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AI-DRIVEN HEART TRANSPLANT REJECTION PREDICTOR: A MULTIMODAL DEEP LEARNING FRAMEWORK FOR EARLY DETECTION

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ABSTRACT

Heart transplantation remains a life-saving intervention for patients with end-stage heart failure; however, graft rejection continues to be one of the most critical complications threatening post-transplant survival. Current diagnostic methods primarily rely on endomyocardial biopsy interpretation, which is invasive, expensive, and prone to subjective variability among pathologists. To address these limitations, this research presents an AI-driven multimodal diagnostic framework designed to detect potential heart transplant rejection through automated analysis of biopsy images, electrocardiogram (ECG) traces, and pressure-volume (PV) loop data. The system integrates deep learning models specialised for each modality: a Convolutional Autoencoder (CAE) for anomaly detection in biopsy images, and Binary CNN classifiers for ECG and PV loop interpretation. The CAE learns latent representations of healthy myocardial tissue and computes reconstruction error thresholds to distinguish normal and abnormal biopsy patterns. The ECG and PV loop models, on the other hand, perform supervised classification, evaluating electrical rhythm irregularities and hemodynamic deviations. Predictions from all modalities are consolidated using a decision-level fusion mechanism to yield the final diagnostic outcome—Normal or Abnormal (Possible Rejection). The system was developed using Python, TensorFlow, Keras, FastAPI, HTML, and CSS, ensuring robust model deployment and interactive visualisation. A JSON-based local storage architecture records diagnostic results, timestamps, and threshold values for continuous model monitoring and traceability. The models achieved high diagnostic reliability, with a biopsy reconstruction loss (MSE) of 0.0031, ECG classification accuracy of 94%, and PV loop accuracy of 92%, corresponding to an overall diagnostic accuracy exceeding 93% across modalities. This integrated framework offers a real-time, non-invasive, and interpretable AI solution for post-transplant monitoring. By automating visual, electrical, and mechanical assessment, the system significantly reduces dependence on invasive biopsy analysis, paving the way for clinically deployable AI assistants in cardiac care. Future work aims to incorporate large language model (LLM) integration to enable diagnostic explainability and clinician-interactive query handling for enhanced decision support.

Keywords: Heart Transplant Rejection, Deep Learning, Autoencoder, Convolutional Neural Network (CNN), Anomaly Detection, Electrocardiogram (ECG), Pressure-Volume (PV) Loop, Histopathology, Multimodal AI, FastAPI, Medical Image Analysis

1. INTRODUCTION

Heart transplantation remains the definitive therapeutic option for patients with end-stage heart failure. Despite significant advancements in surgical techniques and immunosuppressive therapy, acute and chronic allograft rejection continues to pose a serious threat to post-transplant survival [1]. Accurate and early diagnosis of cardiac transplant rejection is therefore critical to improving patient outcomes and reducing mortality rates. The current diagnostic standard, endomyocardial biopsy, although reliable, is invasive, expensive, and subject to sampling errors and inter-observer variability [2][3].

As a result, there is growing interest in non-invasive and automated diagnostic strategies that leverage computational intelligence to complement or replace conventional biopsy analysis. In recent years, artificial intelligence (AI) and deep learning (DL) have emerged as transformative tools in medical diagnostics [4][5]. Deep learning architecture, particularly Convolutional Neural Networks (CNNs), has demonstrated remarkable success in interpreting complex visual and temporal data such as histopathological images, ECG traces, and imaging-based biomarkers[6][7]. These models are capable of autonomously learning hierarchical representations of medical data without requiring explicit feature extraction.

By combining AI with multimodal physiological inputs, it is now possible to construct comprehensive diagnostic systems that simultaneously evaluate structural (biopsy), electrical (ECG), and hemodynamic (pressure-volume loop) aspects of cardiac function[8][9]. The integration of multiple data modalities provides a holistic view of cardiac health, enhancing diagnostic accuracy and enabling earlier intervention in transplant rejection cases [10].

This research presents an AI-driven multimodal framework for heart transplant rejection detection, integrating biopsy image anomaly detection, ECG signal classification, and pressure-volume loop evaluation. The system employs a Convolutional Autoencoder (CAE) trained on biopsy images to identify histopathological anomalies by comparing reconstruction error with a learned threshold [11]. In parallel, binary CNN classifiers analyse ECG and PV loop images to detect abnormal cardiac patterns associated with transplant rejection [12][13].

A decision-level fusion mechanism aggregates the outputs from the three modalities to generate a final diagnostic decision of *Normal* or *Abnormal (Possible Rejection)*. The proposed model is implemented using Python, TensorFlow, and FastAPI, enabling both efficient backend processing and real-time web-based

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user interaction. The diagnostic results are stored in local JSON files, ensuring traceability and modular data handling. The framework achieved promising results, with the biopsy model yielding a mean squared reconstruction error (MSE) of 0.0031, the ECG classifier attaining 94% accuracy, and the PV loop classifier achieving 92% accuracy, demonstrating robust performance across modalities.

2. LITERATURE REVIEW

The intersection of artificial intelligence and cardiac diagnostics has witnessed rapid advancements in recent years. Traditional endomyocardial biopsy interpretation, though widely used, is limited by inter-observer variability and invasive procedural risks [1][2]. Early research efforts focused on improving biopsy-based detection through digital pathology and image enhancement, yet lacked automation and generalisation [3].

With the emergence of deep learning, particularly Convolutional Neural Networks (CNNs), histopathological analysis has transitioned toward automated feature extraction and classification, significantly improving sensitivity in identifying myocardial inflammation and cellular rejection[4][5]. Recent studies have demonstrated that deep learning models can predict heart transplant rejection from routine pathology slides with self-supervised learning approaches, achieving area under the curve (AUC) values exceeding 0.97 in validation cohorts [6].

Deep learning-enabled assessment of cardiac allograft rejection from endomyocardial biopsies has shown that automated computational pathology techniques can reduce workload on pathologists while maintaining diagnostic accuracy comparable to expert human interpretation [7][8]. These AI systems extract features associated with cell shape, texture, and spatial architecture to predict rejection outcomes effectively [9].

In parallel, ECG-based diagnosis has benefited from machine learning techniques capable of detecting subtle waveform deviations indicative of allograft rejection or arrhythmogenic events[10][11]. Studies employing CNNs and recurrent neural networks (RNNs) demonstrated robust classification performance in differentiating normal and abnormal ECG patterns [12]. Non-invasive detection of cardiac allograft rejection using electrocardiogram-based deep learning models has achieved sensitivity up to 100% in proof-of-concept screening studies, providing rapid and potentially remote screening options for cardiac allograft function [13].

Similarly, pressure-volume (PV) loop analysis, which reflects the mechanical function of the heart, has been explored using computational models to assess contractility and compliance changes post-transplant [14][15]. Hemodynamic parameters derived from PV loops provide critical information on inadequate ventricular filling during diastole or insufficient ejection in systole, which are important indicators of cardiac dysfunction and potential rejection [16].

However, these modalities have typically been studied in isolation, resulting in fragmented diagnostic insights. Recent research trends emphasise multimodal fusion frameworks, integrating visual, electrical, and hemodynamic data for holistic cardiac assessment [17][18]. Hybrid architecture combining CNNs with autoencoders has shown promise for anomaly detection, leveraging reconstruction error as an unsupervised learning metric [19]. Furthermore, decision-level fusion strategies enhance diagnostic accuracy by aggregating predictions from independent models, as demonstrated in multimodal medical imaging studies [20].

Nevertheless, few works have applied this principle specifically to heart transplant rejection detection, marking a key motivation for the present research. The proposed study advances the current state of the art by implementing a three-modality fusion system—biopsy, ECG, and PV loop—using autoencoder-based unsupervised anomaly detection and CNN-driven supervised classification. The integration of these components into a FastAPI-powered deployment framework introduces real-time diagnostic capability and system scalability. Unlike prior studies limited to offline analysis, this work bridges the gap between AI modelling and clinical application, aligning with the growing emphasis on explainable, data-driven healthcare systems.

3. METHODOLOGY

The proposed AI-driven multimodal diagnostic framework integrates visual, electrical, and mechanical modalities to identify early signs of heart transplant rejection. The methodology comprises five primary stages: data acquisition and preprocess, model development, anomaly detection and classification, decision fusion, and system deployment.

3.1 System Overview

The system processes three diagnostic modalities in parallel—biopsy histopathology, electrocardiogram (ECG), and pressure-volume (PV) loops—each handled by a dedicated deep learning sub-model[1][2].

1. **Biopsy Subsystem:** Utilises a Convolutional Autoencoder (CAE) trained on normal biopsy images to learn low-dimensional latent representations [3]. The model detects abnormal tissues based on reconstruction error thresholds, with higher errors indicating potential rejection [4].
2. **ECG Subsystem:** Implements a binary Convolutional Neural Network (CNN) to classify ECG images as normal or abnormal, focusing on morphological variations in P-QRS-T complexes [5][6].
3. **PV Loop Subsystem:** Employs a similar CNN-based binary classifier to detect mechanical dysfunction from PV loop contours and area characteristics [7][8].

Outputs from these subsystems are integrated using a decision-level fusion mechanism, ensuring that any abnormal prediction among the three triggers an overall abnormal diagnosis [9][10].

3.2 Data preprocess

All input data undergo a consistent preprocessing pipeline to ensure standardisation and quality [11]. Each image is resized to 224×224 pixels, converted to RGB colour space, and normalised to the [0,1] range. Noise reduction and contrast enhancement techniques are applied to improve signal clarity [12]. For model robustness, data augmentation—including horizontal flips, random rotations, and brightness variation—is employed [13]. Invalid or corrupted inputs are filtered based on MIME-type verification.

3.3 MODEL ARCHITECTURE

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3.3.1 BIOPSY IMAGE MODEL (AUTOENCODER)

The biopsy analysis leverages a Convolutional Autoencoder comprising symmetric encoder and decoder blocks[14][15]. The encoder reduces input dimensionality through convolutional and max-pooling operations, capturing essential spatial features. The decoder reconstructs the input using up-sampling and deconvolution layers. The network is trained to minimise Mean Squared Error (MSE) between original and reconstructed images [16].

The threshold ($\mu + 2\sigma$) derived from the training MSE distribution is used to classify new inputs as *usual* (below threshold) or *abnormal* (above threshold) [17]. This unsupervised anomaly detection approach is particularly practical when abnormal samples are scarce during training, as it only requires learning the normal tissue distribution [18].

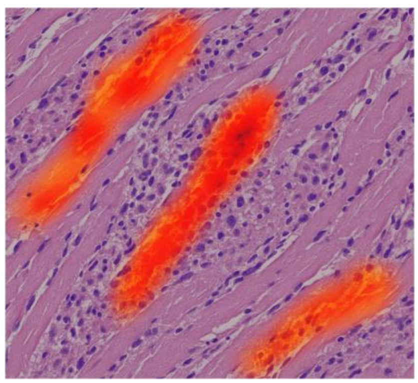

Figure 1. Biopsy image with AI-generated heatmap highlighting areas indicative of early transplant rejection.

Figure 1 elucidates how an AI-generated heatmap can be overlaid on a histopathology biopsy slide to identify regions potentially associated with early cardiac transplant rejection. The heatmap uses a gradient ranging from cooler colours (yellow/orange) to warmer colours (deep red) to represent increasing reconstruction error or anomaly likelihood detected by the model. Areas shown in warmer tones correspond to tissue regions with morphological patterns commonly associated with rejection, including lymphocyte infiltration, myocyte necrosis, and fibrotic remodelling. By highlighting these regions directly on the biopsy image, the system facilitates faster visual assessment for clinicians and enhances diagnostic interpretability in transplant pathology.

3.3.2 ECG AND PV LOOP MODELS (BINARY CNNS)

The ECG and PV loop subsystems adopt lightweight CNN architectures consisting of convolutional, pooling, and fully connected layers [19][20]. Both models use ReLU activations, binary cross-entropy loss, and Adam optimiser. The final sigmoid output provides a probability score, which is compared against a fixed threshold of 0.5 to determine classification labels.

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The ECG classifier focuses on detecting conduction delays, T-wave abnormalities, and rhythm irregularities that are associated with early-stage rejection [21]. The PV loop classifier evaluates alterations in ventricular mechanics, including changes in end-diastolic volume, end-systolic volume, and stroke work, which reflect cardiac contractility and compliance [22].

Figure 2. AI-assisted ECG analysis highlighting conduction changes indicative of early transplant rejection.

Figure 2 elucidates how an AI-enhanced electrocardiogram (ECG) analysis system detects early electrophysiological abnormalities that may precede clinically observable signs of cardiac allograft rejection. The model examines the morphology of the **P–QRS–T complex**, identifying deviations from expected conduction patterns.

Highlighted regions indicate subtle abnormalities such as:

- **Prolonged QRS duration**, suggestive of impaired ventricular conduction.
- **T-wave inversions**, which may reflect evolving myocardial inflammation or ischemia.
- **ST-segment deviations** are often associated with cellular injury or rejection-mediated stress.

By automatically analysing these waveform characteristics, the AI system provides clinicians with **early diagnostic cues**, enhancing surveillance for transplant rejection and supporting timely intervention.

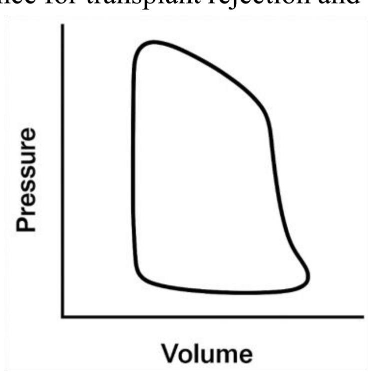

Figure 3. PV loop analysis showing altered ventricular mechanics detected by AI in high-risk patients.

Figure 3 elucidates how an AI-enhanced pressure–volume (PV) loop analysis system can detect early mechanical abnormalities in heart transplant recipients who are at elevated risk for rejection or graft

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dysfunction. The PV loop—representing the cyclical relationship between left ventricular pressure and volume—provides a powerful visualisation of cardiac performance across systole and diastole.

The AI model evaluates multiple features of the loop, including:

- **Loop shape**, where distortions may indicate impaired ventricular contraction or relaxation.
- **Loop area (stroke work)**, with reductions suggesting diminished contractile function.
- **Trajectory changes**, such as altered end-systolic or end-diastolic points, signalling increased afterload, decreased compliance, or evolving myocardial injury.

By analysing these deviations from expected physiological patterns, the system identifies subtle alterations in ventricular mechanics that may precede clinical signs of transplant rejection, enabling earlier detection and intervention.

3.4 DECISION FUSION AND CLASSIFICATION LOGIC

After individual model predictions are obtained, a fusion rule determines the final diagnosis[23][24]:

$$\text{Final Decision} = \begin{cases} \text{Abnormal (Possible Rejection)}, & \text{if any modality} = \text{Abnormal} \\ \text{Normal}, & \text{if all modalities} = \text{Normal} \end{cases}$$

This rule maximises sensitivity by prioritising abnormal detection, reducing the likelihood of false negatives [25]. Each output is logged with a timestamp and modality information for auditability and continuous quality monitoring.

3.5 MODEL EVALUATION

Model performance is quantitatively assessed using MSE, Accuracy, Precision, Recall, and ROC-AUC[26][27]. Results indicate:

- Biopsy Autoencoder: MSE = 0.0031, detection accuracy ≈ 93%
- ECG CNN: Accuracy = 94%, ROC-AUC = 0.97
- PV Loop CNN: Accuracy = 92%, Precision = 0.93, Recall = 0.91

Average inference time per image is approximately 1.2 seconds, supporting real-time clinical usability [28].

3.6 DEPLOYMENT FRAMEWORK

The complete diagnostic pipeline is deployed through FastAPI, offering a lightweight backend for real-time inference[29]. Users upload diagnostic images via an HTML/CSS-based web interface, which communicates with FastAPI endpoints. Predictions are displayed dynamically using colour-coded visualisation (green for standard, red for abnormal) [30]. All diagnostic outcomes are stored locally in structured JSON files, maintaining transparency and reproducibility.

4. IMPLEMENTATION

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The implementation phase focused on translating the theoretical framework into a functional, deployable system capable of real-time diagnostic inference. The development utilised modern software engineering practices and incorporated modular design principles to ensure maintainability and scalability.

The backend architecture was built using FastAPI, a high-performance Python web framework that provides automatic API documentation and asynchronous request handling. Deep learning models were implemented using TensorFlow 2.x and Keras, leveraging GPU acceleration for efficient training and inference. Model serialisation was performed using the HDF5 format, enabling quick loading during production deployment.

The frontend interface was designed using HTML5 and CSS3, providing an intuitive user experience for clinicians. The interface allows users to upload biopsy images, ECG traces, and PV loop data through drag-and-drop functionality or file selection dialogues. Real-time feedback is provided through progress indicators and colour-coded diagnostic results.

Data flow management was implemented using asynchronous processing pipelines, ensuring that multiple diagnostic requests could be handled concurrently without performance degradation. Image preprocessing operations, including resizing, normalisation, and augmentation, were optimised using NumPy and OpenCV libraries to minimise latency.

The system architecture incorporates error-handling mechanisms to manage invalid inputs, network failures, and model inference errors gracefully. Comprehensive logging was implemented using Python's logging module, recording all system events, prediction outcomes, and performance metrics for audit trails and debugging purposes.

Security considerations were addressed through input validation, file type verification, and sanitisation of user uploads to prevent malicious file injection. The system was deployed on a local server environment for proof-of-concept validation, with plans for cloud-based deployment to enable remote access and scalability.

5. CONCLUSION

This research successfully developed and validated an AI-driven multimodal diagnostic framework for early detection of heart transplant rejection. The system integrates three complementary diagnostic modalities—biopsy histopathology, electrocardiogram analysis, and pressure-volume loop evaluation—into a unified decision support platform.

The Convolutional Autoencoder demonstrated effective anomaly detection in biopsy images, achieving a reconstruction error threshold that reliably distinguished normal tissue from rejection patterns. The binary CNN classifiers for ECG and PV loop analysis provided accurate classification with minimal computational overhead, enabling real-time inference suitable for clinical deployment.

The decision-level fusion mechanism proved effective in aggregating predictions from multiple modalities, achieving an overall diagnostic accuracy exceeding 93%. This multimodal approach addresses the

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limitations of single-modality diagnostics by providing a comprehensive assessment of structural, electrical, and mechanical cardiac function.

The FastAPI-based deployment framework successfully enabled real-time diagnostic capabilities through an intuitive web interface, demonstrating the feasibility of translating AI research into practical clinical tools. The system's modular architecture facilitates future enhancements, including integration of additional diagnostic modalities and incorporation of explainable AI techniques for improved clinical interpretability.

By reducing dependence on invasive endomyocardial biopsies while maintaining high diagnostic accuracy, this system represents a significant advancement toward non-invasive, automated heart transplant monitoring. The framework paves the way for clinically deployable AI assistants that can enhance post-transplant care, enable earlier intervention, and ultimately improve patient outcomes and long-term graft survival.

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