Classification of Histopathological Images for Early Detection of Breast Cancer Using Deep Learning

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Breast cancer is one of the most common and deadly types of cancer that develops in the breast tissue of women worldwide. This is why researchers and experts are interested in developing a computer-aided diagnostic system (CAD) for diagnosing histopathological images of breast cancer. CAD has contributed to increasing the diagnostic accuracy of the biopsy tissue using eosin stained and hematoxylin images. Most CAD systems have used traditional methods to extract handcrafted features, which are imprecise in diagnosis and time-consuming. The diagnostics by both CAD and the calculations are used to reduce the pathologist's workload and improve accuracy. In this study, the proposed convolutional neural network (AlexNet) approach to extract the deepest features from the BreaKHis dataset to diagnose breast cancer as either benign or malignant. In the current proposal, the study performed four experiments according to a magnification factor (40X, 100X, 200X and 400X). Each experiment contains 1407 images. The network was trained and validated on 80 % tissue images and 20 % for testing. The proposed system obtained accuracy, sensitivity, specificity, and AUC, 95 %, 97 %, 90 % and 99.36 % respectively.

Keywords: convolutional neural network, Breast cancer, BreakHis Dataset, Transfer learning.

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1. Introduction

In the field of biomedicine, the diagnosis of microscopic images, that represent human organs, plays an important role in understanding different tissues and biological functions. Several different computer-aided applications have been developed for classifying microscopic images. Breast cancer is one of the most common cancers in the world among women whose ages range from 20 to 50 years [1]. Early diagnosis of breast cancer gives a high survival rate of up to 80 % [2]. Mammography and biopsy are two methods applied for diagnosing breast cancer. It was noted that the mortality rate decreased upon early radiological diagnosis by the radiologist [3, 4]. In this approach, histology samples have been taken from the affected area, and imaged under a microscope are diagnosed. Biopsy is a diagnostic method for diagnosing all types of cancer, including breast cancer [5, 6]. Because of the similarity in characteristics and irregular appearance between benign and malignant lesions, manual diagnosis is difficult and imprecise [7]. Computer-assisted diagnostic techniques extract characteristics from the nuclei to provide important information for diagnosing a lesion, either benign or malignant. There are several clustering algorithms and statistical methods for extracting features, segmentation, and classification of nuclei [8]. In medical image diagnostics, there are many algorithms for diagnosing histopathological images that are rapidly developing, but there is still a demand for a highly effective diagnosis [9]. Therefore, such systems are desirable because they give accurate and correct results. Complex image processing stages such as pre-processing, segmentation, and feature extraction are a reason for low diagnostic accuracy [10]. Therefore, to overcome the machine learning problem, deep learning is introduced to extract the relevant features of the input raw images and use them for the classification process with high accuracy [11]. In deep learning, features are extracted using convolution layers and assembly layers represent high precision [12]. In recent years, convolutional neural networks have been used to diagnose biomedical images, such as detecting and diagnosing tumors [13], chronic diseases [14], and diagnosing micrographs of breast cancer [15]. Convolutional neural networks work very well with large data sets and less accurate on small data sets [16]. Pre-trained CNNs are working to extract a set of image features and apply them to a smaller data set [17, 18]. In the system proposed by Karabatak, M., et al. (2015) for breast cancer database performance evaluation, they proposed the Naïve Bayesian (NB) weighted technique to diagnose breast lesions. They have conducted several trials to evaluate a balanced NB network with 5-fold cross-validation. They reached an accuracy of 98.54 %, a sensitivity of 99.11 %, and specificity of 98.25 % [19].

In the research paper proposed by Khan, S.et al (2019), they proposed a new framework by using deep learning technology for detecting and classification of cytology images of breast cancer. Transfer learning aims to learn a problem and solve another related problem. Feature extraction uses pre-trained through deep learning techniques namely, VGGNet and ResNet, which fed features to fully connected layers to classify images into benign or malignant cells. The proposed system is evaluated on the breast cancer dataset, the proposed framework has reached to high accuracy [20].

In the evaluation proposed by Spanhol, F. A. et al (2017), the automated detection of breast lesions makes the diagnosis more accurate, efficient and less error-prone. Their DeCAF proposal serves as reuse of feature vectors in the CNN pre-trained network and uses it as an input to a classifier trained for the new classification task. The system achieved an accuracy of 90.3 % when using the magnification factor of 200X on the Patient Level, and the system achieved the highest accuracy of 88.7 % when using the magnification factor of 200X on the Image Level [21]. In the evaluation proposed by Zhang, Q. et al. (2016), their study aimed to extract automatic features from image data by shear-wave electrography (SWE), and evaluation of DL to distinguish between benign and malignant neoplasms. They used the restricted Boltzmann machine (RBM) and the point-wise gated Boltzmann machine (PGBM) to build DL architecture to extract the SWE features. PGBM contains related hidden units that are connected to the RBM. The evaluation was performed on a dataset consisting of 135 benign tumors, a set of 227 SWE images, and 92 malignant tumors [22]. In the study presented by Xu, J et al. (2015), they used Stacked Sparse Autoencoder (SSAE). SSAE method learns features from pixel intensities so that they can distinguish nuclei features. Each image is inputted and high-level features are obtained via an auto encoder, and it is fed into the classifier to diagnose each patch as nuclei or not nuclei. SSAE achieved an improved F-measure of 84: 49 % [23]. In the study conducted by Bharat., Et al (2018), to evaluate the Wisconsin dataset on several classifiers, the dataset contains ten extracted features. They used the classifiers Decision Tree (CART), K-Nearest Neighbors (KNN), Support Vector Machine (SVM) and Naive Bayes (NB) to classify the inputted features as either a benign or malignant lesion. They reached accuracy over 92 % for the classifiers KNN, CART and NB [24].

In the research paper presented by Bhardwaj, A., et al. (2015), to evaluate the performance of their proposed system on the WBCD dataset, they proposed a Genetically Optimized Neural Network (GONN) algorithm for classifying a dataset. GONN has obtained superior performance in classifying WBCD dataset as malignant or benign [25]. In the system proposed by Guo, Y., et al. (2018), they proposed Scheme of Diagnosis of Grand Challenge on Breast Cancer History Images.

First, it is the convolutional neural network GoogLeNet technology hybrid with essential information in the decision. Second, it is the implementation of the bagging method with hierarchical voting to improve system performance and reduce generalization errors. Finally, their system has worked to transfer learning and augmenting data to overcome the small data set problem [26]. In the system proposed by Vesal, S., et al (2018), an approach based on transfer learning is employed to classify four types of breast histology images. First, the BACH 2018 Grand Challenge dataset was processed and normalized to correct different colors when preparing slides. The system reached good results. When using Patch-Wise, the accuracy was 92.95 %, 92.95 % for Inception-V3 and ResNet50 respectively [27]. In this work, the new model for histopathology image classification has taken global features from the image. The main contributions to this work are summarized in the following:

1- More information was integrated for decision-making, as both global and local information were combined to obtain high diagnostic performance.

2- To improve the performance of the system and reduce the generalization error, the hierarchical voting technique is applied. Various models are trained, then images are classified by patch-level and image-level voting application.

3- The learning transfer and data augmentation strategy were applied to prevent overfitting and reduce training time. The lowest level features in ImageNet for breast cancer diagnosis are weighted by re-initializing the pre-trained network in our model.

2. Materials and Methods

In this section, the proposed convolutional neural network AlexNet system describes the diagnosis of breast lesions. The approach has included four steps as shown in Fig. 1 AlexNet architecture. First, pretreatment is utilized to improve the microscopic images, normalize spots on histology images, and improve image contrast. This step improves diagnostic performance. Second, this work has introduced a data augmentation technique to increase the amount of training data effectively. Third, the augmented dataset is used to train the network on images of various multi-scales, and then the deep features of the breast histology are extracted. Fourth, the deep features are fed into the fully connected layer, which classifies the microscopic images into malignant or benign.

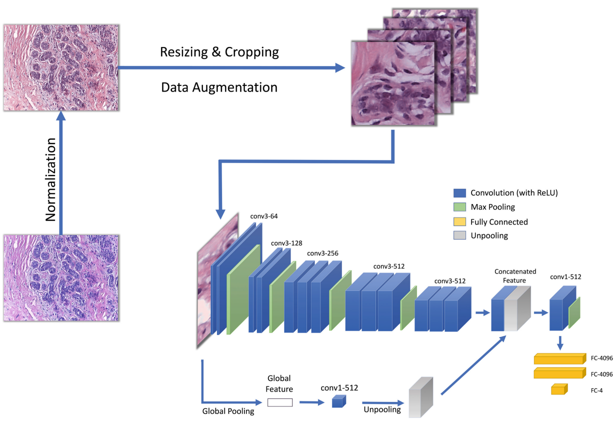

Fig. 1. CNN AlexNet architecture.

2.1. BreakHis Dataset

The Breast Cancer Histopathological (BreakHis) database contains 9,109 breast histology images taken from 82 patients under a magnification factor (40X, 100X, 200X, and 400X). The database is divided into two types: benign lesions, which consist of 2,480 histology images, and malignant lesions, which contain 5,429 histology images. All microscopic images were taken in RGB color space with 460 x 700 pixels. The database was created in collaboration with P&D laboratories, which has become available to researchers and experts as a useful tool for diagnosing breast lesions. Fig. 2 shows an image of tissues under magnification factor 40X, 100X, 200X, and 400X.

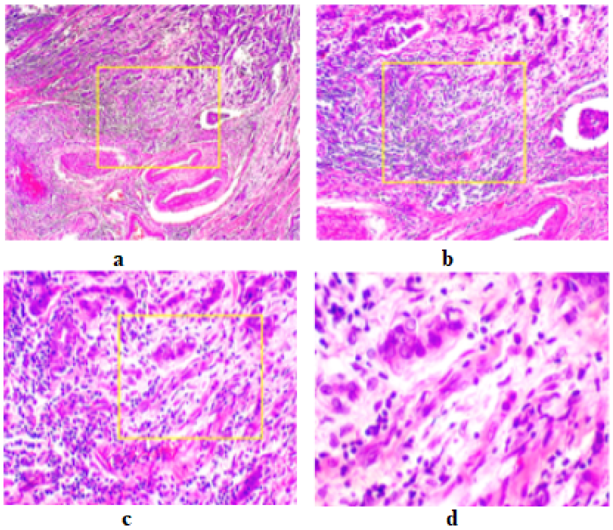

Fig. 2. different magnification factors:(a) 40X, (b) 100X, (c) 200X, and (d) 400X.

2.2. Data Pre-Processing and Augmentation Processing

Pre-treatment is necessary to remove noise from histology images. To perform high-precision diagnostics, convolutional neural networks require a large dataset size. One of the challenges in CNN is insufficient medical data set size, and the over-fitting problem that means CNN performed in terms of accuracy is high for the training dataset, but it performs less with the test dataset. Therefore, in the proposed system, the present study has used the data augmentation technique to solve the problems of data set size and over-fitting. In the data augmentation technique, the number of each microscopic image was increased by geometric transformations such as translation, scaling, rotation and flipping [28, 29]. By Bilinear Interpolation, the image has been resized to 224x224 pixels. The stain normalization method is essential for the image enhancement process since when biopsy is taken, histology staining and inconsistent cuts [30].

2.3. Feature Extraction

The histology images contain many cell shapes, texture features, histology structures, etc. Characterization of features is regarded as an important task of the classification stage. Manual extraction of features requires high knowledge and experience in the field, which distinguishes features that are difficult to be extracted. CNN is worked on extracting representative features of histology images. In the proposed system, the AlexNet model was used to extract deep features. The AlexNet convolutional neural network contains 5 convolutional layers that extract deep features from histology images. The CNN architecture is best suited for identifying features based on texture and histology structures and avoids overfitting problems. The histology images were inputted on the convolutional layers, as the first layers in CNNs, which contain 16 kernels of 7 x 7 pixels, as they give an output of 16 different channels. These channels are fed to the pooling layers to reduce the dimensions of the extracted features (to represent samples of the features). One of the most important layers in the CNN architecture is convolution layers, which is responsible for extracting features from images.

2.4. Transfer learning

As mentioned earlier, the scarcity of breast histology images has become a barrier to AlexNet training. So the study has applied transfer learning [18] and fine-tuned AlexNet pre-trained on the ImageNet dataset [19][. Transfer learning is one of the most important steps in learning a machine that learns to solve a problem and apply it to solve other related problems. Initially, the network is trained on the relevant data set to perform a specific task. Then, it is transferred to perform another task on the target data set [20]. The learning process is divided into two steps. The first step is employed to identify the pre-trained model and the size of the problem, and the second is similarity. The pre-trained model is chosen according to the target problem. If the size of the target data set is smaller and similar to the size of the training data set, then the overfitting is high. If the target data set is larger and similar to the size of trained data, then overfitting is low that requires fine-tuning the data set for the pre-trained model. In the proposed approach, the CNN AlexNet model was used in which properties were shared to impart learning and fine-tuning. AlexNet architecture is trained on the ImageNet dataset and adapts learning transfer to the target dataset. The microscopic images are classified fully by the connected layers. In the AlexNet model, the last three layers that yield 1000 classes are deleted and replaced with a fully connected layer. AlexNet contains three fully connected layers. The first connected layer receives 9,216 neurons and outputs 4,096 neurons, the second connection layer receives and outputs 4,096 neurons, and the third connected layer produces two neurons as malignant or benign according to the number of classes in the data input.

3. Results

This study has conducted four experiments with the BreaKH dataset to evaluate the performance of the AlexNet network. Each Experiment contained 1,407 histology images with a magnification factor. The dataset was divided into 80 % for training and 20 % for testing and validation. The proposed system was evaluated by a confusion matrix and an AUC (Area Under the Curve) through a ROC (receiver operating characteristic) curve. Fig. 3 shows the confusion matrix for the test data set and ROC when evaluating the proposed system on the dataset with a magnification factor of 400X.

The proposed system has obtained Super results in terms of accuracy, sensitivity, specificity and AUC as shown in Table 1. Where accuracy is the number of positive and negative samples that have been correctly classified (TP and TN) and divided by all samples (TP, TN, FP and FN) as shown by Eq. 1. Sensitivity is the number of positive samples (TP) that have been correctly classified and divided by all positive samples (TP and FN) as shown by Eq. 2. Specificity is the number of negative samples (TN) that were correctly classified and divided by all negative samples (TN and FP) as shown by Eq. 3. AUC is the rate of positive samples that are classified correctly and divided by the percentage of incorrect classified positive samples, or the sensitivity divided by the specificity as shown in Eq. 4.

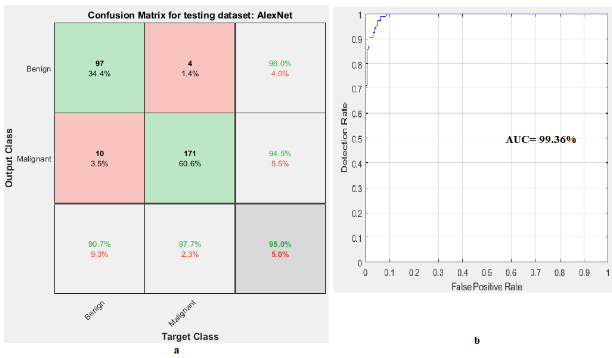

Fig. 3. a) Confusion matrix b) AlexNet performance by AUC.

$$\textbf{Accuracy} = \frac{TP+TN}{TP+TN+FP+FN} \times 100\% \quad (1)$$

$$\textbf{Sensitivity} = \frac{TP}{TP+FN} \times 100\% \quad (2)$$

$$\textbf{Specificity} = \frac{TN}{TN+FP} \times 100\% \quad (3)$$

$$\textbf{AUC} = \frac{\text{True Positive Rate}}{\text{False Positive Rate}} = \frac{\text{Sensitivity}}{\text{Specificity}} \times 100\% \quad (4)$$

As shown in Table 1, the system obtained the following accuracy: 95 % at 40x magnification factor, 91.5 % at 100x magnification factor, 91.8 % at 200x magnification factor, 95 % at 400x magnification factor.

Table 1. Results for Breast Lesion Diagnosis (Malignant and Benign) Using CNN AlexNet Classifier.

Evaluation	40x	100x	200x	400x
Accuracy %	95.00	91.50	91.80	95.00
Sensitivity %	95.40	91.40	94.90	97.70
Specificity %	93.50	91.60	86.90	90.70
AUC %	98.46	97.71	98.42	99.36
Validation %	94.67	90.67	93.33	93.78

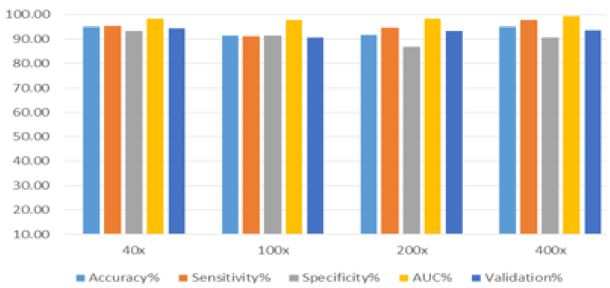

Fig. 4. Display Performance of AlexNet for Detection of Breast Lesion.

The system got the highest AUC of 99.36 % at 400X magnification factor. It is noted that the best performance of the proposed system was based on the magnification factor of 400X. Fig. 4 Displays AlexNet performance on the BreaKHis dataset with four enlargements.

The diagram shows that when using the dataset with a magnification factor of 40x, the system achieved accuracy, sensitivity and specificity of 95.00 %, 95.40 % and 93.50 %, respectively. And when using the dataset with a magnification factor of 100x, the system achieved accuracy, sensitivity and specificity of 91.50 %, 91.40 % and 91.60 % respectively. And the dataset with a magnification factor of 200x, the system obtained accuracy, sensitivity and specificity of 91.80 %, 94.90 %, 86.90 %. We note that the system got the best performance for diagnosing malignant lesions when using the dataset with a 400x magnification factor, where the system got a sensitivity of 97.7 %. While the system got the best performance for diagnosing benign lesions when using the dataset with a magnification factor of 40x, where the system reached a specificity of 93.50 %.

4. Comparative Study

The evaluated the performance of the proposed system in several methods that have been evaluated in the literature. As shown in Table 2, the performance evaluation of several systems in previous related studies. The results of previous studies can be observed in Table 2 in methods [21–28] that give an accuracy ranging from 74.70 % to 90.4 % at the magnification factor of 40x, the accuracy ranging from 78.60 % to 91.9 % at the magnification factor of 100x, the accuracy ranges from what Between 83.40 % to 90.3 % at the magnification factor of 200x, and the accuracy ranges between 81.70 % to 89.70 % at the magnification factor of 400x. While our proposed system showed a performance superior to the previous systems.

Table 2. Comparison of the performance of our proposed system with previous studies.

Previous studies	**40x**	**100x**	**200x**	**400x**
PFTAS [31]	83.80	82.10	85.10	82.30
GLCM [31]	74.70	78.60	83.40	81.70
CNN [32]	90.40	87.40	85.00	83.80
Inception [33]	90.20	91.90	93.70	88.90
CNN [21]	88.50	88.50	90.30	87.10
AlexNet [34]	-	-	84.00	-
GoogLeNet [35]	-	-	-	89.70
CNN [36]	83.10	83.20	84.60	82.10
VGG [37]	86.20	85.90	87.20	86.30
Proposed model	**95.00**	**91.50**	**91.80**	**95.00**

5. Conclusions

In this approach, a transfer learning method is used for classifying breast cancer histology images. The network has learned the deep features with the AlexNet architecture, which is pre-trained on ImageNet. BreaKHis dataset has been classified into malignant or benign images. The dataset contained 7909 images from 82 patients. The images were taken with four magnification factors (40X, 100X, 200X and 400X). In our proposal, 5628 images were classified with four magnification factors (1407 images for each magnification factor), which were divided into 3492 malignant images and 2136 benign images. The dataset was divided into 80 % for training and validation, and 20 % for system performance testing. Transfer learning is used as an effective and accurate method for classifying breast cancer histology images. The network can transfer ImageNet knowledge as convolutional features for image histology problem classification. Although the number of images in the target data set (BreaKHis) is small, AlexNet achieved

Superior results in terms of accuracy, sensitivity, privacy and AUC on the dataset with the four magnification factors.

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