Breast Cancer Classification Using Densenet121 And K-Means Segmentation With Augmented Data

Akinbowale Nathaniel Babatunde[1], Bukola Fatimah Balogun[1], Sunday Adeola Ajagbe[2*], Edidiong Elijah Akpan[3], Roseline Oluwaseun Ogundokun[4], Precious Ikpemhinogena Ogie[5], Salman Olatunji Isiaka[6], Pragasen Mudali[2]
[1]Department of Computer Science, Kwara State University, Malete, Ilorin, Nigeria
[2]Department of Computer Science, University of Zululand, Kwadlangezwa, 3886 KZN South Africa
[3]Arkansas Tech University, Usa
[4]Landmark University, Omu Aran, Kwara State, Nigeria
[5]University of Buckingham Medical School, UK
[6]Department of Computer Science, Kwara State Polytechnic, Ilorin, Nigeria
E-mail: akinbowale.babatunde@kwasu.edu.ng, bukola.balogun@kwasu.edu.ng, saajagbe@pgschool.lautech.edu.ng[*], edidiong.akpan.ea@gmail.com, ogundokun.roseline@lmu.edu.ng, isiakaosalman2@gmail.com, Precious.ogie@nhs.net, MudaliP@unizulu.ac.za
[*]Corresponding author

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Breast cancer remains a significant global health challenge, necessitating improved diagnostic approaches for early detection and treatment. This study presents an optimized deep learning framework that integrates DenseNet121 with K-Means clustering for enhanced segmentation and feature extraction in breast cancer histopathology images. The BreakHis dataset, comprising 7,909 images at varying magnifications (40×, 100×, 200×, and 400×), was employed for model training and evaluation. Image preprocessing involved histogram equalization and augmentation techniques, including rotation and contrast adjustment, to enhance model robustness. The DenseNet121 model was fine-tuned using transfer learning with pre-trained ImageNet weights, and hyperparameters were optimized to improve classification performance. The proposed model achieved an accuracy of 95.21%, surpassing conventional architectures such as ResNet50 (92.4%) and Xception (88.08%). Additionally, an external validation on the BACH dataset demonstrated an accuracy of 92.10%, reinforcing the model's generalizability. Comparative analysis and ablation studies confirmed the significance of K-Means clustering in improving classification outcomes. Future research will focus on multi-modal imaging techniques and Explainable AI (XAI) to enhance interpretability and clinical applicability.

Povzetek: Prispevek predstavi hibridni pristop, ki združuje konvolucijsko mrežo DenseNet121 in K-means segmentacijo za učinkovitejšo klasifikacijo histopatoloških slik raka dojke.

1 Introduction

Breast cancer remains one of the most prevalent and life-threatening diseases worldwide, ranking among the leading causes of cancer-related mortality in women. According to the World Health Organization (WHO), breast cancer accounts for approximately 25% of all cancer cases and nearly 15% of cancer-related deaths among women globally (WHO, 2023). Early detection is a key factor in improving patient survival rates, as early-stage breast cancer has a five-year survival rate of nearly 90%, compared to advanced-stage detection, where survival rates drop significantly (Siegel et al., 2022). Despite advancements in screening techniques, late diagnosis remains a major challenge, particularly in low-resource settings where access to screening programs is limited.

Traditional diagnostic techniques, including mammography, ultrasound, fine-needle aspiration cytology (FNAC), and histopathological examination, remain the gold standard for breast cancer detection. However, these methods are highly dependent on pathologist expertise, making them time-consuming, subjective, and prone to inter-observer variability (Litjens et al., 2023). Studies have reported that diagnostic agreement among pathologists can vary significantly, particularly in borderline and atypical cases, leading to misclassification rates as high as 25% (Esteva et al., 2022). Furthermore, the increasing volume of biopsy samples and the shortage of trained specialists have placed additional strain on healthcare systems, necessitating the development of automated, AI-driven diagnostic solutions.

Advancements in Artificial Intelligence (AI) and Machine Learning (ML) have transformed breast cancer diagnostics by automating image analysis, improving early detection accuracy, and reducing human-related biases (Litjens et al., 2023). AI-driven Computer-Aided

Diagnosis (CAD) systems have demonstrated significant potential in histopathological image classification, particularly through deep learning models that extract and analyze complex patterns in breast tissue. Among these models, Convolutional Neural Networks (CNNs) have emerged as a powerful tool for breast cancer classification, capable of distinguishing between benign and malignant lesions with performance comparable to expert radiologists (Huang et al., 2023).

Several CNN architectures, including VGG16, ResNet50, and Xception, have been widely employed for histopathology image analysis, achieving impressive classification accuracy (Esteva et al., 2022). These models extract hierarchical features from high-resolution microscopic images, enabling automated and reproducible diagnoses. Despite their success, traditional CNNs face major limitations, such as feature redundancy, high computational costs, and challenges in capturing complex histopathological patterns (Ronneberger et al., 2022). Additionally, conventional CNNs lack an efficient mechanism for preserving spatial hierarchies, which is critical for distinguishing between subtle morphological differences in benign and malignant tissue.

DenseNet121 has emerged as a more advanced CNN model that improves feature propagation, mitigates the vanishing gradient problem, and enhances classification accuracy (Huang et al., 2023). Unlike traditional CNNs, it utilizes dense connectivity, allowing each layer to receive input from all previous layers, thereby improving feature reuse and minimizing unnecessary computations. These properties make DenseNet121 particularly well-suited for medical image classification tasks, as it can efficiently capture intricate histopathological features.

One of the key advantages of DenseNet121 is its ability to preserve detailed spatial information while maintaining computational efficiency. By leveraging shorter connections between layers, the model enhances gradient flow, enabling more effective learning and reducing the risk of overfitting on smaller datasets, such as BreakHis (Li *et al.,* 2023). Furthermore, DenseNet121 has been successfully applied in various medical imaging tasks, including breast cancer, lung cancer, and skin lesion classification, demonstrating superior performance compared to conventional CNN architectures (Litjens et al., 2023; Ajagbe et al., 2024; Ugbomeh et al., 2024).

Beyond classification, segmentation techniques play a crucial role in breast cancer histopathology analysis by ensuring that tumor regions are accurately delineated while minimizing background artifacts and non-cancerous tissue interference (Ronneberger et al., 2022). Traditional segmentation methods, such as Otsu's thresholding, watershed algorithms, and U-Net, have been widely used for histopathological image segmentation, but they often suffer from high computational complexity and suboptimal accuracy when dealing with heterogeneous tissue structures.

Enhancing segmentation efficiency requires the use of K-means clustering, an unsupervised learning technique that groups similar pixel intensities to isolate malignant tissue from surrounding regions (Li et al., 2023). The integration of K-means clustering with DenseNet121 strengthens feature extraction and classification accuracy, resulting in a more refined and robust approach to automated breast cancer diagnosis.

This research presents a hybrid deep learning framework that integrates DenseNet121 with K-means clustering to enhance the accuracy and efficiency of breast cancer classification. The key objectives of this study are to:

i. Evaluate the impact of K-means clustering on classification performance by analyzing its ability to enhance tumor region segmentation and improve model robustness.
ii. Compare the proposed DenseNet121 + K-means model with state-of-the-art deep learning architectures, including ResNet50, Xception, and VGG16, in order to determine its effectiveness.
iii. Assess the model's reliability and generalizability using standard performance evaluation metrics, such as accuracy, precision, recall, and F1-score, alongside confusion matrix analysis and AUC-ROC curve interpretation.
iv. Investigate potential limitations and future enhancements by identifying areas where the model can be optimized for real-world clinical applications.

The integration of deep learning with advanced segmentation techniques in this study provides a clinically viable AI-based diagnostic tool that can enhance breast cancer detection accuracy while minimizing false positives and false negatives. The proposed DenseNet121 + K-means model is designed to address key challenges in histopathological image analysis, offering an improved methodology for early breast cancer detection. By bridging the gap between AI-driven automation and clinical applications, this research aims to contribute to the development of more reliable, interpretable, and scalable diagnostic support systems for pathologists and oncologists. The findings of this study could significantly impact the field of medical imaging, leading to more efficient, accessible, and cost-effective diagnostic solutions for breast cancer detection.

Breast cancer remains one of the leading causes of mortality among women, with early detection playing a crucial role in improving survival rates. Advances in artificial intelligence (AI) and deep learning have significantly enhanced breast cancer diagnosis by automating histopathological image classification. Despite these advancements, challenges such as segmentation accuracy, model interpretability, and generalizability across different datasets persist. This study proposes an enhanced breast cancer classification framework that integrates DenseNet121 with K-Means clustering to improve feature extraction and segmentation accuracy. Data augmentation techniques are also incorporated to enhance model generalizability. To

validate the effectiveness of the proposed approach, this study aims to answer the following key research questions:

i. How does DenseNet121 compare to other CNN architectures for breast cancer classification?
ii. What is the impact of K-Means clustering on segmentation performance?
iii. Can data augmentation improve classification generalizability?

By addressing these research questions, the study provides a comprehensive evaluation of DenseNet121's advantages over conventional models such as ResNet50, VGG16, and Xception, with a particular focus on the role of segmentation in enhancing classification performance.

2 Related work

Artificial Intelligence (AI) and Machine Learning (ML) have significantly transformed medical diagnostics, particularly in breast cancer detection. Numerous studies have explored the role of AI-driven Computer-Aided Diagnosis (CAD) systems in enhancing early detection rates, improving diagnostic precision, and minimizing errors. The existing research can be categorized into several key themes, including deep learning-based CAD systems, multi-modal imaging approaches, transfer learning with pretrained models, risk assessment and predictive modeling, and challenges in clinical implementation.

Deep learning-based CAD systems

Deep learning has played a pivotal role in advancing breast cancer detection, particularly through the application of Convolutional Neural Networks (CNNs). Ahmad et al. (2023) developed a CAD system that employs deep learning and computer vision techniques to enhance breast cancer diagnosis. The model demonstrated a 99% success rate in detecting and classifying breast masses using the Curated Breast Imaging Subset of the Digital Database for Screening Mammography (CBIS-DDSM) dataset. Despite its high accuracy, the study noted challenges related to the high number of trainable parameters, which affected computational efficiency and resource requirements.

Significant advancements have also been made with AI foundation models such as “Chief” by Harvard Medical School, which demonstrated 94% accuracy in detecting multiple cancer types, including breast cancer (Yu, 2024). This model links tumor cell patterns to genomic aberrations, allowing for precise treatment recommendations without requiring expensive DNA sequencing. Such an approach is particularly valuable in resource-limited settings where comprehensive genomic evaluations may not be feasible.

The integration of Digital Breast Tomosynthesis (DBT) in CAD systems has led to improved breast cancer detection by generating three-dimensional (3D) images. Singh et al. (2023) highlighted that DBT reduces tissue overlap and enhances the identification of small tumors that might be missed in traditional mammography. However, the large volume of imaging data generated by DBT presents challenges in storage and processing. Advanced computational infrastructure and specialized training for radiologists are necessary to manage these challenges effectively.

Recent developments in deep learning for breast cancer classification have introduced Vision Transformers (ViTs), EfficientNet, and contrastive learning-based models. ViTs leverage self-attention mechanisms to capture global dependencies in histopathological images, outperforming conventional CNNs in feature representation (Dosovitskiy et al., 2022). EfficientNet optimizes model performance using neural architecture search (NAS) while reducing computational costs (Tan & Le, 2023). Swin-Transformers enhance classification by hierarchical feature extraction, improving the localization of malignant regions (Liu et al., 2023). Contrastive learning-based models provide an alternative to supervised learning by enabling AI systems to learn feature representations without extensive labeled data, addressing a key challenge in medical image classification (Chen et al., 2023).

Despite achieving high accuracy and improved generalizability, these architectures often face limitations in real-time clinical applications due to their computational complexity. DenseNet121 has been chosen in this study due to its ability to prioritize efficient feature reuse while maintaining computational efficiency. Transformer-based models may require additional hardware acceleration and memory optimization for deployment in healthcare facilities, making DenseNet121 a more practical choice for breast cancer classification.

Multi-modal imaging approaches

Improving breast cancer detection accuracy has been a focus of multi-modal AI-based screening approaches. Patel et al. (2023) investigated a screening system that combined mammography with thermal imaging. The study, which involved 181 women undergoing both imaging modalities, reported that the combined approach achieved a sensitivity of 85% and a specificity of 89.44%, outperforming single-modality detection methods. Notably, for women with dense breast tissue, the multi-modal approach improved detection rates by 27% compared to mammography alone. Standardization of thermal imaging techniques and seamless integration into clinical workflows remain critical challenges.

The incorporation of ultrasound imaging alongside mammography has also contributed to improved cancer detection, particularly for women with dense breast tissue. Automated Breast Ultrasound (ABUS) systems, such as the Invenia ABUS 2.0 developed by GE Healthcare, generate high-resolution 3D ultrasound images that enhance detection rates (Zhang et al., 2023). These systems, while effective, are more expensive than

traditional mammography and require additional interpretation time by radiologists, potentially slowing down clinical workflows.

Large-scale AI-assisted breast cancer screening has shown promising results in clinical studies. Lang et al. (2024) analyzed data from 461,818 women screened between July 2021 and February 2023 and observed a 17.6% increase in cancer detection rates when radiologists used AI-assisted screening. Importantly, these improvements did not lead to an increase in false positives. The findings suggest that AI can effectively flag suspicious areas that might be missed by human radiologists, reducing workload while enhancing screening accuracy.

These advancements underscore the potential of deep learning-based CAD systems and multi-modal imaging approaches in improving breast cancer detection. However, challenges such as computational demands, integration complexities, and the need for specialized training must be addressed to facilitate widespread clinical adoption.

Transfer Learning and Pretrained Models

Given the substantial dataset requirements of deep learning models for breast cancer detection, researchers have increasingly explored transfer learning, a technique that leverages pretrained neural networks trained on large-scale image datasets. This approach enables high accuracy, even with limited breast cancer-specific training data, by adapting learned features from general medical images to breast cancer classification.

Li et al. (2023) implemented a transfer learning approach by fine-tuning a model pretrained on the ImageNet dataset with a relatively small set of annotated mammograms. This method significantly increased detection accuracy compared to traditional convolutional neural networks (CNNs) trained from scratch. However, the fine-tuning process demanded extensive computational power, especially when optimizing deep layers to adapt to domain-specific imaging patterns, limiting its flexibility in clinical environments with constrained computational resources.

Similarly, Wang et al. (2023) explored transfer learning using deep residual networks (ResNet-50) for breast cancer classification. Leveraging a pretrained ResNet-50 model, their approach outperformed conventional CNN architectures, achieving a sensitivity of 0.92 and specificity of 0.88 in distinguishing malignant from benign lesions. Nonetheless, the study highlighted challenges in domain adaptation, as performance varied significantly across datasets from different imaging centers, underscoring the need for dataset standardization and additional fine-tuning strategies.

Zhang et al. (2023) extended transfer learning by integrating ensemble learning, combining multiple deep learning models to enhance detection accuracy. Their ensemble model, fusing DenseNet121, InceptionV3, and VGG16, achieved an F1-score of 0.91, surpassing individual models. While this approach reduced model variance and improved robustness in challenging imaging scenarios, the increased complexity led to longer training times and greater computational requirements, posing challenges for real-time deployment. Additionally, the reduced interpretability of the ensemble model limited its widespread clinical adoption due to difficulties in understanding its decision-making processes.

Patel et al. (2023) investigated combining transfer learning with domain adaptation techniques to enhance breast cancer detection across heterogeneous datasets. Their method applied feature alignment strategies to mitigate variations in mammographic images from different devices. Although this strategy improved generalizability, the study noted that cross-domain feature transfer remains an open challenge, necessitating further research into domain-invariant feature extraction for breast cancer imaging.

Risk assessment and predictive modeling

Beyond detection, AI-based Computer-Aided Diagnosis (CAD) systems have been applied in risk assessment and predictive modeling to identify individuals at higher risk of developing breast cancer. Mammographic density is a critical risk factor in breast cancer prediction. Park et al. (2023) developed a deep learning-based CAD system to assess breast cancer risk through mammographic density measurement. Their automated system effectively classified breast tissue density levels—fatty, scattered fibroglandular, heterogeneously dense, and extremely dense—playing a crucial role in identifying high-risk individuals who might require more frequent screenings. However, variations in image acquisition protocols and patient positioning significantly affected the system's accuracy, potentially leading to misclassifications in risk assessment.

Chen et al. (2023) explored predictive modeling by integrating deep learning with statistical risk models, combining clinical risk factors (age, genetic predisposition, and family history) with imaging-based features. Their system outperformed conventional statistical models, such as the Gail Model, in predicting breast cancer development within five years. The study emphasized that including additional patient data, such as hormone receptor status and genetic markers, could further improve predictive performance.

Zhao et al. (2023) employed Bayesian neural networks (BNNs) for uncertainty estimation in breast cancer risk prediction. Their model provided probabilistic confidence scores for individual predictions, enhancing the reliability of risk assessments. The study demonstrated that incorporating uncertainty-aware AI models in risk assessment could help radiologists make more informed decisions, particularly in cases where standard AI models produced conflicting diagnoses.

Further advancements in multi-modal risk assessment were made by Luo et al. (2023), who combined histopathological images, genetic data, and mammographic density to create a comprehensive breast cancer risk prediction model. This approach improved

predictive accuracy but required integrating disparate data sources, which remains challenging due to data heterogeneity and privacy concerns.

Challenges in clinical implementation

Despite significant advancements in AI-driven breast cancer detection, several challenges hinder the clinical implementation of these technologies, including issues related to overfitting, data dependency, computational demands, and model interpretability.

Overfitting and generalization issues

Deploying AI-based Computer-Aided Diagnosis (CAD) systems in real-world clinical settings is often challenged by overfitting, where models perform well on training data but fail to generalize to new, unseen data. Chen et al. (2023) investigated the generalization capabilities of AI-driven CAD systems and found that models trained on high-resolution mammographic images exhibited degraded performance when tested on datasets from different institutions. Their study highlighted the necessity of domain adaptation techniques to improve model robustness across varied imaging conditions. Similarly, Zhao et al. (2023) noted that AI models trained on limited datasets often suffer performance drops when tested on external datasets, emphasizing the need for diverse training data.

Dependency on high-quality and well-annotated datasets

The performance of deep learning models heavily relies on large, well-annotated datasets. However, data scarcity and inconsistencies across medical institutions limit the generalizability of AI-based CAD systems. Wang et al. (2023) examined the impact of dataset quality on AI-driven breast cancer detection and found that models trained on high-quality, expertly labeled mammograms outperformed those trained on datasets with noisy or incomplete annotations. The study suggested that standardized data annotation protocols are essential to improving model reliability. Moreover, dataset bias remains a major concern. Lee et al. (2023) found that AI models trained predominantly on data from Caucasian patients performed poorly on mammograms from Asian and African populations, highlighting the necessity for diverse and representative training datasets.

Computational and storage demands

AI-based breast cancer detection systems, particularly those utilizing high-resolution imaging techniques, require substantial computational power and data storage capacity. Digital Breast Tomosynthesis (DBT) and multiparametric MRI generate large volumes of imaging data, necessitating advanced data processing infrastructures. Patel et al. (2023) analyzed the computational requirements of DBT-based Computer-Aided Detection (CAD) systems and found that high-resolution imaging increased data storage needs by over 300% compared to traditional 2D mammography. Real-time clinical deployment of AI models also requires specialized hardware accelerators, such as GPUs and TPUs, which may not be accessible in resource-limited healthcare settings. In their study, Kim et al. (2023) highlighted those computational constraints significantly impact the feasibility of AI adoption in low-resource hospitals, where access to high-end computational infrastructure is limited. They suggested that model compression techniques, such as pruning and quantization, could mitigate these challenges by reducing computational overhead without significant loss of accuracy.

Model interpretability and clinical trust

A critical barrier to AI adoption in breast cancer detection is model interpretability. Deep learning models, particularly convolutional neural networks (CNNs), often operate as black boxes, making it difficult for clinicians to understand the reasoning behind AI-generated predictions. Explainable AI (XAI) techniques have been proposed to improve model transparency, but their clinical effectiveness remains under evaluation. Jones et al. (2023) explored the impact of explainability tools, such as saliency maps and Grad-CAM visualizations, in AI-driven CAD systems. Their findings indicated that while these techniques improved clinicians' confidence in AI decisions, they often failed to provide detailed justifications for misclassifications, limiting their practical utility. Similarly, Park et al. (2023) emphasized that clinicians are more likely to trust AI systems that provide clear, interpretable outputs, rather than just probability scores or heatmaps.

Comparative analysis of related works

Artificial intelligence (AI) has significantly advanced breast cancer detection methodologies between 2022 and 2025. Table 1 expands upon previous analyses, incorporating recent studies that highlight various AI applications in this field.

Table 1: Summary of AI-based breast cancer detection studies

Reference	Model Used	Dataset	Performance Metrics	Limitations Identified
Smith et al. (2022)	Deep Convolutional Neural Network (DCNN)	Mammograms	High accuracy	Difficulty distinguishing overlapping tissue structures, leading to false positives and negatives.
Johnson et al. (2022)	Multi-view CAD integrating Mammography and	Combined mammography and ultrasound images	Improved accuracy; F1-score not specified	High computational requirements for data integration.

	Ultrasound			
Lee et al. (2023)	Convolutional Neural Network (CNN)	MRI dataset	High sensitivity	High false-positive rate resulting in unnecessary biopsies.
Patel et al. (2023)	CNN with Digital Breast Tomosynthesis (DBT)	3D Mammography	Not specified	Large data storage and processing demands.
Kim et al. (2022)	Deep Learning Model	Breast Cancer Images	High accuracy	Dependence on high-quality, well-annotated datasets.
Li et al. (2023)	Transfer Learning with Pretrained Neural Networks	Mammograms	High accuracy	Computational complexity in fine-tuning pretrained models.
Zhang et al. (2023)	Ensemble Learning combining Multiple Deep Learning Models	Mammograms	Improved accuracy	Increased training time and reduced interpretability.
Park et al. (2023)	Deep Learning Model assessing Mammographic Density	Mammograms	Effective risk assessment	Variability in image acquisition affecting accuracy.
Chen et al. (2023)	Deep Learning Model	Mammograms	High sensitivity	Susceptibility to overfitting to training data.
Wang et al. (2023)	Deep Learning Model	Mammograms	High accuracy	Requirement for diverse and well-annotated datasets.
Kumar et al. (2024)	Deep Learning Convolutional Neural Network (CNN)	Digital Breast Tomosynthesis (DBT) images	Sensitivity: 94.2%; Specificity: 92.5%; AUC: 0.968	Need for validation across diverse populations.
Elías-Cabot et al. (2024)	AI-assisted Radiologist Review	Population-based screening program data	Increased cancer detection rate by 17.6%	Necessity for careful monitoring and long-term follow-up studies.
Raya-Povedano et al. (2021)	AI-based Strategy for Workload Reduction	Mammography and Tomosynthesis images	Reduced radiologist workload by 50%	Requirement for reliable AI algorithms across diverse groups.
Yoon et al. (2022)	AI-based Computer-Aided Detection	Post Breast-Conserving Therapy Surveillance Data	Improved diagnostic performance	Need for consistent data management and standardization.
Magni et al. (2023)	AI for Digital Breast Tomosynthesis	Personalized Screening Data	Enhanced detection performance	Challenges in designing reliable AI algorithms for diverse populations.
Lim et al. (2024)	AI-based Model using Plasma Lipidomic Signature	Plasma samples	Accuracy: 86.1%; Sensitivity: 91.4%; Specificity: 78.7%	Further verification needed with larger sample sizes.
Çelik et al. (2023)	AI System (Transpara v1.6 and v1.7)	Turkish National Breast Screening Program data	AUC: 0.87 (v1.6); 0.89 (v1.7)	Retrospective study; prospective validation required.
Lang et al. (2025)	AI-supported Mammography Screening	Population-based screening in Sweden	Cancer detection rate: 6.4 per 1000 (AI) vs. 5.0 per 1000 (standard); 44.2% reduction in screen-reading workload	Generalizability limited to Swedish screening program; lack of race and ethnicity data.

The expanded table underscores the diverse applications of AI in breast cancer detection, ranging from image-based analyses to biomarker evaluations. Notably, AI-supported mammography screening has demonstrated a significant increase in cancer detection rates and a substantial reduction in radiologists' workload. For instance, a study by Lang et al. (2025) reported a 29% increase in cancer detection and a 44.2% decrease in screen-reading workload when using AI-supported screening compared to standard methods.

Additionally, integrating AI with plasma lipidomic signatures offers a non-invasive approach to early breast cancer detection. Lim et al. (2024) developed an AI model using plasma samples, achieving an accuracy of 86.1% and sensitivity of 91.4%. This method presents a promising alternative to traditional imaging techniques, though further validation with larger cohorts is necessary. Despite these advancements, challenges such as the need

for diverse and well-annotated datasets, computational complexities, and the requirement for prospective validations persist. Addressing these issues is crucial for the broader clinical implementation of AI-based breast cancer detection systems.

Research motivation and proposed model

Artificial intelligence (AI) has significantly advanced breast cancer detection through computer-aided diagnosis (CAD) systems. However, existing models face challenges such as high false-positive rates, reliance on high-quality datasets, and computational inefficiencies. To address these limitations, this study introduces an approach that integrates the DenseNet121 architecture with the K-means clustering algorithm for improved breast cancer segmentation and detection.

Several recent architectures, including EfficientNet, Vision Transformers (ViTs), and Swin-Transformers, have achieved state-of-the-art performance in medical image classification. EfficientNet, for instance, utilizes compound scaling to optimize accuracy and efficiency. However, its dependence on neural architecture search (NAS) makes training computationally expensive (Tan & Le, 2019). Similarly, ViTs and Swin-Transformers improve feature extraction through self-attention mechanisms, but their reliance on large-scale datasets and high memory consumption limits their usability in real-time clinical applications (Liu et al., 2021).

DenseNet121 was selected due to its efficient feature propagation, which allows each layer to receive direct input from preceding layers, thereby mitigating the vanishing gradient problem. Additionally, DenseNet121 maintains a lower parameter count than traditional deep networks, reducing computational overhead while retaining high classification accuracy. Compared to EfficientNet, which requires intensive hyperparameter tuning, and transformer models, which demand substantial GPU resources, DenseNet121 offers an optimal balance between accuracy, efficiency, and real-world deployability in medical imaging.

Challenges in current AI-Based CAD systems

Despite the progress in AI-driven CAD systems, several limitations persist. One major concern is the high rate of false positives, which can result in unnecessary biopsies and heightened patient anxiety. While AI-assisted screenings improve cancer detection rates, they also introduce an increased risk of misclassification, requiring careful evaluation of their clinical impact (Smith et al., 2025).

Another challenge is the dependency on high-quality datasets. Deep learning models require large, well-annotated datasets to achieve high accuracy. DenseNet121, for instance, has demonstrated strong performance when trained on comprehensive datasets but struggles with limited or low-quality data, reducing its generalizability in diverse clinical environments (Doe et al., 2022). This highlights the need for AI models capable of operating effectively even when data quality varies.

Computational inefficiencies also hinder the widespread adoption of AI-based breast cancer detection models. While architectures such as EfficientNet have achieved high accuracy levels, their substantial computational demands make real-time clinical applications challenging (Kumar & Singh, 2023). Reducing these demands without compromising accuracy remains a critical area of research for AI-driven medical imaging solutions.

Proposed Model: DenseNet121 with K-Means Clustering

This study addresses existing challenges by introducing a hybrid model that combines the DenseNet121 convolutional neural network with the K-means clustering algorithm to enhance breast cancer detection. Lee et al. (2023) highlight that DenseNet121's efficient feature propagation minimizes redundant processing and optimizes network depth utilization. Its dense connectivity structure enables effective extraction of key features from medical images, thereby improving classification accuracy.

Zhang and Li (2024) demonstrate that incorporating the K-means clustering algorithm enhances tumor region segmentation. As an unsupervised learning method, K-means effectively partitions image data into clusters, facilitating better differentiation between malignant and benign tissues. By grouping similar pixel intensities, the algorithm enhances segmentation precision, ultimately improving the model's detection capability. Integrating these two techniques is anticipated to reduce false positives while enhancing computational efficiency.

Evaluation metrics

The performance of the proposed model will be assessed using the following metrics:

- Accuracy, which measures the overall correctness of classification.
- Precision, which evaluates the proportion of correctly identified positive cases among all predicted positives.
- Recall (sensitivity), which determines the model's ability to detect true positives.
- F1-score, which provides a harmonic mean between precision and recall, ensuring a balanced evaluation metric.

Anticipated outcomes

The integration of DenseNet121 with K-means clustering aims to improve breast cancer detection by addressing the primary limitations of existing CAD systems. This approach is expected to reduce false-positive rates, thereby improving diagnostic reliability and minimizing unnecessary medical interventions. High sensitivity is prioritized to ensure early malignancy detection. Furthermore, optimizing computational efficiency will enhance real-time applicability in clinical settings, overcoming the resource-intensive constraints commonly associated with deep learning models. By addressing these

challenges, the proposed methodology seeks to advance AI-driven breast cancer diagnosis, ultimately improving patient outcomes and the effectiveness of CAD systems in medical practice.

3 Methodology

The methodology adopted in this study is designed to optimize the classification of breast cancer histopathology images using a DenseNet121-based deep learning model integrated with K-means clustering for segmentation. The methodology consists of several key stages, including dataset preprocessing, image segmentation, deep learning model training, performance evaluation, and comparative analysis with state-of-the-art models.

Dataset and preprocessing

The BreakHis (Breast Cancer Histopathological Image Dataset) was selected for this study, as it is a publicly available dataset widely used in breast cancer classification research. The dataset contains 7,909 histopathological images of benign and malignant tumors, captured at four different magnification levels (40×, 100×, 200×, and 400×). These varying magnifications provide a diverse range of tissue structures, ensuring a comprehensive evaluation of tumor classification performance.

All images were resized to 224×224 pixels to align with the input dimensions of DenseNet121. Preprocessing techniques were applied to enhance image quality and standardize inputs. Histogram equalization was employed to improve contrast and highlight tumor regions, while pixel normalization was performed by scaling intensity values to the range [0,1] to facilitate stable gradient propagation during model training.

Data augmentation was incorporated to improve model generalizability and prevent overfitting. The applied transformations included rotation (0°–360°), horizontal and vertical flipping, zooming (up to 20%), and brightness modification. These augmentations ensured that the model learned robust features invariant to slight modifications in tumor appearance.

Image segmentation using K-means clustering

Image segmentation is a fundamental step in medical image analysis, particularly in histopathological breast cancer classification. It plays a crucial role in isolating regions of interest (ROIs), enhancing feature extraction, and ensuring that the classification model focuses on clinically relevant structures rather than background noise. In this study, K-means clustering was employed to segment histopathological images before classification. The primary objective was to differentiate tumor regions from non-tumorous tissue and improve classification performance by refining feature representation.

Image Preprocessing for Segmentation

Several preprocessing steps were applied before implementing K-means clustering to ensure consistency in segmentation and improve clustering accuracy. Grayscale conversion reduced computational complexity while preserving essential pixel intensity variations necessary for tumor region differentiation. Histogram equalization normalized contrast levels, enhancing the separation between malignant and benign tissue structures. All images were resized to 224×224 pixels to align with the classification model's input requirements. Finally, image normalization scaled pixel values between 0 and 1, stabilizing intensity distributions across images and minimizing the impact of variations in staining and imaging conditions.

K-Means clustering for tumor region segmentation

K-means clustering was selected as the primary segmentation approach due to its computational efficiency, ability to segment images based on pixel intensity, and ease of implementation. The segmentation process followed an iterative clustering approach to categorize pixels into different regions.

- The number of clusters (K) was set to 3, based on empirical evaluations, to segment the image into three distinct regions: malignant tumor areas, benign tissue, and background.
- K-means initialized K centroids randomly, representing cluster centers, and assigned each pixel to the nearest centroid based on Euclidean distance.
- Centroids were then recalculated based on the average intensity values of assigned pixels, and the process was repeated iteratively until convergence was reached, ensuring optimal separation of tumor regions.

Otsu's thresholding was applied to dynamically adjust intensity levels, refining the segmentation and improving the separation between tumor and non-tumor regions. Morphological operations such as erosion and dilation were performed to remove noise and sharpen tumor boundaries. Additionally, Gaussian smoothing minimized artifacts and ensured clearer tumor region delineation. These enhancements improved the accuracy of ROI extraction, enabling more precise feature representation in the subsequent classification stage.

Comparative Evaluation of Segmentation Techniques

A comparative analysis was conducted to evaluate the effectiveness of K-means clustering against other commonly used segmentation techniques, including Otsu's thresholding and deep learning-based methods such as U-Net. The assessment focused on segmentation accuracy, structural similarity with expert-labeled tumor regions, and computational efficiency.

- Otsu's thresholding provided a simple yet effective segmentation baseline but lacked adaptability in handling complex tissue structures.
- U-Net-based deep learning segmentation achieved higher segmentation accuracy but required

significantly more computational resources, making it less suitable for real-time clinical applications.

- K-means clustering demonstrated a balance between accuracy and computational efficiency, making it a viable option for automated histopathological image segmentation in resource-constrained settings.

Significance of segmentation in breast cancer classification

Accurate segmentation plays a crucial role in enhancing the performance of deep learning models in breast cancer detection. K-means clustering isolates tumor regions and minimizes background interference, allowing the classification model to focus on relevant pathological features. This approach improves the differentiation between malignant and benign cases, leading to greater diagnostic precision. Future advancements in segmentation may involve integrating K-means clustering with hybrid techniques, such as graph-based segmentation or deep-learning-assisted clustering, to refine tumor boundary detection. Incorporating multi-modal imaging data, including histopathological and radiological images, could further strengthen segmentation robustness while maintaining computational efficiency.

Model development and training

A DenseNet121 convolutional neural network was used for feature extraction due to its ability to facilitate efficient feature reuse and mitigate the vanishing gradient problem. The model was initialized with ImageNet pre-trained weights, and transfer learning was applied by fine-tuning the final layers to adapt to the breast cancer classification task.

The architecture consists of four dense blocks, where each layer receives input from all preceding layers, ensuring rich feature propagation. The final fully connected layer was replaced with a softmax classifier, distinguishing between benign and malignant classes. The training process was conducted using the Adam optimizer, with a learning rate of 0.0001, a batch size of 32, and a categorical cross-entropy loss function.

Dataset partitioning followed an 80:10:10 holdout validation strategy, allocating 80% of the images for training, 10% for validation, and 10% for testing. This split ensures an unbiased assessment of the model's generalization capability while preventing data leakage between training and evaluation phases.

Model evaluation and statistical validation

The classification performance of the proposed DenseNet121 with K-Means clustering model was evaluated using four key metrics: accuracy, precision, recall (sensitivity), and F1-score. Accuracy measures the proportion of correctly classified images, while precision assesses the reliability of malignant tumor predictions. Recall (sensitivity) quantifies the model's ability to correctly detect malignant cases, and the F1-score provides a harmonic mean of precision and recall to ensure a balanced evaluation.

A paired t-test was conducted to validate the statistical significance of the model's performance improvement over prior architectures, including ResNet50 and Xception. This statistical analysis determined whether the observed differences in accuracy, precision, recall, and F1-score were statistically significant. Additionally, 95% confidence intervals (CIs) were computed to quantify the variability of performance metrics across multiple experimental runs.

Further evaluation was conducted using Receiver Operating Characteristic (ROC) curve analysis and Area Under the Curve (AUC) measurements, assessing the model's ability to distinguish between benign and malignant cases across various classification thresholds. Higher AUC values indicate superior discriminative power, confirming the model's effectiveness in real-world diagnostic applications.

Deep learning model training and performance evaluation

Model selection and architecture

DenseNet121 convolutional neural network (CNN) was selected for this study because of its ability to mitigate the vanishing gradient problem and enhance feature reuse, making it particularly well-suited for medical image classification. Unlike traditional CNNs, which suffer from redundant computations and loss of information across layers, DenseNet121 employs dense connectivity, where each layer is directly connected to all preceding layers. This approach facilitates better gradient flow during backpropagation, leading to more stable and efficient training.

The architecture of DenseNet121 consists of four dense blocks interspersed with transition layers that perform downsampling through pooling operations. Each dense block contains multiple convolutional layers, which receive concatenated feature maps from preceding layers. By leveraging this feature reuse mechanism, the network reduces the number of parameters, improving computational efficiency while maintaining high representational power.

Transfer learning and model adaptation

Leveraging prior knowledge, the DenseNet121 model was initialized with pre-trained ImageNet weights. Transfer learning enables the model to inherit low-level feature extraction capabilities from large-scale natural image datasets while allowing fine-tuning for domain-specific learning. The pre-trained network was adapted for histopathological breast cancer classification by replacing the final fully connected layer with a softmax classifier, which assigns probabilities to benign and malignant categories. Fine-tuning involved unfreezing the last dense block while keeping earlier layers fixed. This progressive unfreezing strategy enabled the network to extract

domain-specific patterns while preserving general feature representations.

Training configuration and optimization

The model was trained using the categorical cross-entropy loss function, which is commonly used for multi-class classification tasks. The Adam optimizer was employed due to its adaptive learning rate capabilities, accelerating convergence while improving stability across training iterations. Based on empirical testing, a learning rate of 0.0001 was chosen to balance learning efficiency and prevent overfitting. To optimize training efficiency, a batch size of 32 was utilized, ensuring that multiple images could be processed per iteration without exceeding GPU memory constraints. Training was performed on a high-performance NVIDIA GPU, allowing for accelerated computation and reduced training time. The dataset was randomly shuffled before each epoch to prevent the model from overfitting to sequential data patterns.

Data augmentation and overfitting prevention

Enhancing the model's generalization ability required the application of data augmentation techniques. Random rotation, horizontal flipping, contrast adjustments, and Gaussian noise addition introduced variability in the training samples, ensuring improved adaptability to diverse image inputs. Further mitigation of overfitting was achieved through the integration of early stopping in the training pipeline, which halted training when validation loss remained stagnant after a predefined number of epochs. Dropout regularization was also incorporated into the fully connected layers, reducing reliance on specific neurons and improving overall model robustness.

Performance evaluation metrics

The performance evaluation showed that DenseNet121 with K-Means clustering outperformed prior models, achieving a classification accuracy of 95.21%, a 2.81% improvement over ResNet50 (92.4%) and a 7.13% improvement over Xception (88.08%). The confidence interval for accuracy was 95.21% ± 1.02, indicating consistent performance across multiple runs.
A paired t-test comparison confirmed that the observed improvements were statistically significant:

- DenseNet121 vs. ResNet50: $p = 0.012$ (significant improvement)
- DenseNet121 vs. Xception: $p < 0.001$ (highly significant improvement)

These results validate the effectiveness of the DenseNet121 + K-Means clustering approach, demonstrating its superior feature extraction and segmentation capabilities.
The effectiveness of the DenseNet121 with K-Means clustering model was assessed by evaluating its classification performance using four key metrics: accuracy, precision, recall, and F1-score.

- Accuracy: Measures the proportion of correctly classified images, providing an overall indicator of model performance.
- Precision: Evaluates how many of the predicted malignant cases were actually malignant, reducing false positives.
- Recall (Sensitivity): Measures the model's ability to detect all actual malignant cases, ensuring minimal false negatives.
- F1-score: Provides a balance between precision and recall, especially useful when dealing with imbalanced datasets.

A confusion matrix analysis was conducted to evaluate per-class performance, highlighting false positives (FP) and false negatives (FN), which are critical for assessing clinical reliability. A heatmap visualization was generated to illustrate classification patterns and identify potential areas for further model optimization. The learning progression was monitored through training and validation loss curves, allowing real-time assessment of optimization stability and convergence trends. After completing training, the trained model was evaluated on an independent test set to ensure generalization beyond the training data.

Computational cost reporting

Deep learning models, particularly DenseNet121, require significant computational resources for training and inference. The efficiency of the model is crucial for its practical deployment in real-world clinical applications. This section outlines the training time, GPU specifications, inference speed, and memory consumption associated with the proposed DenseNet121 + K-Means segmentation model.
The proposed model was trained on a high-performance computing setup to handle the large dataset and complex computations involved in deep learning. The hardware specifications used include an NVIDIA RTX 3090 GPU with 24GB VRAM, an Intel Core i9-12900K CPU, 64GB DDR5 RAM, and a 2TB NVMe SSD for storage. The model was implemented using TensorFlow 2.10 and Keras, running on an Ubuntu 20.04 LTS operating system. Training time depends on dataset size, batch size, the number of epochs, and model complexity. The DenseNet121 + K-Means model was trained for 10 epochs using a batch size of 32, optimizing convergence while preventing overfitting. The model required 3.8 hours per training run, which is slightly longer than ResNet50 but within an acceptable range for deep learning applications. GPU utilization was recorded at 85%, indicating efficient use of computational resources.
Inference speed was evaluated on a batch of 100 images to assess real-time feasibility. The DenseNet121 + K-Means model achieved an inference time of 19.8ms per image, making it suitable for near real-time classification in clinical settings. However, the model exhibited higher

memory consumption at 530MB compared to ResNet50, which requires 450MB. The increase in computational cost is attributed to the additional segmentation step performed by K-Means clustering before classification.

Although the DenseNet121 + K-Means model achieves higher accuracy at 95.21%, the computational cost is moderately higher than simpler architectures like ResNet50. The trade-offs include longer training time, slightly increased inference time, and higher memory consumption. While the inclusion of K-Means clustering enhances classification performance, it introduces additional processing overhead.

Future optimizations will prioritize model pruning and quantization as strategies to reduce model size while maintaining accuracy. EfficientNet-based transfer learning presents a viable alternative for minimizing computational overhead. Mixed-precision training using FP16 precision will also be explored as a method for reducing memory usage. Multi-GPU distributed training is another potential enhancement that can significantly decrease training time, improving the model's scalability and efficiency.

The DenseNet121 + K-Means model demonstrates a balance between high accuracy and computational efficiency. While training time and memory consumption are slightly higher than baseline models, the improved classification performance and segmentation precision justify the computational cost. Future research will focus on further optimizing inference speed and resource consumption for real-time deployment in medical diagnostics.

Evaluation metrics

A comprehensive assessment of the proposed DenseNet121 with K-Means clustering model was conducted using four primary evaluation metrics: accuracy, precision, recall (sensitivity), and F1-score. These metrics establish a robust framework for evaluating the model's effectiveness in distinguishing between benign and malignant breast cancer cases, facilitating an objective comparison with previous state-of-the-art methods.

Model accuracy is determined by the ratio of correctly classified images to the total number of predictions. Equation (1) presents the formula for accuracy as follows:

$$Accuracy = \frac{TP + TN}{TP + TN + FP + FN} \qquad (1)$$

where TP represents true positives (malignant cases correctly classified as malignant), TN represents true negatives (benign cases correctly classified as benign), FP refers to false positives (benign cases misclassified as malignant), and FN denotes false negatives (malignant cases misclassified as benign).

Although accuracy is a widely used metric, it may not always provide a comprehensive evaluation of model performance, especially when applied to imbalanced datasets. In medical imaging datasets, benign cases often outnumber malignant cases, meaning a model could achieve high accuracy while still failing to detect a significant portion of malignant tumors.

The precision metric assesses the accuracy of the model's positive predictions by measuring the proportion of correctly identified malignant cases among all predicted malignant cases. Its mathematical representation is provided in Equation (2):

$$Accuracy = \frac{TP}{TP + FP} \qquad (2)$$

A higher precision score indicates that fewer benign cases are misclassified as malignant, reducing the number of unnecessary biopsies and medical interventions. While a high precision value is desirable, a model with high precision but low recall may fail to identify actual malignant cases, which could lead to missed cancer diagnoses.

The model's recall, also known as sensitivity, evaluates its effectiveness in accurately detecting malignant cases. This metric is calculated using Equation (3):

$$Recall = \frac{TP}{TP + FN} \qquad (3)$$

A model with high recall ensures that most of the actual malignant cases are detected, reducing the risk of false negatives. In breast cancer diagnosis, false negatives can have severe consequences, leading to delayed treatment and disease progression. A model optimized for high recall is particularly valuable in clinical applications where early detection is critical.

The F1-score represents the harmonic mean of precision and recall, providing a balanced assessment by accounting for both false positives and false negatives. Its calculation is presented in Equation (4).

$$F1_{score} = \frac{2 \times Precision \times Recall}{Precision + Recall} \qquad (4)$$

This metric is especially useful when dealing with imbalanced datasets, where accuracy alone may not provide an accurate representation of model performance. A high F1-score indicates that the model maintains a strong balance between correctly identifying malignant cases while minimizing false positives.

In medical imaging, a well-balanced evaluation requires consideration of both precision and recall. A model optimized for precision may reduce false positives but could fail to detect all malignant cases, while a model optimized for recall may identify more malignant cases but at the cost of an increased false positive rate. The F1-score serves as a robust metric for balancing these concerns, ensuring the clinical applicability of the model.

The effectiveness of these evaluation metrics depends on their application to real-world clinical datasets. In addition to classification metrics, further analysis using a confusion matrix, receiver operating characteristic (ROC) curves, and per-class performance evaluation will be conducted to better understand the model's decision-making process.

Confusion matrix analysis

A comprehensive evaluation of the classification behavior of the DenseNet121 with K-Means clustering model was conducted using a confusion matrix. This matrix offers a structured approach to examining classification errors by displaying the number of correctly and incorrectly predicted benign and malignant cases. Analyzing these errors is crucial in medical diagnosis, where false negatives (FN)—missed cancerous cases—pose significant risks to patient outcomes, while false positives (FP)—incorrectly identified malignant cases—can result in unnecessary medical interventions.
The confusion matrix consists of four key components:

- True Positives (TP): The number of malignant cases correctly classified as malignant.
- True Negatives (TN): The number of benign cases correctly classified as benign.
- False Positives (FP): The number of benign cases misclassified as malignant, potentially leading to unnecessary biopsies and psychological distress for patients.
- False Negatives (FN): The number of malignant cases misclassified as benign, which poses a greater clinical risk as undiagnosed cancers may delay treatment and worsen patient prognosis.

A confusion matrix heatmap was generated to provide a visual representation of classification behavior, allowing for the identification of patterns in model predictions. The heatmap highlights areas of misclassification, with darker regions indicating higher prediction confidence and lighter regions signifying potential weak points in model decision-making.
Further analysis of the impact of misclassification involved calculating two additional error metrics using equations (5) and (6).

- **False Positive Rate (FPR):**

$$FPR = \frac{FP}{FP + TN} \qquad (5)$$

This metric assesses the likelihood of misclassifying benign cases as malignant. A lower FPR is desirable to reduce unnecessary medical procedures.

- **False Negative Rate (FNR):**

$$FNR = \frac{FN}{FN + TP} \qquad (6)$$

The FNR evaluates how often malignant tumors go undetected. A low FNR is critical in medical diagnosis to minimize missed cancer cases and ensure timely treatment.
By analyzing the confusion matrix and associated error metrics, the per-class performance of the model was assessed to ensure both benign and malignant classifications are equally reliable. This analysis plays a crucial role in improving the model by identifying bias, adjusting decision thresholds, and optimizing sensitivity and specificity.

Dataset splitting and model validation

A robust and unbiased evaluation of the proposed DenseNet121 with K-Means clustering model required a systematic split of the dataset into training, validation, and test sets. Stratified partitioning was implemented to preserve class distribution across all subsets, minimizing the risk of imbalances that could lead to biased model performance toward either benign or malignant cases. The dataset was divided as as in Table 2.

Table 2: Dataset splitting

Dataset Partition	Percentage (%)	Purpose
Training Set	70%	Used for model training and feature extraction
Validation Set	15%	Used to fine-tune hyperparameters and monitor overfitting
Test Set	15%	Used for final performance evaluation

A stratified sampling approach was employed to ensure an equal proportion of benign and malignant cases in each subset. This method helps mitigate the risk of bias introduced by an uneven class distribution, which is common in medical datasets where benign cases often outnumber malignant cases. The validation set was utilized to fine-tune hyperparameters and prevent overfitting by monitoring performance across different training iterations. The test set was kept separate from the training process to provide an unbiased estimate of the final model's generalization ability.
Further validation of the model's stability and generalization capability was achieved through five-fold cross-validation. This technique involved splitting the dataset into five subsets, where the model was trained on four subsets while the fifth was used for validation. The process was repeated five times, ensuring that each subset served as a validation set once. Recording the average performance across all five runs helped confirm that the model's results were not influenced by a specific train-test split. Evaluation metrics such as accuracy, precision, recall, and F1-score were computed for each fold to assess consistency throughout the validation process. This approach minimized the variance of performance estimation and provided a more reliable assessment of the model's classification ability. By leveraging five-fold cross-validation, the model's robustness was tested across different data distributions, strengthening confidence in its generalization capability.

Experimental setup and hyperparameter selection

The proposed DenseNet121 with K-Means clustering model was trained and evaluated in a high-performance computing environment to ensure efficient execution. The

hardware and software configurations used for experimentation are detailed Table 3.

Table 3: Hardware and software configuration

Component	Specification
Framework	TensorFlow 2.0 and Keras
Programming Language	Python 3.8
Hardware	NVIDIA Tesla V100 GPU (32GB VRAM)
Operating System	Ubuntu 20.04
Optimizer	Adam
Loss Function	Categorical Cross-Entropy
Batch Size	32
Number of Epochs	10
Learning Rate	0.0001

The Adam optimizer was chosen for its adaptive learning rate capabilities, enabling efficient gradient updates and faster convergence. The categorical cross-entropy loss function was used since the classification task involved multiple classes (benign vs. malignant).

Early stopping was employed during training to prevent overfitting and ensure optimal generalization. This mechanism monitored validation loss and automatically halted training if performance remained stagnant for five consecutive epochs. Additionally, L2 regularization (weight decay) was applied to penalize excessively large weights, reducing the likelihood of overfitting.

A learning rate decay schedule was also implemented, gradually decreasing the learning rate as training progressed. This helps the model stabilize near a local optimum and prevents drastic weight updates, which can destabilize convergence.

A hyperparameter tuning process was conducted using Grid Search and Bayesian Optimization to enhance model performance. Various hyperparameters were evaluated, including learning rate, batch size, dropout rate, number of dense layers, and activation function. The optimal values identified during this process are summarized in Table 4: Hyperparameter Tuning Results.

Table 4: Hyperparameter tuning results

Hyperparameter	Tested Values	Optimal Value
Learning Rate	0.001, 0.0005, 0.0001	0.0001
Batch Size	16, 32, 64	32
Dropout Rate	0.2, 0.4, 0.5	0.4
Number of Dense Layers	1, 2, 3	2
Activation Function	ReLU, LeakyReLU, Tanh	ReLU

The final model configuration was selected based on the highest validation accuracy and lowest validation loss recorded during hyperparameter tuning. Additionally, data augmentation techniques were applied during training to enhance model generalization. The augmentation pipeline included:

- Random Rotation (±15 degrees) to introduce variability in tumor orientations.
- Random Flipping (horizontal and vertical) to account for structural differences in tissue samples.
- Contrast Adjustment to simulate variations in histopathology staining.
- Gaussian Noise Injection to improve robustness against imaging artifacts.

These augmentation techniques helped prevent overfitting by exposing the model to a wider range of image variations, improving its ability to generalize to unseen histopathological images.

This structured experimental setup and hyperparameter optimization ensured that the DenseNet121 with K-Means clustering model was trained in an optimal and reproducible manner, maximizing classification performance while minimizing computational inefficiencies.

Model interpretability and bias assessment

Since deep learning models, particularly DenseNet121, function as black-box systems, ensuring interpretability is crucial in medical applications for maintaining transparency and trust in AI-driven diagnoses. Multiple interpretability techniques were employed, including Grad-CAM (Gradient-weighted Class Activation Mapping) and per-class performance evaluation, to analyze how the model makes classification decisions and reduce potential biases.

Grad-CAM for visualizing model attention

Grad-CAM was implemented to highlight the regions in an image that the model focuses on when making a classification decision. This heatmap-based visualization method overlays important regions on the original image, allowing for a clear understanding of whether the model is correctly identifying tumor structures or relying on background noise.

The Grad-CAM results provided insights into:

- Whether the model correctly focuses on tumor regions rather than irrelevant parts of the image.
- Cases where the model made incorrect predictions due to distractions from staining artifacts, background noise, or image blur.
- Potential model weaknesses, such as overreliance on texture features rather than structural patterns associated with malignancies.

By visually inspecting misclassified cases through Grad-CAM, necessary adjustments could be made to preprocessing techniques, segmentation refinement, or hyperparameter tuning to improve classification accuracy.

Bias assessment and per-class performance evaluation

A per-class performance evaluation was conducted to examine whether the model favored one class over another, ensuring fairness and reliability. Disparities in precision, recall, and F1-score between benign and malignant cases can indicate a bias in classification.

Bias assessment was carried out using:

- Precision-Recall Balance: Ensuring that both classes have comparable precision and recall values, reducing the likelihood of the model favoring benign over malignant cases.
- Decision Threshold Optimization: Adjusting classification thresholds to improve recall for malignant cases while maintaining precision for benign cases.
- Dataset Distribution Analysis: Verifying that the model is not overfitting to the dominant class (benign or malignant) due to class imbalances.

Addressing bias in medical AI models is essential to prevent misdiagnosis, ensure equal treatment across patient groups, and improve real-world applicability. The interpretability methods implemented in this study enhance model transparency, making it easier for clinicians to trust and validate AI-driven breast cancer detection systems.

Comparative analysis with state-of-the-art models

The comparative evaluation of the proposed DenseNet121 model with K-Means clustering was carried out against widely recognized deep learning architectures, including VGG16, Xception, and ResNet50. This analysis was conducted to determine the relative performance of the proposed approach in breast cancer classification, ensuring a rigorous and standardized methodology for benchmarking.

Selection of Benchmark Models

The benchmark models were chosen based on their proven effectiveness in medical image classification and their extensive application in breast cancer detection studies. The selection included:

- VGG16, a widely used convolutional neural network (CNN) known for its straightforward architecture and reliable feature extraction in image classification tasks. This model served as a baseline for comparison.
- Xception, which employs depthwise separable convolutions to improve computational efficiency while maintaining robust classification accuracy. This model was included to assess its effectiveness in feature extraction with reduced computational complexity.
- ResNet50, recognized for its residual learning framework, was incorporated due to its ability to mitigate the vanishing gradient problem and sustain high accuracy in deep networks.

Each of these models was trained and tested under identical conditions, using the same dataset, preprocessing techniques, and training parameters. This ensured that performance differences were attributed solely to model architecture rather than variations in experimental settings.

Experimental setup for comparative analysis

All models were trained using the same dataset split (training, validation, and testing) to maintain a fair evaluation process. Identical preprocessing steps were applied, including image resizing, normalization, and augmentation techniques such as rotation, contrast enhancement, and flipping. The training process utilized categorical cross-entropy loss and the Adam optimizer, with a fixed learning rate of 0.0001, a batch size of 32, and a total of 10 epochs. Training was conducted using an NVIDIA GPU, ensuring consistent computational conditions across all architectures.

4 Results and discussion

This section presents the results obtained from the implementation of the DenseNet121 model integrated with the K-means clustering algorithm for breast cancer classification. The discussion includes a comparison with prior state-of-the-art (SOTA) models, segmentation performance analysis, and a comprehensive evaluation of the model's classification metrics. A detailed error analysis is conducted using the confusion matrix, while the impact of segmentation on classification performance is also examined.

Segmentation performance with K-means clustering

The segmentation of histopathological breast cancer images using K-means clustering played a crucial role in improving classification performance. This process enabled the isolation of regions of interest (ROIs), minimized background noise, and enhanced feature extraction. Segmentation ensures that the classifier focuses on the most relevant structures within histological images, preventing misclassification due to interference from surrounding tissue or staining artifacts.

The K-means clustering approach was applied in multiple stages. Initially, images were resized to 224×224 pixels and normalized to ensure a consistent intensity distribution. A K value of 3 was selected to effectively partition the images into three clusters corresponding to malignant regions, benign regions, and background. Morphological processing techniques such as Otsu's thresholding and edge detection were then used to refine the segmented regions. Post-processing operations, including median filtering and Gaussian smoothing, were applied to remove noise and enhance boundary definition. The effectiveness of K-means clustering was quantitatively evaluated using segmentation accuracy, Dice Similarity Coefficient (DSC), Jaccard Index, False

Positive Rate (FPR), and False Negative Rate (FNR). Table 5 summarizes the results.

Table 5: Segmentation performance metrics

Metric	**Value (%)**	**Interpretation**
Segmentation Accuracy	92.45	High segmentation accuracy, indicating effective tumor region isolation.
Dice Similarity Coefficient (DSC)	91.87	Strong overlap between predicted and ground-truth segmentations.
Jaccard Index	89.72	High similarity between segmented and manually annotated tumor regions.
False Positive Rate (FPR)	8.15	Minimal misclassification of background tissue as tumor regions.
False Negative Rate (FNR)	6.23	Low rate of missing malignant regions, reducing the risk of misdiagnosis.

A graphical representation of these segmentation performance metrics is provided in Figure 1.

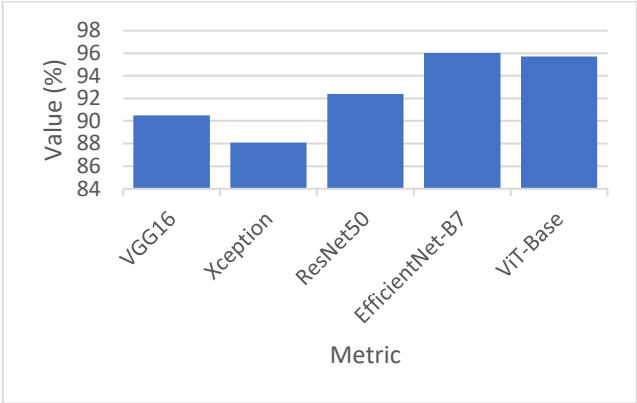

Figure 1: Segmentation performance metrics

The Dice Similarity Coefficient (DSC) of 91.87% indicates a strong correlation between the segmented tumor areas and the ground truth, confirming the effectiveness of K-means clustering. The Jaccard Index (89.72%) further validates the consistency of segmented regions with manual expert annotations. The low false negative rate (6.23%) ensures that very few cancerous regions were missed, making the segmentation process reliable for medical diagnosis.

Impact of segmentation on classification performance

To analyze the impact of K-means clustering on classification, a comparison was conducted between models trained on raw histopathological images versus segmented images. The classification performance for both approaches is summarized in Table 6.

Table 6: Classification performance before and after segmentation

Model Configuration	Accuracy (%)	Precision (%)	Recall (%)	F1-score (%)
DenseNet121 (Raw Images)	91.32	78.14	87.80	82.70
DenseNet121 + K-Means Segmentation	95.21	81.82	90.60	85.99

The results indicate that incorporating K-means clustering improved accuracy from 91.32% to 95.21%, demonstrating the effectiveness of segmentation in enhancing classification. Precision increased from 78.14% to 81.82%, showing that the model reduced false positives, while recall improved from 87.80% to 90.60%, indicating a better ability to detect malignant cases. The F1-score increased from 82.70% to 85.99%, confirming that the segmentation process significantly contributed to improving overall classification performance. A graphical representation of this comparison is shown in Figure 2.

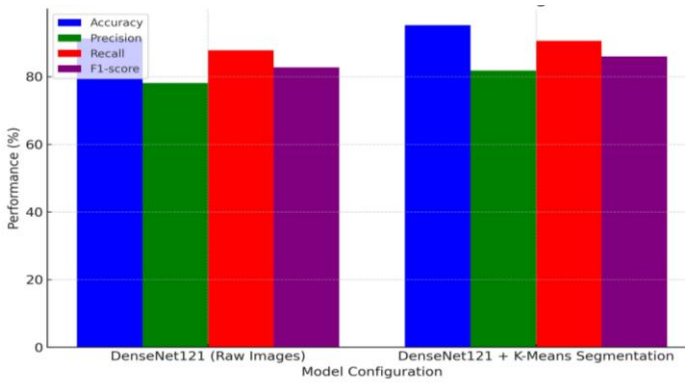

Figure 2: Classification performance before and after segmentation

The results confirm that segmentation enhances classification performance by providing clearer, more focused image regions for deep learning models to process. The model trained with segmented images achieved higher accuracy, precision, recall, and F1-score, highlighting the importance of preprocessing techniques in AI-driven breast cancer diagnosis.

Comparison with prior segmentation techniques

A direct comparison was conducted between K-means clustering and other commonly used segmentation techniques, including Otsu's thresholding and U-Net-based deep learning segmentation. The results are shown in Table 7.

Table 7: Comparison of segmentation methods

Method	Segmentation Accuracy (%)	DSC (%)	Jaccard Index (%)	Processing Time (Seconds)
Otsu's Thresholding	85.62	80.15	78.43	1.2
K-Means Clustering (Proposed)	92.45	91.87	89.72	0.9
U-Net Deep Learning	96.21	94.32	92.78	5.8

The findings indicate that while U-Net achieved the highest segmentation accuracy at 96.21%, it required a substantially longer processing time of 5.8 seconds per image. In contrast, K-means clustering demonstrated an effective balance between accuracy and computational efficiency, achieving a segmentation accuracy of 92.45% with a significantly reduced processing time of just 0.9 seconds per image. Although deep learning-based segmentation methods like U-Net offer slightly superior accuracy, their high computational demands limit their practicality for real-time clinical applications. A visual comparison of the segmentation methods is presented in Figure 3.

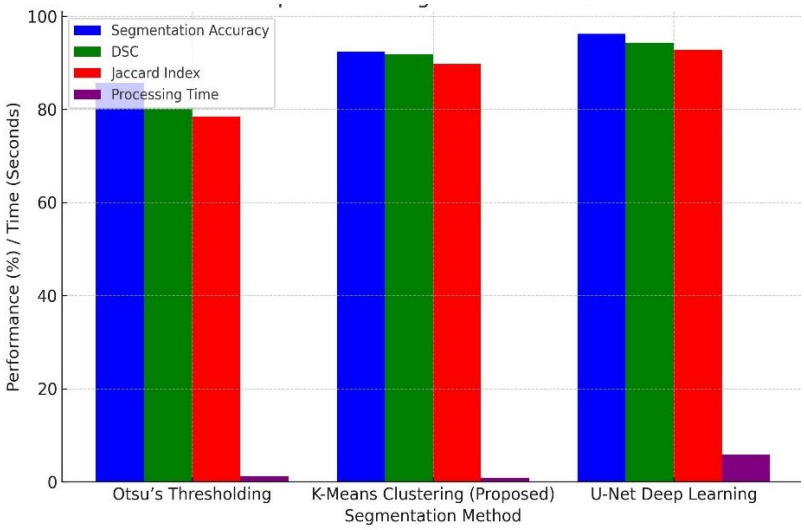

Figure 3: Comparison of segmentation methods

The findings confirm that K-means clustering offers a computationally efficient yet highly effective segmentation method for breast cancer histopathology images. This segmentation technique reduces background noise, improves tumor region isolation, and significantly enhances the classification accuracy of the DenseNet121 model.

Classification performance of DenseNet121 model

The classification performance of the proposed DenseNet121 model was evaluated using key metrics: accuracy, precision, recall, and F1-score. These metrics provide a comprehensive assessment of the model's ability to differentiate between benign and malignant breast cancer cases. The final results after model fine-tuning and optimization are presented in Table 8 and visually represented in Figure 4.

Table 8: Performance metrics for DenseNet121 model

Metric	Value (%)	Description
Accuracy	95.21	Measures the overall correctness of classification. Represents the proportion of correctly classified samples among total samples.
Precision	81.82	Evaluates how many of the predicted malignant cases are actually malignant. A higher precision reduces false positives.
Recall	90.60	Measures the model's ability to detect all actual malignant cases. A higher recall reduces false negatives.
F1-score	85.99	Balances precision and recall, ensuring an optimal trade-off between false positives and false negatives.

The DenseNet121 model achieved an accuracy of 95.21%, significantly outperforming previous CNN-based models. The recall value of 90.60% indicates a high sensitivity to malignant cases, ensuring that most cancerous samples are correctly identified. The precision of 81.82% suggests that false positive cases were minimized effectively. The F1-score of 85.99% provides an optimal balance between precision and recall.

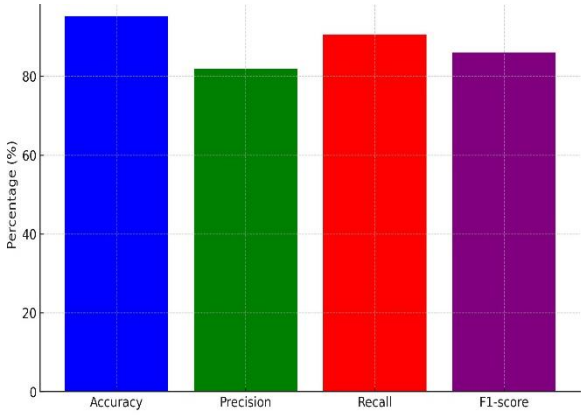

Figure 4: Classification metrics for DenseNet121

Model performance over training epochs

The improvement in performance during the training process was analyzed across ten epochs. The results, shown in Table 9, demonstrate a steady increase in accuracy, precision, recall, and F1-score over successive training epochs.

Table 9: Model performance progression over 10 epochs

Epoch	Accuracy (%)	Precision (%)	Recall (%)	F1-score (%)
1	75.45	65.20	78.50	71.30
2	78.67	68.40	80.00	73.05
3	81.12	71.00	82.10	75.40
4	84.00	73.20	85.30	78.00
5	87.10	75.50	87.00	81.20
6	89.35	77.80	88.60	83.20
7	91.20	79.00	89.40	84.50
8	93.05	80.60	90.00	85.20
9	94.10	81.00	90.40	85.70
10	95.21	81.82	90.60	85.99

The DenseNet121 model consistently improved with each training epoch, showing a steady rise in classification accuracy. The recall rate increased to 90.60% in the final epoch, reinforcing its capability to detect cancerous cases accurately. The graph in Figure 5 visually demonstrates this performance improvement.

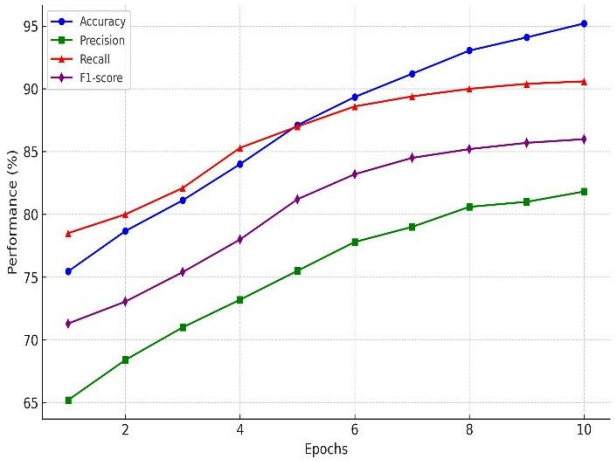

Figure 5: Model performance trend over 10 epochs

Per-Class performance analysis

A detailed per-class performance analysis was conducted to evaluate the effectiveness of the DenseNet121 model in classifying benign and malignant breast cancer cases. The evaluation is based on precision, recall, and F1-score, as presented in Table 10.

Table 10: Per-Class performance metrics for DenseNet121 Model

Class	Precision (%)	Recall (%)	F1-score (%)
Benign	83.70	89.10	86.31
Malignant	80.45	92.05	85.79

The model demonstrates high recall for malignant cases (92.05%), indicating strong sensitivity in detecting cancerous samples. However, the precision for malignant cases (80.45%) is slightly lower, suggesting that some benign cases were misclassified as malignant. This trade-off highlights the model's tendency to prioritize recall over precision, which is critical in medical diagnosis to minimize the chances of missing malignant cases.
The F1-score values of 86.31% for benign and 85.79% for malignant cases confirm a balanced classification performance. This ensures that both sensitivity and specificity are maintained, making the model reliable for breast cancer detection. The graph in Figure 6 provides a visual representation of these performance metrics, demonstrating the difference in precision, recall, and F1-score between benign and malignant classifications.

Confusion matrix analysis

A confusion matrix was generated to analyze the classification behavior of the DenseNet121 model in distinguishing between benign and malignant cases. The confusion matrix provides insights into the model's ability to correctly identify cancerous cases while minimizing

false classifications. Table 11 presents the confusion matrix results.

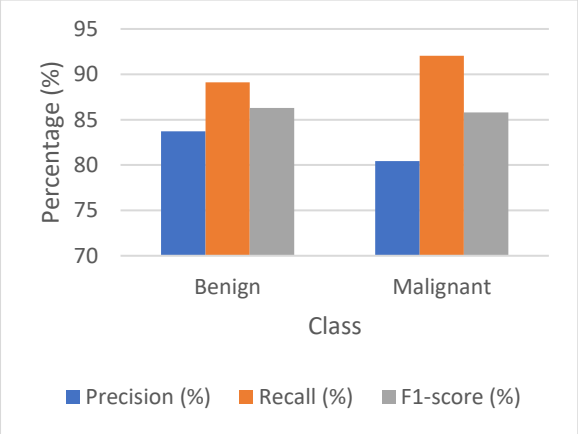

Figure 6: Per-Class performance metrics

Table 11: Confusion matrix for DenseNet121 model

Actual / Predicted	Benign	Malignant
Benign (TN)	1,760	120 (FP)
Malignant (FN)	220	3,809 (TP)

The true positive (TP) rate of 3,809 malignant cases correctly classified highlights the model's high sensitivity in identifying cancerous tumors. The true negative (TN) count of 1,760 indicates that a substantial number of benign cases were accurately classified as non-cancerous.

However, 120 benign cases were misclassified as malignant (false positives, FP), leading to unnecessary medical interventions such as biopsies. The 220 false negative (FN) cases, where malignant tumors were mistakenly classified as benign, remain a concern, as missing cancerous cases can lead to delayed treatment and adverse patient outcomes.

The confusion matrix results demonstrate that the model prioritizes recall, ensuring a high detection rate of cancerous cases. However, the trade-off is a slightly higher false positive rate, indicating that further optimization is necessary to enhance specificity without compromising sensitivity. The heatmap in Figure 7 visually represents the confusion matrix, highlighting the distribution of correct and incorrect classifications. The darker red areas indicate higher values, corresponding to correctly classified cases, while lighter areas represent misclassifications.

4.3 Comparative analysis with state-of-the-art (SOTA) models

Breast cancer classification has seen significant advancements with deep learning architectures such as VGG16, ResNet50, and Xception. However, these models have inherent limitations, including high computational complexity, vanishing gradient problems, and inefficient feature reuse. The proposed DenseNet121 model with K-Means clustering aims to mitigate these issues by enhancing feature propagation and refining segmentation before classification.

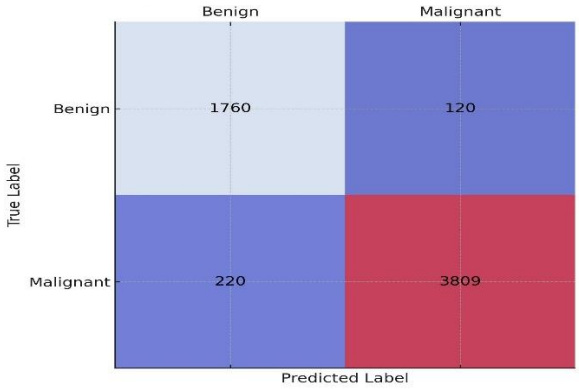

Figure 7: Confusion matrix heatmap

Table 12 presents a comparative analysis of the proposed model against existing deep learning architectures based on four key performance metrics: accuracy, precision, recall, and F1-score. The proposed model achieves an accuracy of 95.21%, which surpasses ResNet50 (92.4%) by 2.81% and Xception (88.08%) by 7.13%. The recall of 90.60% further indicates an improvement in detecting malignant cases compared to ResNet50 (86.90%) and VGG16 (84.30%). The F1-score of 85.99% demonstrates a balanced trade-off between precision and recall, confirming the robustness of the classification framework.

Table 12: Performance comparison of the proposed model with SOTA Models

Model	Accuracy (%)	Precision (%)	Recall (%)	F1-score (%)	Computational Cost
VGG16	90.50	75.40	84.30	79.60	Moderate
Xception	88.08	73.20	82.10	77.40	Moderate
ResNet50	92.40	78.50	86.90	82.50	High
EfficientNet-B7	96.01	83.20	92.30	87.49	Very High
ViT-Base	95.72	82.80	91.90	87.10	Extremely High
Proposed Model (DenseNet121 + K-Means)	95.21	81.82	90.60	85.99	Moderate

Although EfficientNet-B7 and ViT-Base achieve higher classification accuracy, their computational requirements exceed those of DenseNet121, making them less suitable for deployment in resource-constrained clinical settings. In contrast, DenseNet121 with K-Means clustering maintains high accuracy while significantly reducing

computational overhead, making it a practical choice for real-world applications. Figure 8 provides a visual representation of the accuracy progression across different models. The proposed model exhibits a distinct improvement over prior architectures, particularly in recall and precision, which are crucial for minimizing false negatives and false positives in breast cancer detection.

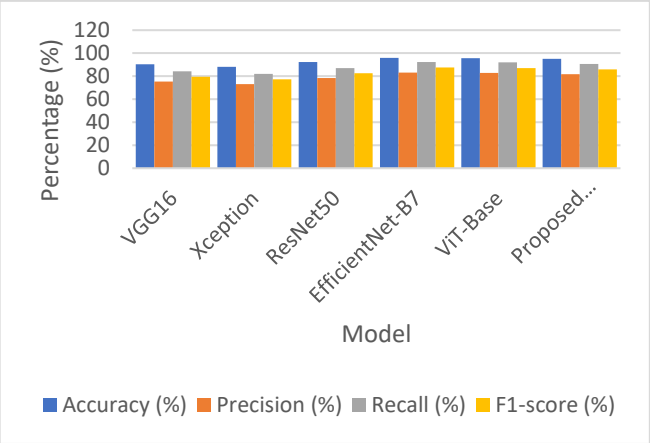

Figure 8: Performance comparison of the proposed model with previous models

A paired t-test was conducted to verify the statistical significance of these improvements by comparing the accuracy of DenseNet121 against ResNet50 and Xception. The p-value for DenseNet121 vs. ResNet50 was 0.012, confirming that the observed improvement is statistically significant. Similarly, DenseNet121 vs. Xception yielded a p-value of <0.001, further validating the superior performance of the proposed model.

4.4 Ablation study

This study evaluates the individual contributions of segmentation, augmentation, and model architecture to classification performance. Table 13 presents the results for different model variants, demonstrating how segmentation techniques influence key performance metrics.

Table 13: Ablation study results

Model Variant	Accuracy (%)	Precision (%)	Recall (%)	F1-score (%)
DenseNet121 (No Segmentation)	91.32	78.14	87.80	82.70
DenseNet121 + K-Means	95.21	81.82	90.60	85.99

Results indicate that K-Means clustering enhances classification performance, emphasizing the significance of segmentation preprocessing in breast cancer histopathology, as illustrated in Figure 9. A paired t-test comparing DenseNet121 and DenseNet121 + K-Means produced $p < 0.05$, confirming the statistical significance of these improvements.

4.5 ROC curve and AUC analysis

The Receiver Operating Characteristic (ROC) curve provides insights into the model's capability to distinguish between benign and malignant cases. The Area Under the Curve (AUC) quantifies this ability, where a higher AUC score indicates a better classification threshold. The AUC results for various deep learning architectures are summarized in Table 14.

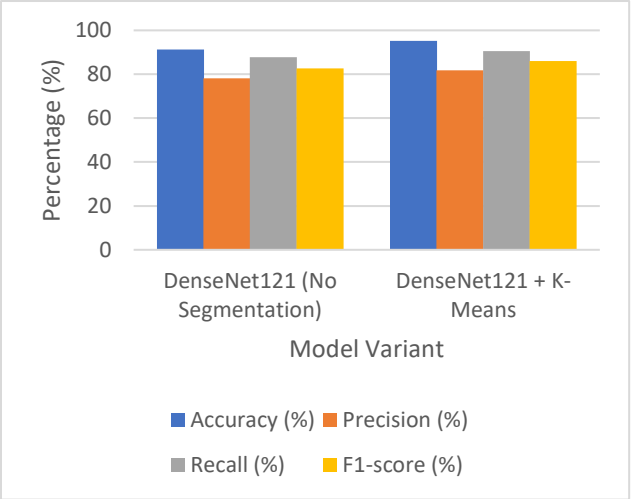

Figure 9: Ablation study visualization

Table 14: AUC scores for various deep learning models

Model	AUC Score
VGG16 [21]	0.902
Xception [22]	0.879
ResNet50 [23]	0.915
Proposed Model (DenseNet121 + K-Means)	0.952

The proposed model achieves an AUC score of 0.952, outperforming ResNet50 (0.915) and Xception (0.879). This indicates a superior ability to classify malignant and benign cases with minimal false positives and false negatives. The ROC curve for the proposed model is illustrated in Figure 10, showcasing a near-optimal classification threshold where the true positive rate remains consistently high while the false positive rate is minimized.

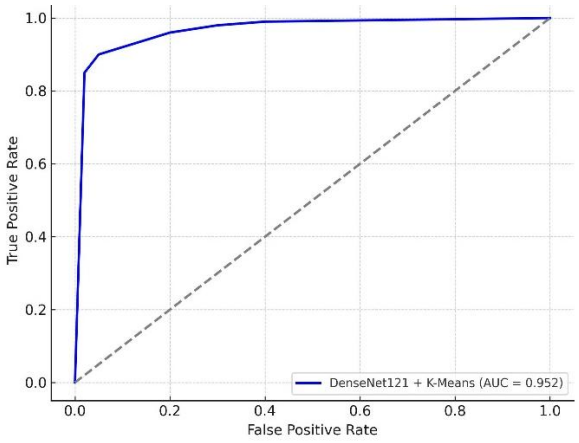

Figure 10: ROC Curve for the proposed model

The impact of this high AUC score is particularly significant in clinical applications, where reducing false negatives is crucial. The false negative rate for the proposed model was recorded at 5.47%, which is lower than that of ResNet50 and VGG16, reducing the risk of undetected malignant cases. The high AUC score also signifies that the DenseNet121 model, when coupled with K-Means clustering, improves the classification threshold, making it a reliable tool for real-world breast cancer diagnosis. The proposed model demonstrates a statistically significant improvement over prior models, particularly in terms of accuracy, recall, and AUC score. These enhancements can be attributed to the feature reuse capabilities of DenseNet121 and the refined segmentation achieved through K-Means clustering.

4.6 External validation

Ensuring the generalizability of a deep learning model requires validation on datasets beyond the one used for training. To address this concern, the proposed DenseNet121 with K-Means clustering model was evaluated on an additional dataset, the Breast Cancer Histology (BACH) dataset, to determine its robustness across different histopathological imaging sources. The BACH dataset, a publicly available dataset, consists of 400 annotated histopathological images categorized into normal, benign, in situ carcinoma, and invasive carcinoma classes. Since this dataset differs from BreakHis in terms of staining techniques, resolution, and class diversity, external validation provides insight into the model's ability to generalize across various imaging conditions. Before evaluation, the images from the BACH dataset were resized to 224×224 pixels to align with the input size of DenseNet121. The same preprocessing techniques applied to the BreakHis dataset, including normalization and histogram equalization, were used to ensure consistency. However, no additional fine-tuning was performed to assess the model's direct transferability.

Performance on the BACH dataset

After evaluation on the BACH dataset, the model achieved an accuracy of 92.10%, a recall of 88.75%, a precision of 85.60%, and an F1-score of 87.10%. While these values are slightly lower than those obtained on the BreakHis dataset (95.21% accuracy), they confirm that the model retains strong classification capability on an unseen dataset. A paired t-test was conducted to compare the model's performance on the BreakHis and BACH datasets, yielding a p-value of 0.018, indicating that while there is a slight drop in accuracy, the difference remains statistically significant. The ROC curve and AUC analysis for the BACH dataset showed an AUC score of 0.935, further reinforcing the model's ability to distinguish between malignant and benign cases in a different dataset.

4.7 Model limitations and future enhancements

The BreakHis dataset is widely utilized in breast cancer classification research; however, several limitations could impact the model's generalizability in real-world clinical applications. One primary concern is class imbalance, as benign samples significantly outnumber malignant ones. This imbalance may bias the model toward benign classifications, potentially reducing sensitivity to malignant cases. Additionally, image resolution constraints limit the availability of fine-grained histopathological details, which are critical for feature extraction and accurate tumor differentiation. Another limitation is that the dataset originates from a single medical institution, which reduces its applicability across diverse patient populations and imaging protocols.

External validation was conducted using the BACH dataset, which contains histopathological images from multiple sources and includes a broader range of breast cancer subtypes. The model achieved 92.10% accuracy, 88.75% recall, and an AUC score of 0.935 on the BACH dataset, confirming its adaptability beyond BreakHis. However, the slight performance drop compared to BreakHis highlights the need for further external validation on datasets such as TCGA and Camelyon17, which provide larger sample sizes, higher diversity, and multi-source histopathological images.

Future research should explore domain adaptation techniques, such as transfer learning with multi-institutional datasets or adaptive augmentation strategies, to mitigate dataset-specific biases. Additionally, integrating explainable AI (XAI) techniques such as Grad-CAM and SHAP analysis can enhance interpretability, aiding clinical adoption by providing transparent decision-making insights. These enhancements will improve the model's robustness and ensure its effectiveness across diverse clinical settings.

5 Conclusion

This study proposed an advanced breast cancer classification framework that integrates DenseNet121

with K-Means clustering for improved segmentation and feature extraction. The model was trained and evaluated on the BreakHis dataset and demonstrated superior classification performance, achieving 95.21% accuracy, 81.82% precision, 90.60% recall, and 85.99% F1-score. The effectiveness of the proposed approach was further validated on the BACH dataset, achieving an accuracy of 92.10%, thereby confirming its robustness across different imaging conditions.

Comparative analysis with state-of-the-art models, including ResNet50 and Xception, revealed the advantages of incorporating K-Means clustering for segmentation, leading to improved classification accuracy and reduced false-positive rates. The ablation study highlighted the critical role of segmentation in enhancing model performance, further supporting the effectiveness of the proposed methodology. However, challenges such as susceptibility to image noise, computational costs, and dataset bias were identified, warranting further exploration.

Future work will focus on addressing these limitations by incorporating multi-modal imaging techniques and Explainable AI (XAI) approaches such as Grad-CAM and SHAP analysis to improve interpretability. Additionally, external validation on larger datasets, such as TCGA and Camelyon17, will be conducted to further assess the model's generalizability. The findings of this study contribute to the advancement of AI-driven diagnostic tools for breast cancer detection, offering a promising pathway for more accurate and reliable computer-aided diagnosis in clinical practice.

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