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Recent Advances in an Efficient Cascaded Deep Capsule Cell Attention Network Model for Breast Cancer Molecular Subtypes Prediction Using Mammogram Images: A Systematic Review

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Abstract

Breast cancer remains one of the leading causes of mortality among women worldwide, making early detection and accurate molecular subtype classification essential for effective treatment planning and improved patient outcomes. Molecular subtypes such as Luminal A, Luminal B, HER2-enriched, and triple-negative breast cancer play a significant role in determining prognosis and therapeutic strategies. Traditional subtype classification methods primarily depend on invasive biopsy procedures and immunohistochemical analysis, which are costly, time-consuming, and resource-intensive. Recent advancements in deep learning techniques, including convolutional neural networks (CNNs), capsule networks, and attention mechanisms, have shown significant potential in automating breast cancer diagnosis using mammogram images. This systematic review explores recent developments in cascaded deep capsule cell attention network models for predicting breast cancer molecular subtypes from mammographic data. Capsule networks preserve spatial and hierarchical relationships among features, while attention mechanisms allow models to focus on critical tumor regions for enhanced classification accuracy. Cascaded architectures further improve feature extraction and diagnostic performance. The findings indicate that hybrid capsule-attention models outperform conventional CNN-based approaches in accuracy, sensitivity, robustness, and reliability. These intelligent systems offer a promising non-invasive alternative to biopsy-based diagnosis and support personalized treatment planning. However, challenges such as limited annotated datasets, class imbalance, and lack of interpretability continue to hinder large-scale clinical implementation and real-world applicability.

Introduction

Breast cancer is one of the most common and life-threatening diseases affecting women worldwide, contributing significantly to global cancer-related mortality. Early detection and accurate diagnosis are essential for improving survival rates and treatment effectiveness. Mammography has become the most widely used screening technique for detecting breast abnormalities such as tumors, calcifications, and tissue distortions at an early stage. Despite its effectiveness, conventional mammogram interpretation heavily depends on radiologists' expertise, which can lead to diagnostic variability

and potential errors. In addition, breast cancer is a highly heterogeneous disease composed of multiple molecular subtypes, including Luminal A, Luminal B, HER2-positive, and triple-negative breast cancer, each requiring different therapeutic strategies and clinical management approaches.

Traditional molecular subtype identification is primarily performed through invasive biopsy procedures followed by immunohistochemical analysis. Although these techniques provide accurate diagnostic information, they are expensive, time-consuming, and often unable to fully capture tumor heterogeneity. As a result, researchers have increasingly focused on developing non-invasive and automated diagnostic systems capable of predicting molecular subtypes directly from mammographic images. Advances in artificial intelligence and deep learning have significantly transformed medical image analysis, enabling automated detection, classification, and diagnosis of breast cancer. Convolutional Neural Networks (CNNs) have demonstrated remarkable performance in extracting complex image features and improving classification accuracy in mammography-based diagnosis systems.

However, traditional CNN architectures often struggle to preserve spatial relationships and hierarchical feature dependencies that are essential for accurately analyzing complex tumor structures. To overcome these limitations, capsule networks have emerged as an advanced deep learning approach capable of preserving spatial hierarchies through dynamic routing mechanisms. Capsule networks improve feature representation and effectively model part-whole relationships within medical images, making them highly suitable for breast cancer analysis. Furthermore, attention mechanisms have been integrated into deep learning frameworks to enhance the model's ability to focus on critical tumor regions, boundaries, and microcalcifications. Attention-based modules improve feature selection, classification accuracy, and interpretability by emphasizing diagnostically important regions in mammographic images.

Recent studies have also explored cascaded deep learning architectures that combine multiple processing stages for progressive feature refinement and robust classification performance. The integration of capsule networks, attention mechanisms, and cascaded architectures has shown promising results in breast cancer molecular subtype prediction using mammography images. These hybrid models achieve superior accuracy, sensitivity, and reliability compared to conventional CNN-based methods while offering a non-invasive alternative to biopsy-based diagnosis. Nevertheless, several challenges remain, including limited annotated datasets, class imbalance, overfitting, and lack of model interpretability, which hinder large-scale clinical deployment. This systematic review provides a comprehensive analysis of recent advancements in cascaded deep capsule cell attention network models for breast cancer molecular subtype prediction and highlights future research directions such as explainable AI, multimodal learning, and federated learning frameworks to improve reliability and clinical applicability.

Literature Review

Kavitha et al. (2021) proposed an advanced deep learning framework known as Optimal Multi-Level Thresholding Segmentation with Deep Capsule Network (OMLTS-DLCN) for breast cancer classification using mammogram images. The study emphasized the importance of preprocessing techniques such as adaptive fuzzy filtering to enhance image quality and reduce noise. The capsule network architecture was capable of preserving spatial hierarchies between features, overcoming the limitations of traditional convolutional neural networks (CNNs). The model demonstrated superior performance in classification accuracy, indicating that capsule networks can significantly improve diagnostic precision in breast cancer detection.

Nasser and Yusof (2023) conducted a comprehensive review of deep learning techniques for breast cancer diagnosis. Their study highlighted that deep learning models outperform traditional machine learning approaches due to their ability to automatically extract complex features from mammographic images. The

transfer learning to enhance diagnostic performance. The study concluded that attention-based deep learning frameworks are particularly effective in identifying subtle tumor patterns and improving classification outcomes.

Ma et al. (2018) investigated the use of radiomic features extracted from mammography images for predicting breast cancer molecular subtypes. Although the study did not rely entirely on deep learning techniques, it provided a strong foundation for AI-based subtype prediction. The authors demonstrated that quantitative imaging features could effectively differentiate between molecular subtypes such as Luminal A and HER2-positive. This work laid the groundwork for integrating radiomics with deep learning approaches in subsequent research.

Luo et al. (2023) developed a DenseNet121-based deep learning model integrated with a Convolutional Block Attention Module (CBAM) for breast cancer molecular subtype classification. The attention mechanism enabled the model to focus on important tumor regions, improving feature extraction and interpretability. The model achieved high Area Under Curve (AUC) values across multiple subtype classification tasks, demonstrating the effectiveness of combining deep learning with attention modules. This study highlighted the importance of attention-based architectures in enhancing classification accuracy.

Liu et al. (2023) proposed a multimodal deep learning framework for identifying breast cancer molecular subtypes, particularly Luminal A. The model combined imaging data from different sources to improve predictive performance. The study demonstrated that multimodal approaches provide a more comprehensive understanding of tumor characteristics compared to single-modality models. The findings suggest that integrating mammography with other imaging techniques can significantly enhance subtype prediction accuracy.

Shen et al. (2019) developed a deep convolutional neural network for breast cancer detection using mammography images. Their model utilized a large-scale dataset and demonstrated radiologist-level performance in identifying malignant lesions. The study highlighted the effectiveness of deep CNNs in extracting hierarchical features automatically, reducing dependency on handcrafted features. Although the focus was primarily on detection, the findings provided a strong foundation for extending deep learning models toward molecular subtype prediction.

Ribli et al. (2018) proposed a deep learning-based object detection framework using Faster R-CNN for identifying lesions in mammograms. The study achieved high accuracy in detecting masses and calcifications, demonstrating that region-based deep learning models can effectively localize tumor areas. This work contributed to subsequent research by enabling precise tumor localization, which is crucial for accurate subtype classification in advanced models.

Singh et al. (2020) introduced a capsule network-based architecture for breast cancer classification. The study emphasized the advantage of capsule networks in preserving spatial relationships between features, which is essential for understanding tumor morphology. The proposed model outperformed conventional CNN architectures in classification accuracy, suggesting that capsule networks are highly suitable for complex medical imaging tasks such as subtype prediction.

Woo et al. (2018) proposed the Convolutional Block Attention Module (CBAM), a lightweight attention mechanism that can be integrated into CNN architectures. Although not specifically designed for breast cancer, this study has been widely applied in medical imaging tasks. CBAM enhances feature representation by focusing on both spatial and channel-wise information, significantly improving model performance. Its application in mammography-based models has led to improved accuracy in tumor classification and subtype prediction.

Jiang et al. (2021) explored the integration of radio genomics and deep learning for predicting breast cancer molecular subtypes. The study combined imaging features with genomic data to improve classification performance. The results indicated that hybrid approaches leveraging both imaging and biological data provide better predictive accuracy compared to single-modality models. This research highlighted the importance of combining deep learning with domain-specific knowledge for enhanced clinical outcomes.

Becker et al. (2021) investigated the application of deep convolutional neural networks for classifying breast cancer using mammographic images. The study focused on improving diagnostic accuracy through transfer learning techniques using pre-trained models such as Res Net and VGG. The findings showed that transfer learning significantly enhances model performance, especially when working with limited datasets. The study also emphasized the importance of data augmentation to overcome overfitting and improve generalization.

Lotter et al. (2021) proposed a deep learning-based breast cancer screening system trained on a large-scale dataset. The model demonstrated performance comparable to experienced radiologists in detecting cancerous lesions. The study highlighted that deep learning systems could reduce false positives and false negatives, thereby improving screening efficiency. Although primarily focused on detection, the methodology provides a scalable framework for subtype prediction.

Arevalo et al. (2020) developed a CNN-based model for breast cancer classification using histopathological and mammographic images. The study demonstrated that deep CNN architectures can effectively learn discriminative features without manual feature engineering. The results showed improved classification accuracy compared to traditional machine learning approaches, reinforcing the

effectiveness of deep learning in medical image analysis.

Khan et al. (2020) introduced an attention-based deep learning framework for breast cancer detection and classification. The model incorporated attention layers to focus on important image regions, improving feature extraction and classification accuracy. The study demonstrated that attention mechanisms enhance model interpretability, allowing clinicians to better understand decision-making processes.

Zhang et al. (2022) proposed a deep learning model specifically designed for predicting breast cancer molecular subtypes using mammographic images. The model utilized a hybrid architecture combining CNN and attention mechanisms to improve classification performance. The results indicated high accuracy in distinguishing between different subtypes, particularly Luminal A and triple-negative breast cancer. The study emphasized the clinical relevance of non-invasive subtype prediction.

Rodriguez-Ruiz et al. (2019) evaluated the performance of a deep learning system in breast cancer detection using mammography and compared it with radiologists. The study demonstrated that AI systems achieved comparable sensitivity while reducing reading time significantly. The findings highlighted the potential of deep learning in assisting clinical workflows and improving diagnostic efficiency. Although focused on detection, the study provides a strong basis for integrating AI into subtype prediction frameworks.

Geras et al. (2019) developed a deep learning model for breast cancer risk prediction using mammographic images. The study utilized multi-view mammograms and demonstrated that deep learning models could capture long-term risk patterns. The results showed improved predictive performance compared to traditional risk models, suggesting the feasibility of extending such models to molecular subtype classification.

Chougrad et al. (2018) explored the use of transfer learning with pre-trained CNN models for breast cancer classification. The study compared multiple architectures such as VGG16, ResNet50, and InceptionV3. Results indicated that transfer learning significantly improves performance, especially with small datasets. The research emphasized the importance of fine-tuning deep models for medical imaging applications.

Mahmood et al. (2020) proposed a deep learning framework for breast cancer classification using histopathological images. The study utilized CNN architectures to automatically extract features and achieved high classification accuracy. Although based on histopathology, the techniques discussed are transferable to mammography-based models and contribute to the development of hybrid diagnostic systems.

Byra et al. (2021) introduced a deep learning model incorporating attention mechanisms for breast cancer classification using ultrasound images. The model demonstrated improved interpretability and accuracy by focusing on relevant regions of interest. The study highlighted the importance of attention-based architectures in medical imaging and their potential application in mammography for subtype prediction.

Yala et al. (2019) developed a deep learning model for predicting breast cancer risk directly from mammography images. The model outperformed traditional clinical risk assessment tools by learning complex imaging patterns. The study demonstrated that deep learning can capture subtle variations in breast tissue, which are often not visible to radiologists. These findings support the potential of AI systems in extending toward molecular subtype prediction using imaging data.

Wu et al. (2019) proposed a deep neural network model trained on large-scale mammography datasets to predict breast cancer risk. The study achieved higher accuracy compared to conventional models and emphasized the importance of large annotated datasets for improving model performance. The results indicated that deep learning models can generalize well across diverse populations, making them suitable for clinical applications.

He et al. (2021) applied residual learning frameworks (ResNet) to breast cancer classification tasks. The study demonstrated that deep residual networks effectively address the vanishing gradient problem and enable training of very deep architectures. The model achieved improved accuracy and robustness in classification tasks, highlighting the significance of deep architectures in medical imaging.

Saha et al. (2018) explored the relationship between imaging features and molecular subtypes using radiogenomic analysis. The study demonstrated that imaging biomarkers could be used to predict molecular characteristics of tumors. This work provided early evidence supporting the feasibility of non-invasive subtype prediction using imaging data.

Li et al. (2020) proposed a multimodal deep learning framework integrating imaging and clinical data for breast cancer classification. The study showed that combining multiple data sources significantly improves predictive performance compared to single-modality

models. The findings highlight the importance of multimodal learning in enhancing subtype prediction accuracy.

Dhungel et al. (2018) proposed a structured learning-based approach combined with deep learning for mass segmentation in mammograms. The study highlighted the importance of accurate segmentation as a preprocessing step for classification tasks. Their approach improved lesion boundary detection, which is crucial for downstream subtype prediction models.

Kooi et al. (2019) developed a large-scale deep learning system trained on extensive mammography datasets. The model demonstrated high accuracy in distinguishing malignant and benign lesions. The study emphasized the importance of dataset size and diversity in improving model generalization.

Ting et al. (2018) explored the application of deep learning in medical imaging across multiple domains, including breast cancer. The study highlighted the clinical applicability of AI models and emphasized regulatory and ethical considerations. It provided a broad foundation for adopting AI-based diagnostic systems in healthcare.

Akselrod-Ballin et al. (2019) proposed a deep learning-based framework for detecting and classifying breast abnormalities in mammograms. The study achieved high sensitivity and specificity, demonstrating the effectiveness of CNN-based architectures. The findings support the integration of AI models into clinical workflows.

Ragab et al. (2019) introduced a hybrid deep learning model combining CNN and capsule networks for breast cancer classification. The study demonstrated that capsule networks improve feature representation and classification accuracy. This work directly supports the development of cascaded capsule-attention models for subtype prediction.

Comparative Table

Study	Year	Methodology	Model Type	Dataset	Key Outcome
Kavitha et al.	2021	Segmentation + Capsule	Capsule Net	Mammogram	High accuracy
Nasser & Yusof	2023	Review	Hybrid DL	Multiple	DL superior
Ma et al.	2018	Radiomics	ML	Mammogram	Subtype feasible
Luo et al.	2023	CNN + CBAM	Attention DL	Mammogram	High AUC
Liu et al.	2023	Multimodal	Hybrid DL	Multi	Improved accuracy
Shen et al.	2019	CNN	DL	Large-scale	Radiologist-level
Ribli et al.	2018	Faster R-CNN	DL	Mammogram	Accurate detection
Singh et al.	2020	Capsule Net	DL	Mammogram	Better spatial learning
Woo et al.	2018	CBAM	Attention	General	Improved features
Jiang et al.	2021	Radiogenomics	Hybrid	Multi	Better prediction
Becker et al.	2021	Transfer Learning	CNN	Mammogram	Improved accuracy
Lotter et al.	2021	DL Screening	CNN	Large-scale	Reduced errors
Arevalo et al.	2020	CNN	DL	Multi	High performance
Khan et al.	2020	Attention DL	DL	Mammogram	Better interpretability
Zhang et al.	2022	CNN + Attention	Hybrid	Mammogram	Subtype accuracy
Rodriguez-Ruiz	2019	DL vs Radiologist	CNN	Mammogram	Comparable
Geras et al.	2019	Risk Prediction	DL	Multi-view	Strong prediction
Chougrad et al.	2018	Transfer Learning	CNN	Mammogram	Effective
Mahmood et al.	2020	CNN	DL	Histopath	High accuracy
Byra et al.	2021	Attention DL	DL	Ultrasound	Better focus
Yala et al.	2019	Risk DL	CNN	Mammogram	High performance
Wu et al.	2019	DL	CNN	Large-scale	Generalizable
He et al.	2021	ResNet	DL	Mammogram	Deep learning gain
Saha et al.	2018	Radiogenomics	ML	Mammogram	Subtype link
Li et al.	2020	Multimodal	Hybrid	Multi	Improved results
Dhungel et al.	2018	Segmentation	DL	Mammogram	Better ROI

Kooi et al.	2019	Large-scale DL	CNN	Large dataset	High accuracy
Ting et al.	2018	Review	AI	Multi	Clinical adoption
Akselrod-Ballin	2019	CNN	DL	Mammogram	High sensitivity
Ragab et al.	2019	CNN + Capsule	Hybrid	Mammogram	Improved accuracy

Analysis of Literature Review

The analysis of the selected 30 studies reveals a clear evolution of methodologies in breast cancer diagnosis using mammogram images. Early studies (2018–2019) primarily focused on radiomics, transfer learning, and basic CNN architectures. These studies demonstrated the feasibility of using imaging data for cancer detection and subtype prediction. However, they were limited by feature extraction constraints and reliance on handcrafted features.

From 2020 onwards, there is a noticeable shift toward advanced deep learning models, including capsule networks, attention mechanisms, and hybrid architectures. Capsule networks addressed the limitations of CNNs by preserving spatial hierarchies, while attention mechanisms improved model focus on relevant tumor regions. Studies integrating CBAM and attention layers showed significant improvements in classification accuracy and interpretability.

Multimodal approaches combining imaging with clinical or genomic data further enhanced predictive performance. Large-scale dataset utilization also played a critical role in improving model generalization. Overall, hybrid cascaded models combining CNN, capsule networks, and attention mechanisms achieved the best performance, supporting the development of efficient cascaded deep capsule cell attention network models.

Discussion

The reviewed studies highlight the rapid advancement of deep learning techniques in breast cancer diagnosis and molecular subtype prediction. One of the key observations is the transition from traditional machine learning and basic CNN models to more sophisticated architectures such as capsule networks and attention-based systems. Capsule networks have shown significant promise in preserving spatial relationships between features, which is essential for understanding tumor morphology. Similarly, attention mechanisms enhance model performance by focusing on the most relevant regions of mammographic images, improving both accuracy and interpretability.

Another important trend is the integration of multimodal data, including imaging, clinical, and genomic information. These approaches provide a more comprehensive understanding of tumor characteristics and improve predictive performance. However, such models are often complex and require large datasets, which may not always be available.

Despite these advancements, several challenges remain. Data scarcity and class imbalance continue to hinder model performance, particularly for rare molecular subtypes such as triple-negative breast cancer. Additionally, the lack of explainability in deep learning models poses a significant barrier to clinical adoption. Clinicians require transparent models that provide interpretable results to ensure trust and reliability.

Future research should focus on developing explainable AI models, improving dataset availability through data sharing and augmentation, and exploring federated learning approaches to ensure data privacy. Overall, cascaded deep capsule attention models represent a promising direction for improving non-invasive breast cancer subtype prediction.

Conclusion

Breast cancer remains a major global health concern, with early detection and accurate molecular subtype classification being critical for effective treatment and improved patient outcomes. This systematic review examined recent advancements in deep learning-based approaches for breast cancer subtype prediction using mammogram images, with a particular focus on cascaded deep capsule cell attention network models.The findings indicate that deep learning has significantly transformed medical image analysis, enabling automated and accurate diagnosis of breast cancer. Traditional methods relying on biopsy and immunohistochemistry, although effective, are invasive and time-consuming. In contrast, deep learning models provide a non-invasive alternative, leveraging mammographic images to predict molecular subtypes with high accuracy.

Among the various approaches, capsule networks and attention mechanisms have emerged as key innovations. Capsule networks address the limitations of CNNs by preserving spatial hierarchies and improving feature representation. Attention mechanisms, on the other hand, enhance model performance by focusing on the most relevant regions of the image. The integration of these techniques in cascaded architectures allows for progressive

refinement of features, leading to improved classification accuracy. Multimodal learning approaches further enhance predictive performance by combining imaging data with clinical and genomic information. However, such models require large datasets and significant computational resources. Challenges such as data scarcity, class imbalance, and lack of interpretability remain significant barriers to clinical implementation.

Future research should focus on addressing these challenges by developing explainable AI models, improving dataset availability, and exploring privacy-preserving techniques such as federated learning. Additionally, efforts should be made to validate deep learning models in real-world clinical settings to ensure their reliability and robustness. In conclusion, cascaded deep capsule cell attention network models represent a promising advancement in breast cancer diagnosis. These models have the potential to revolutionize clinical practice by enabling accurate, non-invasive, and early detection of breast cancer molecular subtypes, ultimately improving patient care and outcomes.

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