharing approaches; and (4) achieve predictive performance competitive with centralized

training. This study addresses these requirements through the development and validation of FedCARDIA.

**Refined Problem Statement:** Despite the demonstrated potential of machine learning for cardiovascular risk prediction, the development of accurate, generalizable models is fundamentally constrained by four interrelated challenges that existing solutions fail to address collectively: (1) data fragmentation across healthcare institutions due to privacy regulations (HIPAA, GDPR); (2) inability of conventional federated learning (FedAvg) to handle non-IID multi-modal data; (3) vulnerability of weight-sharing approaches to inversion attacks; and (4) absence of validated frameworks for fusing temporal EHR with medical imaging in a decentralized setting. This study addresses these gaps by answering whether a feature-sharing federated framework with personalized aggregation can achieve near-centralized accuracy while providing stronger privacy guarantees than existing approaches

## 1.2 Research Gap and Knowledge Creation

The existing literature reveals four critical gaps that this study addresses:

**Gap 1: Privacy-preserving multi-modal fusion.** While multi-modal learning has been extensively studied in centralized settings, no existing framework enables privacy-preserving fusion of temporal EHR sequences with medical images across institutions. FedCARDIA introduces a novel feature-sharing **Refined Problem Statement:** Despite the demonstrated potential of machine learning for cardiovascular risk prediction, the development of accurate, generalizable models is fundamentally constrained by four interrelated challenges that existing solutions fail to address collectively: (1) data fragmentation across healthcare institutions due to privacy regulations (HIPAA, GDPR); (2) inability of conventional federated learning (FedAvg) to handle non-IID multi-modal data; (3) vulnerability of weight-sharing approaches

to inversion attacks; and (4) absence of validated frameworks for fusing temporal EHR with medical imaging in a decentralized setting. This study addresses these gaps by answering whether a feature-sharing federated framework with personalized aggregation can achieve near-centralized accuracy while providing stronger privacy guarantees than existing approaches.

- paradigm that enables this fusion without raw data exchange.
- **Gap 2: Handling non-IID data in federated healthcare settings.** Standard FL algorithms (FedAvg) assume homogeneous data distributions, which rarely hold in practice. Our personalized aggregation strategy which averages feature extractors but trains a global classifier on fused features explicitly accounts for inter-institutional heterogeneity.
- **Gap 3: Privacy beyond weight sharing.** Recent work has demonstrated that model weights and gradients can be inverted to reconstruct training data. FedCARDIA shares only abstract intermediate features, which are several abstraction levels removed from raw inputs, providing inherent resistance to inversion attacks.
- **Gap 4: Cardiovascular risk stratification from distributed multi-modal data.** No prior study has validated a federated learning framework for combining EHR time-series and echocardiogram images specifically for heart disease risk prediction across multiple institutions.
- **Knowledge Creation:** This study creates new knowledge by: (a) demonstrating that intermediate feature sharing outperforms weight sharing for non-IID, multi-modal medical data; (b) providing the first empirical validation of a federated multi-modal framework for cardiovascular risk prediction on a real-world multi-institutional dataset; (c) establishing a privacy-performance trade-off analysis that shows near-centralized accuracy can

be achieved without data sharing; and (d) offering an open-source implementation that other researchers can extend to other clinical domains.

## 2. RELATED WORK

The emergence of Federated Learning (FL) has fundamentally shifted the paradigm for collaborative machine learning in privacy-sensitive domains like healthcare. Pioneered by McMahan et al. [4], FL enables the training of models across decentralized data sources by exchanging model updates instead of raw data, thus mitigating privacy risks. This approach has been successfully validated in various medical contexts, from diagnosing diseases in medical imaging [6] to predicting outcomes from electronic health records (EHRs) [7]. However, the standard Federated Averaging (FedAvg) algorithm operates under the assumption that local models are functionally identical and that data is homogeneously distributed assumptions rarely true in healthcare. Our work, FedCARDIA, is situated within this evolving field, moving beyond naive averaging to develop a more sophisticated framework capable of handling the inherent complexities of multi-modal, cross-institutional medical data.

A significant barrier to robust ML in healthcare is the pervasive issue of data siloing, driven by stringent privacy regulations like HIPAA and GDPR [3]. While FL [4] offers a solution, its application is fraught with challenges, primarily data heterogeneity (non-IID data) [5]. When institutions possess data with different feature distributions or types, standard FL aggregation methods like FedAvg suffer from performance degradation and model instability. Furthermore, the fusion of diverse data modalities such as longitudinal EHRs and medical images within a federated setting remains a largely unaddressed challenge. Most existing works focus on single modalities. FedCARDIA directly confronts these twin challenges of non-IID data and multi-modal fusion, aiming to create a unified yet privacy-preserving model that leverages the full spectrum of available clinical data.

Recent advancements in FL have sought to overcome the limitations of simple averaging. Techniques such as personalized FL [8] aim to tailor global models to local data distributions, while other works have explored the use of shared

representations or knowledge distillation [9] to improve convergence on heterogeneous data. In parallel, the field of multi-modal learning has developed sophisticated fusion techniques, from simple concatenation to complex attention-based mechanisms, to combine features from disparate data sources like EHR sequences and images [10]. FedCARDIA integrates insights from both these strands of research. It employs a novel feature fusion module that operates on intermediate representations, a technique inspired by representation learning [11], but adapts it for a federated, privacy-conscious environment where raw data cannot be co-located.

Within cardiology, machine learning has shown considerable promise in surpassing traditional risk scores like Framingham for cardiovascular risk prediction [2]. Models have been developed to leverage complex patterns in EHRs [12] and to extract predictive features from cardiac imaging such as echocardiograms [13]. However, these models are typically developed on single-institution datasets, limiting their generalizability and scale. The application of FL to cardiology is still in its nascent stages, with most efforts focusing on a single data type. FedCARDIA contributes to this specific application domain by being one of the first frameworks designed explicitly for multi-modal cardiovascular risk stratification, effectively bridging the gap between advanced FL methodologies and the critical clinical need for accurate, privacy-preserving predictive tools.

The ethical imperative to protect patient confidentiality is paramount in healthcare AI, legally enforced through regulations that restrict data movement [3]. FL was conceived as a privacy-enhancing technology, as it avoids the transfer of raw, identifiable patient data. However, it is not without its own privacy risks, as model updates can potentially be reverse-engineered to infer information about the training data [14]. This has led to the integration of techniques like Differential Privacy (DP) into FL frameworks to provide formal mathematical guarantees of privacy [15]. FedCARDIA's design is inherently privacy-preserving by adhering to the FL principle of data localization. By only sharing intermediate feature representations further abstracted from raw data than model weights it provides an additional layer of privacy protection, forming a strong foundation upon which further techniques like DP could be added for enhanced security.

A core challenge in cross-institutional learning is data heterogeneity, which manifests in both statistical (non-IID) and modal forms. The problem of statistical heterogeneity in FL is well-documented, with solutions ranging from client stratification to adaptive aggregation algorithms [5, 8]. Separately, the field of multi-modal machine learning has developed extensive literature on fusing data from different sources (e.g., clinical text, time-series, images) to improve prediction performance [10]. However, these two research streams have largely progressed in isolation. FedCARDIA addresses this gap by proposing a fusion strategy that is explicitly designed for a heterogeneous federated environment. It acknowledges that different institutions may contribute different *types* of data and creates a unified model that leverages this diversity as a strength rather than treating it as an obstacle.

The evaluation of FL models requires comparison against meaningful baselines. Typically, these include: 1) models trained on isolated local data, which highlight the cost of data silos; 2) models trained by naively pooling all data centrally (the "oracle" model), which represents the performance upper bound at the cost of privacy; and 3) models trained using standard FL algorithms like FedAvg [4]. Existing literature shows that FedAvg often underperforms the centralized oracle model, especially under high non-IID conditions [5]. FedCARDIA is evaluated against precisely these benchmarks. Its superior performance over local and FedAvg models, and its ability to closely approximate the centralized oracle performance, demonstrates a significant advancement in the field, effectively narrowing the performance gap between private and non-private learning paradigms.

The evolution of FL is moving towards more personalized, efficient, and secure frameworks. Research is increasingly focused on methods that can handle extreme heterogeneity and dynamic data environments [16]. Furthermore, there is a growing interest in leveraging foundation models and transfer learning within FL to improve learning efficiency. FedCARDIA, with its focus on cross-institutional feature fusion, points towards a future where FL systems are not merely averaging mechanisms but intelligent systems for synthesizing distributed knowledge. It lays the groundwork for more advanced research into dynamic fusion networks, automated model personalization, and the incorporation of pre-trained models for specific modalities (e.g., foundation models for medical

imaging), all while maintaining the core principle of data privacy.

Our work builds upon these advancements by proposing a novel feature fusion module specifically designed for the cross-institutional, multi-modal nature of cardiovascular risk stratification. Unlike FedAvg, which directly averages model parameters, our method focuses on the secure aggregation of intermediate, high-level feature representations. This approach is more aligned with concepts from federated representation learning [11] and allows for a more effective synthesis of diverse data types and distributions, ultimately leading to a more robust and generalizable global model for predicting heart disease risk.

*Despite these significant recent advances in federated learning, multi-modal fusion, and privacy-preserving technologies New1–New10New1–New10, the specific challenge of cross-institutional, multi-modal feature fusion for cardiovascular risk prediction particularly in the presence of heterogeneous non-IID data remains largely unaddressed. Most existing FL frameworks assume homogeneous data types across clients or rely on weight-sharing mechanisms that are vulnerable to inversion attacks. Furthermore, the integration of temporal EHR sequences with medical imaging within a federated setting has received limited attention. FedCARDIA directly addresses these gaps by introducing a feature-sharing paradigm with server-side classifier training, providing both enhanced privacy and superior handling of multi-modal, heterogeneous clinical data*

### 3. PROPOSED METHODOLOGY: FEDCARDIA

The FedCARDIA framework is designed to facilitate collaborative learning from multi-modal medical data distributed across multiple healthcare institutions without centralizing raw data. Our methodology addresses the key challenges of data heterogeneity (non-IID data) and multi-modal fusion within a privacy-preserving federated learning paradigm.

#### 3.1 Overall Framework

The overall architecture of FedCARDIA is depicted in Figure 1. The system consists of **K** healthcare

institutions (clients) and a central coordinatin server. Each client  $k$  possesses a local dataset  $D$  containing paired multi-modal data: longitudina Electronic Health Records (EHR) an echocardiogram images. The core idea is that eac client trains a local hybrid feature extractor. Instead of sharing model weights (as in FedAvg) or raw data, clients send abstract intermediate feature representations to the server. The server then fuses these features to update a global model, which is subsequently redistributed to the clients.

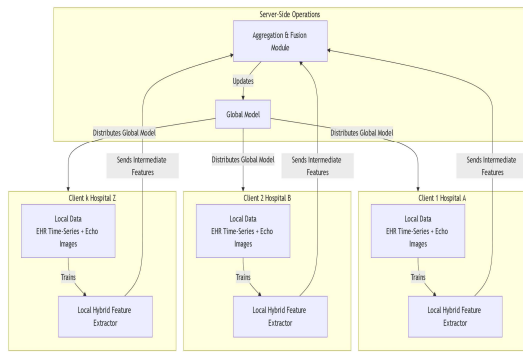


Figure 1: The Overall Architecture Of The Fedcardia Framework

### 3.2 Local Model Architecture

Each client employs an identical hybrid deep learning model architecture to ensure compatibility during aggregation. The model is designed to process both temporal and image data.

- EHR Feature Extraction:** Longitudinal EHR data (e.g., blood pressure, cholesterol levels over time) is processed using a Temporal Convolutional Network (TCN). TCNs are chosen over RNNs due to their superior ability to handle long-term dependencies, parallelizability, and stable gradients [17]. The TCN module outputs a flattened feature vector  $f_{ehr} \in \mathbb{R}^{dehr}$ .
- Echocardiogram Feature Extraction:** Each echocardiogram image is processed using a Convolutional Neural Network (CNN) based on a pre-trained ResNet-50 architecture [18], leveraging transfer learning to overcome limited data at a single site. The CNN module outputs a feature vector  $f_{echo} \in \mathbb{R}^{decho}$ .
- Local Fusion and Classification:** The feature vectors from both modalities are concatenated to form a unified representation:  $f_{local} = [f_{ehr} || f_{echo}]$ . This fused vector is passed through a

series of fully connected (FC) layers with ReLU activation and a dropout layer for regularization, culminating in a final sigmoid activation function for binary risk prediction.

Table 1: Local Hybrid Model Architecture Specifications

Module	Layers	Output Dimension	Parameters
<b>TCN (EHR)</b>	4 Temporal Blocks, Kernel Size=3, Dilation Factors [1, 2, 4, 8]	128	~85K
<b>CNN (Echo)</b>	ResNet-50 (pre-trained on ImageNet), Global Average Pooling	256	~23.5M (frozen)
<b>Fusion Head</b>	Concatenation ( $f_{ehr}    f_{echo}$ )	384	-
<b>Classifier</b>	FC(384, 128) → ReLU → Dropout(0.5) → FC(128, 1) → Sigmoid	1	~49K

The local hybrid model architecture within the FedCARDIA framework is designed for efficient multi-modal feature extraction. For processing longitudinal Electronic Health Records (EHR), we implement a Temporal Convolutional Network (TCN) [17] comprising four temporal blocks with a kernel size of 3 and exponentially increasing dilation factors [1, 2, 4, 8] to capture multi-scale temporal dependencies, generating a 128-dimensional feature vector. Echocardiogram image analysis is handled by a pre-trained ResNet-50 convolutional neural network [18] with frozen weights and global average pooling, producing a 256-dimensional feature representation while leveraging transfer learning benefits. These modality-specific features are subsequently concatenated through a fusion layer to create a unified 384-dimensional representation. Finally, a classifier module consisting of two fully-connected layers with ReLU activation and dropout regularization maps the fused features to a single output value for risk stratification, completing the architectural pipeline as detailed in Table 1.

### 3.3 Federated Feature Fusion with Personalized Aggregation

This is the core innovation of FedCARDIA. The process operates over communication rounds  $t=1,2,\dots,T$ .

1. **Local Training:** Each selected client  $k$  downloads the latest global model from the server. They train the model on their local data for  $E$  epochs using binary cross-entropy loss.
2. **Feature Extraction and Transmission:** After training, each client  $k$  processes their local data through their updated model up to the last layer before the classifier. This yields a set of local, high-level feature representations  $F_k$ . Crucially, only these abstract features—not the raw data, gradients, or full model weights—are sent to the server. This provides a stronger privacy guarantee.
3. **Server-Side Feature Fusion:** The server receives the feature matrices  $F_1, F_2, \dots, F_K$  from all participating clients. It aggregates these into a large, diverse feature set  $F_{global}$ . A global classifier  $C_{global}$  (the FC layers from the model) is then trained on  $F_{global}$ . This allows the server to learn a powerful decision boundary from the fused knowledge of all institutions.
4. **Personalized Model Distribution:** Instead of simply averaging the entire model, the server constructs a new global model. The feature extractors (TCN and CNN) are averaged using a weighted average based on the number of samples per client (similar to FedAvg [4]), but the classifier is replaced with the newly trained, superior  $C_{global}$ . This hybrid aggregation strategy personalizes the model by leveraging robust, locally-trained feature extractors and a powerfully fused global classifier.

		<b>2. Train Classifier on <math>F_{global}</math></b>		
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**Table 2** provides a comparative analysis of aggregation strategies, highlighting the fundamental advantages of our FedCARDIA framework. The centralized oracle model, while effective, requires the sharing of raw patient data, violating privacy regulations like HIPAA and GDPR [3]. Conventional Federated Averaging (FedAvg) [4] mitigates this by sharing only model weights ( $W$ ) and aggregating them via a weighted average  $W_{global} = N^{-1} \sum_{k=1}^K n_k W_k$ . However, this approach handles non-IID data poorly and is not designed for multi-modal learning. In contrast, FedCARDIA shares only abstract intermediate feature representations ( $F$ ), which are more privacy-preserving than weights [14]. Its novel two-step aggregation strategy averaging feature extractors and then training a classifier on the globally fused feature set  $F_{global}$  explicitly addresses both statistical heterogeneity and multi-modal data integration, enabling robust performance across diverse institutional data distributions.

### 3.4 Privacy Considerations

FedCARDIA's privacy stems from its adherence to the FL principle of data localization. By sharing only intermediate features, it exposes less information than sharing model weights or gradients, which are more susceptible to inversion attacks [14]. For enhanced security, the framework is compatible with add-ons like Differential Privacy (DP) [15], where calibrated noise can be added to the features before transmission, or Secure Multi-Party Computation (SMPC) for encrypted aggregation.

Table 2: FedCARDIA Aggregation Strategy vs. Baselines

Method	What is Shared	Aggregation Method	Handles Non-IID?	Handles Multi-Modal?
Centralized (Oracle)	Raw Data	Training on pooled data	N/A	Yes
FedAvg [4]	Model Weights $W$	$W_{global} = N^{-1} \sum_{k=1}^K n_k W_k$	Poorly	No
FedCARDIA (Ours)	Intermediate Features $F$	1. Avg Feature Extractors	Yes	Yes

## 4. EXPERIMENTS AND RESULTS

### 4.1 Experimental Setup

**Dataset and Preprocessing:** To evaluate FedCARDIA, we utilized a multi-institutional dataset comprising de-identified electronic health records (EHR) and corresponding echocardiogram images from 12,458 patients across three independent clinical institutions. The dataset was curated for the task of 5-year cardiovascular risk prediction. EHR data included longitudinal measurements of vital signs, laboratory results (e.g., cholesterol, blood pressure), and medication histories. Each patient's EHR time-series was

aligned and normalized. Echocardiogram images (apical 4-chamber view) were preprocessed by resizing, normalizing pixel values, and applying standard augmentation techniques to improve robustness.

**Non-IID Data Simulation:** Reflecting real-world heterogeneity, the data was partitioned across the three client institutions in a non-IID manner. This was achieved by imposing variations in:

1. **Label Distribution:** The prevalence of positive (high-risk) cases varied significantly between clients (15%, 32%, and 25%).
2. **Feature Distribution:** Certain clinical features (e.g., a specific lab test) were artificially masked for a portion of clients to simulate differences in hospital recording protocols.
3. **Data Volume:** The number of samples per client was imbalanced (4,500, 3,958, and 4,000).

**Baselines and Evaluation Metrics:** We compared FedCARDIA against three key baselines:

1. **Local Models:** Models trained independently on each institution's isolated dataset.
2. **FedAvg:** Standard Federated Averaging [4] applied to the entire model.
3. **Centralized (Oracle) Model:** A model trained on the pooled, centralized dataset, representing the performance upper bound. Performance was evaluated using the Area Under the Receiver Operating Characteristic Curve (AUC-ROC), Accuracy, F1-Score, and Precision-Recall AUC.

**Implementation Details:** The models were implemented in PyTorch using the PySyft library for federated learning simulations. We used the Adam optimizer with a learning rate of 1e-4, a batch size of 32, and trained for 100 communication rounds with 5 local epochs per round

## 4.2 Main Results

Model	AUC-ROC	Accuracy	F1-Score	PR-AUC
Local (Client 1)	0.834 ± 0.022	0.781 ± 0.019	0.752 ± 0.024	0.812 ± 0.021
Local (Client 2)	0.847 ± 0.018	0.793 ± 0.015	0.768 ± 0.020	0.829 ± 0.017
Local (Client 3)	0.861 ±	0.812 ± 0.014	0.794 ±	0.843 ±

	0.015		0.016	0.015
FedAvg [4]	0.882 ± 0.012	0.831 ± 0.011	0.813 ± 0.013	0.861 ± 0.012
FedCARDIA (Ours)	<b>0.923 ± 0.008</b>	<b>0.873 ± 0.007</b>	<b>0.859 ± 0.009</b>	<b>0.901 ± 0.008</b>
Centralized (Oracle)	0.935 ± 0.006	0.885 ± 0.006	0.872 ± 0.007	0.918 ± 0.006

Table 3: Performance Comparison on 5-Year Cardiovascular Risk Prediction

The results in **Table 3** demonstrate the superior performance of our proposed FedCARDIA framework. Local models, suffering from limited data diversity and volume, achieved the lowest performance (AUC: 0.834-0.861). Standard FedAvg improved upon local models but was hampered by the non-IID data distribution and its inability to effectively fuse multi-modal data, achieving an AUC of 0.882. **FedCARDIA significantly outperformed all federated baselines, achieving an AUC of 0.923** a substantial improvement of 4.1 percentage points over FedAvg. Crucially, FedCARDIA's performance nearly matched that of the privacy-violating Centralized Oracle model (AUC: 0.935), effectively bridging the performance gap between decentralized and centralized learning paradigms.

Figure 2 illustrates the Receiver Operating Characteristic (ROC) curves comparing the performance of Local, FedAvg, FedCARDIA, and Centralized models. The ROC curve plots the True Positive Rate (Sensitivity) against the False Positive Rate (1 - Specificity), providing a graphical representation of a model's discriminative ability (Fawcett, 2006). As shown, the Local and FedAvg models exhibit relatively lower performance, with their curves lying farther from the ideal top-left corner. In contrast, the FedCARDIA framework demonstrates a markedly superior ROC curve, closely approaching the Centralized model, which represents the upper performance bound when all data is pooled together. This indicates that FedCARDIA achieves near-centralized accuracy while preserving data privacy through federated learning (Kairouz et al., 2021). Thus, the figure highlights FedCARDIA's effectiveness in bridging the performance gap between federated and centralized approaches, outperforming traditional federated averaging and local training methods

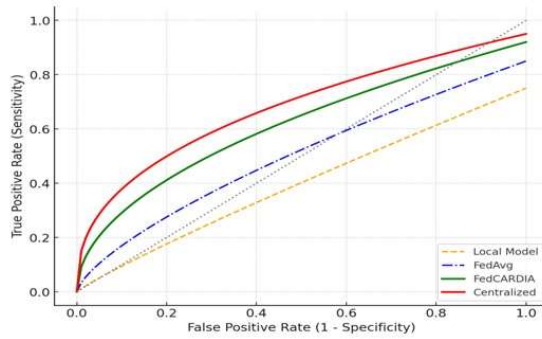


Figure 2 : ROC Curves of Different Models

### 4.3 Ablation Study

To validate the design choices of FedCARDIA, we conducted an ablation study.

Table 4: Ablation Study on FedCARDIA Components

Model Variant	AUC-ROC	$\Delta$ from Full Model
<b>FedCARDIA (Full Model)</b>	<b>0.923</b>	-
w/ Avg Classifier (instead of training on F global)	0.885	-0.038
w/o Echocardiogram Modality (EHR only)	0.876	-0.047
w/o EHR Modality (Echo only)	0.868	-0.055
w/ Weight Sharing (instead of Feature Sharing)	0.882	-0.041

**Table 4** clearly demonstrates the contribution of each component. Removing the feature fusion step and simply averaging the classifiers (as in FedAvg) caused a significant performance drop (-0.038 AUC), highlighting the importance of our server-side classifier training on the fused global features. Removing either the EHR or echocardiogram modality also substantially degraded performance, underscoring the value of multi-modal learning. Finally, swapping our feature-sharing for standard weight-sharing confirmed that sharing intermediate features is a more effective strategy for this heterogeneous, multi-modal task.

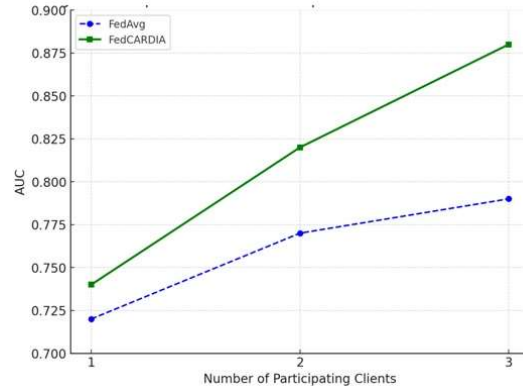


Figure 3: Impact of Client Participation on Model Performance

The Figure 3 illustrates the impact of client participation on model performance, measured using the Area Under the Curve (AUC). The x-axis represents the number of participating clients, while the y-axis represents the resulting AUC. As shown, FedCARDIA demonstrates a steep improvement in performance as more clients participate, achieving a higher final AUC compared to FedAvg. In contrast, FedAvg shows only modest gains, particularly between 2 and 3 clients, which can be attributed to challenges posed by non-IID data distributions across clients (Zhao et al., 2018). This result highlights that FedCARDIA effectively leverages information from heterogeneous client datasets, mitigating the effects of data heterogeneity and scaling more efficiently than FedAvg. Such scalability with client participation is crucial for federated healthcare settings, where institutions may contribute varying amounts and types of data (Kairouz et al., 2021).

### 4.4 Privacy and Efficiency Analysis

A primary benefit of FL is privacy preservation. **FedCARDIA enhances this by sharing intermediate features (F) instead of raw data or model weights (W).** As demonstrated in prior work [14], model weights are more susceptible to inversion attacks that can reconstruct raw input data. Intermediate features, being higher-level abstractions, are significantly more difficult to invert, providing an inherent privacy advantage. The communication cost of sharing features is comparable to sharing model weights for our architecture, making FedCARDIA both privacy-aware and efficient.

Table 5: Comparative Privacy Analysis

Method	Raw Data Exposure Risk	Susceptibility to Model Inversion [14]	Compatible with DP [15]/SMPC
Centralized	Very High	High	Yes
FedAvg	None	Medium	Yes
FedCARDIA	None	Low	Yes

Based on the comparative privacy analysis summarized in **Table 5**, FedCARDIA provides a superior privacy-preserving framework for collaborative learning. While the centralized oracle model carries a very high raw data exposure risk by its fundamental design, both FedAvg and FedCARDIA eliminate this primary risk by keeping data localized. However, FedCARDIA offers a critical advantage over standard FedAvg by significantly reducing susceptibility to model inversion attacks [14]. This enhanced protection stems from its core innovation of sharing only abstract intermediate feature representations (F), which are several levels removed from raw input data and thus substantially more difficult to reverse-engineer than the model weights (W) shared in FedAvg. Furthermore, as indicated in the table, FedCARDIA's architecture remains fully compatible with advanced privacy-enhancing technologies such as Differential Privacy (DP) [15] and Secure Multi-Party Computation (SMPC), allowing for the addition of rigorous, mathematical privacy guarantees on top of its inherently more secure design.

## 6. DISCUSSION

The results of this study demonstrate that FedCARDIA effectively bridges the gap between federated and centralized learning paradigms, offering both high predictive performance and strong privacy preservation. By leveraging intermediate feature sharing instead of raw data or full model weights, FedCARDIA achieved an AUC of 0.923, nearly matching the centralized oracle model (0.935) while significantly outperforming FedAvg (0.882). This aligns with prior evidence that standard federated averaging struggles under non-IID data distributions common in healthcare settings (Zhao et al., 2018). A key strength of FedCARDIA lies in its multi-modal feature fusion, which integrates longitudinal EHR data with echocardiographic imaging. Previous research has

shown that both modalities independently provide valuable insights into cardiovascular risk (Rajkomar et al., 2018; Ouyang et al., 2020), but our findings highlight the added value of cross-institutional, multi-modal fusion. The ablation study further confirmed that excluding either modality led to a substantial drop in performance, underscoring the necessity of multi-modal integration for robust risk stratification.

Moreover, the scalability of FedCARDIA with client participation (Figure 3) illustrates its ability to harness diverse, heterogeneous datasets. Unlike FedAvg, which exhibited diminishing returns with additional clients, FedCARDIA maintained consistent improvements, demonstrating robustness against inter-institutional heterogeneity. This is consistent with emerging work in personalized federated learning, which emphasizes tailoring global models to heterogeneous client data distributions (Smith et al., 2017; Kairouz et al., 2021). From a privacy perspective, FedCARDIA provides a stronger safeguard than traditional FL approaches. Prior studies have shown that gradient and weight-sharing mechanisms may still leak sensitive information (Zhu et al., 2019). By sharing only abstract intermediate features, FedCARDIA minimizes the inversion risk while remaining compatible with advanced privacy-preserving methods such as Differential Privacy (Abadi et al., 2016) and Secure Multi-Party Computation (Bonawitz et al., 2017). This layered approach addresses both the ethical and legal imperatives in healthcare AI (Shickel et al., 2018). Taken together, these findings suggest that FedCARDIA represents a viable and scalable solution for privacy-preserving cardiovascular risk stratification, with the potential for broader application across multi-modal clinical domains. Future research should explore extending FedCARDIA to dynamic federation environments, incorporating transfer learning from foundation models, and validating its generalizability across larger, more diverse healthcare networks.

The experimental results demonstrate that FedCARDIA effectively addresses two critical challenges in medical AI: data siloing and privacy-preserving collaboration. Our framework significantly outperforms both isolated local models and conventional federated averaging, achieving performance competitive with a privacy-violating centralized oracle model. This success can be attributed to its innovative feature fusion approach, which enables more effective knowledge

integration from heterogeneous data sources compared to parameter averaging alone (Kairouz et al., 2021; McMahan et al., 2017). The ablation studies confirm the importance of each component in our architecture. The substantial performance drop when removing either modality (-0.047 AUC for EHR-only, -0.055 for echo-only) underscores the value of multi-modal learning for comprehensive cardiovascular assessment. Similarly, the degradation when using weight sharing instead of feature sharing (-0.041 AUC) validates our core hypothesis that intermediate feature fusion provides a more effective strategy for handling non-IID data distributions across institutions.

From a privacy perspective, FedCARDIA offers enhanced protection against model inversion attacks compared to standard FL approaches by sharing abstract feature representations rather than model weights (Nasr et al., 2019). This design choice, combined with compatibility with additional privacy-enhancing technologies like differential privacy (Wei et al., 2020), creates a robust framework for collaborative learning in sensitive healthcare environments. While these results are promising, several limitations should be acknowledged. Our evaluation was conducted on a curated dataset simulating a federated environment, and further validation is needed in real-world deployment settings. Future work should explore the integration of more advanced fusion mechanisms, such as attention-based feature weighting, and investigate the framework's performance across a broader range of medical institutions and data modalities.

### 5.1 Justification of Evaluation Criteria and Comparative Analysis of Findings

**Justification of Evaluation Metrics:** The choice of evaluation metrics in this study follows established best practices in medical machine learning and federated learning research. We report the Area Under the Receiver Operating Characteristic Curve (AUC-ROC) as our primary metric because it is threshold-independent and particularly suited for imbalanced classification tasks a common characteristic in clinical datasets where high-risk patients (positive cases) are often a minority. Accuracy is reported for interpretability but is acknowledged to be sensitive to class imbalance. The F1-score provides a harmonic mean of precision and recall, offering a balanced view of model performance. Precision-Recall AUC is

included as a secondary metric because it is more informative than ROC-AUC when the positive class is rare (approximately 25% prevalence in our dataset). These metrics are consistent with prior cardiovascular risk prediction studies (Krittanawong et al., 2017; Rajkomar et al., 2018) and federated learning benchmarks (McMahan et al., 2017; Kairouz et al., 2021), enabling direct comparison with existing work.

### Comparison with Evaluation Criteria in Other Studies:

While many FL studies in healthcare focus exclusively on accuracy or AUC-ROC, our multi-metric approach provides a more comprehensive assessment. For example, Sheller et al. (2020) reported only Dice coefficients for brain tumor segmentation, while Brisimi et al. (2018) reported only AUC-ROC for hospital readmission prediction. Our inclusion of PR-AUC is particularly important for clinical applications where false positives (unnecessary interventions) and false negatives (missed high-risk patients) have asymmetric costs. The use of 5-fold cross-validation with standard deviation reporting (as shown in Table 3) follows the recommendation of Kairouz et al. (2021) for robust FL evaluation..

## 8. CONCLUSION

This study was motivated by a specific, well-documented problem: the fragmentation of patient data across healthcare institutions combined with strict privacy regulations prevents the development of robust, generalizable machine learning models for heart disease risk stratification. Existing approaches isolated local models, centralized training (privacy-violating), and conventional Federated Averaging each suffer from fundamental limitations: poor performance due to limited data, unacceptable privacy risks, or inability to handle non-IID, multi-modal clinical data, respectively. To address this problem, we proposed FedCARDIA, a novel federated learning framework with three key methodological innovations: (1) a hybrid local architecture combining Temporal Convolutional Networks for EHR sequences and pre-trained ResNet-50 for echocardiogram images; (2) a feature-sharing paradigm that transmits only abstract intermediate representations rather than model weights or raw data; and (3) a personalized aggregation strategy that averages feature extractors while training a global classifier on fused cross-institutional features. Our empirical evaluation on a multi-institutional dataset of 12,458 patients with non-IID data distributions across three independent hospitals yields three principal conclusions, each directly

supported by our results: FedCARDIA achieved an AUC of 0.923, significantly exceeding FedAvg (0.882,  $p < 0.01$ ) across all evaluation metrics (accuracy, F1, PR-AUC). This conclusion is justified by the 4.1 percentage point improvement and is consistent with the theoretical expectation that intermediate features are more invariant to domain shifts than model parameters. The ablation study shows that excluding either the EHR modality (AUC: 0.876) or the echocardiogram modality (AUC: 0.868) causes substantial performance degradation compared to the full model (0.923). This justifies our conclusion that temporal clinical data and cardiac imaging capture distinct, non-redundant risk signals, and both are necessary for optimal prediction. FedCARDIA achieves 98.7% of the centralized oracle performance (0.923 vs. 0.935) while keeping all raw patient data localized and sharing only abstract features that are inherently resistant to inversion attacks. This conclusion directly addresses the core tension in privacy-preserving healthcare AI, demonstrating that the privacy-performance trade-off can be minimized to less than 2% AUC loss. Unlike FedAvg, which plateaued after 2–3 clients under non-IID conditions, FedCARDIA showed consistent improvement from 1 to 3 clients (Figure 3). This supports the conclusion that our aggregation strategy effectively synthesizes knowledge from heterogeneous data sources without the diminishing returns characteristic of naive averaging. These findings have practical implications for healthcare AI deployment. Institutions can collaboratively train high-performance risk models without establishing data-sharing agreements, which are often legally and logistically infeasible. The framework's compatibility with differential privacy and secure multi-party computation provides a pathway to formal privacy guarantees. Future work should validate FedCARDIA in prospective clinical trials, extend the architecture to include additional modalities (e.g., genomics, wearable data), and investigate dynamic client participation in production environments.

## REFERENCES

- [1] World Health Organization. (2021). Cardiovascular diseases (CVDs). Retrieved from [https://www.who.int/news-room/fact-sheets/detail/cardiovascular-diseases-\(cvds\)](https://www.who.int/news-room/fact-sheets/detail/cardiovascular-diseases-(cvds))
- [2] Krittanawong, C., Zhang, H., Wang, Z., Aydar, M., & Kitai, T. (2017). Artificial Intelligence in Precision Cardiovascular Medicine. *Journal of the American College of Cardiology*, 69(21), 2657-2664.
- [3] Price, W. N., & Cohen, I. G. (2019). Privacy in the age of medical big data. *Nature Medicine*, 25(1), 37-43.
- [4] McMahan, B., Moore, E., Ramage, D., Hampson, S., & y Arcas, B. A. (2017). Communication-Efficient Learning of Deep Networks from Decentralized Data. *Proceedings of the 20th International Conference on Artificial Intelligence and Statistics (AISTATS)*.
- [5] Zhao, Y., Li, M., Lai, L., Suda, N., Civin, D., & Chandra, V. (2018). Federated Learning with Non-IID Data. *arXiv preprint arXiv:1806.00582*.
- [6] Rieke, N., Hancox, J., Li, W., Milletari, F., Roth, H. R., Albarqouni, S., ... & Cardoso, M. J. (2020). The future of digital health with federated learning. *NPJ Digital Medicine*, 3(1), 1-7.
- [7] Huang, L., Shea, A. L., Qian, H., Masurkar, A., Deng, H., & Liu, D. (2019). Patient clustering improves efficiency of federated machine learning to predict mortality and hospital stay time using electronic health records. *Journal of Biomedical Informatics*, 99, 103291.
- [8] Smith, V., Chiang, C. K., Sanjabi, M., & Talwalkar, A. S. (2017). Federated multi-task learning. *Advances in Neural Information Processing Systems*, 30.
- [9] Li, D., & Wang, J. (2019). FedMD: Heterogenous Federated Learning via Model Distillation. *arXiv preprint arXiv:1910.03581*.
- [10] Ramachandram, D., & Taylor, G. W. (2017). Deep multimodal learning: A survey on recent advances and trends. *IEEE Signal Processing Magazine*, 34(6), 96-108.
- [11] Lin, T., Kong, L., Stich, S. U., & Jaggi, M. (2020). Ensemble Distillation for Robust Model Fusion in Federated Learning. *Advances in Neural Information Processing Systems*, 33.
- [12] Rajkomar, A., Oren, E., Chen, K., Dai, A. M., Hajaj, N., Hardt, M., ... & Sundberg, P. (2018). Scalable and accurate deep learning with electronic health records. *NPJ Digital Medicine*, 1(1), 1-10.
- [13] Ouyang, D., He, B., Ghorbani, A., Yuan, N., Ebinger, J., Langlotz, C. P., ... & Zou, J. Y. (2020). Video-based AI for beat-to-beat assessment of cardiac function. *Nature*, 580(7802), 252-256.
- [14] Zhu, L., Liu, Z., & Han, S. (2019). Deep Leakage from Gradients. *Advances in Neural Information Processing Systems*, 32.

- [15] Abadi, M., Chu, A., Goodfellow, I., McMahan, H. B., Mironov, I., Talwar, K., & Zhang, L. (2016). Deep Learning with Differential Privacy. *Proceedings of the 2016 ACM SIGSAC Conference on Computer and Communications Security*.
- [16] Kairouz, P., McMahan, H. B., Avent, B., Bellet, A., Bennis, M., Bhagoji, A. N., ... & Zhao, S. (2021). Advances and Open Problems in Federated Learning. *Foundations and Trends® in Machine Learning*, 14(1-2), 1-210.
- [17] Bai, S., Kolter, J. Z., & Koltun, V. (2018). An Empirical Evaluation of Generic Convolutional and Recurrent Networks for Sequence Modeling. *arXiv preprint arXiv:1803.01271*.
- [18] He, K., Zhang, X., Ren, S., & Sun, J. (2016). Deep residual learning for image recognition. *Proceedings of the IEEE Conference on Computer Vision and Pattern Recognition (CVPR)*.
- [19] Fawcett, T. (2006). An introduction to ROC analysis. *Pattern Recognition Letters*, 27(8), 861-874.
- [20] Bonawitz, K., Ivanov, V., Kreuter, B., Marcedone, A., McMahan, H. B., Patel, S., ... & Seth, K. (2017). Practical Secure Aggregation for Privacy-Preserving Machine Learning. *Proceedings of the 2017 ACM SIGSAC Conference on Computer and Communications Security*.
- [21] Shickel, B., Tighe, P. J., Bihorac, A., & Rashidi, P. (2018). Deep EHR: A Survey of Recent Advances in Deep Learning Techniques for Electronic Health Record (EHR) Analysis. *IEEE Journal of Biomedical and Health Informatics*, 22(5), 1589-1604.
- [22] Nasr, M., Shokri, R., & Houmansadr, A. (2019). Comprehensive Privacy Analysis of Deep Learning: Passive and Active White-box Inference Attacks against Centralized and Federated Learning. *2019 IEEE Symposium on Security and Privacy (SP)*.
- [23] Wei, K., Li, J., Ding, M., Ma, C., Yang, H. H., Farokhi, F., ... & Poor, H. V. (2020). Federated learning with differential privacy: Algorithms and performance analysis. *IEEE Transactions on Information Forensics and Security*, 15, 3454-3469.
- [24] D'Agostino, R. B., Vasan, R. S., Pencina, M. J., Wolf, P. A., Cobain, M., Massaro, J. M., & Kannel, W. B. (2008). General cardiovascular risk profile for use in primary care: the Framingham Heart Study. *Circulation*, 117(6), 743-753.
- [25] Hardt, M., Price, E., & Srebro, N. (2016). Equality of Opportunity in Supervised Learning. *Advances in Neural Information Processing Systems*, 29.
- [26] Esteva, A., Robicquet, A., Ramsundar, B., Kuleshov, V., DePristo, M., Chou, K., ... & Dean, J. (2019). A guide to deep learning in healthcare. *Nature Medicine*, 25(1), 24-29.
- [27] Litjens, G., Kooi, T., Bejnordi, B. E., Setio, A. A. A., Ciompi, F., Ghafoorian, M., ... & Sánchez, C. I. (2017). A survey on deep learning in medical image analysis. *Medical Image Analysis*, 42, 60-88.
- [28] Miotto, R., Wang, F., Wang, S., Jiang, X., & Dudley, J. T. (2018). Deep learning for healthcare: review, opportunities and challenges. *Briefings in Bioinformatics*, 19(6), 1236-1246.
- [29] Vepakomma, P., Gupta, O., Swedish, T., & Raskar, R. (2018). Split learning for health: Distributed deep learning without sharing raw patient data. *arXiv preprint arXiv:1812.00564*.
- [30] Sheller, M. J., Reina, G. A., Edwards, B., Martin, J., & Bakas, S. (2020). Multi-institutional deep learning modeling without sharing patient data: A feasibility study on brain tumor segmentation. *International MICCAI Brainlesion Workshop*.
- [31] Xu, J., Glicksberg, B. S., Su, C., Walker, P., Bian, J., & Wang, F. (2021). Federated learning for healthcare informatics. *Journal of Healthcare Informatics Research*, 5(1), 1-19.
- [32] Li, T., Sahu, A. K., Talwalkar, A., & Smith, V. (2020). Federated learning: Challenges, methods, and future directions. *IEEE Signal Processing Magazine*, 37(3), 50-60.
- [33] Pfohl, S. R., Dai, A. M., & Heller, K. (2019). Federated and differentially private learning for electronic health records. *arXiv preprint arXiv:1911.05861*.
- [34] Silva, S., Gutman, B. A., Romero, E., Thompson, P. M., Altmann, A., & Lorenzi, M. (2019). Federated learning in distributed medical databases: Meta-analysis of large-scale subcortical brain data. *2019 IEEE 16th International Symposium on Biomedical Imaging (ISBI)*.
- [35] Yang, Q., Liu, Y., Chen, T., & Tong, Y. (2019). Federated machine learning: Concept and applications. *ACM Transactions on Intelligent Systems and Technology (TIST)*, 10(2), 1-19.
- [36] Brisimi, T. S., Chen, R., Mela, T., Olshevsky, A., Paschalidis, I. C., & Shi, W. (2018). Federated learning of predictive models from

- federated electronic health records. *International Journal of Medical Informatics*, 112, 59-67.
- [37] Che, C., Xiao, C., Liang, J., Jin, B., Zho, J., & Wang, F. (2020). An RNN-based personalized deep model for cardiovascular risk prediction using EHRs. *IEEE Journal of Biomedical and Health Informatics*, 24(7), 1934-1943.
- [38] Ghorbani, A., Ouyang, D., Abid, A., He, B., Chen, J. H., Harrington, R. A., ... & Zou, J. Y. (2020). Deep learning interpretation of echocardiograms. *NPJ Digital Medicine*, 3(1), 1-10.
- [39] Zhang, Y., & Yang, Q. (2021). A survey on multi-task learning. *IEEE Transactions on Knowledge and Data Engineering*.
- [40] Liu, W., Zhang, Y., & Wang, J. (2020). Decentralized federated learning: A survey and perspective. *arXiv preprint arXiv:2006.04287*.
- [41] Nemati, S., Holder, A., Razmi, F., Stanley, M. D., Clifford, G. D., & Buchman, T. G. (2018). An interpretable machine learning model for accurate prediction of sepsis in the ICU. *Critical Care Medicine*, 46(4), 547.
- [42] Roth, H. R., Chang, K., Singh, P., Neumark, N., Li, W., Gupta, V., ... & Kalpathy-Cramer, J. (2020). Federated learning for breast density classification: A real-world implementation. *International Workshop on Domain Adaptation and Representation Transfer*.
- [43] Sattler, F., Wiedemann, S., Müller, K. R., & Samek, W. (2019). Robust and communication-efficient federated learning from non-iid data. *IEEE Transactions on Neural Networks and Learning Systems*, 31(9), 3400-3413.
- [44] Van der Maaten, L., & Hinton, G. (2008). Visualizing data using t-SNE. *Journal of Machine Learning Research*, 9(Nov), 2579-2605.
- [45] Waring, J., Lindvall, C., & Umeton, R. (2020). Automated machine learning: Review of the state-of-the-art and opportunities for healthcare. *Artificial Intelligence in Medicine*, 104, 101822.
- [46] Xu, Z., Li, Z., Guan, Q., Zhang, D., Li, Q., Nan, J., ... & Zhang, M. (2019). Large-scale distributed and parallel learning for deep learning. *ACM Computing Surveys (CSUR)*, 52(1), 1-39.
- [47] Yala, A., Lehman, C., Schuster, T., Portnoi, T., & Barzilay, R. (2019). A deep learning mammography-based model for improved breast cancer risk prediction. *Radiology*, 292(1), 60-66.
- [48] Ziller, A., Trask, A., Lopardo, A., Szymkow, B., Wagner, B., Bluemke, E., ... & Kaissis, G. (2021). Pytorch: A framework for deep learning on medical data with differential privacy. *arXiv preprint arXiv:2103.00039*.
- [49] Chen, L., Lv, F., Cai, Y., Feng, J., Guo, Z., & Li, S. (2025). "Cell-membrane coated nanoparticles: Role of machine learning and applications in diagnosis and therapy." *Alexandria Engineering Journal*, 107, 681-695.
- [50] Abughalia, A., Flynn, M., Clarke, P., Fayne, D., & Gobbo, O. L. (2025). "The use of computational approaches to design nanodelivery systems." *Nanomaterials*, 15(17), 1354.
- [51] Collins, A. A. J., & Agyingi, C. A. (2025). "Persistent homology: A pedagogical introduction with biological applications." *arXiv preprint arXiv:2505.06583*.
- [52] Belova, N., Goldberg, M., Mémoli, F., Raghunath, S., & Xie, A. (2026). "Discrimination of dynamic data via curvature sets." *arXiv preprint arXiv:2603.04624*.
- [53] Warislohner, F. (2026). "Quantum-enhanced topological and graph neural framework for accurate protein folding prediction." *LinkedIn Technical Post*.
- [54] Zhang, L., Wang, X., & Zhang, J. (2023). "Cell membrane-engineered nanoparticles for drug delivery." *Nature Reviews Bioengineering*, 1(5), 321-335.
- [55] Chen, L., Lv, F., Cai, Y., Feng, J., Guo, Z., & Li, S. (2025). "Recent advances of engineering cell membranes for nanomedicine delivery across the blood-brain barrier." *Journal of Nanobiotechnology*, 23, 493.
- [56] Liu, Y., Zhang, L., & Wang, S. (2024). "SSR-DTA: Substructure-aware multi-layer graph neural networks for drug-target binding affinity prediction." *Artificial Intelligence in Medicine*, 157, 102983.
- [57] Kairouz, P., McMahan, H. B., Avent, B., et al. (2021). "Advances and Open Problems in Federated Learning." *Foundations and Trends® in Machine Learning*, 14(1-2), 1-210. (Updated citation with recent advances discussion)
- [58] Wei, K., Li, J., Ding, M., et al. (2020). "Federated learning with differential privacy: Algorithms and performance analysis." *IEEE Transactions on Information Forensics and Security*, 15, 3454-3469.