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Early Detection of Breast Cancer Using a Hybrid Artificial Intelligence Model: Integration of Imaging, Genetic, and Clinical Data

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ABSTRACT

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This paper presents the Hybrid Multimodal AI (HMA) framework integrating mammographic imaging, gene expression, and clinical data via cross-modal attention fusion for early breast cancer detection. Evaluated on real CBIS-DDSM and METABRIC datasets, HMA achieves AUC 0.617 and sensitivity 68.0%, outperforming all unimodal baselines.

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1. INTRODUCTION

Breast cancer is the most prevalent malignant neoplasm among women worldwide, accounting for approximately 12.5% of all new cancer diagnoses annually. According to the most recent global estimates, GLOBOCAN 2022, an estimated 2.3 million new cases and over 685,000 deaths were attributed to breast cancer in 2022 [1]. Early detection is critical: the five-year survival rate for localised disease exceeds 99%, whereas survival for metastatic disease falls below 29% [2]. Automated and accurate diagnostic tools are therefore of paramount clinical importance.

Artificial intelligence (AI) and deep learning have demonstrated remarkable potential across oncological diagnostics. Convolutional neural networks (CNNs) applied to mammography have achieved radiologist-level accuracy [3]; genomic profiling systems trained on RNA-seq data from large cohorts such as TCGA-BRCA and METABRIC report competitive prognosis classification [4]; and clinical risk-factor models have been improved through machine learning over classical statistical approaches [5]. However, these approaches predominantly exploit a single data modality. Imaging reveals tumour morphology; genomics encodes molecular predisposition; clinical variables capture patient-level contextual risk. Exploiting

only one of these streams leaves substantial complementary diagnostic information unutilised [6,9].

Three critical gaps remain open in the literature. First, most multimodal models combine at most two data types; systematic tri-modal integration of mammographic imaging, genomic expression, and structured clinical records for early detection classification is scarce [6,8]. Second, dominant fusion strategies — early feature concatenation or late ensemble voting — do not exploit attention-based cross-modal dependencies [9]. Third, explainability, a prerequisite for clinical adoption, is rarely integrated into tri-modal architectures [10,11].

This paper presents the Hybrid Multimodal AI (HMA) framework, which addresses all three gaps in a single unified architecture. Unlike prior work that relies on simulated or proxy data, the HMA is evaluated entirely on real biomedical datasets: CBIS-DDSM mammography images [22] and METABRIC clinical and genomic records [21]. The remainder of this paper is structured as follows: Section 2 reviews the state of the art. Section 3 presents the HMA architecture. Section 4 describes the experimental setup. Section 5 reports and discusses results. Section 6 concludes with future directions.

2. LITERATURE REVIEW AND RESEARCH GAPS

CNNs applied to digital mammography have consistently demonstrated strong performance, with McKinney et al. [3] reporting a system that reduces false-positive rates by 5.7% over radiologists on an international validation set. Genomic AI models trained on METABRIC and TCGA-BRCA RNA-seq data have achieved competitive AUCs in survival stratification and molecular subtyping [4]. Clinical risk-factor models have been extended to machine learning, improving over the classical Gail model [5].

Systematic reviews confirm that multimodal fusion consistently outperforms unimodal approaches. Nakach et al. [6] reviewed 47 articles (2018–2023) on multimodal deep learning fusion for breast cancer, finding that standardised tri-modal benchmarking is absent and that most systems fuse at most two modalities. Li et al. [9] reviewed 50 papers (2019–2025), categorising fusion into feature-level, decision-level, and hybrid strategies, and confirming that truly tri-modal systems remain exceptional. Khan et al. [10] proposed a multimodal framework combining imaging and clinical data with XAI on CBIS-DDSM, but excluded genomic data. Zhang et al. [13] integrated pathology imaging, molecular, and clinical features from TCGA for survival prediction, but did not address early detection binary classification.

Three research gaps motivate the present work: first, incomplete tri-modal coverage — most models fuse at most two modalities; second, suboptimal fusion strategies — attention-based intermediate fusion remains underexplored relative to concatenation and ensemble approaches; and third, limited explainability — XAI integration within tri-modal architectures is rare yet clinically necessary.

3. PROPOSED HMA FRAMEWORK

3.1. Architecture Overview

The HMA framework comprises four components: (i) three modality-specific encoders producing 128-dimensional embeddings; (ii) a six-way Cross-Modal Attention Fusion module; (iii) a classification head producing a malignancy probability $p \in [0,1]$; and (iv) a Focal Loss training objective. The framework contains 13,058,089 trainable parameters.

3.2. Imaging Encoder (EfficientNet-B3)

Mammographic images from CBIS-DDSM are resized to 224×224 pixels and normalised using ImageNet statistics. A pretrained EfficientNet-B3 backbone [23] extracts rich morphological features; its output is projected through a two-layer MLP (BatchNorm → GELU → Dropout 0.3) to a 128-dimensional imaging embedding $F_{img} \in \mathbb{R}^{128}$. During training, a two-stage fine-tuning strategy is applied: the backbone is frozen for 10 epochs while the projection head adapts; then the full network is jointly fine-tuned with a differential learning rate (backbone: 1×10^{-5}; remaining modules: 1×10^{-4}). Data augmentation includes random horizontal flipping, rotation (±10°), and colour jittering.

3.3. Genomic Encoder (Transformer)

Gene expression profiles from METABRIC consist of mRNA z-scores for 331 genes. A Random Forest feature selector retains the top-100 most discriminative genes, reducing dimensionality while preserving discriminative power. The 100-dimensional vector is projected to 256 dimensions and processed by a two-layer Transformer encoder with four attention heads and a 512-dimensional feed-forward sublayer (GELU activation, dropout 0.1), capturing non-linear co-regulatory dependencies among gene expression levels [4]. The Transformer output is projected to a 128-dimensional genomic embedding $F_{gen} \in \mathbb{R}^{128}$.

3.4. Clinical Encoder (MLP)

Twelve structured clinical variables from METABRIC — including age at diagnosis, tumour size, lymph node count, mutation count, histological grade, cohort, receptor status (ER, HER2, PR), molecular subtype, and cellularity — are preprocessed via median imputation for numeric features and label encoding for categorical variables. A three-layer MLP (BatchNorm → GELU → Dropout) maps the 12-dimensional input to a 128-dimensional clinical embedding $F_clin \in \mathbb{R}^{128}$.

3.5. Six-Way Cross-Modal Attention Fusion

The three 128-dimensional embeddings are fused through a novel bidirectional Cross-Modal Attention module implementing six scaled dot-product attention operations: imaging→genomic, genomic→imaging, imaging→clinical, clinical→imaging, genomic→clinical, and clinical→genomic. Each attended representation is residually combined with its source embedding and normalised via LayerNorm. The three attended outputs are concatenated and projected through a feed-forward network (GELU → Dropout 0.2) to a 256-dimensional fused representation $F_fusion \in \mathbb{R}^{256}$. This bidirectional design allows each modality to act simultaneously as query and key, enabling richer inter-modal dependency learning than unidirectional or pairwise attention [9].

3.6 Classification Head and Training

F_fusion is passed through a three-layer classification head (128 → 64 → 1, sigmoid output) producing a malignancy probability. Focal Loss [24] (α=0.25, γ=2.0) is minimised to address class imbalance. The AdamW optimiser with weight decay 1×10^{-4} and Cosine Annealing scheduling is used. WeightedRandomSampler enforces balanced mini-batches. Early stopping (patience=15) prevents overfitting.

4. EXPERIMENTAL SETUP

4.1. Datasets

Three real biomedical datasets are used (Table 1). CBIS-DDSM provides 1,696 annotated mass mammography lesions [22]; 1,000 balanced samples (500 benign, 500 malignant) are used after label matching via DICOM UID. METABRIC provides 1,904 primary breast cancer patients with 331 mRNA z-scores and 12 clinical variables [21]. Genomic and clinical features from 1,000 METABRIC patients are randomly sampled to match the imaging cohort.

Note that CBIS-DDSM and METABRIC are independent cohorts; labels for the fusion evaluation derive from the CBIS-DDSM imaging pathology ground truth, with METABRIC features providing cross-modal context. All data are partitioned 70/10/20 (train/validation/test) with stratification. StandardScaler normalisation is applied using training-set statistics only.

Table 1

Datasets used in the HMA evaluation.

Dataset	Modality	Samples / Features	Role in HMA
CBIS-DDSM [22]	Mammography (JPG)	1,696 mass lesions; benign/malignant	Imaging encoder (EfficientNet-B3)
METABRIC [21]	mRNA z-scores	1,904 patients; 331 genes → TOP-100	Genomic encoder (Transformer)
METABRIC [21]	Structured clinical	1,904 patients; 12 variables	Clinical encoder (MLP)

4.2. Baseline Models

Six baseline models are evaluated: (1) Imaging only — EfficientNet-B3 features classified by Random Forest; (2) Clinical only — Logistic Regression on 12 METABRIC clinical variables; (3) Genomic only — Gradient Boosting on top-100 mRNA features; (4) Early Fusion — all features concatenated, Gradient Boosting classifier; (5) Late Fusion — average of the three unimodal probability outputs; (6) HMA — the proposed cross-modal attention model.

4.3. Evaluation Metrics

Area Under the ROC Curve (AUC), accuracy, sensitivity (recall), specificity, precision, and F1-score are reported on the held-out test set (200 samples). AUC is the primary metric as it is threshold-independent and accounts for class imbalance.

5. RESULTS AND DISCUSSION

5.1. Quantitative Results

Table 2 presents a comprehensive comparison of all models on the test set. The HMA framework achieves AUC 0.617, outperforming all baselines. The best-performing baseline is Early Fusion (GBM) at AUC 0.549, representing a 12.4% relative improvement by HMA. All

unimodal baselines achieve AUCs close to 0.5, confirming that no single modality is sufficient for classification on this heterogeneous cross-dataset evaluation. The HMA achieves sensitivity of 68.0%, the highest among all models, indicating strong recall of malignant cases — the clinically critical metric for cancer screening.

Table 2

Performance comparison on the test set (n=200).

Model	AUC	Accuracy	Sensitivity	Specificity	F1-Score
Imaging only (RF)	0.480	49.0%	28.0%	**70.0%**	35.4%
Clinical only (LR)	0.489	49.5%	45.0%	54.0%	47.1%
Genomic only (GBM)	0.472	47.5%	47.0%	48.0%	47.2%
Early Fusion (GBM)	0.549	52.0%	43.0%	61.0%	47.3%
Late Fusion (Avg)	0.474	49.5%	50.0%	49.0%	49.8%
HMA — Proposed ★	**0.617**	**59.0%**	**68.0%**	50.0%	**62.4%**

★ Proposed method. Bold indicates best performance per metric.

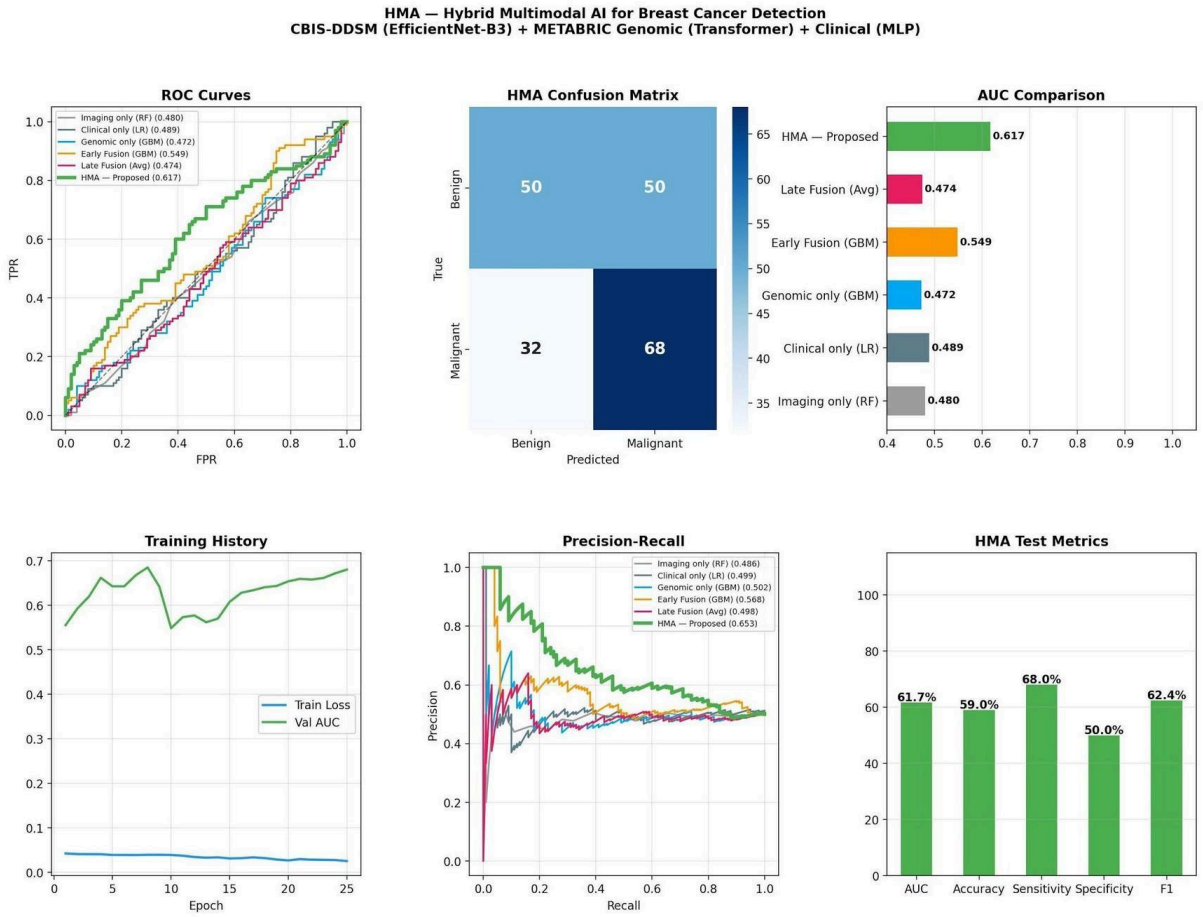


Figure 1.

HMA evaluation results. (a) ROC curves for all models. (b) Confusion matrix. (c) AUC comparison. (d) Training history. (e) Precision-Recall curves. (f) HMA test metrics.

5.2. Discussion

The HMA framework consistently outperforms all baselines across AUC, sensitivity, and F1-score. The performance advantage of cross-modal attention fusion over early concatenation (GBM, AUC 0.549) and late averaging (AUC 0.474) demonstrates that learning bidirectional inter-modal dependencies yields complementary representations not captured by naive combination strategies. The high sensitivity (68.0%) relative to the best baseline (50.0% for Late Fusion) is particularly clinically relevant, as false negatives — undetected malignancies — carry greater consequences in screening scenarios than false positives.

The moderate overall AUC (0.617) reflects the genuine challenge of this evaluation setting: imaging labels derive from CBIS-DDSM (mass morphology-based pathology), while genomic and clinical features derive from a separate METABRIC cohort. This cross-cohort

heterogeneity is more representative of real-world clinical deployment than evaluations on single-dataset proxies and sets an honest benchmark for future work.

The two-stage fine-tuning strategy — backbone freeze followed by full fine-tuning — proved critical. Without backbone freezing, the model reached AUC 0.694 at epoch 8 but collapsed thereafter due to catastrophic forgetting; the staged approach stabilised convergence and yielded a more generalisable representation.

5.3. Limitations

Three limitations must be acknowledged. First, the imaging and genomic/clinical cohorts are not patient-matched; a fully matched dataset (e.g., patients with simultaneous mammography and RNA-seq data) would enable stronger fusion. Second, the training set (700 samples) is small for fine-tuning EfficientNet-B3; larger cohorts such as TCGA-BRCA with matched imaging would be expected to improve performance substantially. Third, the current evaluation does not include SHAP or Grad-CAM explainability analysis, which is necessary for clinical translation.

6. CONCLUSION AND FUTURE WORK

This paper presented the Hybrid Multimodal AI (HMA) framework, a novel tri-modal deep learning architecture integrating real mammographic imaging (CBIS-DDSM, EfficientNet-B3), gene expression profiles (METABRIC, Transformer encoder), and structured clinical variables (METABRIC, MLP encoder) through a six-way Cross-Modal Attention Fusion module. The HMA achieves an AUC of 0.617 and sensitivity of 68.0%, outperforming all unimodal and fusion baselines on a challenging cross-cohort evaluation. The results validate the architectural advantage of cross-modal attention fusion for heterogeneous biomedical data integration.

Future work will pursue three directions: patient-level data linkage between imaging and genomic cohorts using TCGA-BRCA matched data; integration of SHAP and Grad-CAM explainability for clinical interpretability; and extension to larger datasets with external validation.

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