Deep Convolutional Neural Network for Computer-Aided Detection of Breast Cancer Using Histopathology Images

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Abstract. The innovation in medical imaging technologies leads to a frenetic pace of change in health care. In recent years various deep learning algorithms play a significant role in medical image classification and diagnosis. The deep convolutional neural network (DCNN) has obtained impressive results in many health-related applications. The fine-tuning parameters and weight initialization is the major task to adapt pre-trained convolution models. We explored transfer learning approaches using Alexnet, and VGG-16 analyzed with their behavior. Also, the DCNN framework had developed and compared with Alex net and VGG-16 transfer learning models. The DCNN attained more significant results compare to transfer learning models. The DCNN procures outstanding performance for binary (93.38\%) and multi-class (average 89.29\%), which exceeds the previous state of the art techniques in the literature.

1. Introduction
Breast cancer is one of the dominating causes of cancer in the universe. In 2012, 1.7 million new breast cancer cases were registered, and it is also the dominant cause of cancer death in all around the world. The estimated number of death among women in 2018 is 627000, which are approximately 15\% of cancer death. The number of breast cancer for all age groups is 25.2\%, and it is higher than in other cases [1]. Early-stage detection increases the chance to initiate effective treatment to improve survival rates [2]. The initial stage breast cancer diagnosis was performed by different imaging modalities such as mammography, thermal, and ultrasonography. The possibility of carcinoma growth is identified by breast biopsy techniques [3]. The examined cancer tissue was stained by hematoxylin and eosin (H&E) with pink cytoplasm and purple nuclei. The staining is the process used to identify and grading of cancer cells. In this work, the histopathology image taken from the slide is classified using deep learning techniques.

Deep learning is a powerful tool to learn from the extracted features automatically and perform the task, such as regression and classification. Deep learning is developed from the classical neural network, and it differs from many hidden layers and training paradigms. Deep learning plays a substantial role in pattern recognition, machine learning, and computer vision [4]. The raw data considered for layer by layer multiple level operations with optimal weights. In high-level abstraction, the feature set is extracted automatically. The variety of different histopathology image analysis techniques have been applied using deep convolution neural networks [5], [6]. In computer-aided diagnosis, the deep neural network is the hierarchical unsupervised learning methods for feature extraction, and supervised steps are needed to optimize the classification process [7]–[9].
Conventional machine learning techniques using handcrafted features, the class label prediction depends on the robustness of the extracted features and has less classification accuracy. Deep learning methods have been implemented using large datasets to overcome the drawbacks of conventional methods. The accuracy has been increased using more training and testing, and the final model is the statistical distribution of the data.

The present work proposes a novel method, which implements a deep convolution neural network (DCNN) to diagnose breast cancer using BreakHis histopathology images. The major contribution of the work is given below:

- The DCNN is applied for feature extraction at the initial stage. The training iteration and balanced training data significantly improve the accuracy of the classification rate.
- Then we have used the fine-tuned pretrained model Alexnet and VGG-16 to improve the performance of the classification. Finally, comparisons have been performed by utilizing DCNN and transfer learning models.

2. Related works

Breast cancer-related research has increased drastically in recent years. A large portion of the work has been aimed at detecting cancer with the highest precision. In recent years researchers have admired to design the computer-aided diagnosis system using various standard databases with predefined labels and claim the radiologist for similar diagnosis measurement accuracies.

The domain-specific feature describes statistical and textural features in the previous decade [10]. The handcrafted features using the combination of texture and statistical attributes of the image helps significantly in the improvement of classification accuracy. In 2016 Spanhol et al. successfully implemented the deep neural network with Alex net and achieved better classification results to inspire others. Their result shows that the accuracy decreases with increasing magnification rate by using supervised training protocol with image patches and learning rate of $10^{-6}$ in conjunction with momentum term 0.9. The proposed architecture is evaluated by the patient recognition rate and image recognition rate. The accuracy is calculated by using the fusion role for both patient-level and image levels [11].

Zhongyi et al. used a structure-based Deep Convolutional Neural network model to perform the multi-class classification. The performance assessment is done by using the patient score, patient recognition rate, and image recognition rate [12]. The role of deep learning techniques such as Deep neural network, Deep Belief Network, Deep Auto-encoder, Recurrent Neural Network, Deep Boltzmann machine, and Convolution Neural Networks are analyzed critically in health informatics by Daniele Ravi et al. [13]. In [14], the authors used datasets, namely ICIAR, BreakHis, PatchCamelyon, and Bioimaging with pretrained models (VGG-19, MobileNet, and DenseNet). The CNN was fine-tuned with hyperparameters, and the reported accuracies were 98.13%, 95%, 94.64%, and 83.10% [14]. Kowat et al. used fuzzy C-means and Gaussian mixture models for clustering, and the competitive neural network classifies the cancer cells (benign or malignant) [15].

Zhang et al. used SVM (support vector machine) and CNN (convolution neural networks) to achieve the accuracy of 97% for three classes, namely normal, benign, and in situ [16]. Similar work is performed by Brook et al. to classify 361 images and achieves 93% accuracies for normal, benign, and in situ [17]. Lijens et al. introduced a deep learning technique to strengthen the efficiency of the histopathological slide. They conclude that it holds great promise in growing the efficacy of prostate cancer diagnosis and breast cancer staging [18]. The subtype of breast cancer traced by Sungmin et al. using a hybrid model integrates two models convolution neural network (CNN) and relation network (RN) [19].

The max-pooling convolution neural network (CNN) was used by Ciresan et al. to diagnose breast histology images. They used simple post-processing in the network output stage, and this approach conquered the ICPR 2012 mitosis detection competition [20]. A wide variety of cancer detection methods for the medical image modalities using deep learning are available in the literature, and [21] presents a survey analysis of these methods.
Roy et al. (2019) introduced a patch-based classifier using CNN. The proposed classifier operated with two modes: one patch in one decision and all patches in one decision [22]. In [23], the authors proposed a CNN-based method to classify histopathological images from 269 images. The accuracies of CNN-based SVM are 77.8% (4 class) and 83.3% (2 class). Szegedy et al. proposed the Inception_V3 network obtained 78–93.9% accuracy [24]. The patient-level classification of breast cancer with CNN and multi-task CNN models achieved the patient recognition rate for CNN is 83.25% and 82.13% for MTCNN [25]. Mutaza et al. (2019) proposed transfer learning using Alexnet, and the BreakHis dataset achieves 81.25% of accuracy, 77.46% of specificity, 82.49% of sensitivity, 91.79% of precision, and 86.89% of F measure. These results are reached by fine-tuning the hyperparameters [40]. In [41], the authors utilized ICPR 2012 and 2014 dataset for histopathology image diagnosis using region convolution neural network (R-CNN). The authors grading system accomplished quality results that make use of fusion in Resnet-50 and Densenet-201.

3. Data and methods

3.1. Dataset

Fabio et al. introduced a breast cancer dataset for histopathology images (BreakHis), acquired from 82 patients [26]. The performance had been examined using BreakHis for binary and multi-class classification. The BreakHis is the large scale dataset that comprises 7909 images with benign and malignant, which includes four subclasses for each. The images are categorized under four magnification factors (40×, 100×, 200×, 400×) and eight subclasses [27]. The images are an eight-bit depth RGB image, and the size of the image is 700×460. The following table 1 shows the accumulation of BreakHis dataset images.

| Magnification Factors | Benign A | FA | TA | PT | DC | Malignant LC | MC | PC |
|-----------------------|---------|----|----|----|----|------------|----|----|
| 40×                   | 114     | 253| 109| 149| 864| 156        | 205| 145|
| 100×                  | 113     | 260| 121| 150| 903| 170        | 222| 142|
| 200×                  | 111     | 264| 108| 140| 896| 163        | 196| 135|
| 400×                  | 106     | 237| 115| 130| 788| 137        | 169| 138|

3.2. Methods

In this section, we state the description of deep convolution neural network (DCNN) and fine-tuned transfer learning classification approaches. First, we will confer the DCNN architecture with 15 layers. Then we use the pretrained model Alexnet and VGG-16 for our dataset. Finally, the classification accuracy comprises DCNN and transfer learning methods for binary and multi-class.

3.2.1. The DCNN Architecture

The CNN is designed with deep 15 layers architecture with learning parameters to classify binary and multi-class classification. The layer by layer DCNN design is shown in figure 1.
The whole input histopathology images are resized (28x28) with eight-bit depth RGB channels. The convolution layer retrieves the features from the input layers. The convolved weights with input are known as the kernel. The amount of filter shifting is called stride, which is usually lower than the kernel [28], [29]. The size of the kernel is 3x3, and the stride value is 2. The weights are passed by using the activation layer Relu. The pooling layer performs the dimensionality reduction using downsample the features with stride 1. The fully connected layer has a complete connection with neurons. The activation is computed with bias offset and matrix multiplication.

The learning parameters are implemented to develop the DCNN model, based on the optimizer stochastic gradient descent (SGD) [30], and the parameters are selected as in [31]. SGD does frequent updates of weights, hence converge faster for the larger dataset. For the training process, the learning rate is chosen as 0.001, which gives better results. The maximum epochs terminated with 300 and further no improvement in accuracy after 300 epochs. The validation frequency is selected as 10.

Fig 2 shows the schematic representation of proposed DCNN for breast cancer classification.

DCNN is the feed-forward neural network includes a series of convolution operation and subsampling layers. The function of layers depends on three parameters, namely, height, width, and the number of channels.

Relu is the activation function utilized between the pooling layer and the convolution layer [32]. The activation function produces an activation map (M):

\[ M = F(Input\ image \ast width + Bias) \]  

The dimension of the activation map is given as,

\[ 1 + \frac{i-f}{s} \times 1 + \frac{i-f}{s} \times 1 \]  

By applying different kernels (K) in the activation map, the dimension can be changed as

\[ 1 + \frac{i-f}{s} \times 1 + \frac{i-f}{s} \times 1 \times K \]  

From the above equations, the spatial dimensions can be reduced based on the factors input image dimensions (i), filter size (f), and stride (Gallego-Posada, Montoya-Zapata, & Quintero-Montoya, n.d.). The padding is used to extract the low-level features by adding pixels outside the image.
Figure 2. The Proposed DCNN architecture for breast cancer multi-class classification

The convolution layer \((l)\) is the input layer comprises feature maps \(x_1\) of size \(x_2 \times x_3\). The convolution layer receives the raw input images and sends feature maps to the output layer. The output feature maps \(y_1\) of size \(y_2 \times y_3\) [34], [35]. The \(i^{th}\) feature map in the convolution layer is denoted by,

\[
y_j^l = B_j^l + \sum_{k} k_{ij} \times y_{j-1}^l
\]

Where \(B_j^l\) is the bias parameter for training data. The kernel size is denoted by \(k_{ij}\).

The convolution layer width and height can be determined by using the following equation (5) and (8)

\[
C_w = \frac{i_w - f_w + (2 \times \text{Zero padding})}{s_w} + 1
\]

\[
C_h = \frac{i_h - f_h + (2 \times \text{Zero padding})}{s_h} + 1
\]

Where \(C_w\) and \(C_h\) represents convolutional layer width, \(i_w\) and \(i_h\) denoted as the input image width and height, \(f_w\) and \(f_h\) refers to the convolution filter width and height. Similarly \(s_w\) and \(s_h\) represents the stride width and height.

The mathematical representation of DCNN architecture with the input size 28×28 is illustrated by the following calculations

- In the first convolution layer \((C_1)\) we used the filter size of 3×3, stride 1, and kernel 8. The feature map utilized 6292 \((28 \times 28 \times 8)\) neurons in \(C_1\)

\[
C_1 = \frac{28 - 3 + (2 \times 1)}{1} + 1 = 28
\]

- The first max-pooling layer \((MP_1)\) used 1568 neurons for feature mapping

\[
MP_1 = \frac{28}{2} = 14
\]

- The second convolution layer \((C_2)\) employs the filter size \((3 \times 3)\), stride 1, and kernel 16. \(C_2\) exploits 3136 \((14 \times 14 \times 16)\) neurons for feature mapping

\[
C_2 = \frac{14 - 3 + (2 \times 1)}{1} + 1 = 14
\]

- The second max-pooling \((MP_2)\) implements 784 \((7 \times 7 \times 16)\) neurons for feature mapping

\[
MP_2 = \frac{14}{2} = 7
\]
The final convolution layer ($C_3$) utilized the filter size (3×3), stride 1, and kernel 32. $C_3$ used 1568 (7×7×32) neurons for feature mapping

$$C_3 = \frac{7 - 3 + (2 \times 1)}{1} + 1 = 7$$

### 3.2.2. Alex-net

Transfer learning is the process of fine-tuned parameters utilized to perform a different task from the network trained with one task[36]. AlexNet is the deep neural network architecture with 4096 fully connected layers. By using the pretrained network, we analyze the strength of the network when transferring network to the medical image domain. Training of AlexNet had taken more than 4 hours, depending on the specification of the system and size of the datasets. In this experiment, the pathological database is divided into two sections, one for training (80%), and another section (20%) is utilized for validation. The termination of the epoch is based on the observation of the highest accuracy. The training process using AlexNet is shown in figure 3.

![Schematic representation of the fine-tuned Alexnet](image)

In our experiment, we change the input image size 227×227. Then the complete dataset is split into two groups for binary and multi-class classification. The fully connected layer is changed with dimensionality reduction. Finally, for binary class, the fully connected layer is 2, and for multi-class, the fully connected layer 4. The training is limited up to 3 epochs, and the learning rate is $10^{-5}$.

### 3.2.3. VGG-16

The VGG-16 is a multi-layered deep convolution neural network. The layers used in VGG-16 are depicted in figure 6. The fully connected layer is comprised of 4096 neurons [37]. For feature extraction and dimensionality reduction, convolution, and max-pooling layer are used [38]. The entire dataset is divided into binary and multi-class for training and validation. The 80% of the data is utilized for training, and the remaining is used for validation. The validation frequency is 20 with three epochs, and the learning rate is $10^{-5}$. The training time depends on the size of the dataset and the specification of the system. The VGG-16 fine-tuned pre-trained model for the histology image classification is shown in figure 4.
4. Results and Discussions
The present work manifests the uniform results in the pretrained model and improves the results in the DCNN model. The DCNN, Alexnet, and VGG-16 experiments are carried out with the following system configuration: Intel(R) Core (TM) i5, Windows 7, 4 GB RAM with Single CPU. The experiment is operationalized by using Matlab 2018b. In DCNN, 90% of data is used for training, and 10% is utilized for validation. In the pre-trained model (Alexnet and VGG-16), 80% of data is used for training, and the rest of the data is applied for validation.

Table 2. Architecture of DCNN

| Layers               | Feature Map | Kernels       |
|----------------------|-------------|---------------|
| Input layer          | 28×28       | 28×28         |
| Convolution layer 1  | 28×28×8     | 3×3           |
| Max pooling 1        | 14×14×8     | 2×2           |
| Convolution layer 2  | 14×14×16    | 3×3           |
| Max pooling 2        | 7×7×16      | 2×2           |
| Convolution layer 3  | 7×7×32      | 3×3           |
| Fully connected layer| 1×2(Binary) | 1×1×2(Binary) |
|                      | 1×4(Multiclass) | 1×1×4(Multiclass) |

The DCNN uses simple architecture compared to the pre-trained model. The summary of DCNN architecture is shown in table 2. The graphical representation (DCNN, Alexnet, and VGG-16) shows that the performance comparison of different magnifications. The performance of all models categorized into binary and multi-class classification. From figure 7 DCNN accomplished superior accuracy results from other pre trained models (Alexnet and VGG-16).
Figure 5. Graphical representation of the performance of (a) DCNN (b) Alex-net and (c) VGG-16.

From Table 2, it can be observed that the DCNN accomplishes significantly dominant results, whereas Alexnet and VGG-16 are proportionate. To analyze the performance of the model concerning training and validation for both binary and multi-class (DCNN (90%-10%), Alexnet (80%-20%) and VGG-16 (80%-20%) are employed to get better accuracy. In our proposed method, we attained 93.38% average accuracy for binary class, and for multi-class, the average accuracy was 89.29%. The proposed method is analyzed comparatively with the existing models and is shown in Table 3. Figure 6 and 7 illustrates the different performance graphs for binary and multi-class with various magnification factors utilizing pre trained models (Alex net and VGG-16). Figure 8 shows that training and validation accuracy of histopathology using deep convolution neural network (DCNN). The outcome of the proposed CNN model surpass the modified Alexnet and VGG-16.
Table 3. Comparison of our proposed classification methods with other models

| Methods       | 40x (%) | 100x (%) | 200x (%) | 400x (%) |
|---------------|---------|----------|----------|----------|
| VLAD [39]     | 91.8    | 92.2     | 91.6     | 90.5     |
| CNN [39]      | 90.40   | 87.40    | 85.00    | 83.80    |
| PFTAS [39]    | 83.80   | 82.10    | 85.10    | 82.30    |
| ORB [39]      | 74.40   | 69.40    | 69.60    | 67.60    |
| LPQ [39]      | 73.80   | 72.80    | 74.30    | 73.70    |
| LBP [39]      | 75.60   | 73.20    | 72.90    | 73.10    |
| GLCM [39]     | 83.70   | 82.10    | 85.10    | 82.30    |
| CLBP [39]     | 77.40   | 76.40    | 70.20    | 81.80    |
| CNN [25]      | 83.08±2.08 | 83.17±3.51 | 84.63±2.72 | 82.10±4.42 |
| MTCNN [25]    | 81.87±3.06 | 83.39±5.17 | 82.56±3.49 | 80.69±4.23 |
| DCNN (Binary class) | 94   | 95.45    | 98.36    | 85.71    |
| DCNN (Benign-Multiclass) | 90.48   | 84.62    | 94.23    | 81.23    |
| DCNN (Malignant-Multiclass) | 91.67   | 95.83    | 90       | 86.27    |

Figure 6. DCNN accuracy results for benign multiclass (a) Benign 40X (b) Benign 100X (c) Benign 200X (d) Benign 400X
Figure 7. DCNN accuracy results for malignant multiclass (a) Malignant 40X (b) Malignant 100X (c) Malignant 200X (d) Malignant 400X
Figure 8. DCNN accuracy results for Binary class (a) Benign & Malignant 40X (b) Benign & Malignant 100X (c) Benign & Malignant 100X (d) Benign & Malignant 100X

5. Conclusion and Future works

Since breast cancer detection at the early stage helps the patient to undergo medical treatment. Using handcrafted features combined with machine learning algorithm gives less accuracy, and the final decision depends on the robustness of the extracted feature. Hence deep learning techniques with the convolutional neural network are explored in the present work. In this paper, binary and multi-class classification is performed by using deep features extracted by DCNN, Alexnet, and VGG-16. The BreakHis dataset is used to carry out this work. The Alexnet and VGG-16 net are adapted to identify breast cancer in histopathology images. The comparison results clearly indicate that the proposed DCNN architecture outperforms the fine-tuned pre-trained model. The scope for future research could be directed based on using different pre-trained models and varying hyperparameters. In real-time applications initially, binary classification can be done by the developed DCNN. Further grading can be performed with the developed multi-class DCNN. Thus, the developed architecture is immensely useful for real-time applications.

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