International Journal of Electrical and Computer Engineering (IJECE)
Vol. 14, No. 5, October 2024, pp. 6006~6015
ISSN: 2088-8708, DOI: 10.11591/ijece.v14i5.pp6006-6015

Performance analysis of breast cancer histopathology image classification using transfer learning models

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Article Info

Article history:

Received May 10, 2024
Revised Jul 12, 2024
Accepted Jul 17, 2024

Keywords:

BreakHis
Breast cancer
Deep learning
Histopathology images
Image classification
Transfer learning

ABSTRACT

Convolutional neural networks (CNN) which are deep learning-based methods are being currently successfully deployed and have gained much popularity in medical image analysis. CNN can handle enormous amounts of medical data which makes it possible for accurate detection and classification of breast cancer from histopathological images. In the proposed method, we have implemented transfer learning-based classification of breast cancer histopathological images using DenseNet121, DenseNet201, VGG16, VGG19, InceptionV3, and MobileNetV2 and made a performance analysis of the different models on the publicly available dataset of BreakHis. These networks were pre-trained on the ImageNet database and initialized with weights which are fine-tuned by training with input histopathological images. These models are trained with images of the BreakHis dataset with multiple image magnifications. From the comparative study of these pre-trained models on histopathology images, it is inferred that DenseNet121 achieves the highest breast cancer classification accuracy of 0.965 compared to other models and contemporary methods.

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1. INTRODUCTION

Breast cancer is the second most prominent reason for cancer deaths occurring in women globally. To extend the lifespan of women diagnosed with breast cancer, early identification with prompt treatment is crucial. Early breast cancer detection allows for the selection of a suitable treatment, which effectively decreases the death rate. A significant number of handcrafted methods and deep learning-based methods have been employed for feature extraction and breast cancer histology image classification since the advent of pattern recognition and machine learning. To achieve maximum classification accuracy, while reducing the number of selected features, feature extraction is an essential process in image classification. Convolutional neural network architecture which is used to implement deep learning algorithms has the ability of autonomous feature extraction, data retrieval, and performing conceptual data representations for classification. Consequently, they are able to solve the issues with conventional feature extraction techniques. One of the main objectives of computer aided diagnosis (CAD) methods for breast cancer diagnosis is the automated categorization of histopathological images into benign and malignant tumors. Deep learning-based methods perform at achieving this objective by automated feature extraction and classification of the histopathology images. The problem addressed in this paper involves evaluating the efficacy and efficiency of different transfer learning models for the classification of breast histopathology images. The proposed solution is to give an insight into how performance metrics such as accuracy, recall, and precision can be

enhanced through a transfer learning approach in the applicability of breast cancer diagnosis. A variety of pre-trained convolutional neural network (CNN) models, which include DenseNet, VGG, inception, and MobileNet have the advantages of applying connections between layers, fewer parameters, stronger propagation, and feature reuse. The network may be trained more quickly and easily as a result of the increased parameter efficiency. Using transfer learning, the information about data is gained from one task, and another associated task is solved using that information through which the computational complexity is greatly reduced. The model's performance during training and testing can be increased in an efficient manner. In this paper, transfer learning-based breast cancer diagnosis techniques have been proposed and the method is validated on the BreakHis dataset with a comparative analysis of the different pre-trained CNN models. The contributions of the article include i) implementing transfer learning-based breast histopathology images classification, ii) comparative analysis of the different pre-trained models on BreakHis dataset, and iii) comparison of the transfer learning-based classification of breast cancer histopathology images with the recent methods of literature.

A method of selection of patches from breast histopathology images and a transfer learning-based method were suggested for classification from a few training images. Their proposed work performed three different types of experiments that support vector machine-based classification of deep features, patch-wise classification, and image-wise classification [1]. A method that adapted a pre-trained CNN model using deep feature extraction and transfer learning techniques was proposed. In this study, feature extraction was done using VGG16 and AlexNet models, and final fine-tuning was done using AlexNet. Support vector machines (SVM) were used to classify the collected features [2].

An ensemble of deep learning methods was proposed for the classification of histopathology images of breasts into benign or malignant. In this work, the pre-trained models of the fine-tuned VGG16, fine-tuned VGG19, fully-trained VGG16, and fully-trained VGG19 were implemented, and 5-fold cross-validation was employed [3]. Transfer learning method coupled with fine-tuning on blocks was suggested for the classification of both binary and 8-class images of the BreakHis dataset [4].

A modified residual neural network (ResNet) technique was proposed for the detection of breast tumors from images of histopathology which attained better results on the dataset of BreakHis [5]. A combination of a saliency detector and a fully convolutional classifier network was proposed to label the entire slide pixel-wise. Followed by a polling method of the majority to perform ultimate slide-level diagnosis [6].

An approach that utilized CNN, a bag of features, and handcrafted features for the count of mitosis and then performed classification of breast histopathology images was proposed [7]. A stacked generalized ensemble (SGE) algorithm was implemented for classifying images from breast cancer datasets as either benign or malignant [8]. An ensemble model of ResNet50 and extreme learning machine (ELM) was implemented whose kernels were weighted for computer-aided diagnosis of breast cancer [9]. The CNN architecture of ResNet-34 was proposed based on residual learning, for the classification of malignancy and benign cases of breast histopathology images [10]. A transfer learning-based method was suggested which utilized two pre-trained models of DenseNet-161 and ResNet-50 for the breast histopathology images classification [11].

The method of cascaded SVM and multi-level features was proposed to classify images of breast cancer histopathology into different grades: low, intermediate, and high grades [12]. A computer-aided diagnosis system was implemented for the classification of images from the BreakHis dataset [13]. A method based on extreme gradient boosting and deep learning was proposed for which the pre-processing techniques of stain normalization and data augmentation were employed [14]. A method comprising of convolutional long short-term memory model and optimized SVM was proposed to classify breast cancer images [15].

A tree-based multi-classification model called BrT (breast tumor) was employed utilizing deep learning techniques to extract distinctive features and achieve improved performance while utilizing fewer computational resources [16]. A generative adversarial network (GAN) for classifying an imbalanced breast cancer dataset was proposed by Saini and Susan [17]. A nucleus-guided transfer learning (NucTraL) approach to develop an accessible and cost-effective algorithm for breast tumor classification was suggested and evaluated on the publicly accessible BreakHis dataset [18]. The CNN architecture of BreastNet was proposed, which incorporated a residual architecture with attention modules to classify breast cancer images [19]. A breast histopathology image classification method that utilized a bag of visual words (BoW) approach to combine shape features and manually designed features was proposed [20]. Ensembles of CNN models were proposed to classify breast cancer histopathology images [21]–[27]. A classification method for breast histopathology images which included the steps of image enhancement, nucleus segmentation, extraction of features, and detection of breast cancer was proposed [28]. A deep learning-based Heterogeneous Ensemble method for the classification of nuclei into mitotic and non-mitotic in breast histopathological images was proposed [29]. The method employed techniques of feature invariance, region homogeneity, and residual learning. A novel loss function called concentric loss was proposed in CNN-based weakly supervised breast cancer diagnosis and the method was validated on the ICPR2014 MITOSIS dataset and AMIDA13 dataset

[30]. A fully convolutional auto-encoder to learn the leading structural models and a multiple instance learning method were proposed to detect breast cancer in Histopathology images [31], [32].

Based on the literature survey, it is inferred that transfer learning-based methods give promising results in detecting breast cancer from histopathology images. The major advantages of transfer learning are that it requires fewer training images, and the requirement of computational resources is less. Hence in the proposed method, the pre-trained models including VGG16, VGG19, DenseNet121, DenseNet201, InceptionV3, and MobileNet are fine-tuned for the detection and classification of breast cancer histopathology images. The performance of these models on the breast cancer histopathology images dataset is analyzed and compared based on different performance metrics.

The rest of the section is organized as follows. Section 2 discusses CNN, transfer learning, pre-trained models, and the proposed method, experimental results and analysis are discussed in Section 3 with a conclusion in Section 4. The novelty of the proposed work is the application of different transfer learning models for the classification of breast cancer histopathology images and a comparative analysis is done on the different models and with other methods.

2. METHOD

2.1. Convolutional neural network

Convolutional neural network (CNN) architecture comprises of input layer, several convolution layers with rectified linear units, pooling layers, and dense layers. CNN architecture's basic component is the convolutional layer which extracts the features from the input images. Pooling layers in convolutional networks typically comprise down-sampling layers that gradually reduce the size of the feature representation. Convolution and pooling processes together generate high-level features that can be used for categorization. CNNs' end-to-end learning architecture provides feature extraction and also classification. A large number of parameters in the CNN architecture are optimized during the training phase. The standard backpropagation algorithm is typically used for CNN training.

2.2. Transfer learning

The process that learns data from one problem and applies it to different related problems for feature extraction and classification is called transfer learning (TL). Transfer learning is performed using pre-trained models that have previously been trained on a large amount of data. The pre-trained model is additionally trained and tuned using an original dataset comprising of small quantity of images. Recently, transfer learning has been applied to many image processing applications since fine-tuning a pre-trained model is typically quicker and simpler when compared to train a CNN model from scratch whose weights are randomly initialized. Deep learning's requirement for large quantities of data is one of its primary features. Under-fitting will happen during training if there is not sufficient data and hence the method of transfer learning is suggested as a way to train with deep learning on a smaller dataset. Accurate and effective image categorization can be accomplished with smaller datasets using transfer learning's learning capacity. For a newly formed task, if there is insufficient training data, the popular CNN models like VGG16 are pre-trained on the ImageNet dataset comprising 1.2 million images belonging to one thousand classes to acquire the characteristics of the ImageNet dataset. In the proposed work, transfer learning based on VGG16, VGG19, DenseNet121, DenseNet201, InceptionV3, and MobileNet is implemented for the classification of breast cancer histopathological images into benign and malignant categories. The pre-trained models on the ImageNet dataset are used and fine-tuned using the BreakHis dataset and the proposed strategy has achieved enhancement in classification accuracy based on the small dataset.

2.3. Pre-trained models

In this research, the pre-trained models of DenseNet121, DenseNet201, VGG16, VGG19, InceptionV3, and MobileNetV2 are implemented for binary breast histopathology image classification into benign and malignant. Every layer in DenseNet is feed-forwardly linked to all previous layers of the network. DenseNet has the benefit of improved feature rebuilding, which dramatically increases the design's efficiency. DenseNet has been gradually enhancing its accuracy while also enhancing its feature set without leading to overfitting or performance loss. DenseNet also has the ability to save a lot of time by increasing the number of features that can be reused in subsequent tasks. The VGG architecture is a significant development in the field of deep learning since it is an implementation of CNN with a dense set of connections of layers to represent the visual data in a structured form for functioning. Even though many subsequent efforts improved the VGG structure, in this paper, we have included the implementation of VGG16 and VGG19 for analysis of breast cancer histopathology image classification.

VGG16 contains sixteen weight layers and VGG19 convolutional neural network contains 19 layers, sixteen of which are convolutional layers, and three layers are fully connected. Feature extraction is done using 16 convolutional layers, while classification is done through the following three fully connected layers. This model imports an image with a size of 224×224 and produces the classification output label as a benign or malignant tumor.

Inception-V3 network architecture is a pre-trained model trained on the ImageNet dataset and its size is 89 MB. The input image size is 299×299 pixels and a total of 350 connected layers are available in the Inception-V3Net directed acyclic graph (DAG) network architecture. Inception modules exist in InceptionNet and they consist of blocks of layers that learn both global and local features from the input images using 1×1, 3×3, and 5×5 convolutional layers. The InceptionNet uses a modular design so that the network learns feature maps at different scales. Filter Concatenation is performed on these feature maps to represent the input data in a more widespread manner inclusive of both higher-level and low-level features. MobilenetV2 is being deployed because of its small size and its performance is better on mobile devices. It utilizes depth-aware independent convolutions, which means that each color channel performs a separate convolution rather than being combined and smoothed.

MobilenetV2 architecture consists of two residual blocks with stride of 1 and 2, which is used for downsampling. Three layers are present in each block which are the 1×1 convolution layer with ReLU6, depth-wise convolution with ReLU6, and the third layer is linear 1×1 convolution. The advantages of MobileNet are that it is a lightweight deep neural network and depth-wise convolutions are used so that the number of parameters is greatly reduced when compared with other networks.

2.4. Proposed method

The flow diagram of the proposed transfer learning-based histopathology image classification is shown in Figure 1. The histopathological images belonging to the dataset of BreakHis are partitioned into training images and testing images in the ratio of 0.8:0.2. The input images are subjected to normalization and dataset balance as pre-processing steps. The pre-trained CNN models – DenseNet121, DenseNet201, VGG16, VGG19, InceptionV3, and MobileNetV2 are used for feature extraction, and the weights of these models were already initialized through training on millions of images from the ImageNet dataset.

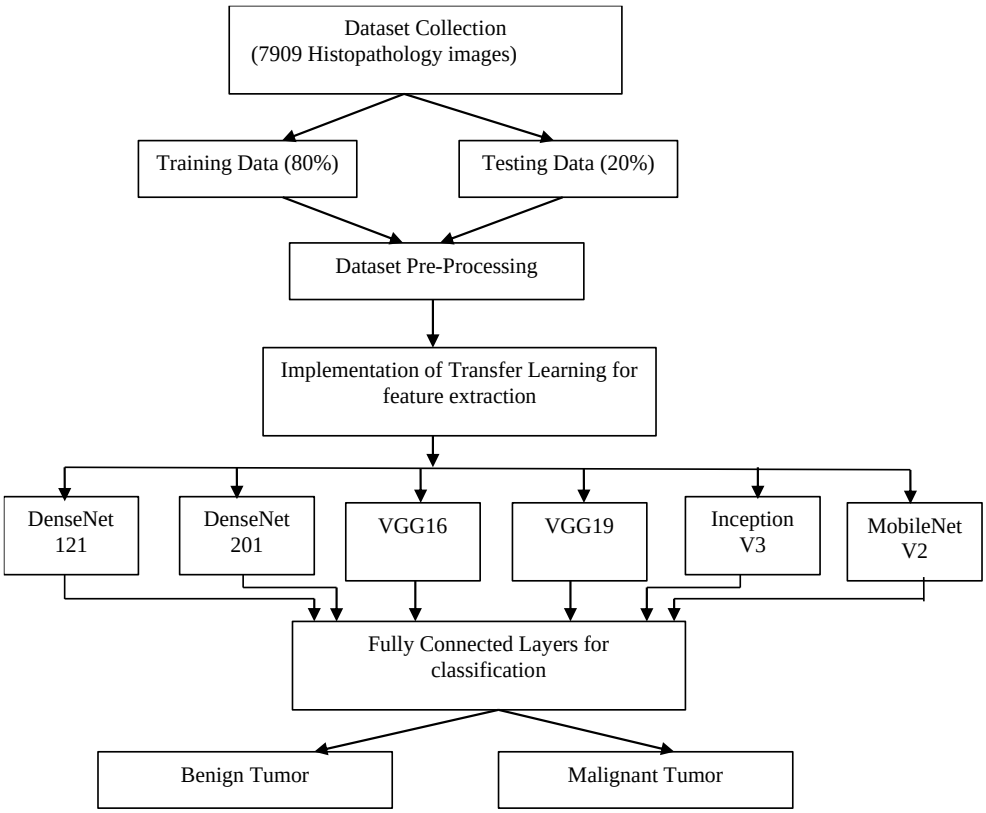

Figure 1. Flow diagram of the transfer learning-based histopathology images classification

The top dense layers of these networks are removed and replaced with three fully connected layers for binary classification as benign and malignant tumors. The network is trained and fine-tuned using the breast histopathology images from the train dataset and then validated using images from the test dataset. An analysis of the performance of the different transfer learning models is done with regard to classification performance metrics of precision, recall, accuracy, and F1-score.

The size of the input images is 224×224×3 and the input images are first pre-processed in which normalization is done. The dataset is imbalanced as inferred from Table 1. The amount of benign images and malignant images in the 40x dataset are 625 and 1370 respectively and the total images are 1995. Hence, upsampling is done for the benign images from 625 to 1,370 and hence the dataset becomes balanced with a total number of images as 2,740. The pre-trained models of DenseNet121, DenseNet201, VGG16, VGG19, InceptionV3, and MobileNetV2 are loaded with weights of the ImageNet dataset, and the top dense layers of these models are removed. Then, flattened layers, dropout layers, and dense layers are added for binary classification. The model is compiled with the optimizer of Adam at 0.00001 learning rate, with a batch size of 256, and runs for 60 epochs. The model is trained using the training dataset with the above parameters and validated with the testing images. A performance evaluation of all the models on the BreakHis dataset is done and a comparative analysis with other methods in the literature is done.

Table 1. Description of the BreakHis dataset

Magnification factor	Benign images	Malignant images	Total images
40x	625	1370	1995
100x	644	1437	2081
200x	623	1390	2013
400x	588	1232	1820
Total Images in the BreakHis dataset			7909

3. RESULTS AND DISCUSSION

3.1. Description of the dataset and performance metrics

The breast tumor histopathological images belonging to two different categories, benign and malignant, were gathered for the BreakHis collection via clinical investigations. All patients identified with breast cancer were notified to the Brazilian P&D lab to take part in the investigation during the time period if they had any clinical symptoms of the disease. Hematoxylin and Eosin staining were used to gather samples during surgical open biopsy (SOB). Pathologists at the R&D laboratory can annotate these photos for histological studies. The 7,909 microscopic images of breast tumor tissue belonging to benign and malignant categories from 82 people that make up the BreakHis dataset were taken using a microscope (including 40x, 100x, 200x, 400x). Based on the way the cancerous cells are seen underneath the microscope, both classes of breast tumors are further classified into sub-categories. A breast tumor's prognosis and possible treatment of therapy can vary depending on its type or subtype. There are four forms of benign breast tumors and four forms of malignant breast tumors. In this experiment, 20% of the samples are used for testing, while 80% are used for training. It is ensured that the training images are not used during testing in order to successfully apply the task of categorization.

Figure 2 shows the sample histopathological images of breast cancer from the BreakHis dataset. The sub-categories of benign images are Tubular Adenoma, Adenosis, Phyllodes Tumor, and Fibroadenoma. The sub-categories of malignant tumors are Lobular Carcinoma, Ductal Carcinoma, Papillary Carcinoma, and Mucinous Carcinoma.

The proposed method of transfer learning-based breast cancer histopathology image classification is evaluated by means of the confusion matrix obtained while classification. There are four terms in this evaluation matrix. True positive represents images that have been correctly recognized as benign, and false positive refers to malignant images that are incorrectly identified as benign. True negative refers to correctly diagnosed malignant images, whereas false negative indicates images from the benign class that are incorrectly classified as malignant. Four metrics are used to evaluate the performance of the proposed transfer learning-based classification of breast cancer histopathological images from the test dataset which include accuracy, recall, precision, and F1-score. Precision is expressed as the proportion of benign images correctly categorized out of all predicted images of the same class.

$$Precision = \frac{True\ Positive}{True\ Positive + False\ Positive} \quad (1)$$

Recall is expressed as the ratio of benign images truly categorized out of all predicted images of the malignant class.

$$Recall = \frac{True\ Positive}{True\ Positive + False\ Negative} \quad (2)$$

Accuracy measures the number of images that were correctly identified out of all the testing images and evaluates how accurately a model performs.

$$Accuracy = \frac{True\ Positive + False\ Negative}{Total\ number\ of\ images} \quad (3)$$

F1-score shows the equilibrium value of recall and precision and is typically used for improving a model for recall or precision.

$$F1\ Score = \frac{2 * Precision * Recall}{Precision + Recall} \quad (4)$$

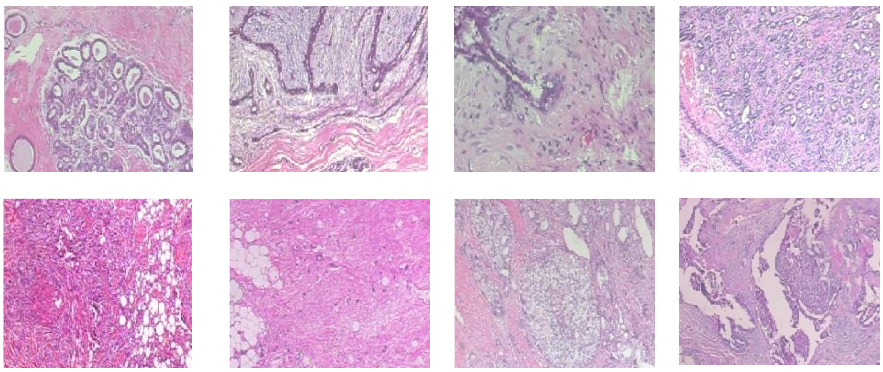

Figure 2. Histopathology images from the dataset of BreakHis

3.2. Experimental results

The experiments are carried out with six pre-trained models: VGG16, VGG19, DenseNet 121, DenseNet201, MobileNetV2, and InceptionV3 on breast cancer histopathology images. The proposed method is evaluated using the publicly available BreakHis dataset comprising 7909 real images, categorized into two subsets of benign and malignant samples of quantity 2,480 and 5,429 respectively. These images belong to different magnification factors of 400x, 200x, 100x, and 40x. We obtained accuracy and loss plots and confusion Matrices for all the magnification factors and the results obtained for DenseNet121 architecture on the 100x dataset are shown in Figure 3. The results based on the experiments obtained for the proposed transfer learning-based method are shown in Tables 2 to 5 for images of different magnification factors of 40x, 100x, 200x, and 400x respectively. The graphical results for the performance analysis of the proposed method on the 40x dataset are shown in Figure 4.

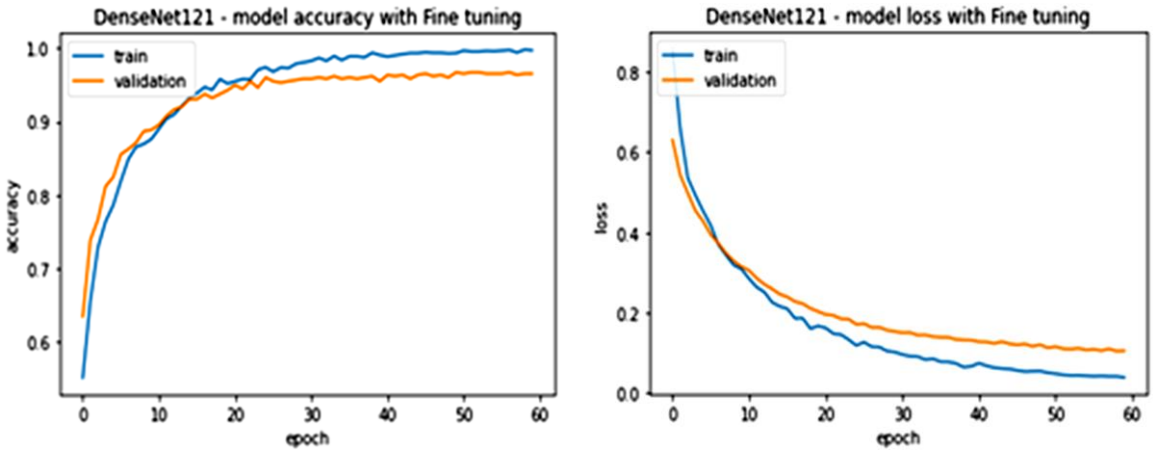

Figure 3. Accuracy and loss plots for DenseNet121 on 100x dataset

Table 2. Comparison of performance metrics of different pre-trained models on 40x images

Performance metrics	Classification accuracy	Precision	Recall	F1-Score
DenseNet 121	0.944	0.967	0.922	0.944
DenseNet 201	0.938	0.981	0.897	0.937
Inception V3	0.938	0.977	0.901	0.937
VGG 16	0.907	0.933	0.883	0.907
VGG 19	0.872	0.898	0.848	0.872
Mobile Net	0.938	0.970	0.908	0.938

Table 3. Comparison of performance metrics of different pre-trained models on 100x images

Performance metrics	Classification accuracy	Precision	Recall	F1-Score
DenseNet 121	0.965	0.972	0.958	0.965
DenseNet 201	0.953	0.982	0.924	0.952
Inception V3	0.934	0.953	0.913	0.933
VGG 16	0.906	0.930	0.879	0.904
VGG 19	0.887	0.906	0.865	0.885
Mobile Net	0.941	0.957	0.924	0.940

Table 4. Comparison of performance metrics of different pre-trained models on 200x images

Performance metrics	Classification accuracy	Precision	Recall	F1-Score
DenseNet 121	0.955	0.973	0.934	0.953
DenseNet 201	0.962	0.974	0.949	0.961
Inception V3	0.942	0.955	0.926	0.94
VGG 16	0.899	0.906	0.886	0.896
VGG 19	0.867	0.881	0.842	0.861
Mobile Net	0.906	0.914	0.893	0.903

Table 5. Comparison of performance metrics of different pre-trained models on 400x images

Performance metrics	Classification accuracy	Precision	Recall	F1-Score
DenseNet 121	0.935	0.956	0.908	0.932
DenseNet 201	0.957	0.962	0.95	0.956
Inception V3	0.938	0.977	0.901	0.937
VGG 16	0.907	0.933	0.871	0.901
VGG 19	0.878	0.905	0.838	0.87
Mobile Net	0.909	0.945	0.863	0.902

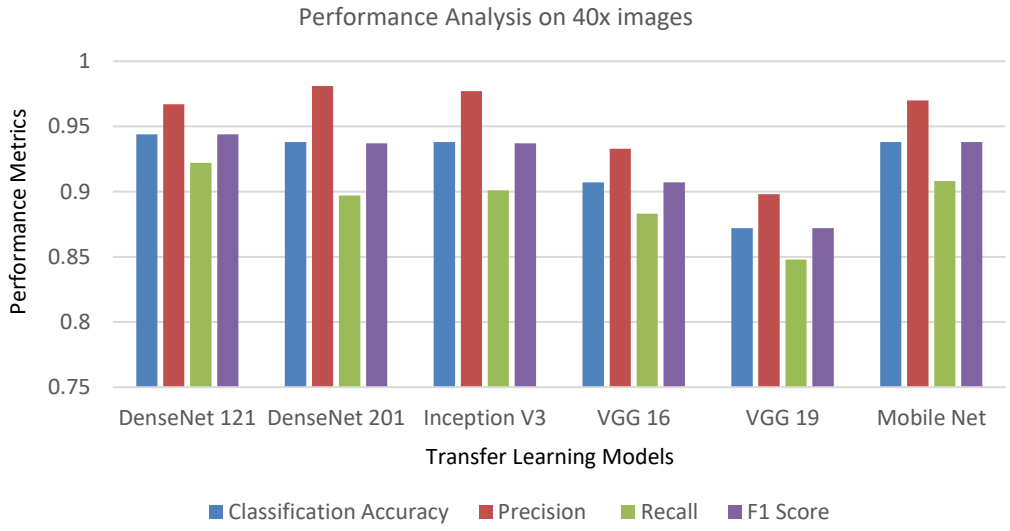

Figure 4. Performance analysis of different pre-trained models on 40x images

As inferred from the results obtained from the different experiments conducted, DenseNet121 and DenseNet201 architectures give the best performance compared to other models with a classification accuracy of 0.96. Next to the DenseNet, InceptionV3 and MobileNet give higher classification accuracy of

0.94 and then VGG16 and VGG19 give classification accuracy of 0.90. Table 6 shows the comparison of the proposed method with the method proposed by Zhu *et al*. [24], which shows improvement in classification accuracy by 9%.

Table 6. Comparison of classification accuracy of proposed method with method in literature

Method	40x	100x	200x	400x
Method proposed by [24]	0.852	0.835	0.841	0.793
Proposed transfer learning-based method with DenseNet121 pre-trained model	0.944	0.965	0.955	0.935

3.3. Discussion on the results

A comprehensive analysis of the different performance metrics of classification accuracy, precision, recall, and F1-score were done on the BreakHis dataset for the classification of breast histopathology images into benign and malignant tumors. From Table 2, it is inferred that the DenseNet121 CNN model achieved the highest classification accuracy, recall, and F1-score of 0.944, 0.922, and 0.944 respectively while the highest precision of 0.981 is obtained for DenseNet201 on the 40x dataset. Similarly, on the 100x dataset, as shown in Table 3, the highest values of 0.965, 0.958, and 0.965 are obtained for classification accuracy, recall, and F1-score respectively and the highest precision of 0.982 is obtained for DenseNet201. The classification results on the 200x dataset as shown in Table 4 indicate that the highest values of 0.962, 0.974, 0.949, and 0.961 are obtained for classification score, precision, recall, and F1-score respectively by DenseNet201 architecture. The classification results on the 400x dataset as shown in Table 5 indicate that the highest values of 0.957, 0.950, and 0.956 are obtained for classification score, recall, and F1-score respectively by DenseNet201 architecture while the highest value of 0.977 is obtained for precision by InceptionV3 architecture. The highest values of performance metrics are shown in bold in the respective tables. Dense connections are established between all of the previous and succeeding layers in the DenseNet architecture and hence better performance is achieved for DenseNet with reduced computational cost and less parameters compared to VGG, Inception, and MobileNet architecture. In the inception architecture, multiple convolutional kernels are employed to extract information from different scales of the image and finally, the features are concatenated to better represent the image. The results of inception architecture are second highest on the BreakHis dataset for all magnification factors of 40x, 100x, 200x, and 400x. The VGG architecture consists of multiple Convolutional layers with rectified linear unit activation function and pooling layers for feature extraction. Finally, three fully connected layers are used for classification with a SoftMax activation function. The basic unit of MobileNet comprises depthwise convolution and pointwise convolution. In depthwise convolution, dissimilar convolution kernels are used for each input channel and pointwise convolution uses kernels of 1x1 convolution. The experimental results indicate that the performance of DenseNet and Inception architecture is superior to the VGG and MobileNet architecture by approximately 4% for breast cancer histopathology image classification.

4. CONCLUSION

In this paper, a transfer learning-based method for classifying breast cancer histopathology images is proposed, utilizing the BreakHis dataset. We implement six popular pre-trained models, for automatic feature extraction for binary classification into benign and malignant categories. To evaluate the performance, we employed various metrics including accuracy, precision, sensitivity (recall), and F1-score for four different magnification factors. For binary classification into benign and malignant tumors, the highest classification accuracy of 96.5% is attained for the DenseNet121 architecture which is better compared to the recent method in literature. A comparative analysis of the six different pre-trained models is also done. The proposed transfer learning-based approach gives an enhancement in accuracy of 9% over the state-of-the-art method.

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