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Original Research Article

Classification of breast cancer from histopathology images using an ensemble of deep multiscale networks

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ABSTRACT

Manual delineation of tumours in breast histopathology images is generally time-consuming and laborious. Computer-aided detection systems can assist pathologists by detecting abnormalities faster and more efficiently. Convolutional Neural Networks (CNN) and transfer learning have shown good results in breast cancer classification. Most of the existing research works employed State-of-the-art pre-trained architectures for classification. But the performance of these methods needs to be improved in the context of effective feature learning and refinement. In this work, we propose an ensemble of two CNN architectures integrated with Channel and Spatial attention. Features from the histopathology images are extracted parallelly by two powerful custom deep architectures namely, CSAResnet and DAMCNN. Finally, ensemble learning is employed for further performance improvement. The proposed framework was able to achieve a classification accuracy of 99.55% on the BreakHis dataset.

1. Introduction

Breast cancer is one of the most common forms of cancer and it is the second leading cause of cancer death in women. Since 2007, breast cancer death rates have been steady in women younger than 50, but have continued to decrease in older women. In recent years, incidence rates have increased by 0.5 % per year. Changes or mutations in DNA can cause normal breast cells to become cancerous cells [1]. Breast cancer is metastatic cancer and is capable of spreading to other organs in the human body. According to breast cancer statistics, the number of new cases in 2020 is 2,261,419 worldwide. The mortality rate of breast cancer is the highest in the majority of the countries [2]. Although the exact cause of breast cancer is undiscovered, specific risk factors have been identified. One of the most important causes of breast cancer is genetics and family history of the disease. Weight gain and high-calorie intake also increase the risk of breast cancer in

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post-menopause women. Alcohol and smoking are also important factors that may cause the development of breast tumours [3].

Efficient diagnosis of breast cancer in the early stages can reduce tissue damage and can provide a higher probability of recovery. Numerous procedures are followed in the clinical diagnosis of breast cancer. Magnetic Resonance Imaging (MRI), Mammography, Histopathology, and Ultrasound are commonly used modalities for clinical screening [4]. MRI is preferred to enhance detection when compared to other screening methods [5]. Histopathology provides important predictive information which may help in identifying crucial targets beforehand [6]. In this process, a tissue sample from the affected area is collected and tested under a microscope for the identification of the tumour as normal, benign, or malignant. The benign tissues are non-cancerous and are an abnormality that can be cured. Whereas, malignant cells are cancerous cells that multiply in number and grow irregularly. Histopathology images are usually examined at a lower magnification level allowing extensive analysis at the tissue level. In general, cancer cells are examined based on the shape and size of cells, the shape, and size of cell nuclei, and the distribution of cells [7]. The histopathological analysis is important before proceeding with surgery to estimate the tumour size as accurately as possible [8].

Analysis of the histopathology images manually is a complex, tedious and challenging task due to the heterogeneity existing in the morphology of the cancer cells [9]. Various pre-processing and enhancement techniques have to be performed on the histopathology images for efficient detection of cancerous cells [10]. However, considering these difficulties, computer-aided diagnosis (CAD) is used in many cases. Compared to manual analysis of Whole Slide Images (WSI) slides, computer-based systems may provide faster and more consistent results. The advancements in the field of machine learning have led to more efficient and intelligent CAD systems [11,12]. These systems play a major role in examining the histopathological images faster and more accurately and identifying the abnormalities. Since, histopathology images contain more information regarding the structural aspect of the underlying tissues, powerful pre-processing techniques, and learning algorithms are required for the diagnosis of cancer cells effectively [13].

2. Related works

In this section, various methods applied for breast cancer classification are reviewed in two categories. Machine learning-based methods and deep learning-based methods are analyzed in the first and second categories respectively.

2.1. *Machine Learning-based methods*

The supervised learning methods for breast cancer classification employ standard algorithms like Nearest Neighbours [15–17,22], Naïve Bayes [16], Logistic Regression [17,23], Decision Trees [15], Random Forests [23], Support Vector Machines (SVM) [15–17,23] etc. Most of these methods utilize handcrafted features to extract morphological features from images followed by classification using a standard machine learning classifier [15–17,19–21]. Ensemble learning has also been adopted by various works for a further increment in stability and performance [15,17,18].

A two-stage approach for breast cancer classification was presented by Karthiga et al. Nuclei segmentation was performed by K-Means clustering followed by a Discrete Wavelet Transform (DWT) method for extracting features [14]. SVM was applied for classification. Gupta et al. presented an approach to extract joint colour-texture image descriptors [15]. Gabor chromatic features and complex wavelet features were some of the image descriptors that were extracted. Finally, an ensemble of various ML classifiers using the majority voting technique was employed. Bikesh et al. presented an approach to extract important features and further classify them using various ML algorithms [16]. It could be observed that SVM performed the best in extracting features and medium k-NN performed best in classification. Khuriwal et al. proposed another method using a univariate feature selection algorithm that computes chi-square stats between non-negative classes and labels [17]. Furthermore, ensemble learning using an adaptive voting technique for the classification of breast cancer was performed. A new approach was introduced by Zhang et al. for breast cancer classification [18]. An ensemble of one-class Kernel Principal Component Analysis (KPCA) models using different image features was proposed. Here, the combination of different image features exploits the complementary strengths of the feature extractors.

Handcrafted features have been widely used for the detection of breast cancer in many research works. Alirezazadeh et al. proposed an approach using domain adaption based on representation learning [19]. Feature vectors were extracted using handcrafted descriptors such as Local Phase Quantization (LPQ), Parameter-Free Threshold Adjacency Statistics (PFTAS), and Local Binary Pattern (LBP) and are mapped to an invariant space. Another approach was presented by Dimitropoulos et al. where breast cancer images are considered as a set of multidimensional spatially-evolving signals that can be modelled efficiently [20]. Moreover, Vector of Linear Aggregated Descriptors (VLAD) on the Grassmannian space to exploit both the dynamics and spatial information of the images was proposed. Bahlmann et. al presented a method to characterize distributions of Haematoxylin and Eosin (H&E) channels separately through the use of descriptors [21]. The descriptor is based on the distribution of intensities in the Haematoxylin and Eosin (H&E) channels. Finally, SVM was employed for the classification of breast cancer. Another supervised learning approach for the Computer-Aided Diagnosis (CAD) of breast cancer was presented by Sudharshan et. al [22]. This work analyzed different state-of-the-art multiple instance learning methods for classification. Samvetmut et al. presented an extended approach by combining histopathology images with clinical, DNA, RNA, and treatment features [23]. The classification was performed using an ensemble classifier consisting of Logistic Regression, Random Forest, and SVM.

The performance of the above-discussed machine learning methods depends on the proper selection of discriminative features. In classical machine learning algorithms,

handcrafted features are learned which require a lot of domain expertise and then fed into a classifier. On the other hand, deep learning algorithms learn the features incrementally through their hidden layers. This eliminates the need for domain expertise and hardcore feature engineering.

2.2. *Deep Learning-based methods*

A substantial amount of research works have been published on breast cancer classification of histopathology images using deep learning methods. CNN is widely applied in the domain of medical image processing because, (1) It can process a huge volume of contextual features that extend well to pathological details (2) the processing paradigm is hierarchical from levels of intensities, textures, physical properties to morphology, anatomy, etc. and exploits the spatial dependencies between the levels (3) the larger receptive field adds to the context, (4) pixel-accurate operations that trace deep links to these levels of feature learning [24].

Transfer learning is a technique that has been employed by a substantial amount of research works. Architectures like Inception V3, VGG16, Resnet, etc. have been widely used for the detection of breast cancer. Chang et al. proposed a method that uses a pretrained Inception-V3 architecture along with various data augmentation techniques for breast cancer classification [25]. The model was trained for 500 epochs to reach the convergence. Hou proposed a method to extract important patches followed by the use of Otsu algorithm for segmenting the background region. Furthermore, GoogleNet was employed for feature extraction and classification of breast cancer [26]. Residual networks reduce the complexity and solve the problem of degradation while keeping good performance. Gupta et al. applied Resnet architecture for feature extraction from histopathology images [27]. Furthermore, Logistic Regression and SVM were employed for classification. In [28], Sun et al. have performed a comparison of Resnet, GoogleNet, and CaffeNet architectures for the classification of breast cancer. It could be inferred that Resnet performed slightly better than the other two architectures. El Aghouri et al. presented an analysis with a Moroccan H&E dataset using Resnet and Xception architectures [29]. Out of the two models, the Xception network performed better in terms of overall classification accuracy and sensitivity. Gour et al. proposed a modified Resnet-50 architecture that consists of only 13 residual blocks for breast cancer classification [30]. Here, transfer learning has been applied to the first 130 layers of the model and the final 22 layers have been trained from scratch. Another approach using a pretrained Resnet-50 architecture along with various pre-processing methods was proposed for the detection of breast cancer [31]. The input dataset was split in the ratio of 75:25 and the model was trained for 200 epochs. Yamlome et al. proposed a modified architecture of AlexNet which consists of the first 17 layers for feature extraction [32]. Finally, three fully-connected layers and a dropout layer were used before classification. Another approach using Alexnet architecture was presented by Spanhol et al. for breast cancer detection [33]. It was inferred that the presented CNN method outperformed the ML-based methods with handcrafted features. Karthiga et al. proposed a method that used a pre-trained VGG16 architecture for breast cancer classification [34]. Here, the authors employed one-hot encoding algorithm to reduce the utilization of memory and training time. Few transfer learning approaches were reported in the literature for the classification of breast cancer. In [35,36], VGG16 architectures were combined with different ML models like Random Forest, SVM, etc. Liew et al. presented an approach where feature extraction was performed by a pretrained CNN architecture namely, Densenet-201 [37]. The dataset was resampled to overcome class imbalance and the classification task was carried out with the XGBoost algorithm. Here, Adam optimizer with a learning rate of 1e-4 was employed to minimize the RMSprop loss function.

Khan et al. presented a novel approach that uses fine-tuned VGG16, Resnet, and GoogleNet for feature extraction from two different breast cancer histopathology datasets [38]. These features are then combined using filter concatenation before classification using the softmax layer. Furthermore, data augmentation was performed and a comparative analysis of different data split ratios was also presented. Another novel method was proposed in [39] that uses Densenet, NASNet, and VGG16 as feature extractors. A global pooling layer is then used to generate feature maps before using the softmax layer for classification. Dropout and batch normalization layers have been utilized to solve the problem of overfitting. In addition to existing pretrained architectures, Dabeer et al. proposed a custom convolution neural network with three convolutional layers to spotlight crucial features for the detection of breast cancer [40]. Here, the authors split the dataset in the ratio of 80:20 for training and testing respectively. Gamble et al. presented an approach to predict the biomarkers from breast cancer histopathology images [41]. Inception V3 was employed for feature extraction and Logistic Regression was used for prediction. In contrast to basic data augmentation techniques, generative adversarial networks have also been used to solve the problem of class imbalance. Wang et al. presented an approach that develops a target-biased generative adversarial network to transform the source images into target style with the help of target bias loss under an adversarial learning mechanism [42]. Sui et al. presented an augmentation approach using Deep Convolution Generative Adversarial Network (DCGAN) for generating new image patches [43]. This work utilized a multi-scale deconvolution network for the detection of breast cancer. Another approach proposed by Saini et al. utilized DCGAN on the minority class to overcome class imbalance [44]. Moreover, a modified VGG16 network with lesser parameters has been used for feature extraction with extensive hyperparameter tuning.

In addition to pre-trained architectures, a few custom CNN architectures were also presented in the recent past for effective detection of breast cancer. Ting et al. presented a 30-layer custom CNN architecture for the detection of breast cancer in histopathology images [45]. Chen et al. customized the VGG architecture with an embedding layer for effective classification [46]. This work involved feature extraction from two parallel branches and was finally concatenated before feeding into Fully-Connected (FC) layers. Chen et al. presented a Holographic Cytometry based approach using a custom CNN with three residual blocks [47]. Another custom CNN was proposed

for mitosis detection from histopathology images [48]. Here, an object-level interobserver agreement study on mitosis counting is also presented. Dalwinder et al. applied a Back Propagation Neural Network (BPNN) for the detection of breast cancer [49]. Moreover, optimal feature weights and parameters were selected using Ant Lion Optimization.

In addition to classification, segmentation of breast cancer images was also performed in many works. Kriti et al. presented an approach to segment breast cancer ultrasound images using an active contour model [50]. Moreover, the images were pre-processed and analyzed using various despeckle filtering algorithms. Priego-Torres et al. have presented an approach to segment breast cancer histopathology images using DeepLabv3 architecture. Mobilenet, Xception, and Resnet architectures were compared for the optimal backbone. It could be inferred that Mobilenet performed the best among the others [51]. In another work, Ye et al. proposed a methodology to segment Digital Breast Tomosynthesis (DBT) images using a Dilated CNN. The images were pre-processed followed by patch extraction before feeding into the network [52]. In [53,54], custom CNN architectures were employed to segment and classify breast cancer images. Y-Net architectures were applied for the segmentation of breast cancer in a few works [55,56]. A two-stage approach for segmentation of breast cancer metastatic lesions was proposed by Moreau et al. Here, they employed a 3D U-Net for segmentation of baseline images and another U-Net for the segmentation of follow-up acquisitions [57].

Apart from the above research works, several reviews were presented for the classification and detection of breast cancer. Gastounioti et al. have presented an extensive review of mammographic phenotyping for breast cancer using Artificial Intelligence [58]. Similarly, reviews on histopathology image analysis using deep learning were presented in [59–62]. In addition to the above-discussed works, a few methods were also presented for designing CAD systems for the diagnosis of breast cancer. Marta et al. presented one such approach to develop a breast cancer CAD model to deal with deformations in the MRI images [63].

2.3. *Research gaps and motivation*

The proposed work addresses the following research gaps in breast cancer classification.

Unlike deep learning methods, machine learning-based methods require domain expertise to identify handcrafted features from histopathology images for effective classification.

In most of the existing research works, class imbalance was observed in the dataset used for training the deep learning models. This imbalance will have a significant impact on generalizing the feature patterns for all classes. Hence, effective data augmentation strategies need to be applied for training deep learning models.

Most of the research works employed a single-path deep learning architecture for classification. It was observed that the false positive and false negative rates were slightly higher for these networks. This can be addressed by employing advanced mechanisms like feature fusion from multiple tracks, ensembling, etc.

2.4. *Research contributions*

The following are the research contributions made towards addressing these gaps.

To tackle the problem of class imbalance, the proposed methodology includes extensive data augmentation to increase the number of training samples. This enabled the proposed network to become more robust and prevent overfitting.

Channel and Spatial Attention (CSA) module was integrated with the Densenet architecture to improve the representation power of the proposed deep network. By doing so, the network was able to learn inter-channel and intra-spatial relationships in an effective way.

Weighted average ensembling was performed with CSAResnet and DAMCNN to reduce the number of false positives and false negatives in the proposed work. This enabled the proposed network to generalize the feature patterns from two different tracks for effective classification.

3. Proposed methodology

The proposed methodology is an ensemble of two state-of-the-art architectures integrated with two types of attention. Spatial attention utilizes the inter-spatial relationship of features to generate a feature map whereas channel attention utilizes the inter-channel relationship of features to generate a feature map. In this work, we have combined both the attention modules for efficient feature refinement. The augmented images are passed as input to both CSAResnet and DAMCNN for training. Finally, to improve the performance and stability of the proposed architecture, weighted ensembling is performed followed by performance evaluation on the test set. Fig. 1 presents the proposed framework used for classification.

3.1. *Channel and spatial attention embedded Resnet-101 (CSAResnet)*

In this section, we have discussed how Resnet-101 architecture was integrated with the channel and spatial attention (CSA) module to make it more efficient and robust at detecting crucial features in breast cancer histopathology images. The Resnet-101 pre-trained model has been employed because its parameters are already optimized resulting in better overall performance.

As illustrated in Fig. 2, the final output layer of the Resnet model has been replaced with a convolutional and a batch normalization layer which is then fed to the CSA module. First, the feature vectors from the previous layers of the Resnet model are passed through the Conv2D layer which then progresses through the batch normalization layer. The nor-

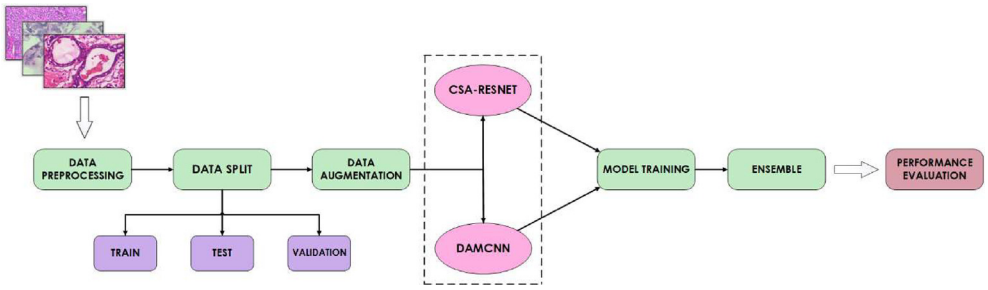

Fig. 1 – Proposed framework for the classification of breast cancer images.

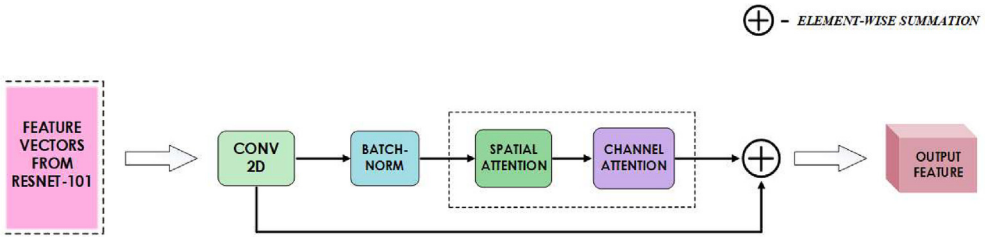

Fig. 2 – Architectural overview of the of CSAResnet.

malized output is then passed through the channel-spatial attention (CSA) block for further feature refinement. The output from the attention block is then summed with the output from the convolutional layer using element-wise summation resulting in an attention-enhanced output feature map.

3.2. *Channel and spatial attention module (CSA Module)*

While the channel attention block learns inter-channel features and the spatial attention block learns inter-spatial features, combining both have resulted in greater representation power. An illustration of the CSA module is presented in Fig. 3. Firstly, the channel attention map is calculated and then the spatial map is obtained from the generated intermediate feature map. Each attention feature map is multiplied individually with the input feature map using element-wise multiplication. Furthermore, both global average-pooling and global max-pooling operations were employed for greater representation power.

A) Channel Attention Module

As shown in Fig. 4, a channel attention map (Qc) is generated using inter-channel features from the input feature map.

The input feature information with dimensions $C \times H \times W$ where C is the number of feature maps, H is the height of a feature map and W is the width of a feature map, is first passed through both global max-pooling and global average-pooling layers producing respective feature descriptors. These descriptors are then passed through fully connected layers. The feature maps generated from both the dense layers are then concatenated using element-wise summation. Finally, these feature maps are passed through a sigmoid function. The sigmoid function is used to normalize the generated feature map.

B) Spatial Attention Module

A spatial attention feature map (Qs) is generated using intel-spatial features from the channel- refined input feature map with dimensions $C \times H \times W$. The output spatial attention feature map has dimensions $1 \times H \times W$. This is illustrated in Fig. 5.

The spatial attention selects the important receptive field of the object from each feature map. Two intermediate feature maps are generated using max-pooling operation and average-pooling operation each with dimensions ($1 \times H \times W$). These feature maps are merged into one and are then passed through a convolutional block of 5x5 kernel size. Finally, the

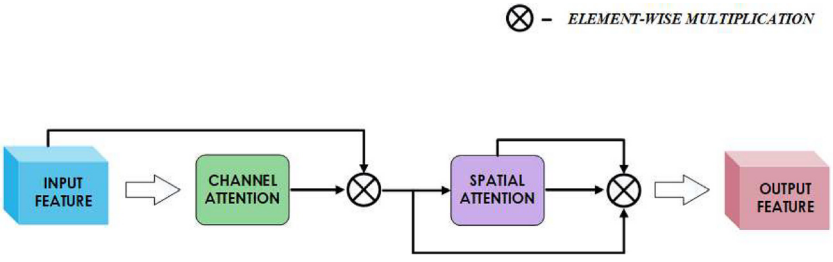

Fig. 3 – CSA module.

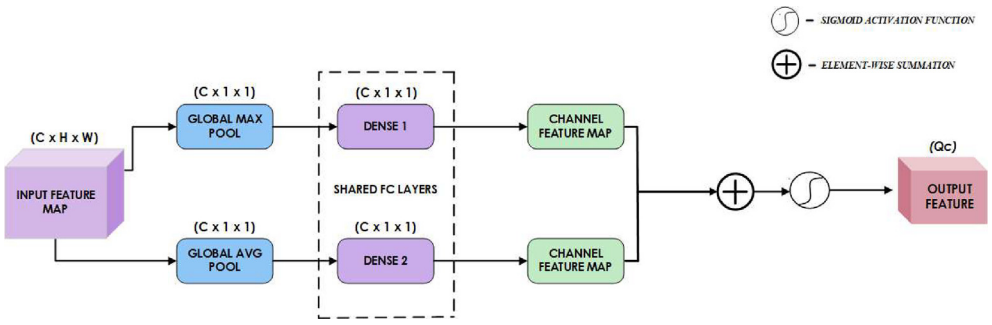

Fig. 4 – Schematic diagram of the Channel Attention Module.

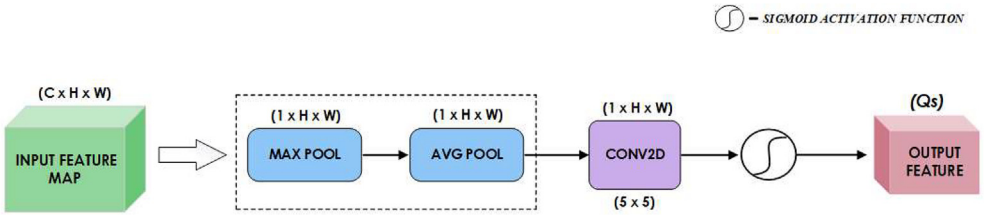

Fig. 5 – Schematic diagram of the Spatial Attention Module.

feature maps generated are passed through a sigmoid function.

3.3. *Dual attention multiscale convolutional neural network (DAMCNN)*

DAMCNN is proposed by combining two powerful state-of-the-art models namely Densenet-201 and Efficientnet-B0. The input images are first passed through these two architectures. The Densenet-201 model has been integrated with channel and spatial attention (CSA) to boost its representation power as illustrated in Fig. 6.

We have used Efficientnet-B0 because of its significantly low parameter size and still manages to achieve state-of-the-art performance on image classification tasks. It consists of a squeeze and excite block which acts as a self-attention layer for dynamic channel-wise feature recalibration. Global average pooling is performed on both the custom architectures to generate individual feature vectors. Finally, the generated feature vectors are fused into a single vector with the help of a concatenate layer. Moreover, optimization is performed to further improve the performance and stability of the neural network. Dropout and batch normalization layers are crucial to overcome the problem of overfitting. Dropout layers are responsible for speeding up the training process. Batch normalization layers are used to normalize the data to improve stability while model training. A dense layer was used between the two dropout and batch normalization blocks. A final dense layer is used before the softmax layer for binary classification of the histopathology images. The proposed DAMCNN architecture has a total of 27,414,711 parameters. The architecture of this proposed system is shown in Fig. 7.

3.4. *Ensemble learning*

Ensemble learning is the process of fusing multiple learning algorithms resulting in a robust and reliable model with better generalization performance. Ensemble learning has proved to be a powerful solution for computer vision tasks. In this work, we have proposed to use the technique of weighted average ensembling. Here, the contribution of each member to the final classification is weighted by the performance of the model. Both the models namely, CSAResnet and DAMCNN are used as ensembles. The proposed ensemble model reduces the margin of error and improves the overall classification performance.

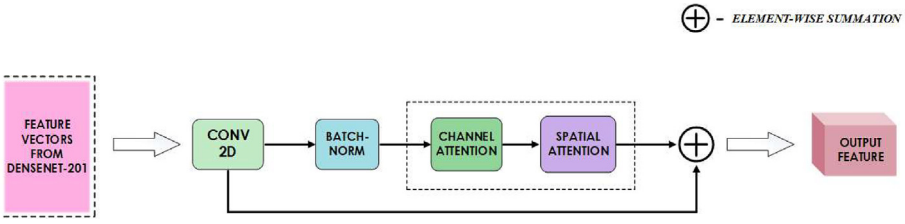

Fig. 6 – Schematic overview of the CSADensenet architecture.

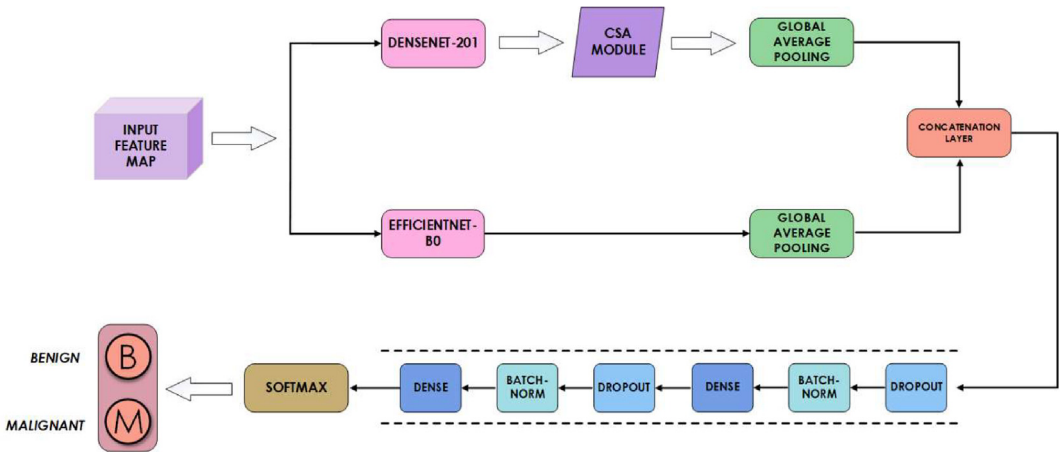

Fig. 7 – Schematic diagram of the proposed DAMCNN architecture.

4. Results

This section presents the dataset description, data augmentation techniques, system setup, ablation studies, and performance evaluation using various performance metrics.

4.1. *Dataset description*

To benchmark the efficacy of the proposed methods, we have used a publicly available histopathology dataset, BreakHis for robust validation of performance. This dataset consists of H&E-stained microscopic images of breast tissue collected from 82 patients with varying magnification levels. Examples of both benign class and malignant class are shown in Fig. 8 and Fig. 9. It is divided into two classes, namely benign tumours, and malignant tumours This dataset has been split into training (80 %), testing (10 %), and validation (10 %) purposes. Further details of the BreakHis dataset can be referred to in Table 1.

4.2. *Data Pre-processing and data augmentation*

In this subsection, we have discussed the image pre-processing and data augmentation techniques. The BreakHis dataset consists of images with 700 × 460 pixels. Before training, the images were resized to 224 × 224 pixels using the Image Data Generator library from Keras. It is to be noted that the input images present in the dataset are of different dimensions. This will have a significant impact on learning the generalized feature patterns and convergence of the network. The dataset is split into a training set (70 %), validation set (20 %), and test set (10 %).

We have performed several data augmentation techniques to increase the size of the dataset. Since the dataset contains

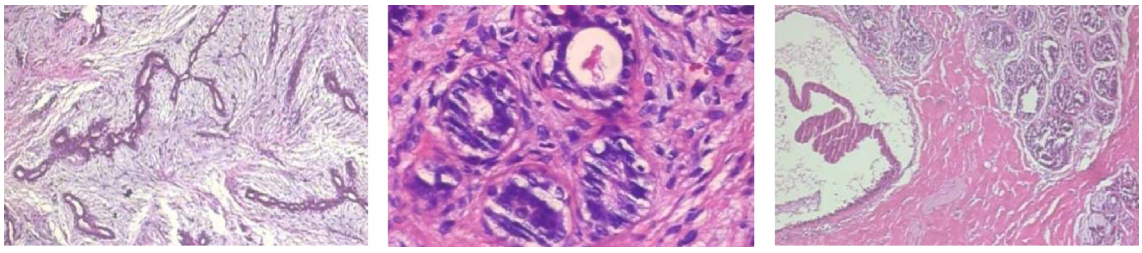

Fig. 8 – Examples of Benign class in different magnification levels (a) 200x (b) 400x (c) 40x.

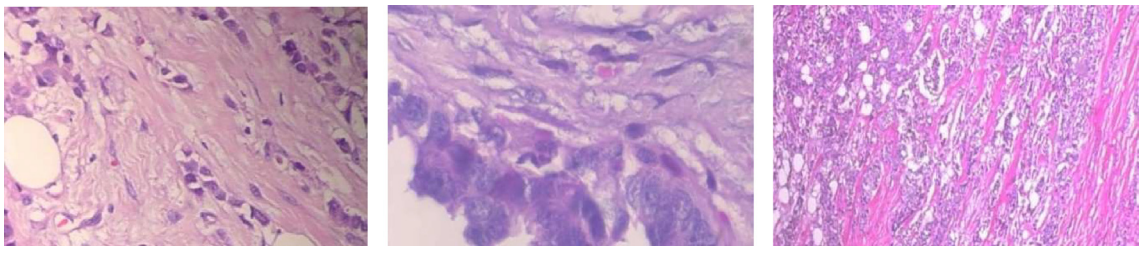

Fig. 9 – Examples of Malignant class in different magnification levels (d) 200x (e) 400x (f) 40x.

Table 1 – Details of BreakHis Dataset.

Magnification	Benign	Malignant	Total
40x	625	1370	1995
100x	644	1437	2081
200x	623	1390	2013
400x	588	1232	1820
Total	2480	5429	7909

more samples of malignant tumours (68.64 %) than benign tumours (31.36 %), the imbalance can cause overfitting and improper convergence during training. To overcome this problem, a set of augmented images have to be generated. The following augmentations were carried out: (1) Randomly zooming in and out by a factor of 2 on the images. (2) Random rotation of the images about the centre between 0° and 90°. (3) Randomly flipping the images horizontally and vertically. (4) Randomly shifting the image horizontally and vertically by a percentage of 0.5 using height shift range and width shift range respectively.

4.3. *Experimental setup*

The proposed models were implemented using Keras, an open-source framework based on python running on top of TensorFlow. All the training and testing were performed on a desktop with Nvidia RTX 2060 Super with 6 GB of GDDR6 VRAM, Ryzen 5 processor with 6 cores and 12 threads @3.6Ghz, and 16 GB of DDR4 RAM. To find optimal model parameters, the loss was minimized using Adaptive Moment Estimation (Adam) with an initial learning rate of 0.0001 and weight decay of 0.00001.

4.4. *Ablation studies*

To validate the various components of the proposed methodologies, ablation analysis was performed. It can be observed that, with the addition of the proposed modules, the model shows a gradual increase in performance overall. The metrics employed to demonstrate the performance of the proposed network are Accuracy, AUC score, Precision, Recall, F1-score, Cohen's Kappa, False Positive Rate, True Negative Rate, and Matthew's Correlation Coefficient.

4.4.1. *Analysis of Resnet and CSAResnet*

This experiment analyses the performance of two models namely Resnet-101 and Resnet-101 integrated with channel and spatial attention (CSAResnet). Initially, the baseline model namely Resnet-101 architecture was trained for 200 epochs. The resultant observations of this model training process are presented in Fig. 10. An accuracy of 86.21 % was obtained on the testing set with the baseline model. To improve the performance of Resnet-101 architecture, channel and spatial attention were added to it. This network was trained for 200 epochs which took 320 min for completion. The resultant observations of the CSAResnet model are presented in Fig. 11. Due to the integration of two types of attention, this model resulted in an accuracy of 93.17 %.

4.4.2. *Analysis of dual attention embedded Multiscale CNN (DAMCNN)*

In this section, we have proposed a multiscale convolutional neural network embedded with an attention mechanism. Efficientnet-B0 and Densenet-201 are the two models that have been used as backbone architectures. The latter has been embedded with channel and spatial attention to

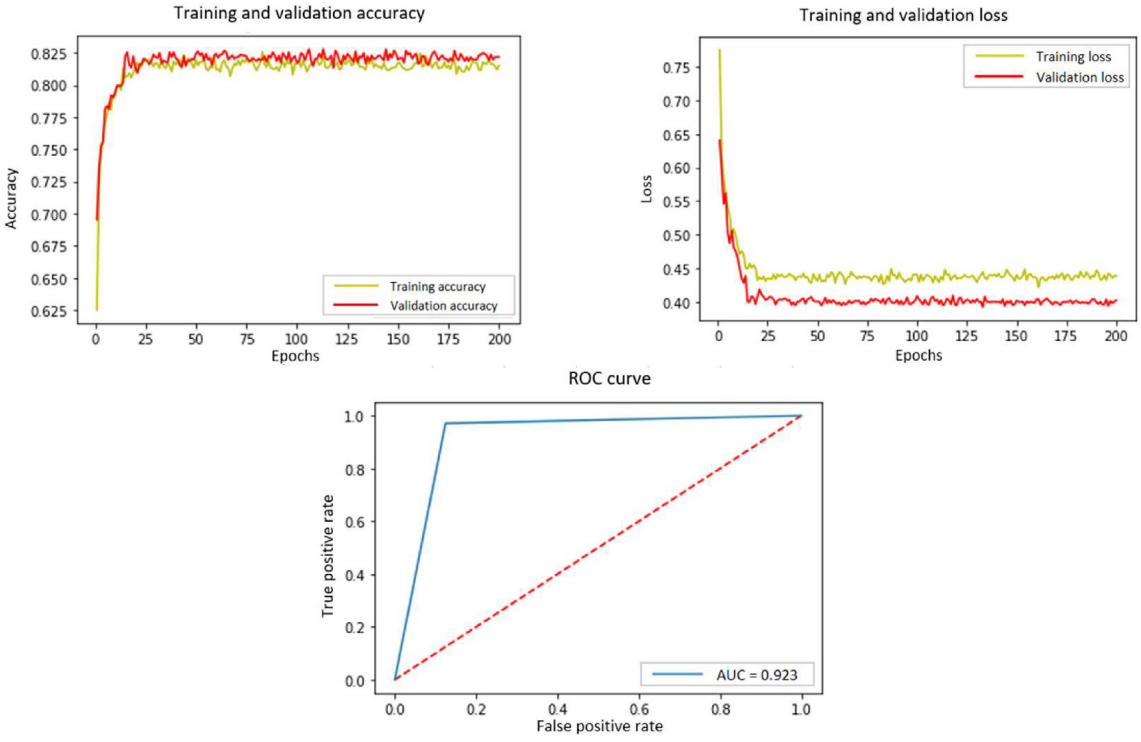

Fig. 10 – Analysis of Resnet-101 backbone architecture (a) Accuracy b) loss c) ROC curve.

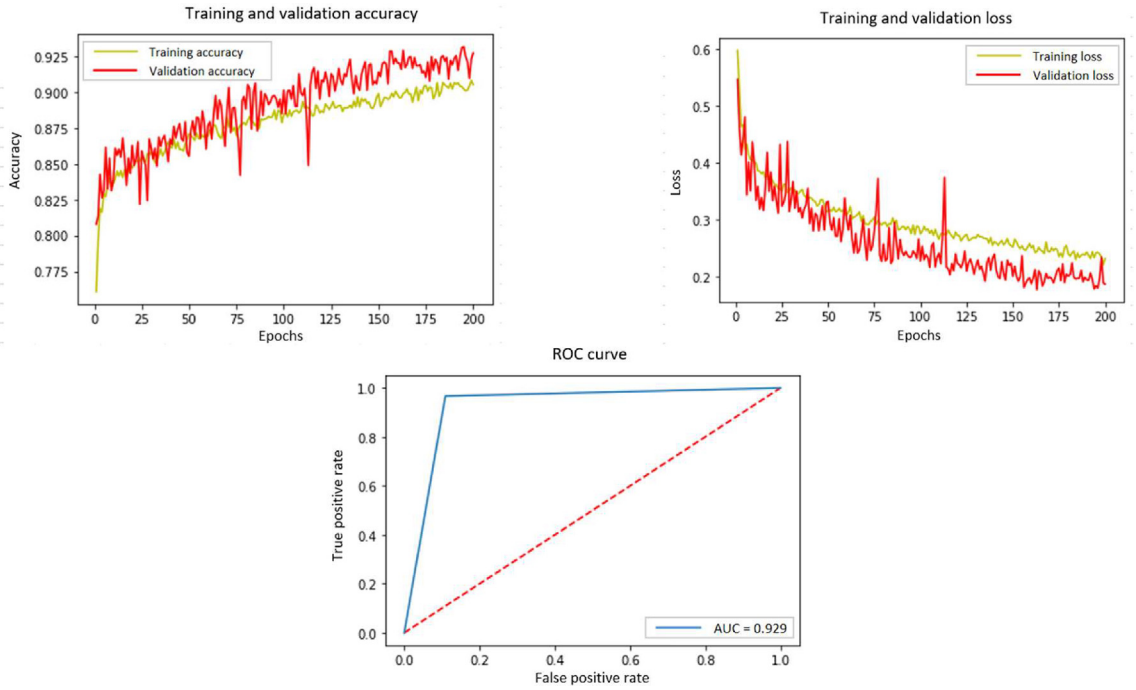

Fig. 11 – Analysis of CSAResnet architecture (a) Accuracy b) loss c) ROC curve.

improve the feature representative power of the neural network. The global average pooling layer is then used to generate corresponding feature maps from both models. Subsequently, concatenate layer is used to merge the feature maps. Finally, two batch normalization and dropout layers have been used before the fully connected (FC) layer to solve the problem of overfitting. Similar to CSAResnet, Adam optimizer was used to fine-tune the weights of the model. This network was trained for 50 epochs which took 150 min for completion. An accuracy of 98.4 % was obtained. The resultant observations for this model are presented in Fig. 12.

4.4.3. *Analysis of proposed ensemble CNN*

We propose an efficient and powerful approach of combining our custom architectures, CSAResnet and Dual Attention Embedded Multiscale CNN (DAMCNN) by the method of ensembling. The CSAResnet learns important and high-level features from the histology images due to the presence of the 2D attention module. Moreover, the dual attention network uses two powerful models parallelly, Densenet201 with 2D attention and EfficientnetB0 for both precise feature extraction. Finally, to improve the stability of the model and prediction accuracy, weighted ensembling is performed using both the custom networks. An accuracy of 99.55 % was obtained on the testing set with the ensemble model. The resultant observations for this model are presented in Fig. 13.

Table 2 summarizes the experimental results of the proposed research. The networks with attention outperform the baseline model significantly. Moreover, DAMCNN shows notable improvement in all the metrics. It implies that the two models integrated with channel and spatial attention are able to generalize well when trained parallelly. Lastly, our proposed ensemble model has resulted in further improvement.

4.4.4. *Analysis of the proposed model with the BACH dataset*

To validate the efficacy of the proposed ensemble CNN, the performance of the model is trained and tested on another breast cancer histopathology dataset namely, the Breast Cancer 2018 Grand Challenge (BACH) dataset [64]. An accuracy of 99.36 % was obtained on the test set. Moreover, the images from both BreakHis and BACH datasets were combined and employed for testing out the proposed model. The resultant observations are presented in Table 3. It can be inferred that even after combining the two datasets to validate the proposed model, the accuracy was almost the same proving its robustness and overall stability.

5. Discussion

In this section, the performance of the proposed model is compared against existing works for breast cancer classification. The proposed approach is compared with existing works and the resultant observations are highlighted in Table 4.

The work presented in this research work exemplifies the emerging fields of digital pathology and Artificial Intelligence. The results attained with the proposed work are compared against existing works that have also employed CNNs for breast cancer classification. To be able to make a fair comparison, we have presented the performance comparison for a majority of the existing works that have used the BreakHis dataset.

Transfer learning-based approaches were employed by a substantial amount of research works [27,30,32,33,38]. Model training using pre-trained weights performs well on a small amount of data since the weights were already optimized to a reasonable extent. Moreover, the time taken to train the model is also reduced. Architectures like Resnet, Inception, VGG, and Densenet are used in a number of works with pre-

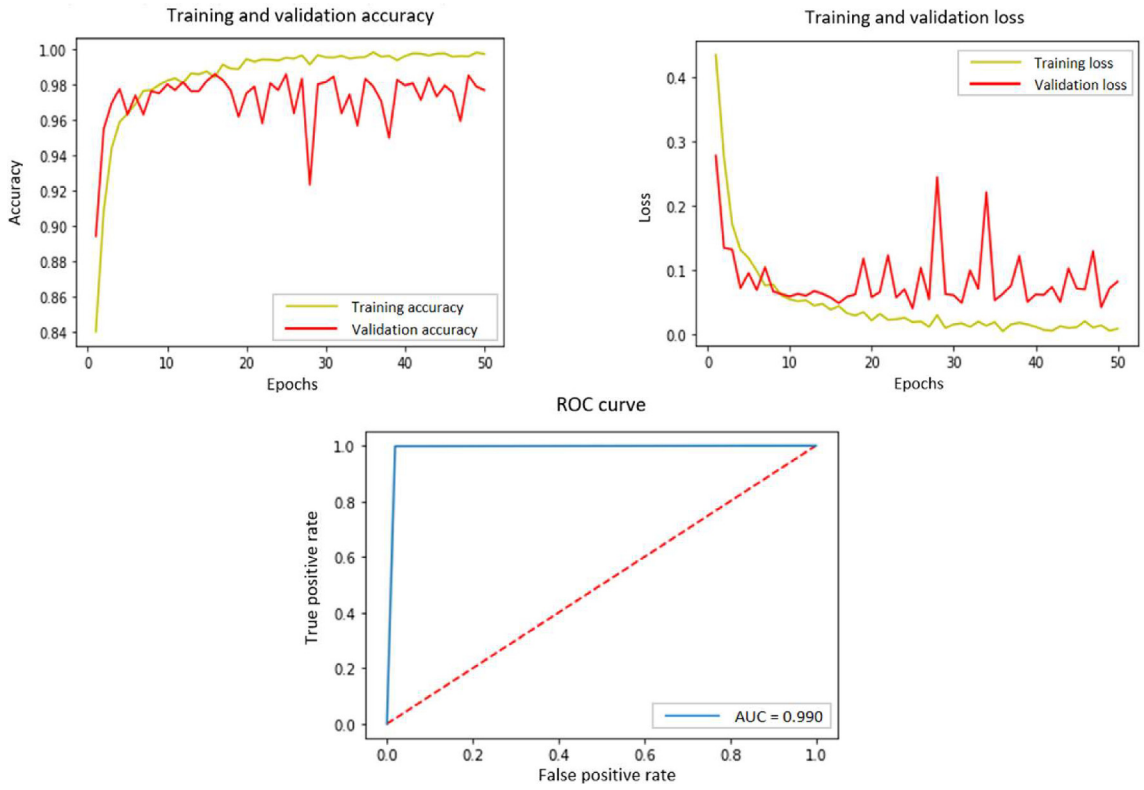

Fig. 12 – Analysis of DAMCNN architecture (a) Accuracy b) loss c) ROC curve.

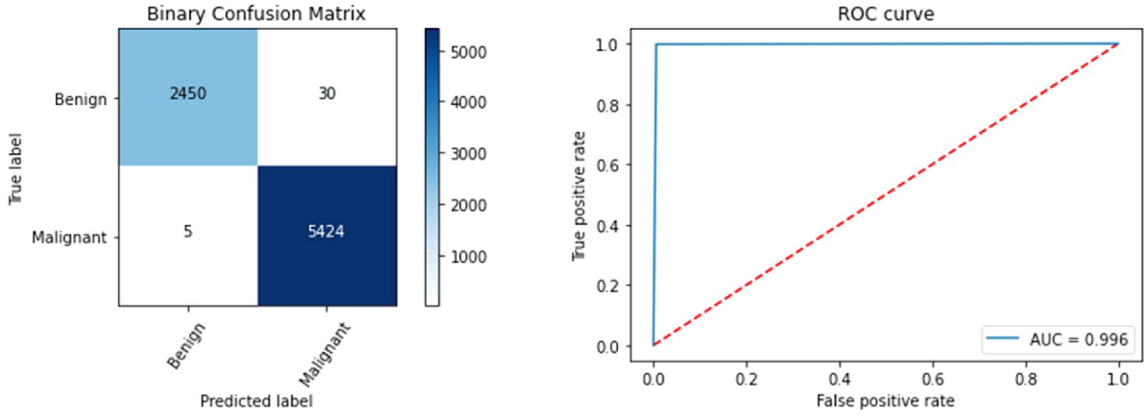

Fig. 13 – Analysis of proposed model (a) Confusion Matrix b) ROC curve.

Table 2 – Summary of the ablation studies.

Model	Precision	Recall	FPR	TNR	F1-Score	Cohen's Kappa	MCC	Accuracy (%)
Resnet-101	0.84	0.84	0.41	0.87	0.83	0.58	0.6	86.21
CSAResnet	0.93	0.93	0.12	0.87	0.93	0.86	0.86	93.17
DAMCNN	0.99	0.99	0.01	0.98	0.99	0.98	0.98	98.4
Proposed Ensemble Model	0.99	0.99	0.01	0.99	0.99	0.99	0.99	**99.55**

Table 3 – Performance Analysis of the proposed model on both BreakHis and BACH.

Dataset	Accuracy in (%)
BreakHis	99.55
BACH	99.36
BreakHis and BACH	99.45

trained weights for effective breast cancer detection. The classification accuracy reported by the transfer learning approaches was in the range of 89.6–99.1 %. Although transfer learning is a powerful approach, it works only on problems with similar initial and target domains. Due to the insufficient availability of data and the problem of class imbalance, a few works have employed GANs to generate synthetic data samples [42,44]. Moreover, Synthetic data can replicate all the important statistical properties of real data. This enables the networks to generalize better and helps to tackle class imbalance. The classification accuracy reported by the GAN-based approaches was in the range of 87.6–96.5 %. Saini et al. presented an approach using DCGAN to generate synthetic histopathology images. Furthermore, classification was performed using transfer learning which resulted in an accuracy of 96.5 %. Despite the ability to generate new images, GANs suffer from problems like non-convergence, mode collapse, and vanishing gradients. The proposed work overcomes class imbalance by applying extensive data augmentation to generate more data samples for the imbalanced classes. In addition to this, Khan et al. employed three pre-trained architectures for feature extraction and concatenated them finally. This multi-scale-based methodology resulted in an accuracy of 99 %. Similarly, we have employed a multi-scale architecture namely, DAMCNN which is embedded with attention to increase the representation power of the network.

Table 5 – Observations of the existing methods with the same data split ratio employed in this work.

S.No	Source	Accuracy in (%)
1	Sun et al. [28]	88.85
2	Spanhol et al. [33]	91.24
3	Hou et al. [26]	89.30
4	Gour et al. [30]	89.23
5	Gupta et al. [27]	94.32
6	Yamlome et al. [32]	95.60
7	Khan et al. [38]	96.55
8	Qasem et al. [31]	99.27
9	Proposed method	99.55

It can be observed that the proposed method has outperformed the existing state-of-the-art approaches with an overall accuracy of 99.55 %. Unlike the existing works, the proposed method utilized an independent attention module to extract spatial and channel features from breast cancer histopathology images. Moreover, we have also ensembled the two different deep architectures for precise feature learning with greater generalization ability. As a result, the number of false negatives and false positives are reduced and it could be observed in the confusion matrix presented in Fig. 13.

To perform a fair comparison against the existing works, these methods were reimplemented with the same data split employed in this work. It could be inferred from Table 5. that the proposed system outperformed the existing works even with the same data split ratio.

6. Conclusion

Breast cancer is one of the leading causes of death in women around the world. Detecting breast cancer at the onset stage plays an important role in initiating medical treatment quickly. However, inherent challenges in interpreting the

Table 4 – Performance analysis with the existing works based on the BreakHis dataset (sorted according to classification accuracy).

Source	Dataset	Method	Accuracy reported in the source (%)
Wang et al. [42]	BreakHis	GAN	87.6
Sun et al. [28]	BreakHis	Transfer Learning	89.60
Spanhol et al. [33]	BreakHis	Transfer Learning	90.0
Hou et al. [26]	BreakHis	Transfer Learning	91.0
El Agouri et al. [29]	Private	Transfer Learning	91.0
Gour et al. [30]	BreakHis	Transfer Learning	92.52
Gupta et al. [27]	BreakHis	Transfer Learning	93.27
Dabeer et al. [40]	BreakHis	Custom CNN	93.45
Yamlome et al. [32]	BreakHis	Transfer Learning	95.27
Albashish et al. [35]	BreakHis	CNN and ML Classifier	96.0
Saini et al. [44]	BreakHis	DCGAN with Transfer learning	96.5
Liew et al. [37]	BreakHis	CNN and ML Classifier	97.0
Khan et al. [38]	BreakHis	Transfer Learning	97.52
Dalwinder et al. [49]	WBC, WDBC and BCCD	BPNN and FW	98.37
Khan et al. [39]	BreakHis	Multi-Scale CNN and Transfer Learning	99.0
Qasem et al. [31]	BreakHis	Transfer Learning	99.1
Proposed Model	**BreakHis**	**Ensemble of DAMCNN and CSAResnet**	**99.5**

histopathological images make it difficult for pathologists to accurately detect abnormalities. In this work, we have proposed an ensemble of two models namely, CSAResnet and DAMCNN to extract features parallelly and combine them for classification. The existing deep architectures have mostly used pre-trained models for breast cancer classification. These models usually employ single-path networks and lack an exclusive attention module for precise feature learning. Therefore, we have proposed a novel multi-path ensembled architecture to extract necessary significant feature patterns for the effective detection of breast cancer. Moreover, the positive impact of the spatial and channel attention module for the detection of breast cancer has been demonstrated and quantified. The proposed method exhibits promising results in identifying malignant and benign images with an accuracy of 99.55 % on the BreakHis dataset. In addition to accuracy, the precision, recall, F1-Score, and AUC obtained are 99.99 %, 99.44 %, 99.71 %, and 0.996 respectively. Further research in this area can focus on reducing the size of the model either by quantization or pruning to make it compact and train faster without compromising on performance. The proposed framework can be extended for the computer-aided diagnosis of prostate cancer, bone cancer, and lung cancer. It can also be extended for other imaging modalities.

CRediT authorship contribution statement

R. Karthik: Conceptualization, Data curation, Methodology, Project administration, Resources. **R. Menaka:** Conceptualization, Writing – review & editing. **M.V. Siddharth:** Data curation, Writing – original draft, Software.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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