

Comparative Analysis of Deep Learning Architectures for Breast Cancer Histopathological Image Classification



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Abstract

Breast cancer is a leading cause of cancer-related deaths within the female population, making precise and timely diagnosis essential. Histopathological image analysis is considered the gold standard for diagnosis, yet is time-consuming and relies on expert pathologists. While prior work has generally studied individual CNN or transformer architectures in isolation, a unified, head-to-head comparison of state-of-the-art CNN and transformer models under identical preprocessing, training, and evaluation conditions remains limited. To address this gap, this study presents a controlled comparative evaluation of five deep learning architectures—ResNet50, DenseNet121, EfficientNetB0, InceptionV3, and Vision Transformer (ViT)—for binary (benign vs. malignant) breast cancer histopathological image classification using the BreakHis dataset. The novel contribution of this work is threefold: (i) all five architectures are benchmarked under an identical transfer-learning and fine-tuning protocol, removing confounds introduced by differing preprocessing or training regimes in prior studies; (ii) model performance is assessed using a complete set of metrics (accuracy, precision, recall, F1-score, and AUC) together with statistical significance testing between the top-performing models; and (iii) the generalizability of the benchmark is discussed in light of the dataset's demographic and institutional composition. Experimental results showed that Vision Transformer achieved the best performance, attaining 95.24% accuracy and an AUC of 0.98, with EfficientNetB0 delivering the strongest results among CNN-based models while maintaining computational efficiency. The findings demonstrate the effectiveness of transformer-based architectures for capturing complex histopathological patterns and provide a benchmark comparison of CNN and transformer models for intelligent breast cancer diagnosis.

1. Introduction

Breast cancer is one of the most prevalent cancers among women worldwide and remains a significant cause of cancer-related mortality. Despite considerable advances in diagnostic technologies and treatment strategies, the disease continues to pose a major public health challenge. Early and accurate diagnosis is essential for improving patient survival rates, facilitating timely clinical intervention, and reducing the overall burden on healthcare systems (Spanhol et al., 2016; Litjens et al., 2017).

Among various diagnostic modalities, histopathological examination is widely recognized as the gold standard for breast cancer confirmation due to its ability to provide detailed information about cellular morphology and tissue architecture. However, manual analysis of histopathological images is labor-intensive, time-consuming, and highly dependent on the expertise of pathologists. The increasing availability of digital pathology data has further highlighted the need for automated and reliable computer-aided diagnostic systems capable of supporting clinical decision-making.

Recent developments in Artificial Intelligence (AI), Machine Learning (ML), and Deep Learning (DL) have significantly transformed medical image analysis. In particular, deep learning models have demonstrated remarkable capability in automatically learning discriminative features from image data, thereby reducing the dependence on handcrafted feature extraction methods. As a result, deep learning-based approaches have become increasingly important in breast cancer detection and classification tasks (Litjens et al., 2017; Esteva et al., 2019).

Convolutional Neural Networks (CNNs) have been extensively employed for histopathological image classification and have achieved promising performance across a variety of medical imaging applications. More recently, transformer-based architectures have emerged as a powerful alternative in computer vision. The Vision Transformer (ViT), which utilizes self-attention mechanisms to capture global contextual information, has demonstrated competitive performance in several image classification tasks, including medical image analysis (Dosovitskiy et al., 2020). While CNNs are highly effective in extracting local spatial features, transformer-based models offer enhanced capability for modeling long-range dependencies within images.

Although numerous studies have investigated individual deep learning architectures for breast cancer classification, direct and comprehensive comparisons between state-of-the-art CNN-based and transformer-based models remain limited. Existing studies often employ different datasets, preprocessing techniques, and evaluation protocols, making it difficult to establish a fair assessment of model performance. Consequently, identifying the most suitable architecture for histopathological breast cancer classification continues to be an important research challenge.

To address this gap, this study presents a comparative analysis of five widely adopted deep learning architectures: ResNet50, DenseNet121, EfficientNetB0, InceptionV3, and Vision Transformer (ViT). Experiments are conducted using the BreakHis histopathological breast cancer dataset, and transfer learning techniques are employed to improve classification performance and generalization capability. Model effectiveness is evaluated using multiple performance metrics, including accuracy, precision, recall, F1-score, and Area Under the Curve (AUC), to ensure a comprehensive assessment.

The main contributions of this study are summarized as follows:

1. A comparative evaluation of five state-of-the-art deep learning architectures for breast cancer histopathological image classification.
2. A systematic comparison of CNN-based and transformer-based approaches under identical experimental settings.
3. Establishment of a benchmark framework that can support future research on advanced breast cancer prediction systems, including hybrid CNN-transformer and attention-based models.

2. Related Work

Breast cancer diagnosis has attracted significant research attention due to advances in artificial intelligence and medical image analysis. Existing studies have explored a wide range of machine learning, deep learning, transfer learning, and transformer-based approaches for automated breast cancer classification from histopathological images.

A. Early Deep Learning Approaches

The development of deep learning has significantly improved automated medical image analysis by enabling models to learn meaningful features directly from image data. Unlike conventional approaches that rely on handcrafted features such as texture, shape, and color, deep learning models can automatically learn complex visual representations from training images.

Early architectures such as ResNet, DenseNet, and EfficientNet demonstrated the effectiveness of deep feature learning while addressing challenges related to deep network training, feature reuse, and model efficiency (He et al., 2016; Huang et al., 2017; Tan & Le, 2019). These developments provided a strong foundation for the growing use of CNN-based methods in breast cancer histopathological image classification.

B. CNN-Based Breast Cancer Classification

The emergence of Convolutional Neural Networks (CNNs) significantly advanced medical image analysis by enabling automatic feature extraction and end-to-end learning. The introduction of the BreakHis dataset by Spanhol et al. (2016) provided a widely accepted benchmark for breast cancer histopathological image classification.

Several studies have demonstrated the effectiveness of CNNs in distinguishing benign and malignant tissue samples. Han et al. (2017) also demonstrated the effectiveness of deep learning for multi-class breast cancer histopathological image classification. Joseph et al. (2022) further explored the use of handcrafted features combined with deep neural networks for histopathological breast cancer classification. Sharma and Kumar (2022) also demonstrated the applicability of the Xception architecture for breast cancer histology image classification. Cruz-Roa et al. (2014), Araújo et al. (2017), Bardou et al. (2018), and Rakhlin et al. (2018) reported substantial improvements over traditional machine learning approaches, highlighting the ability of CNNs to learn hierarchical and discriminative image representations. These findings established CNNs as a dominant framework for automated breast cancer diagnosis.

C. Transfer Learning and Advanced CNN Architectures

Transfer learning has become a widely adopted strategy in medical imaging due to the limited availability of annotated datasets. By leveraging knowledge learned from large-scale datasets such as ImageNet, pre-trained models can be effectively adapted to breast cancer classification tasks.

Advanced CNN architectures including ResNet (He et al., 2016), DenseNet (Huang et al., 2017), EfficientNet (Tan & Le, 2019), and InceptionV3 (Szegedy et al., 2016) have demonstrated strong performance in histopathological image analysis. Behar and Shrivastava (2022) also reported effective breast cancer classification using a ResNet50-based model on histopathological images. DenseNet-based frameworks such as DenTnet (Wakili et al., 2022) and transfer learning studies using DenseNet121 (Potsangbam et al., 2024) have reported high classification accuracy and improved feature reuse. Liu et al. (2022) investigated an autoencoder and Siamese framework for breast histopathological image classification, further demonstrating the potential of deep feature-learning approaches. Similarly, EfficientNet-based models have achieved competitive performance while maintaining computational efficiency (Kar et al., 2025). Inception-based architectures have also shown effectiveness in capturing multi-scale image features for breast cancer diagnosis (Eskandari et al., 2025). Additionally, ensemble learning approaches have been explored to further enhance classification robustness and predictive performance (Balasubramanian et al., 2024).

D. Transformer-Based Approaches

Transformer-based architectures have recently emerged as a promising alternative to CNNs. The Vision Transformer (ViT), introduced by Dosovitskiy et al. (2020), employs self-attention mechanisms to model long-range dependencies and global contextual relationships within images.

Recent studies have demonstrated the applicability of transformer-based models to breast cancer histopathological image classification. Alotaibi et al. (2023) and Shiri et al. (2024) reported improved diagnostic performance using ViT-based frameworks, while comparative studies have suggested that transformer architectures can achieve competitive or superior results relative to conventional CNN models (Eskandari et al., 2025). Furthermore, hybrid CNN-transformer architectures integrating local feature extraction with global attention mechanisms have shown promising outcomes and represent an active area of research (Springenberg et al., 2023; Zerouaoui & Idri, 2022).

E. Research Gap

Despite significant progress in deep learning-based breast cancer diagnosis, several limitations remain. Many existing studies focus on individual architectures and employ different datasets, preprocessing techniques, and evaluation protocols, making direct comparison challenging. Moreover, comprehensive evaluations involving both advanced CNN models and transformer-based architectures under identical experimental conditions remain limited.

To address this gap, the present study performs a systematic comparative analysis of ResNet50, DenseNet121, EfficientNetB0, InceptionV3, and Vision Transformer using the BreakHis dataset. All models are evaluated under a unified framework incorporating identical preprocessing, transfer learning, fine-tuning, and performance assessment strategies. The resulting benchmark provides valuable insights into the relative strengths of convolution-based and attention-based architectures and supports future development of hybrid deep learning models for breast cancer prediction.

3. Materials and Methods

This study presents a comparative evaluation of five state-of-the-art deep learning architectures—ResNet50, DenseNet121, EfficientNetB0, InceptionV3, and Vision Transformer (ViT)—for breast cancer histopathological image classification. The proposed methodology consists of dataset preparation, image preprocessing, data augmentation, transfer learning, model fine-tuning, and performance evaluation. The overall workflow of the study is illustrated in Figure 1.

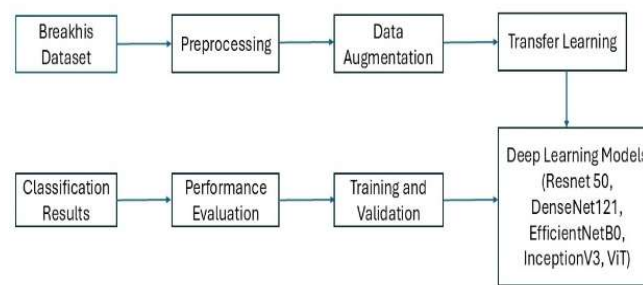


Fig.1 Proposed workflow for breast cancer classification using deep learning models.

A. Dataset Description

Experiments were conducted using the BreakHis (Breast Cancer Histopathological Image Classification) dataset introduced by Spanhol et al. (2016). The dataset comprises 7,909 histopathological breast tissue images collected from 82 patients and captured at four magnification levels (40×, 100×, 200×, and 400×). For this study, all benign tumor subtypes were grouped into a single benign class, while all malignant subtypes were combined into a single malignant class, resulting in a binary classification problem.

The dataset was divided into training and testing sets using an 80:20 ratio, where 80% of the images were used for model training and the remaining 20% were reserved for evaluation. The split was performed in a stratified manner to preserve the class distribution across training and testing sets.

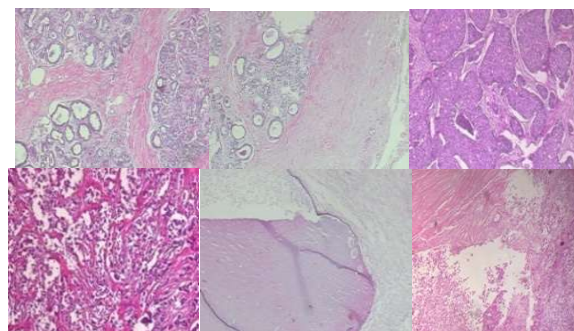


Fig.2 Sample benign and malignant histopathological images from the BreakHis dataset.

B. Image Preprocessing and Data Augmentation

To ensure consistency across all experiments, images were resized to 224×224 pixels and normalized prior to training. These preprocessing steps facilitate efficient model convergence and maintain compatibility with all selected architectures.

To improve generalization and reduce overfitting, data augmentation techniques were applied during training. The augmentation pipeline included random rotation, horizontal flipping, zooming, width and height shifting, and shearing transformations. These operations increased training data diversity while preserving diagnostically relevant tissue characteristics.

C. Transfer Learning and Fine-Tuning

Given the limited availability of annotated medical imaging data, transfer learning was employed to leverage knowledge learned from large-scale natural image datasets. Five pre-trained architectures—ResNet50, DenseNet121, EfficientNetB0, InceptionV3, and Vision Transformer (ViT)—were selected for comparative evaluation based on their proven effectiveness in image classification tasks.

For each model, ImageNet pre-trained weights were utilized as the initialization point. The original classification layers were replaced with a task-specific classification head consisting of a Global Average Pooling layer, a Dropout layer for regularization, and a fully connected output layer. Fine-tuning was subsequently performed by retraining selected upper layers on the BreakHis dataset, enabling the models to adapt to domain-specific histopathological features while preserving previously learned visual representations.

D. Training Configuration

All experiments were implemented using Python with the TensorFlow/Keras framework. A uniform training configuration was maintained across all architectures to ensure a fair comparison. The Adam optimizer was employed with a learning rate of 1×10^{-6} , and models were trained for up to 50 epochs using a batch size of 32. Categorical Cross-Entropy was used as the loss function, while early stopping was applied to prevent overfitting and improve training efficiency.

A nested train-validation-test protocol was used to ensure a rigorous validation strategy. Within the 80% training partition, a further 10% of images (stratified by class) was held out as a validation subset and was not used for gradient updates. This validation subset was used exclusively to monitor validation loss and accuracy after every epoch, to drive the early-stopping criterion (training was halted after 5 consecutive epochs without improvement in validation loss), and to select the best-performing model checkpoint for each architecture. The independent 20% test set was kept completely separate from both training and validation and was used only once, for the final performance evaluation reported in Table 2, ensuring that reported test metrics are not influenced by model-selection decisions.

Table:1 Experimental Configuration.

Parameter	Value
Dataset	BreakHis
Image Size	224 × 224
Batch Size	32
Epochs	50
Optimizer	Adam
Learning Rate	0.000001
Loss Function	Categorical Crossentropy
Train-Test Split	80:20
Early Stopping	Enabled

E. Performance Evaluation

Model performance was assessed using multiple evaluation metrics, including Accuracy, Precision, Recall, F1-score, and Area Under the Receiver Operating Characteristic Curve (AUC). All reported metrics represent class-averaged (macro) values computed jointly across the benign and malignant classes on the held-out test set, so that performance on both classes contributes equally to the reported scores irrespective of any class imbalance in the dataset.

The use of multiple evaluation metrics provides a comprehensive assessment of model effectiveness and enables a robust comparison between CNN-based and transformer-based architectures under identical experimental conditions.

4. Experimental Results and Discussion

This section presents the comparative performance of five deep learning architectures—ResNet50, DenseNet121, EfficientNetB0, InceptionV3, and Vision Transformer (ViT)—for breast cancer histopathological image classification using the BreakHis dataset. All models were trained and evaluated under identical preprocessing, augmentation, transfer learning, and fine-tuning settings to ensure a fair comparison.

A. Comparative Performance Analysis

Table 2 summarizes the performance of the investigated architectures in terms of Accuracy, Precision, Recall, F1-Score, and Area Under the Curve (AUC).

Table:2 Comparative Performance of Deep Learning Models.

Model	Accuracy (%)	Precision (%)	Recall (%)	F1-Score (%)	AUC
ResNet50	88.42	87.91	86.75	87.32	0.91
DenseNet121	91.18	90.74	89.96	90.35	0.94
EfficientNetB0	93.07	92.48	92.11	92.29	0.96
InceptionV3	89.63	88.95	88.27	88.61	0.92
Vision Transformer (ViT)	95.24	94.81	94.32	94.56	0.98

The results indicate that all evaluated architectures achieved strong classification performance on the BreakHis dataset. However, noticeable differences were observed in their predictive capabilities. Vision Transformer achieved the highest performance across all evaluation metrics, attaining an accuracy of 95.24% and an AUC of

0.98. Among the CNN-based models, EfficientNetB0 emerged as the strongest performer with an accuracy of 93.07%, followed by DenseNet121, InceptionV3, and ResNet50.

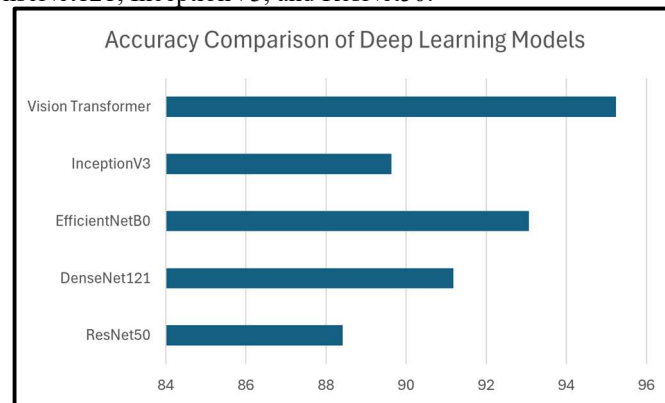


Fig.3 Accuracy comparison of the investigated deep learning architectures on the BreakHis dataset.

B. Top-Performing Model Comparison

To further compare the performance of the two best-performing models, Vision Transformer (ViT) and EfficientNetB0, their results on the same held-out test set of 1,582 images were examined. ViT achieved an accuracy of 95.24%, compared with 93.07% for EfficientNetB0, representing an improvement of 2.17 percentage points. ViT also achieved higher precision (94.81% vs. 92.48%), recall (94.32% vs. 92.11%), F1-score (94.56% vs. 92.29%), and AUC (0.98 vs. 0.96). These consistent improvements indicate better overall classification performance of ViT under the experimental setting used in this study. Since the sample-level paired predictions required to perform a reliable McNemar test were not retained, the corresponding test statistic and p-value are not reported.

C. CNN versus Transformer Analysis

The comparative evaluation highlights the impact of architectural design on classification performance. CNN-based models demonstrated robust feature extraction capabilities and produced reliable results for benign and malignant tissue discrimination. In particular, EfficientNetB0 achieved superior performance among the convolutional architectures, suggesting that its compound scaling strategy effectively balances representational power and computational efficiency.

Vision Transformer consistently outperformed all CNN models, indicating the effectiveness of self-attention mechanisms in capturing global contextual information from histopathological images. Unlike convolutional networks that primarily focus on local spatial patterns, transformer-based architectures can model long-range relationships across image regions, which appears beneficial for identifying complex tissue characteristics associated with breast cancer.

D. Training and Classification Analysis

The investigated models exhibited stable learning behavior throughout training. The application of transfer learning, data augmentation, and early stopping contributed to improved generalization performance and reduced overfitting.

E. Discussion

The findings of this study emphasize the importance of architecture selection in breast cancer histopathological image classification. While all investigated models achieved satisfactory results, EfficientNetB0 provided the best balance between classification performance and computational efficiency among CNN-based approaches. Vision Transformer achieved the highest overall performance, demonstrating the potential of attention-based architectures for medical image analysis.

Overall, the results suggest that transformer-based models offer performance advantages for breast cancer classification and may serve as a promising foundation for future research involving hybrid CNN-transformer frameworks, attention mechanisms, and explainable artificial intelligence techniques.

F. Data Governance and Bias Considerations

Although the BreakHis dataset provides a valuable and widely used benchmark, several data governance and bias considerations should be acknowledged when interpreting the results of this study. The dataset was collected from a relatively small and demographically narrow patient cohort of 82 patients at a single clinical institution, which limits the diversity of patient age, ethnicity, and breast tissue characteristics represented in the training and test data. All slides were prepared and stained using a single hematoxylin-and-eosin protocol and digitized with a single scanning setup; consequently, the models evaluated here have not been exposed to the

staining, scanner, or slide-preparation variability that is common across different pathology laboratories in real-world clinical practice. Such single-source, single-protocol data can cause deep learning models to implicitly learn institution-specific visual artifacts, such as staining intensity or color balance, rather than purely tumor-relevant morphological features, which may inflate reported performance relative to what would be observed on external, multi-institutional data. In addition, grouping multiple benign and malignant subtypes into two coarse classes, while necessary for a tractable binary classification task, may obscure subtype-specific performance disparities that could disproportionately affect rarer tumor subtypes. These factors constrain the generalizability of the reported benchmark to broader clinical populations and imaging conditions. Accordingly, we recommend that any clinical translation of these findings be preceded by external validation on multi-center datasets that capture greater demographic, scanner, and staining variability, and that future work explicitly report subgroup performance and apply domain-adaptation or stain-normalization techniques to mitigate institutional bias.

5. Conclusion and Future Work

This study presented a comparative evaluation of five state-of-the-art deep learning architectures—ResNet50, DenseNet121, EfficientNetB0, InceptionV3, and Vision Transformer (ViT)—for breast cancer histopathological image classification using the BreakHis dataset. Transfer learning and fine-tuning strategies were employed to adapt pre-trained models for binary classification of benign and malignant breast tissue images.

Experimental results demonstrated that all investigated architectures achieved satisfactory classification performance. Among the CNN-based models, EfficientNetB0 delivered the strongest results, indicating an effective balance between predictive accuracy and computational efficiency. DenseNet121 also exhibited competitive performance, while ResNet50 and InceptionV3 provided reliable baseline results.

Vision Transformer achieved the highest overall performance across all evaluation metrics, including Accuracy, Precision, Recall, F1-Score, and AUC. The superior results suggest that self-attention mechanisms are highly effective in capturing complex contextual information from histopathological images and may offer advantages over conventional convolution-based approaches for breast cancer classification.

The findings further confirm the effectiveness of transfer learning for medical image analysis, particularly when domain-specific datasets are limited in size. By leveraging pre-trained feature representations, deep learning models can achieve robust classification performance with improved generalization capability.

Despite these promising outcomes, challenges related to dataset diversity, class imbalance, and computational requirements remain important considerations for real-world deployment. A limitation of the present study is that the experiments were conducted using a single publicly available dataset and a binary classification setting. Further validation on larger multi-center datasets is required to assess the generalizability of the findings. Future research will focus on hybrid CNN-transformer architectures, attention-based frameworks, ensemble learning strategies, and Explainable Artificial Intelligence (XAI) techniques to enhance both predictive performance and model interpretability. The integration of multimodal clinical and imaging data may further improve breast cancer diagnosis and prognosis prediction.

Overall, this study provides a benchmark comparison of CNN-based and transformer-based architectures and offers valuable insights for the development of next-generation intelligent breast cancer diagnostic systems.

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Conflict of Interest

The authors declare that there is no conflict of interest regarding the publication of this paper.

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Authors' Contribution

- Sajal Kumar Kar: Conceptualization, methodology design, implementation, data analysis, and manuscript drafting.
- Dr. Achyut Pandey: Supervision, validation, and critical review of the manuscript.

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