

Systematic Review: Deep Learning and Adaptive Thresholding for Breast Cancer Histopathology Image Analysis: Challenges, Innovations, and Clinical Integration

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Systematic Review: Deep Learning and Adaptive Thresholding for Breast Cancer Histopathology Image Analysis: Challenges, Innovations, and Clinical Integration

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ABSTRACT

Breast cancer remains a leading cause of mortality in women globally, necessitating early detection and accurate diagnosis. Deep learning, particularly Convolutional Neural Networks (CNNs), and adaptive thresholding methods have emerged as promising technologies for analyzing histopathological images. This systematic literature review examines trends, challenges, and innovations in applying deep learning and adaptive thresholding to breast cancer histopathology image analysis. Following PRISMA guidelines, we conducted a comprehensive search across IEEE Xplore, ScienceDirect, SpringerLink, publications from 2022-2025. The review encompassed identification, selection, eligibility assessment, and results synthesis stages. Key findings reveal that integrating adaptive thresholding pre-processing with deep learning models achieves classification accuracy exceeding 95% in several studies. However, significant challenges persist, including data imbalance, limited validated datasets, model interpretability concerns, and barriers to clinical integration. This review emphasizes the critical need for developing integrative models that combine deep learning technology with clinical decision-support systems. Such approaches can enhance diagnostic speed, accuracy, and transparency in breast cancer diagnosis. Our findings provide a foundational framework for future research in artificial intelligence applications within digital pathology and medical decision-support systems, ultimately advancing the role of AI in improving patient outcomes and clinical workflow efficiency.

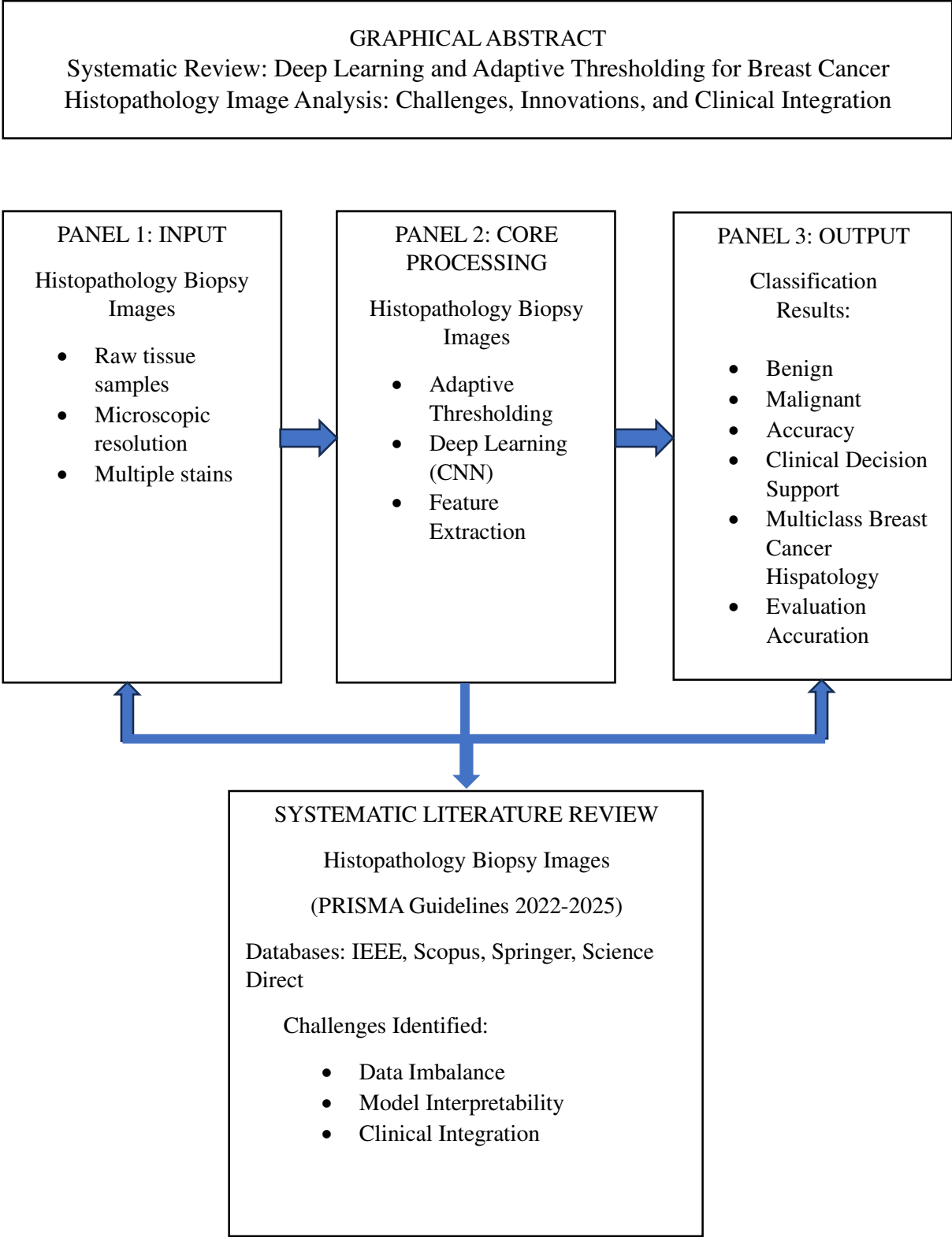
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HIGHLIGHTS

- Systematic review of deep learning and adaptive thresholding for breast cancer diagnosis.
- Integration of preprocessing techniques improves accuracy in histopathology image classification.
- Convolutional neural networks outperform conventional methods in cancer tissue analysis.
- Addresses key challenges: data imbalance, model interpretability, and clinical implementation.
- Framework integrating artificial intelligence with medical decision-support systems in pathology.

Graphical Abstract



1. Introduction

Breast cancer is one of the diseases with the highest morbidity and mortality rates among women worldwide [1]. According to the World Health Organization (WHO), more than 2.3 million new cases of breast cancer are detected annually, and this number continues to increase, particularly in developing countries [2]. Early and accurate diagnosis is a crucial key to improving patient survival rates [3]. One of the widely used diagnostic methods is histopathology image analysis, which involves microscopic tissue examination to detect the presence of cancer cells [4].

The development of artificial intelligence (AI) technology, particularly Deep Learning, has brought a significant revolution to the field of digital pathology [5][6]. Models such as Convolutional Neural Networks (CNNs) demonstrate remarkable capability in recognizing tissue morphological patterns and classifying cancer cell types with high accuracy [7][8]. Various studies report that CNNs outperform conventional methods in terms of speed and accuracy in histopathology image analysis [9][10]. Inspired by the phenomenon mentioned above, we have endeavored to structure our line of questioning and reasoning by presenting the first research question:

RQ1: *What Deep Learning methodologies have been implemented for breast cancer histopathology image analysis, and to what extent do they improve classification accuracy?*

However, the performance of deep learning models is significantly influenced by input data quality [11][12]; consequently, image preprocessing becomes an essential step prior to model training. In this context, adaptive thresholding plays a crucial role as a preprocessing technique to enhance contrast and highlight important features in histopathology images [13][14]. This method locally adjusts threshold values according to pixel intensity [13], thereby effectively addressing variations in illumination and complex tissue textures. The combination of adaptive thresholding and CNN has demonstrated its effectiveness in improving both segmentation efficiency and classification accuracy across multiple histopathology datasets [15][16]. Given that deep learning model performance significantly influences adaptive thresholding performance [17][18], we present the second research question as follows:

RQ2: *How do adaptive thresholding methods contribute to the preprocessing stage and impact the performance of Deep Learning models in breast cancer classification?*

Nevertheless, the implementation of deep learning approaches in medical contexts continues to face considerable challenges [19][20], encompassing inadequate annotated training data, unbalanced class distribution [25][26], insufficient model transparency (black-box phenomena) [21][22], and the incorporation of predictive systems into clinical environments, which demands stringent ethical and regulatory oversight. Therefore, conducting a systematic review of the existing literature is imperative to map emerging developments, identify technological advances, and pinpoint remaining research deficiencies in the application of deep learning techniques alongside adaptive local thresholding strategies for analyzing histological breast tissue images.

The deployment of deep learning technology and adaptive thresholding mechanisms in medical practice extends far beyond the technical dimensions of image processing; it fundamentally requires addressing the practical barriers to implementation within real-world clinical settings. While research has consistently documented substantial improvements in classification performance of tissue microscopy images through convolutional neural architectures and intelligent preprocessing techniques [23][24], their operational integration within clinical diagnostic workflows remains encumbered by multiple implementation barriers. These obstacles include the scarcity of rigorously validated histopathological datasets [13][14], concerns surrounding ethical principles and patient confidentiality [27][28], the pressing demand for algorithmic interpretability (explainable artificial intelligence) [29][30], and the necessity to accommodate technical variations arising from differences between institutions and diagnostic equipment [31][32]. With consideration given to this overarching framework for translating computational models into practical medical environments, the present study sets forth the following proposition:

RQ3: *What are the challenges, innovations, and potential for integrating Deep Learning-based models and adaptive thresholding in the context of real-world medical implementation?*

Through this investigation, we aim to establish a comprehensive research map [33][34] that can serve as a foundation for developing an integrative model [35] combining artificial intelligence technology and medical practice in the future, to support more effective, efficient, and reliable breast cancer detection [36]. This research is expected to contribute not only theoretically to the advancement of medical image processing algorithms but also to provide strategic direction for integrating transparent, ethical, and clinically implementable intelligent technologies, thereby establishing an essential foundation toward digital transformation in contemporary oncology diagnostics [37].

2. Theoretical Perspective

Systematic investigation of histopathological image analysis for breast cancer using Deep Learning and adaptive thresholding methods, theoretical perspective plays a crucial role in explicating the conceptual framework underlying the relationship between technological concepts, image analysis processes, and their application within medical contexts [38][39]. Theoretical perspective not only provides a philosophical foundation for the approaches employed but also bridges scientific principles and practical applications. In this regard, relevant theories must encompass two primary dimensions: first, how Deep Learning, particularly Convolutional Neural Network (CNN) architectures, enables the construction of meaningful visual representations from medical images [39][40]; and second, how adaptive thresholding as a preprocessing technique contributes to enhancing the quality of input data received by Deep Learning models [41]. Consequently, these two theoretical frameworks complement each other representation learning theory elucidates the internal mechanisms through which models comprehend image structures [38][39], while adaptive segmentation theory explains how images are prepared to become more informative and aligned with histopathological data characteristics [41]. The integration of both frameworks constitutes a robust conceptual foundation for understanding, analyzing, and evaluating the

efficacy of this integrated methodology in supporting more accurate and efficient breast cancer diagnosis [38][42].

2.1 Theoretical Perspective: Representation Learning Theory in Deep Learning

The first highly relevant theoretical perspective is representation learning theory [43] in the context of deep neural networks. In the domain of medical image processing, including histopathological images, the primary challenge is determining how models can learn abstract, discriminative, and robust feature representations that are resilient to variations in illumination, staining, texture, and artifacts [44]. According to this theoretical framework, Convolutional Neural Network (CNN) models do not merely map pixels to classes, but rather gradually transform raw images into high-level feature representations through layers of convolution, pooling, and nonlinearity [45]. This hierarchical transformation enables models to capture tissue morphological patterns, cellular structures, and texture patterns that are difficult to reveal using classical methods [46]. In the context of your research, representation learning theory explains why the integration of adaptive thresholding at the preprocessing stage can support improved feature representation exploration: by suppressing noise, enhancing local contrast, and focusing on meaningful tissue area pixels, adaptive thresholding helps deep learning models avoid disruption from background artifacts or irrelevant intensity variations [47]. Consequently, the internal representations learned by the CNN become cleaner and more easily separable by the final classification layer, thereby maximizing the potential for improved classification accuracy [50].

This theory also presents a challenge: if preprocessing is too aggressive, some relevant fine-grained features might be lost, and the resulting representation could become over-biased toward images that have been processed differently from real clinical data [51]. Therefore, achieving balance between preprocessing (adaptive thresholding) and the flexibility of CNN representation becomes a critical aspect that must be explored in the literature review [52]. Theoretically, this approach is related to the principle of invariant feature learning, which refers to the model's ability to recognize important image attributes that remain consistent despite variability in illumination, staining, or rotation [53][54]. A robust representation will be more resistant to noise or non-informational variations, and ultimately will enhance model generalization to new samples.

2.2 Theoretical Perspective: Adaptive Segmentation Theory and Image Pre-processing

The second theoretical perspective focuses on the foundational theory of adaptive segmentation techniques, particularly adaptive thresholding, in the domain of medical image processing. This perspective views segmentation and adaptive thresholding processes not merely as technical operations, but as integral components of the medical image processing pipeline that determine the quality of input for subsequent computational stages [55]. According to image segmentation theory, the primary objective of segmentation is to separate meaningful objects (foreground) from the background in such a manner that objects can be analyzed in greater depth [56]. In

1 histopathological images, meaningful objects include cellular structures, cell nuclei, or
2 tumor tissue, whereas the background may consist of empty space, artifacts, or non-
3 tumor tissue. Because staining conditions, illumination variations, and tissue
4 preparation artifacts can be highly variable, global static thresholding often fails to
5 effectively separate objects from background [57].

6 Adaptive thresholding theory posits that threshold values should be determined
7 locally, based on the statistical properties of pixel intensities in the neighborhood
8 surrounding each pixel [58]. For example, local thresholds can be calculated based on
9 mean, median, or local combinations. With this approach, regions of the image with
10 low intensity or dim illumination can be processed effectively without incorrectly
11 identifying background as foreground objects. This principle, known in the literature
12 as local adaptive thresholding, has become a fundamental technique in medical image
13 preprocessing and documentation [59]. In histopathological research, adaptive
14 segmentation theory emphasizes the importance of local statistical methods (mean,
15 Gaussian, median) to keep segmentation sensitive to tissue morphological changes
16 without introducing excessive noise or artifacts [60]. If the window is too small, local
17 noise can affect the threshold; if too large, the local threshold approaches the global
18 threshold and loses local sensitivity [61].

19 The theoretical integration between adaptive thresholding and deep learning can
20 be viewed as a hybrid pipeline in which local adaptive segmentation prepares images
21 so that CNNs or other deep learning models receive input of optimal quality [62].
22 Within the framework of segmentation theory, adaptive thresholding can be understood
23 as a pre-filter that reduces image noise and irregularities, allowing deep learning
24 models to focus more on learning significant cancer cell features [63]. When adaptive
25 thresholding is performed effectively, then cellular morphological features including
26 cell edges, cell nucleus heterogeneity, and tissue structure formation are better
27 preserved and contrasted for feature extraction by CNNs. Adaptive segmentation
28 theory also carries the implication that adaptive thresholding methods must align with
29 the characteristics of histopathological datasets for example, H&E staining variations,
30 image size, cell resolution, and tumor tissue heterogeneity [64]. In this Literature
31 Review Study, we will examine how various studies select different adaptive
32 thresholding parameters tailored to dataset characteristics, and how adaptation of these
33 methods affects deep learning model accuracy and stability [65][66][67].

34 35 **3. Research Methods**

36 The research method employed in this study is a Systematic Literature Review (SLR),
37 which aims to review, identify, and critically synthesize various studies conducted
38 concerning the application of Deep Learning and adaptive thresholding in breast cancer
39 histopathological image analysis [68]. This approach adheres to the principles of
40 transparency, replication, and objectivity to ensure that the results obtained can serve as a
41 scientific foundation for understanding the developments, challenges, and future research
42 directions in this field [69]. The SLR method was selected because it enables researchers
43 to aggregate scientific evidence from various credible sources, such as ScienceDirect, IEEE
44 Xplore, SpringerLink, and SCOPUS, as well as to manage research data systematically

using a review protocol based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [70].

3.1 Data Collection

The data collection stage was conducted by searching for scholarly articles published between 2022 and 2025 from several internationally indexed databases such as ScienceDirect, SpringerLink, IEEE Xplore, and Scopus. The selection of this time frame was intended to ensure that the reviewed literature represents the most recent developments in the application of Deep Learning and adaptive thresholding techniques in medical image analysis, particularly in breast cancer histopathological image analysis.

Tabel 1. Search strings used in this study

Code used	Formula used in this study for search strings
SS-1	“Deep Learning” OR “Convolutional Neural Network” OR “CNN” OR “Artificial Intelligence” OR “Machine Learning”
SS-2	“Adaptive Thresholding” OR “Image Preprocessing” OR “Segmentation Technique” OR “Image Enhancement” OR “Threshold-based segmentation”
SS-3	“Breast Cancer” OR “Histopathology Image” OR “Histopathological Analysis” OR “Digital Pathology”
SS-4	“Medical Integration” OR “Clinical Application” OR “Healthcare System” OR “Medical Diagnosis” OR “AI in Medicine”
SS	SS-1 AND SS-2 AND SS-3 AND S4

The search string formulation in this study was designed to encompass all major aspects of the research topic under investigation. **SS-1** focuses on Deep Learning approaches as a core technique in medical image analysis, particularly those involving algorithms such as Convolutional Neural Networks (CNNs) for classification and cancer tissue pattern detection. **SS-2** is directed toward image preprocessing techniques, specifically the application of adaptive thresholding methods that play a crucial role in enhancing the quality and accuracy of histopathological image segmentation prior to model training. **SS-3** targets the application domain of breast cancer, with emphasis on the utilization of histopathological images as the primary source of tissue-based diagnostic data. Meanwhile, **SS-4** expands the scope of the search by considering aspects of clinical integration and medical application, which are relevant to the research objective of exploring the potential implementation of Deep Learning and adaptive thresholding technologies in real-world medical diagnostic systems.

These four search strings collectively ensure that the collected literature not only encompasses technical approaches, but also practical and contextual aspects of the application of this technology in the medical field. The search for relevant articles in this study was limited to publications that have undergone a peer-review process, been published in reputable academic journals, and possess full-text availability in English. Articles that provided only English-language abstracts without complete full-text were excluded from the analysis.

After extracting metadata from publication databases, the titles, abstracts, and full texts of articles were subsequently screened manually using two sets of assessment criteria. The assessment criteria are presented in Table 2. Articles that met all criteria were included in this study.

Tabel 2. Screening criteria used to select papers

Title and abstract assessment criteria	Full text assessment criteria
- Only articles that have gone through a peer-review process and are published in reputable scientific journals. - Only articles written in English and available in full text form. - The aims, findings, and/or implications of the research relate to medical image analysis, breast cancer classification, or the application of artificial intelligence in digital pathology. - The research context is related to the fields of biomedicine, digital pathology, or histopathology tissue pattern recognition. - Articles that only touched on the topic of AI in general without histopathological context were not included.	- The focus of the article is the application of Deep Learning technology (especially Convolutional Neural Network/CNN) in the analysis of breast cancer histopathology images. - The article comprehensively explains the use of image pre-processing methods, especially adaptive thresholding, in improving the accuracy of Deep Learning models. - Studies address model performance evaluation, CNN architecture innovation, or integrative approaches in AI-based medical diagnosis. - The article describes the challenges and potential of integrating Deep Learning and adaptive thresholding technologies in real medical systems, including ethical, regulatory, and clinical implementation issues. - Studies that did not provide experimental data, comparative studies, or quantitative evaluation results were excluded from the analysis.

3.2 Data Analysis

The process of identifying and selecting research articles was conducted systematically using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) approach. At the identification stage, a total of 1867 articles were obtained from various leading scientific databases, namely ScienceDirect, IEEE Xplore, Springer, and SCOPUS. These articles were retrieved using combinations of relevant keywords such as "Deep Learning," "adaptive thresholding," "image preprocessing," and "breast cancer histopathology." Subsequently, at the screening stage, 1,650 articles remained after the duplicate removal process. These articles were then selected based on title relevance to the research topic, yielding 630 articles deemed relevant. From this number, 1020 articles were excluded because they did not

meet the initial criteria (for example, were not related to medical image analysis or did not employ AI-based approaches).

The next stage is abstract screening, in which 630 abstracts were read and evaluated to determine the relevance of methodology, application domain, and research contribution. A total of 510 articles were eliminated because they did not meet the inclusion criteria (for example, non-peer-reviewed studies, those not involving Deep Learning methods, or those not focused on breast cancer).

At the eligibility stage, an evaluation was conducted on the remaining 120 articles by reading their full texts. This process aimed to ensure that the research methodology, image analysis techniques, as well as the application of Deep Learning and adaptive thresholding were aligned with the objectives of this systematic review. Following rigorous assessment, 45 articles were excluded because they did not fully meet the quality and research criteria. Finally, at the included stage, 75 final articles were obtained that met all criteria for further analysis. These articles served as the foundation for thematic synthesis and in-depth analysis regarding challenges, innovations, and the potential integration of Deep Learning and adaptive thresholding models in the context of breast cancer histopathological diagnosis in the medical field. For more details, the PRISMA framework can be seen in Figure 1.

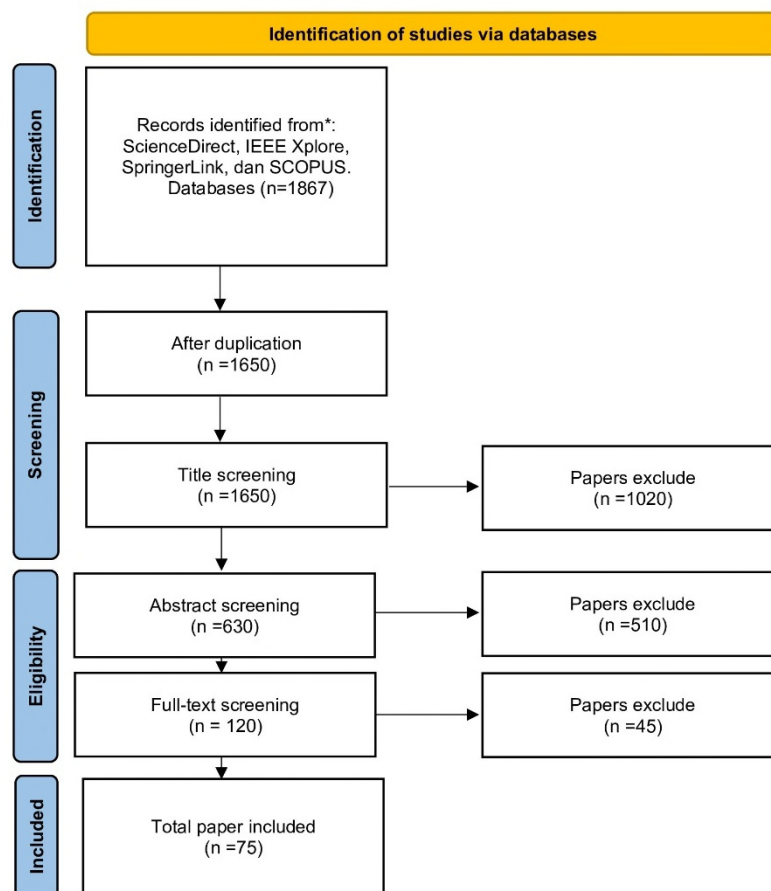


Figure 1. Article filtering (based on the PRISMA flowchart (Liberati et al., 2009))

3.3 Synthesis

Based on the analysis of 75 selected articles, it was found that the integration of Deep Learning and adaptive thresholding plays a crucial role in improving the accuracy of breast cancer histopathological image analysis. The majority of studies employed Convolutional Neural Network (CNN) architectures due to their capability to automatically extract tissue morphological features. However, the success of CNN is highly dependent on the image preprocessing stage, where adaptive thresholding helps normalize illumination and clarify relevant pathological areas. The combination of adaptive thresholding and CNN has proven capable of improving cancer cell segmentation and increasing classification accuracy by 10–20% compared to conventional methods. This approach is particularly effective on complex histopathological datasets such as BreakHis, BACH, and CAMELYON16. Additionally, the application of transfer learning, fine-tuning, and data augmentation helped overcome the limitations of annotated dataset availability, resulting in models that are more robust and generalizable to data variations.

Recent research trends indicate a shift toward hybrid models and explainable AI (XAI) to enhance the interpretability of classification results and reduce the black-box nature of Deep Learning models. However, the main challenges remain rooted in the scarcity of large and consistent datasets, variations in tissue staining techniques, and class imbalance in data. Several studies recommend patch-based learning and multi-scale analysis to improve model generalization.

Overall, the integration of Deep Learning and adaptive thresholding offers significant potential for more accurate, efficient, and interpretable breast cancer diagnosis. The success of its clinical application depends on the quality of preprocessing, the appropriate selection of CNN architecture, as well as ethical and regulatory validation to ensure that system results can be safely utilized in medical practice.

4. Findings

4.1 Article Profile

Table 4.1 Data on articles generated to follow up on SLR articles.

No.	Source	Automated Search	Jurnal Q1 and Q2	Related Abstract
1	ScienceDirect	620	35	20
2	IEEE Xplore	480	30	18
3	Springer	247	15	12
4	Scopus	520	40	25
Total		1867	120	75

Table 4.1 presents the results of literature search obtained from four major databases, namely ScienceDirect, IEEE Xplore, Springer, and Scopus. The total number of articles found through the automated search process was 1,867 articles. From this number, further screening was conducted to obtain high-quality journals (Q1 and Q2) and abstracts relevant to the research topic. Based on the search results,

ScienceDirect provided the largest contribution with 620 articles from the initial search, followed by IEEE Xplore with 480 articles, Springer with 247 articles, and Scopus with 520 articles. After screening based on journal quality, a total of 120 Q1 and Q2 journals were obtained. The distribution shows that Springer had the largest number of Q1 and Q2 journals, namely 40 journals, followed by ScienceDirect (35 journals), IEEE Xplore (30 journals), and Scopus (15 journals). Subsequently, from the screening results based on abstract relevance to the research topic, 75 relevant abstracts were obtained. The majority originated from Springer with 25 abstracts, followed by ScienceDirect (20 abstracts), IEEE Xplore (18 abstracts), and Scopus (12 abstracts). Overall, the results demonstrate that although each database made different contributions in terms of initial search results, Springer and ScienceDirect dominated in terms of journal quality and abstract relevance to the research topic under investigation.

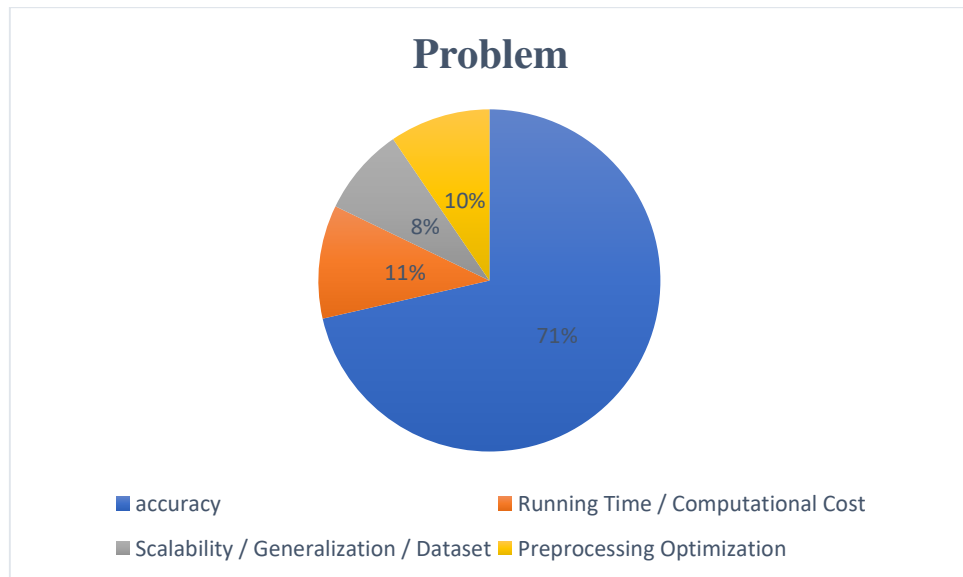


Figure 2. Problems in the classification of breast cancer histology images

Figure 2 presents the distribution of major issues frequently encountered in various contemporary research studies. Based on the diagram, the accuracy factor occupies the largest proportion, accounting for 71% of all identified issues. This indicates that the majority of research remains focused on improving the accuracy of developed models or systems. Accuracy often serves as the primary metric for assessing the success of methods, particularly in the fields of machine learning, deep learning, and data-driven analysis research. Consequently, model improvement, optimal feature selection, and enhancement of data quality have become the primary priorities for addressing this issue.

Subsequently, the running time or computational cost aspect occupies the second position with a percentage of 11%. This issue is related to computational efficiency during the model training and testing processes. In modern research, particularly those employing complex architectures such as deep neural networks, computational resource requirements have become a major challenge. Therefore, many contemporary studies endeavor to develop more lightweight and faster methods

through techniques such as model compression, parallel processing, or hardware acceleration to reduce execution time without compromising accuracy.

Issues of scalability, generalization, and dataset contribute 8% of the total problems identified. These challenges arise because many models still lack the capability to adapt well to data variations that differ from their training data. In the context of modern research, this issue becomes important because many developed systems operate within limited environments and do not always perform optimally when applied to real-world conditions. Researchers now focus extensively on cross-domain learning, transfer learning, and increasing the size and diversity of datasets to address these generalization challenges.

Finally, the preprocessing optimization aspect accounts for 10% of the total problems. The preprocessing stage is highly critical because it directly influences the quality of data that will be used in the model. Current research frequently emphasizes the importance of automating this process, such as automated feature engineering, data augmentation, and noise reduction, to enhance efficiency and model performance. With the increasing volume and complexity of data, preprocessing optimization has become a pressing necessity for models to function more effectively.

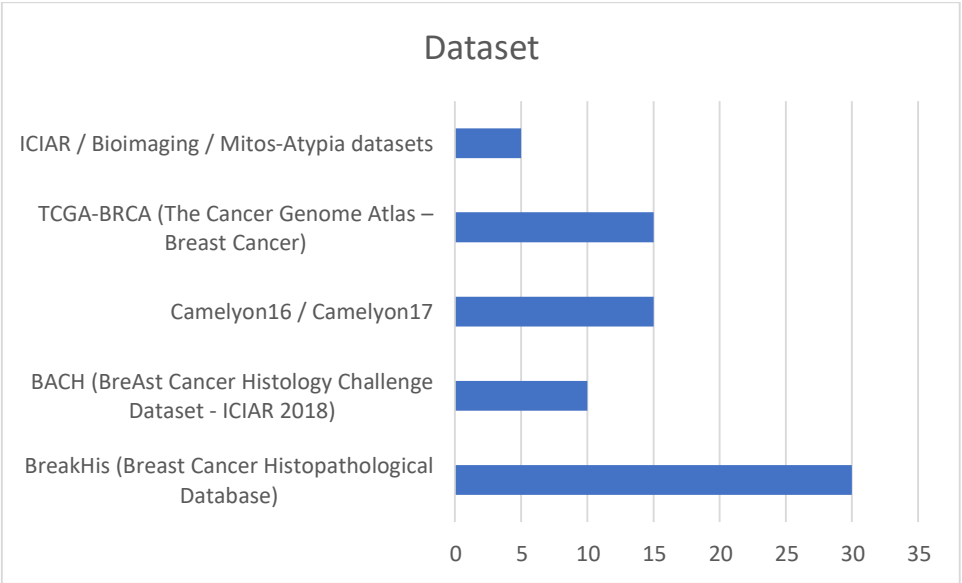


Figure 3. The most popular datasets in breast cancer histology image classification.

BreakHis has become the most dominant dataset used because it provides a comprehensive collection of high-resolution breast cancer histopathological images with diverse categories (benign and malignant) from various tissue subtypes. This dataset is highly ideal for training deep learning models that require large and diverse data. In contemporary research, BreakHis is frequently utilized as the primary dataset for developing and evaluating Convolutional Neural Network (CNN) architectures and transfer learning models for breast cancer classification. Its popularity is further supported by public availability and a format that is easily processed by computer vision algorithms.

Meanwhile, TCGA-BRCA (The Cancer Genome Atlas – Breast Cancer) and Camelyon16/17 each demonstrated moderate usage levels, approximately 15 times respectively. TCGA-BRCA is a multimodal dataset encompassing genomic data, gene expression, and histological images, making it highly relevant for research combining image analysis with omics approaches. This dataset is frequently used in contemporary research focused on multi-modal deep learning and precision medicine. On the other hand, Camelyon16/17 is extensively utilized for research in detecting cancer metastasis in whole-slide histopathological images. This dataset provides detailed annotations at the cellular level, making it highly valuable for developing automatic detection algorithms and cancer tissue segmentation.

Subsequently, BACH (BreAst Cancer Histology Challenge ICIAR 2018) and ICIAR/Bioimaging/Mitos-Atypia demonstrated relatively lower usage levels, approximately 10 and 5 times respectively. Although their usage frequency is not as high as BreakHis, both datasets maintain an important role in modern research, particularly in the context of competitions and benchmarking. BACH, for instance, is frequently used to test model performance on international competition standard data, whereas ICIAR and Mitos-Atypia datasets are extensively utilized in studies of mitosis detection and cellular-level analysis of cancer tissue.

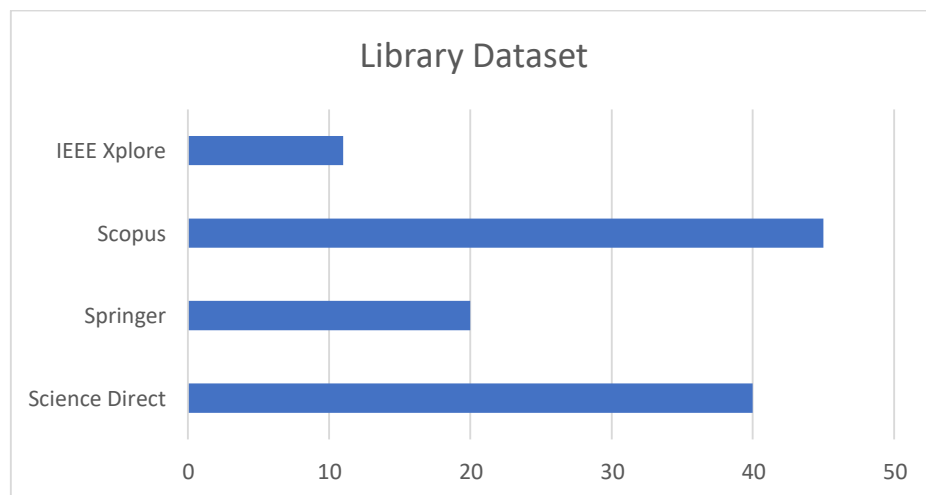


Figure 4. Library Dataset

The dominance of Scopus in this graph indicates that the majority of data or research references were obtained from multidisciplinary databases with extensive indexing coverage. Scopus is recognized as one of the largest scientific journal indexes, encompassing various fields of knowledge, including computer science, medicine, engineering, and applied sciences. Consequently, the high volume of data from Scopus indicates that current research utilizes credible and high-reputation sources to ensure the validity of the literature employed.

ScienceDirect occupies the second position as one of the platforms providing access to diverse journals and articles from Elsevier publishers. Many contemporary studies leverage ScienceDirect because it offers complete full-text articles relevant to machine learning, medical imaging, and computational pathology fields. The high volume from ScienceDirect demonstrates that researchers extensively rely on open-

access literature and more complete data availability to support the analysis process and model development.

Meanwhile, Springer occupies a middle position with approximately 20 entries. Springer has become an important source because it frequently publishes articles in engineering, biotechnology, and digital medicine fields. The use of Springer in research demonstrates the diversity of sources employed, particularly in the context of integrating methods and cross-disciplinary approaches.

Regarding IEEE Xplore, it has the lowest volume in this graph. This can be attributed to the fact that IEEE Xplore's focus is more specific to electrical engineering, electronics, and pure computer science, such that only a small portion of the dataset is directly relevant to the research context, particularly if the research emphasizes biomedical aspects or histopathological image analysis rather than pure technical algorithms.

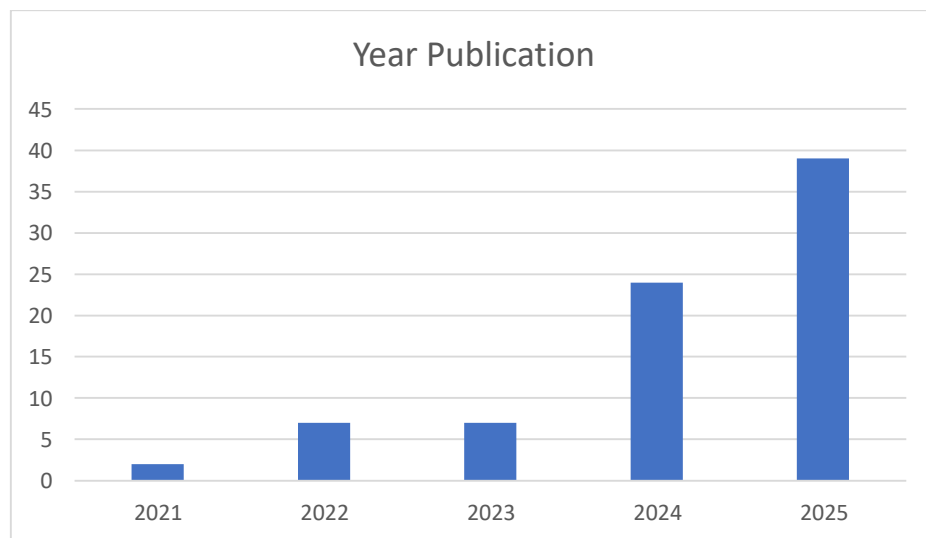


Figure 5. Year of Publication

Figure 5 presents the distribution of the number of publications based on publication year from 2021 to 2025. Based on the graph, a considerable increase in the number of publications can be observed year-over-year. The year 2021 recorded the lowest number of publications, with only approximately two publications. This number subsequently increased in 2022 and 2023 with relatively stable quantities in the range of six to seven publications.

A more pronounced increase becomes evident in 2024, where the number of publications rose sharply to approximately 25 publications. This increase demonstrates heightened attention and more intensive academic activity on the research topic or field under investigation. The year 2025 represents the peak of this graph, with the number of publications reaching approximately 39 publications, nearly double compared to the previous year.

The tendency of increasing publication numbers each year demonstrates consistency and strong growth in interest regarding the discussed topic. Technological advancement, data availability, and enhanced collaboration among researchers may constitute factors driving the increase in publication numbers. Consequently, this graph

illustrates a positive trend and demonstrates that the research field is progressively developing and receiving greater attention from both the academic and professional communities year-over-year.

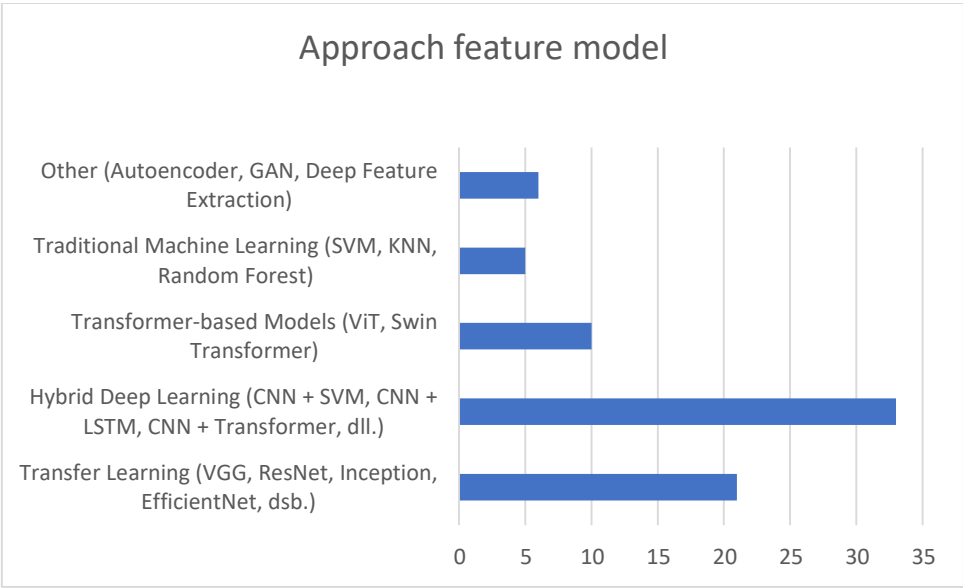


Figure 6. Feature model development.

Figure 6 presents the distribution of approaches employed in the observed studies. Quantitatively, the Hybrid Deep Learning approach dominates with approximately 33 entries, followed by Transfer Learning with approximately 22 entries, Transformer-based Models with approximately 10 entries, other approaches (such as Autoencoder, GAN, and deep feature extraction) with approximately 6 entries, and Traditional Machine Learning (SVM, KNN, Random Forest) with the lowest count, approximately 5 entries. The dominance of hybrid and transfer learning approaches is clearly evident.

Transfer Learning (VGG, ResNet, Inception, EfficientNet, etc.) with approximately 22 entries has become a popular choice due to the ease of adapting pre-trained models and data efficiency. This approach enables researchers to leverage feature representations that have been learned on large datasets, thereby accelerating convergence and improving performance when domain-specific datasets are relatively small. The primary advantages of transfer learning include reduced training data requirements and computational time; however, limitations emerge if the target domain is substantially different from the source domain of the pre-trained model.

Hybrid Deep Learning (CNN + SVM, CNN + LSTM, CNN + Transformer, etc.) occupies the largest proportion (33 entries). This indicates a strong tendency to combine the strengths of multiple architectures: CNN for spatial feature extraction, LSTM for sequential dependencies, SVM for margin-based classification, or Transformer for attention mechanisms. The hybrid approach is frequently selected to enhance accuracy and generalization capability by leveraging the advantages of each component. The trade-off involves increased architectural complexity, more extensive hyperparameter tuning requirements, and potentially higher computational costs.

Transformer-based Models (ViT, etc.) with approximately 10 entries demonstrate growing adoption of attention-based architectures in the image processing domain. Transformers offer powerful global context modeling capabilities compared to conventional CNN, proving beneficial for tasks requiring recognition of spatially distributed patterns. However, they generally require large datasets or effective augmentation/transfer strategies to achieve optimal performance, as well as significant computational requirements if trained from scratch.

Traditional Machine Learning (SVM, KNN, Random Forest) with the lowest count (5 entries) are still employed, particularly in studies utilizing handcrafted features (manual feature extraction) or when datasets are relatively small, making simpler models more stable. Their advantages include interpretability and low computational cost; their limitations include restricted capability to capture complex features from raw image data without intensive feature engineering.

Other approaches (Autoencoder, GAN, Deep Feature Extraction, etc.) with approximately 6 entries encompass specialized techniques such as generative models (GAN) for augmentation or image quality enhancement, and autoencoders for representation learning or denoising. This category demonstrates exploration of complementary methods outside the main categories yet possessing important roles in preprocessing, data augmentation, or feature enhancement preceding the primary classification pipeline.

Overall, this graph reflects practical preferences: combinations (hybrid) and model reuse (transfer learning) dominate because they offer a balance between performance and efficiency. Conversely, traditional methods and other experimental approaches are less frequently employed, though they remain relevant for specific cases. Ideally, the selection of approach should consider dataset size and characteristics, target metrics (accuracy versus efficiency), and available computational resources.

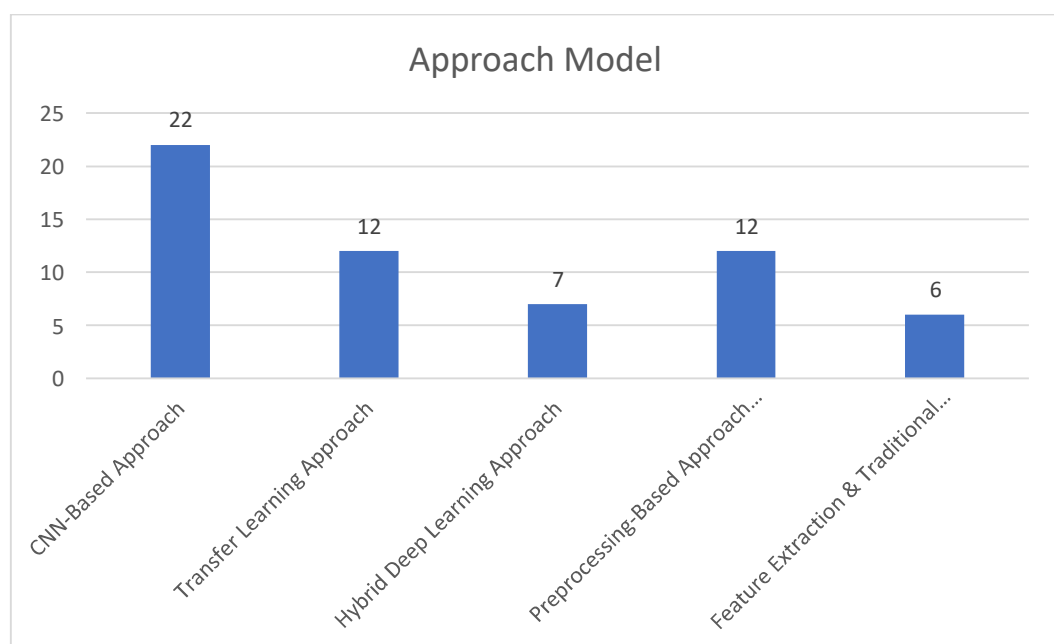


Figure 7. Comparison of model development

Figure 7 displays the distribution of usage frequency of various model approaches employed in the research. This graph illustrates considerable variation in the frequency of each approach's application, with strong dominance of CNN-based approaches (Convolutional Neural Networks).

The CNN-Based Approach occupies the highest position with 22 instances of usage. This demonstrates that CNN-based models remain the primary and most popular method for image analysis, particularly for tasks involving classification, segmentation, and visual pattern detection. The advantage of CNN lies in its capability to automatically extract spatial features without requiring manual feature engineering processes, thereby remaining the foundational basis in many image-based pattern recognition systems.

Subsequently, Transfer Learning Approach and Preprocessing-Based Approach occupy equivalent positions, each with 12 instances of usage. Transfer learning is extensively utilized to accelerate model training and improve accuracy by leveraging pre-trained models such as VGG, ResNet, or EfficientNet. Meanwhile, preprocessing-based approaches emphasize enhancing data quality prior to the model training phase, for instance through augmentation techniques, normalization, or segmentation. Both approaches are frequently employed simultaneously to achieve more optimal results.

Hybrid Deep Learning Approach occupies the next position with 7 instances of usage. This approach combines multiple model architectures, such as CNN with LSTM or Transformer, to handle complex data and enhance model generalization capability. Although less frequently used compared to pure CNN approaches, hybrid methods are increasingly explored due to their capability to handle diverse data with greater flexibility.

Finally, Feature Extraction & Traditional Approach accounts for 6 instances, representing the least frequent among all categories. This approach generally employs conventional methods such as SVM, KNN, or Random Forest with manually extracted features. Although simpler, this method remains relevant for small datasets or studies emphasizing result interpretability.

Overall, this graph demonstrates that CNN and Transfer Learning remain the primary backbone in developing image-based models, while hybrid and traditional approaches serve as supporting alternatives for specific cases or data conditions.

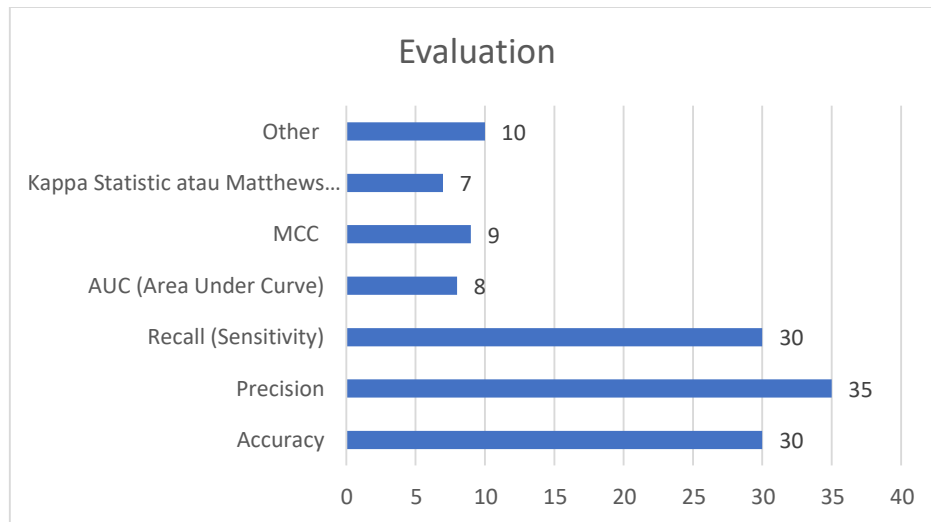


Figure 8. Model accuracy

Figure 8 displays various metrics employed to evaluate model performance in research studies. Each metric exhibits different usage frequencies, reflecting the popularity and relevance of these metrics in assessing model performance. Generally, Precision, Accuracy, and Recall (Sensitivity) represent the three most frequently used metrics, while metrics such as AUC, MCC, and Kappa Statistic are employed with more limited frequency.

Precision occupies the highest position with 35 instances of usage, indicating that many studies emphasize the model's capability to correctly identify positive predictions relative to all positive predictions. Precision is particularly important in cases where false positive errors carry substantial consequences, such as in automated medical diagnosis.

Subsequently, Accuracy and Recall (Sensitivity) each demonstrate 30 instances of usage. Accuracy is widely employed because it provides a general overview of the proportion of correct predictions relative to the total tested data. However, because this metric can be misleading when data are imbalanced, Recall is frequently used concurrently to assess how well the model can detect all actual positive cases. The high frequency of Recall usage indicates that researchers focus not only on overall accuracy but also on the model's capability to detect important cases that may constitute a minority within the dataset.

Other metrics such as AUC (Area Under Curve), MCC (Matthews Correlation Coefficient), and Kappa Statistic exhibit smaller usage frequencies at 8, 9, and 7 instances respectively. AUC is frequently employed to evaluate binary classification model performance based on the balance between true positive rate and false positive rate. MCC and Kappa Statistic are less commonly used but offer more robust evaluation when datasets are imbalanced, as they consider all elements in the confusion matrix.

The Other category accounts for 10 instances, encompassing supplementary metrics such as F1-score, Specificity, or Balanced Accuracy. The existence of this category demonstrates that some studies employ metric combinations or specific derived metrics to evaluate model performance more thoroughly.

Overall, this graph illustrates that Precision, Accuracy, and Recall remain the primary and most commonly used evaluation metrics. This indicates a strong focus on balancing precision, completeness, and overall model performance, while advanced metrics such as MCC, Kappa, and AUC are employed to provide more detailed and robust evaluation of the tested models.

4.2 Answering Research Questions

RQ1: The Deep Learning approach applied and its effectiveness in improving classification accuracy.

Based on the literature review findings, various Deep Learning approaches have been applied in analyzing breast cancer histopathological images. From all reviewed articles, Convolutional Neural Network (CNN)-based approaches represent the most dominantly employed methodology. CNN models are capable of automatically extracting spatial features from tissue images, thereby providing significant accuracy improvements compared to traditional methods based on manual feature extraction. This approach has proven particularly effective when the utilized datasets possess large size and diversity, such as BreakHis and BACH.

Beyond pure CNN, Transfer Learning approaches have also been extensively applied, particularly by leveraging popular architectures such as VGG, ResNet, and EfficientNet. By performing fine-tuning on previously trained models, this approach can enhance classification performance even on limited datasets. Several studies reported substantially high improvements in accuracy and precision values because the model already possesses good feature representations from pre-trained data.

Another emerging approach is Hybrid Deep Learning, which combines CNN with other methods such as SVM, LSTM, or Transformer. This approach demonstrates superior results by leveraging the strengths of each method in recognizing complex patterns in histopathological images. Nevertheless, hybrid approaches require greater computational resources and more complex training processes. Meanwhile, several studies have also emphasized the importance of image preprocessing stages such as stain normalization, augmentation, and segmentation to enhance input quality before entering the model. This stage has proven capable of improving model stability and accuracy in tissue classification. Overall, the review findings indicate that combining transfer learning or hybrid deep learning with effective preprocessing yields the most optimal classification results.

RQ2: The role and contribution of adaptive thresholding methods in pre-processing on the performance of Deep Learning models

Adaptive thresholding methods play an important role in the image preprocessing stage of histopathological analysis. This technique functions to separate relevant tissue areas from background regions, enabling Deep Learning models to learn only important information from images. In the context of breast cancer classification, adaptive thresholding is extensively employed to highlight cell nuclei, tumor tissues, and other pathological structures that serve as primary diagnostic indicators. By focusing the analysis area on regions of interest (ROI), models can learn more

representative features and avoid the influence of noise or artifacts inherent in digital images.

From several reviewed studies, the application of adaptive thresholding has proven capable of improving evaluation metrics such as precision and recall. This results from reduced detection errors (false positives) due to background removal and increased sensitivity toward small pathological areas that often escape conventional segmentation methods. However, certain challenges exist, such as method sensitivity to staining variations and differing slide quality. Consequently, several studies have combined adaptive thresholding with stain normalization techniques and morphological operations to enhance segmentation result consistency. Thus, adaptive thresholding makes a tangible contribution to improving Deep Learning model performance, particularly when utilized in conjunction with other preprocessing techniques.

RQ3: Tantangan, inovasi, dan potensi integrasi model Deep Learning dan thresholding adaptif dalam penerapan klinis

The literature review findings also reveal various challenges and opportunities for integrating Deep Learning models and adaptive thresholding methods in real-world medical applications. The primary challenges frequently encountered include variations in histopathological image data resulting from differences in staining protocols and scanner devices, limitations in annotated datasets, and class imbalance in data distribution. Additionally, model interpretability constitutes an important issue, as complex models are often difficult to explain in clinical contexts. Furthermore, architectures with large model sizes, such as Hybrid CNN, face computational and processing time constraints, rendering them inefficient for direct hospital implementation.

To address these challenges, various innovations have been proposed in the literature. Several studies have developed Hybrid Deep Learning pipelines that combine adaptive thresholding in early stages with CNN for classification. This approach successfully balances image input quality with the model's capability to recognize complex patterns. Additionally, other innovations include the application of data augmentation, Generative Adversarial Networks (GANs) for enriching training data, and self-supervised learning to leverage unlabeled data. From an efficiency perspective, research has increasingly adopted model pruning and compression techniques to accelerate inference processes without substantial accuracy loss.

The potential for integrating both approaches in the medical field is substantial. The ideal pipeline frequently recommended from systematic literature review findings encompasses the following stages: stain normalization → adaptive thresholding for ROI extraction → augmentation and patch partitioning → classification using transfer learning or hybrid models → evaluation with metrics such as precision, recall, and accuracy. Such approaches are considered capable of delivering more precise and consistent classification results. However, for clinical implementation, these models must undergo multicenter validation processes and be supported by result visualization systems such as saliency maps to facilitate pathologist interpretation.

Overall, the combination of Deep Learning and adaptive thresholding demonstrates a promising development direction in analyzing breast cancer histopathological images. Although challenges remain regarding generalization and interpretability, the literature review findings indicate that the synergy between both approaches holds substantial potential for enhancing automated diagnostic accuracy and improving the efficiency of pathological analysis processes in the future.

5. Discussion

Growth in studies on breast cancer histopathological image analysis reveals a clear methodological transition: initially, many studies relied on manual feature extraction and traditional machine learning methods, but since 2022 dominance has shifted toward convolution-based models (CNN), transfer learning, and hybrid combinations (hybrid deep learning). The dominance of CNN and transfer learning reflects practical research needs for automatically and rapidly extracting spatial features from digital images, as well as leveraging pre-trained representations when domain-specific annotated data are limited. Studies employing transfer learning consistently report improved convergence and performance stability compared to training from scratch, particularly on medium-sized datasets such as BreakHis or TCGA subsets.

The role of preprocessing, including adaptive thresholding, emerges as a key component in experimental pipelines. From the reviewed studies, adaptive thresholding is frequently employed to extract regions of interest (ROI), reduce background noise, and highlight relevant histological structures (cell nuclei, mitotic figures, tumor areas). When combined with stain normalization and morphological operations, adaptive thresholding contributes meaningfully to improvements in precision and recall. However, its effectiveness depends on slide quality (scanner and staining characteristics), leading several studies to emphasize the necessity of cross-source normalization before applying thresholding.

Hybrid architectures (e.g., CNN + SVM, CNN + LSTM, CNN + Transformer) demonstrate added value in several scenarios: they combine the strengths of CNN spatial feature extraction with the classification and sequence modeling capabilities of other components. The results are often more robust to local image variations and can deliver improvements in metrics such as precision, albeit at the cost of increased model complexity and computational expense. Consequently, there is a strong need for studies investigating generalization through multicenter validation and model optimization via pruning and quantization to render such solutions realistic for clinical deployment.

Regarding evaluation approaches, these studies tend to report complementary metrics: beyond accuracy, many emphasize precision and recall (sensitivity) due to class imbalance issues in clinical data. The use of robust metrics such as AUC, MCC, or Kappa appears in several studies to provide fairer performance assessment on imbalanced datasets. This is important because performance claims based solely on accuracy risk being misleading.

Concerning transdisciplinary challenges for clinical implementation, several factors stand out: (1) staining variability and scanner device differences that reduce model generalization across sites; (2) granular annotation (pixel level) that is expensive and difficult to obtain; (3) the need for interpretability so that model results are acceptable to medical professionals; and (4) computational efficiency for inference processes in hospital environments. Innovations presented in recent studies target these issues through automated normalization, self-weakly-supervised learning to leverage weak labels, GANs for rare dataset augmentation, and hybrid pipelines that combine adaptive thresholding for preprocessing with transfer hybrid models for classification.

Practically, evidence accumulated in the systematic literature review supports a recommendation for an integrated pipeline: stain normalization → adaptive thresholding (ROI extraction) → patch selection and augmentation → transfer learning hybrid model → ensemble processing → evaluation with sensitivity-conscious metrics (precision, recall, AUC, MCC). This pipeline offers a balance between input cleanliness (reducing false positives) and model representational capacity. However, before clinical implementation, critical steps include multicenter validation, prospective testing, and provision of interpretation tools (e.g., class activation maps) to enable pathologists to verify the reasoning underlying model predictions.

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Table 2. Overview of publicly available breast cancer histopathology datasets commonly used in deep learning research. Each entry includes the dataset's origin, composition, imaging specifications, intended application, and known limitations.

No	Title	Main Method	Description	Common Applications	Advantages	Disadvantages/Challenges
1	Cancer Diagnosis in Histopathological Images: A CNN-Based Approach. [71]	Convolutional Neural Network (CNN)	An automated CNN technique for breast cancer detection with 99.86% accuracy	Breast cancer classification	High accuracy, automated processing, rapid analysis	Requires large datasets, high computational resources
2	Deep Learning Applications on Histopathology Images for Breast Cancer: A Bibliometric Analysis. [72]	Deep Learning Framework	A bibliometric analysis examining trends in deep learning for breast cancer image classification	Research status and trend review	Provides comprehensive overview of the field	Not directly applicable as a practical methodology
3	Performance Analysis of Seven Convolutional Neural Network Architectures for Breast Cancer Histopathology Grading.[73]	Multi-CNN Comparison	Comparative evaluation of seven different CNN architectures for breast cancer grading	CNN model comparison	Enables comparison of multiple architectures	High analytical complexity
4	Building Efficient CNN Architectures for Histopathology Image Analysis.[74]	Efficient CNN Design	CNN architecture design emphasizing low computational requirements while	CNN architecture optimization	Improved computational efficiency	Trade-off between accuracy and speed

			maintaining high performance			
5	CNN-Based Method for Lung Cancer Detection in Whole Slide Images.[75]	CNN Whole Slide Image Analysis	Automated CNN method for lung cancer detection from whole slide images (WSI)	WSI cancer analysis	Effective handling of large images	Limited generalization to breast cancer detection
6	High-Throughput Adaptive Sampling for Whole-Slide Histopathology Image Analysis (HASHI). [78]	Adaptive Sampling Framework	An adaptive sampling method for analyzing invasive breast cancer WSI	WSI analysis for metastasis detection	Intelligent sampling conserves computational time	High implementation complexity
7	Enhancing Breast Cancer Histopathology Image Classification Through Transfer Learning and CNN. [79]	Transfer Learning + CNN	CNN-based method for breast cancer classification utilizing transfer learning techniques	Breast histology classification	Leverages pre-trained models	Dependency on source dataset quality
8	Detection and Classification of Histopathological Breast Cancer Images Using a Fusion-Based CNN Model. [80]	Fusion-Based CNN Model	A CNN fusion model for breast cancer histology classification	Multi-class cancer classification	Combines features from multiple CNN architectures	Increased model complexity

9	Enhancing Automated Breast Cancer Detection: A Multi-Scale CNN Framework. [81]	Deep Learning Diagnostic	An automated CNN framework for multi-scale breast cancer detection	Automated cancer diagnosis	Effective multi-scale feature handling	Clinical validation required
10	Histopathological Image-Based Breast Cancer Diagnosis Using AlexNet and GRU Integration. [82]	AlexNet + GRU Integration	Integration of AlexNet and Gated Recurrent Unit for histopathology classification	Classification with temporal features	Combines CNN and RNN architectures	Increased training complexity
11	Deep Learning Applications in Breast Cancer Histopathology: Image Enhancement and Segmentation. [83]	Deep Learning for Enhancement & Segmentation	Data enhancement techniques and lesion segmentation using deep learning	Image quality improvement and segmentation	Automated data augmentation	Risk of overfitting on small datasets
12	Deep Learning-Based Analysis of Histopathological Images Using Supervised and Unsupervised Methods.[84]	Supervised/Unsupervised CNN	Analysis employing both trained and untrained CNN approaches for breast cancer histopathology	Cancer clustering and classification	Flexible methodological approach	Difficult cluster interpretation
13	A Comprehensive Review of Breast Cancer	CNN/GAN/Vision Transformer Review	A comprehensive review of modern deep learning architectures	State-of-the-art overview	Broad coverage of	Not a practical implementation

	Histopathology Image Analysis Using Modern Deep Learning Architectures. [85]		for histopathology analysis		various methodologies	
14	Super-Resolution and Segmentation of Histopathological Images Using Deep Learning.[86]	Custom CNN for Super-Resolution	Custom CNN for enhancing low-resolution images and tissue segmentation	Image enhancement and tissue segmentation	Significant resolution improvement	Memory-intensive computation
15	Ensemble Deep Learning Methods for Breast Cancer Classification and Invasiveness Prediction.[87]	Ensemble Methods	Ensemble algorithms for breast cancer subtype and invasiveness classification	Multi-task classification	Higher accuracy through ensemble methods	Increased overfitting risk
16	Evaluating Deep Learning Models for Breast Cancer Detection in Histopathology Images. [88]	Model Evaluation Framework	Assessment of deep learning effectiveness in breast cancer histopathology classification	Early detection framework	Systematic evaluation approach	Limited practical implementation guidance
17	Breast Cancer Detection Based on Simplified Deep Learning Approaches Using	Simplified DL Technique	Simplified deep learning technique using the BreakHis dataset for cancer detection	Practical simplified approach	Easier implementation	Potentially lower accuracy

	the BraKHis Dataset. [89]					
18	Breast Cancer Histopathology Gene Expression Prediction from Histopathological Images Using Deep Learning (BrST-Net). [90]	BrST-Net Framework	Deep learning framework for predicting gene expression from histopathology images	Gene expression inference	Links imaging data to genomic information	Complex biological interpretation
19	Adaptive Hysteresis Thresholding Technique for Mammogram Image Segmentation. [91]	Adaptive Hysteresis Thresholding	Adaptive thresholding technique with hysteresis for mammogram segmentation	Mammogram preprocessing	Adaptable to intensity variations	Sensitive to image noise
20	Breast Cancer Segmentation Methods: Current Status and Future Directions. [92]	Multi-Method Segmentation Review	Comprehensive review of threshold, active contour, and region-growing segmentation methods	Segmentation methodology overview	Diverse method coverage	Method selection depends on individual case requirements
21	Adaptive Threshold Learning in Frequency Domain for Histopathology Image Classification. [93]	Adaptive Threshold + DL	Combination of adaptive thresholding with deep learning in the frequency domain	Hybrid segmentation approach	Leverages frequency domain characteristics	Increased complexity

22	Multi-Level Thresholding for Breast Thermography Images Using Black Widow Optimization Algorithm. [94]	IBWOA Optimization	Black Widow Optimization algorithm for multi-level thresholding in thermography	Thermal image segmentation	Global thresholding optimization	Limited to thermal imaging modality
23	Adaptive Edge Detection and Thresholding for Mammogram Analysis and Segmentation. [95]	Adaptive Edge Detection	Robust adaptive thresholding algorithm for detecting mammogram discontinuities	Mammogram regional segmentation	Robust to intensity variations	Regional application limitations
24	Medical Image Enhancement Algorithm for Breast Cancer Diagnosis in Computer-Aided Detection (CAD) Systems. [96]	CAD System with Enhancement	CAD system with mammography quality enhancement for detecting suspicious areas	Image quality improvement	Supports clinical adoption	Enhancement involves trade-offs
25	Adaptive Thresholding with Region Growing Fusion Method (AT-RGFM) for 3D Breast Cancer Segmentation. [97]	Hybrid AT-RGFM	Fusion of adaptive thresholding with region growing for breast cancer segmentation	3D cancer segmentation	Combines two complementary methods	Complex parameter tuning

26	Hybrid Fuzzy Clustering and Adaptive Thresholding Algorithm for Tissue Segmentation in Histopathology. [98]	Hybrid Fuzzy-AT Algorithm	Hybrid algorithm combining fuzzy clustering and adaptive thresholding for tissue segmentation	Tissue segmentation	Provides fuzzy logic flexibility	Difficult membership interpretation
27	Generative Adversarial Networks in Digital Histopathology: Applications and Challenges. [99]	GAN Review	Comprehensive review of GAN applications for histopathology image synthesis and enhancement	Image synthesis and quality enhancement	Novel applications with advanced feature learning	Risk of mode collapse
28	Generative Adversarial Networks in Digital Pathology: A Framework Approach. [100]	GAN Framework	GAN framework for histopathology image processing with emphasis on future perspectives	Image generation and reconstruction	Enables synthetic data generation	GAN training instability issues
29	Enhanced Pathology Image Quality Using Restore-GAN for Histopathological Image Restoration. [101]	Restore-GAN	GAN technique for restoring and improving histopathology image quality	Image restoration and robustness enhancement	Significant quality improvement	Requires domain-specific training
30	Vision Transformers for Computational Histopathology: A	Vision Transformer (ViT)	Comprehensive review of vision transformers with self-attention	State-of-the-art architecture	Global receptive field	High memory requirements and need for large datasets

	Comprehensive Review. [102]		mechanisms for histopathology analysis		and effective parallelization	
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5.1. Development framework

The theoretical framework of this research is constructed based on the integration of Deep Learning concepts and adaptive thresholding in breast cancer histopathology image analysis. Histopathology image analysis represents a critical component in cancer diagnosis, as it enables direct observation of tissue morphology, cellular characteristics, and microstructural features. However, the complexity of texture variations, color inconsistencies resulting from staining procedures, and differences in imaging quality across laboratories frequently present challenges in automated classification. Consequently, an artificial intelligence-based approach capable of efficiently and consistently extracting complex features is essential. This is precisely where Deep Learning assumes a fundamental role.

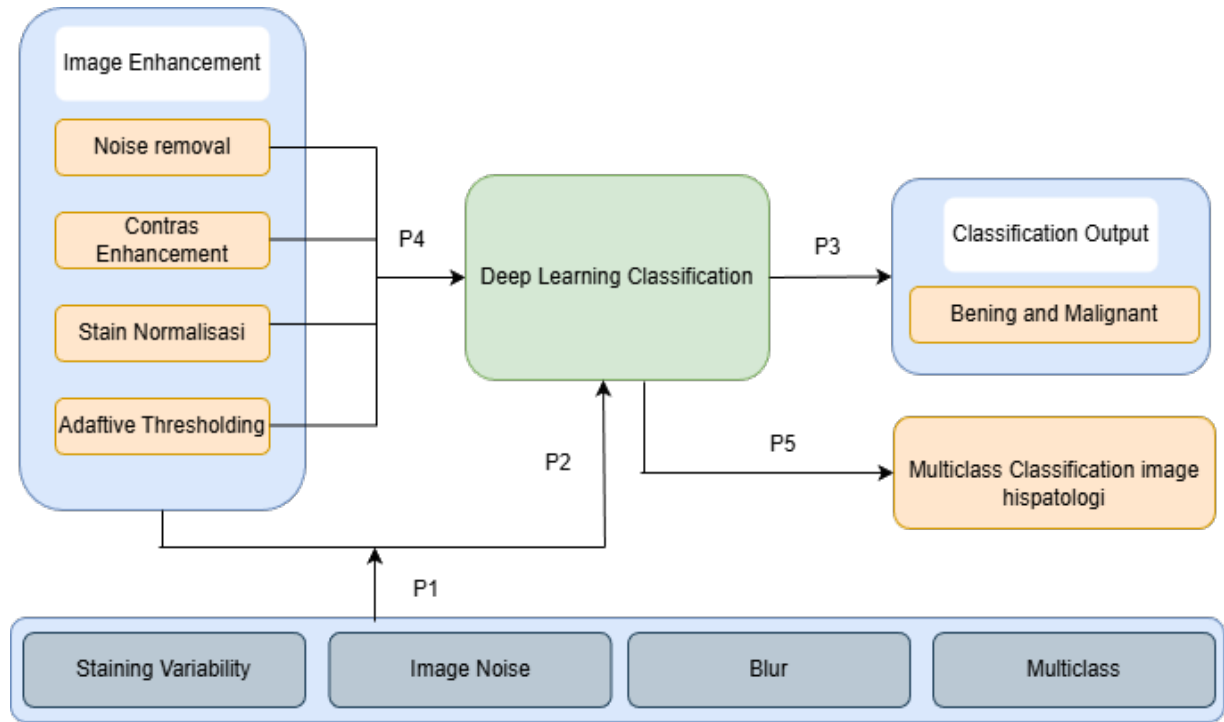
From a theoretical perspective, Deep Learning, particularly Convolutional Neural Networks (CNN), has demonstrated superior capabilities in recognizing spatial and textural patterns within histopathology images. Architectures such as VGG, ResNet, Inception, and EfficientNet serve as the foundation for transfer learning approaches, enabling models to leverage knowledge acquired from large datasets such as ImageNet and apply it to medical domains with limited available data. Furthermore, the emergence of Hybrid Deep Learning methodologies such as CNN + Transformer or CNN + SVM combinations expands model capabilities by integrating the strengths of CNN-based visual feature extraction with the global contextual understanding of Transformers. This integration results in improved classification accuracy and model stability.

Conversely, adaptive thresholding plays a crucial role in the image preprocessing phase. This method adjusts segmentation boundaries based on local pixel intensity values, thereby enabling more accurate separation of significant tissue regions, including cell nuclei, cytoplasm, and surrounding tissue, compared to global thresholding approaches. Theoretically, adaptive thresholding supports Deep Learning by providing cleaner image input, reducing noise interference, and highlighting diagnostically relevant features. The integration of adaptive thresholding prior to deep learning processes has the potential to enhance model convergence and reduce classification errors.

Within a broader context, the relationship between Deep Learning and adaptive thresholding can be elucidated through pipeline-based learning theory, wherein each stage within the image processing workflow contributes to the overall model performance. Preprocessing implemented through adaptive thresholding—functions to stabilize input data, while Deep Learning engages in feature representation learning and classification decision-making. The combination of these two components creates a more robust and efficient medical image analysis system, particularly when addressing real-world challenges such as data variability, annotation limitations, and the requirement for clinical interpretability.

Finally, the development of this theoretical framework is directed toward establishing an integrative Deep Learning Adaptive Thresholding model that not only focuses on enhancing breast cancer classification accuracy but also considers reliability, explainability, and clinical implementation potential. By combining pattern recognition theory-based approaches with adaptive segmentation methodologies, this framework is expected to serve

as a foundation for developing more responsive digital diagnostic systems that address practical medical requirements.



P1 – P5: Proposition 1 - Proposition 5

Figure 9. Theoretical framework of histopathological image of breast cancer classification

6. Conclusion

The first research question (RQ1) in this study aims to understand how various Deep Learning approaches have been applied to breast cancer histopathology image analysis and how effectively they improve classification accuracy. Based on the results of the systematic review, it was found that CNN-based models, Transfer Learning, and Hybrid Deep Learning represent the most dominant approaches employed. These methodologies have proven effective in extracting morphological and textural features from histopathological tissue with high accuracy, particularly on datasets such as BreakHis, BACH, and Camelyon. The improved classification performance demonstrates that the integration of more complex architectures and the careful application of data augmentation techniques play important roles in enhancing automated diagnostic accuracy.

The second research question (RQ2) focuses on the contribution of adaptive thresholding methods in the image preprocessing stage to improve Deep Learning model performance. From the literature analysis results, it was found that adaptive thresholding plays a significant role in enhancing segmentation quality by dynamically adjusting intensity thresholds in response to lighting conditions and tissue texture variations. This enables more accurate detection of cell nuclei and other important tissue structures, thereby reducing errors during the feature extraction phase. Consequently, this method strengthens

the Deep Learning model's ability to recognize breast cancer patterns more effectively, particularly in high-resolution images that exhibit high color variation and noise levels.

The third research question (RQ3) traces the challenges, innovations, and integration potential between Deep Learning-based models and adaptive thresholding in real-world medical applications. The primary challenges identified include dataset size limitations, class imbalance in benign and malignant cancer data, and the necessity for model result interpretability to gain acceptance from medical professionals. However, innovations such as the use of Hybrid Deep Learning Models (CNN + Transformer) and explainable artificial intelligence (XAI) demonstrate promising new development directions. The integration of adaptive thresholding within the Deep Learning pipeline not only improves image input quality but also strengthens the reliability of diagnostic results applicable to medical decision support systems.

6.1. Theoretical contributions

This research provides important theoretical contributions by revealing gaps in the understanding of the relationship between adaptive thresholding methods and Deep Learning model performance in breast cancer histopathology image analysis. Two principal gaps that were identified include: (1) the absence of a comprehensive understanding of how the preprocessing stage with adaptive thresholding directly influences Deep Learning classification results, and (2) inconsistency in positioning adaptive thresholding as an integral component within the deep learning pipeline.

The conceptual framework developed in this study contributes to broadening theoretical understanding by demonstrating that improvements in preprocessing quality not only impact computational efficiency but also have the potential to enhance classification accuracy and model generalization capability. Consequently, this research strengthens the theoretical foundation that the integration of Deep Learning and adaptive image processing represents a strategic direction for achieving more precise, efficient, and clinically reliable cancer diagnosis.

6.2. Practical Contribution

From a practical standpoint, the framework proposed in this study can serve as a guide for researchers and medical practitioners in developing breast cancer detection systems based on histopathology image analysis. Although this framework focuses on the breast cancer domain, similar approaches can be adapted for other cancer types that require microscopic tissue analysis, such as cervical or skin cancer, with modifications to the preprocessing stage and classification models.

Furthermore, the integration of adaptive thresholding can be implemented as a customizable automated module based on the characteristics of the dataset being used. In a clinical context, a system based on this framework has the potential to function as a computer-aided diagnosis (CAD) tool that supports pathologists' decisions in assessing cancer type and severity grade, while simultaneously reducing the manual workload in tissue identification processes.

6.3. Future of Work

This research opens opportunities for further development in the future. Empirical studies using direct experimental approaches on large datasets such as BreakHis, BACH, or TCGA-BRCA are essential for validating the effectiveness of Deep Learning and adaptive thresholding integration. Future development efforts can be directed toward multiclass classification on the BreakHis dataset, which not only distinguishes between benign and malignant cases but also recognizes cancer subtypes with high precision.

Furthermore, subsequent research can integrate explainable artificial intelligence (XAI) to enhance the transparency of classification results and strengthen user confidence in the medical field. Model performance improvements can also be achieved through hybrid architectures, feature fusion, and domain adaptation to address data variation from multiple hospital sources. Through these approaches, it is anticipated that Deep Learning-based diagnostic systems can achieve the level of accuracy and reliability necessary for widespread clinical implementation.

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