Magnification-specific Multicategory Breast Histopathology Image Classification Using Machine and Deep Learning Approaches

Abdelrahman Habib, Jaqueline Leal, Esther Matamoros, Edwing Ulin
Università degli Studi di Cassino e del Lazio Meridionale

Abstract

Breast cancer is a significant health concern worldwide, and accurate classification of breast cancer histopathology images plays a crucial role in diagnosis and treatment planning. In this study, the performance of machine learning (ML) and deep learning (DL) approaches for breast cancer classification is investigated. The ML approach employs Random Forest, Support Vector Machines (SVM), and K-Nearest Neighbors (KNN) algorithms, while the DL approach utilizes transfer learning with DenseNet. The ML models are evaluated using the Area Under the Curve (AUC) metric, while the DL model is assessed based on test accuracy and loss.

The results of the ML approach indicate moderate performance, with AUC values ranging from 0.48 to 0.56 for the tested algorithms. The DL approach achieves an overall test accuracy of 0.7150, indicating that the model correctly classifies breast cancer samples 71% of the time. The analysis of the DL model using ROC curves reveals varying AUC values for different classification classes, ranging from 0.92 to 0.98.

These findings suggest opportunities for improving the classification system's performance. Further exploration of feature engineering, hyperparameter tuning, alternative DL models, and additional preprocessing techniques could enhance the accuracy and effectiveness of breast cancer classification. Ultimately, advancements in ML and DL techniques hold promise for improving breast cancer detection and diagnosis.

Introduction

Using DenseNet(Vulli et al. 2022). Breast cancer is a pervasive and life-threatening disease, affecting a significant number of women worldwide. Its impact on women's health is staggering, with statistics indicating that one in nine women will experience breast cancer during their lifetime. Moreover, breast cancer is the leading risk factor for cancer in women and ranks seventeenth among the major causes of global mortality (Garcia et al. 2021).

Metastatic breast cancers (MBCs), which originate from the lymphatic and blood vessels and spread to distant parts of the body, contribute significantly to breast cancer mortality (Walters et al. 2019). The prognosis, precise diagnosis, and treatment of MBCs pose substantial challenges due to variations in metastasis rate and location, which depend on the tumor subtype.

Accurate examination of lymph nodes is crucial for cancer diagnosis and determining appropriate treatment options. However, the manual screening of numerous slides by pathologists can be laborious and challenging, and patients often need to undergo multiple scans for accurate assessment, which can be hazardous. In recent years, advancements in automated tissue categorization using machine learning techniques have enabled precise identification of metastases in lymph node tissue. Computer-aided diagnosis and digital pathology have made significant progress, allowing for slide digitalization and enhanced image quality similar to traditional light microscopy. Digital pathology reduces human errors and offers remote viewing and analysis capabilities, thereby decreasing the dependence on on-site expertise (Pham et al. 2019).

Although numerous studies have explored the functionality of artificial intelligence (AI) techniques in breast cancer diagnosis, including region of interest (ROI) identification, cell characterization, and classification, deep learning (DL) models have shown great potential due to their ability to automatically extract features and process complex information. DL models, particularly CNNs, have been extensively used for the automated classification of breast cancer histopathological images, with researchers worldwide investing considerable efforts to develop robust computer-aided tools. However, challenges such as overfitting, limited availability of labeled images, and the need for large training datasets still exist(Wakili et al. 2022).

To address these challenges, transfer learning, a technique that leverages knowledge from a related domain to improve model efficiency and performance, has gained prominence in breast cancer diagnosis. Researchers have proposed transfer learning-based approaches to achieve state-of-the-art performance on different datasets, demonstrating the potential of this approach in improving classification accuracy and efficiency. However, further advancements are necessary to refine performance metrics, overcome algorithmic assumptions, and simplify computational complexities (Vulli et al. 2022).

To accomplish this task, the BreakHis dataset (Spanhol et al. 2015) will be utilized. The BreakHis dataset is widely used in breast cancer research and consists of histopathological images with detailed annotations. However, several challenges need to be addressed during the classification process. Firstly, the dataset poses an unbalanced classification problem, with variations in the number of samples available for each class. Secondly, a hierarchical classification approach may be required for multiclass classification, as the dataset includes multiple levels of classification. Lastly, the classification task needs to be performed on multiscale images, which adds complexity to the analysis.

In this paper, the use of machine intelligence and transfer learning in breast cancer diagnosis is explored to enhance the accuracy, efficiency, and generalization ability of classification models. A novel approach is presented that utilizes a pre-trained CNN model, DenseNet, and investigates the benefits of transfer learning in improving the classification performance of breast cancer histopathological images. By addressing the limitations of current methodologies, the aim is to contribute to the development of intelligent algorithms for breast cancer diagnosis.

Methodology

Dataset

General description The BreaKHis dataset (Spanhol et al. 2015) is a comprehensive collection of biopsy images depicting both benign and malignant breast tumors. These images were meticulously gathered through clinical studies conducted from January to December 2014. During this period, patients exhibiting clinical symptoms of breast cancer were invited to participate in the study, and samples were obtained via surgical open biopsy (SOB). These samples were then stained with hematoxylin and eosin to enhance the visibility of cellular structures. The resulting images, which underwent thorough examination by pathologists in the P&D laboratory, serve as valuable resources for histological studies.

Comprising a total of 7,909 images, the BreaKHis dataset encompasses tissue samples from 82 patients. These samples have been categorized into two main groups: benign and malignant tumors. Among them, there are 2,480 images of benign tumors, which originate from 24 patients, and 5,429 images of malignant tumors, gathered from 58 patients. To further classify the tumors, each group is subdivided into four distinct subclasses. The benign tumor category includes adenosis (A), fibroadenoma (F), phyllodes tumor (PT), and tubular adenoma (TA), while the malignant tumor category consists of ductal carcinoma (DC), lobular carcinoma (LC), mucinous carcinoma (MC), and papillary carcinoma (PC).

Magnification	Benign	Malignant	Total
40X	625	1,370	1,995
100X	644	1,437	2,081
200X	623	1,390	2,013
400X	588	1,232	1,820
Total	2,480	5,429	7,909

Table 1: Distribution of the BreakHis dataset by magnification.

All images within the BreaKHis dataset are captured in a true-color space using the RGB model, allowing for a comprehensive representation of color variations. These images exhibit different magnifications, ranging from 40X to 400X, providing insights into tumor morphology at various levels of detail. Each image has a size of 700x460 pixels, offering a substantial amount of information for analysis and research purposes.

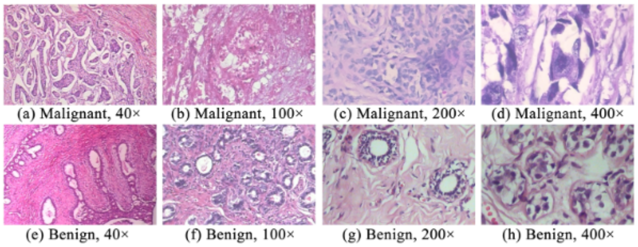

Figure 1: Representative examples of magnifications of BreaKHis dataset.

Data Splitting

The BreakHis dataset was divided into a training set and a test set with a ratio of 60 and 40 respectively. This splitting ratio ensured a sufficient amount of data for training the machine learning models while reserving a separate portion for evaluation. The folder structure of the dataset was rearranged to facilitate organization and easy access to the data. The principal component for rearranging the folder structure was based on the eight classes for tumors, consisting of four malignant types and four benign types. The new folder structure incorporated the concept of magnification levels (40X, 100X, 200X, 400X), allowing for further differentiation and classification of the images.

The magnification levels, played a crucial role in the folder structure rearrangement. Each magnification level was treated as a distinct subset within the dataset, ensuring that images captured at different levels of magnification were appropriately organized.

Data Augmentation

Data augmentation is a widely adopted technique that addresses the challenge of limited training data. By artificially expanding the dataset through the application of diverse transformations and modifications to existing samples, data augmentation enhances model generalization and performance. ImageDataGenerator class from Keras was applied to perform data augmentation. This technique enables the creation of augmented data generators for the training, validation, and testing sets.

The technique was initialized with the target size of the images and the directory paths for the training, validation, and testing data sets. A random seed was set to ensure reproducibility. The training data generator was configured with several augmentation techniques (Re-scaling, Rotation, Width, and Height Shift, Shearing, Zooming, Horizontal Flipping, Brightness Adjustment, and Fill Mode). The training data generator is created, which reads the training images from the specified directory and applies the defined augmentation techniques. The generated batches have a batch size of 32 and follow a categorical class mode. The validation and testing data generators were created. For these sets, only re-scaling is applied to ensure consistency in pre-processing. The validation generator generates batches of size 64, while the testing generator uses a larger batch size of 1,024.

The second approach was addressed with the focal loss function, a specialized loss function designed to address the issue of class imbalance. It introduces a weighting mechanism that assigns higher importance to misclassified samples, particularly those belonging to the minority class. In addition to data augmentation, the focal loss is implemented to further enhance the performance. The focal loss function is defined using TensorFlow and Keras.

Feature Extraction and Selection

In this study, a feature extraction method is employed based on the DenseNet model. The process of feature extraction involved several steps. Firstly, the DenseNet169 with ImageNet weights has been used for feature extraction, enabling it to capture high-level visual patterns.

Next, for each image, the following operations were performed:

- Firstly, the image was loaded and resized to match the input size required by DenseNet169.
- The image was preprocessed ensuring the normalization and formatting necessary for the DenseNet model.
- The preprocessed image was then fed into the DenseNet169 model generating a feature representation capturing the image's distinctive characteristics.
- To facilitate further processing and analysis, the extracted features were flattened into a 1D array.

The method was applied iteratively to process multiple images. Each image was individually processed, resulting in a set of extracted features for each image. These features were collected in a list and subsequently converted into numpy arrays for further processing or analysis.

Following feature extraction, a feature selection is performed using a two-step approach. Initially, the features and corresponding labels were stored. The feature set, represented by array X, was standardized to achieve uniform scaling across features. This standardization process was crucial in avoiding any bias caused by features with disparate magnitudes.

To select relevant features, Lasso regularization is employed with an alpha value of 0.01. Lasso regression introduces a penalty term that encourages sparsity in the feature coefficients. The resulting non-zero coefficient features were then extracted from the data. Furthermore, SelectKBest is employed, a feature selection method based on chi-square tests, to rank the features according to their relevance to the target variable. The top k features with the highest scores were chosen for the machine learning approaches.

Deep Learning Approach

Deep neural networks, which refers to Artificial Neural Networks (ANN) with multiple layers have been considered one of the most powerful tools for decades as it has gained a lot of popularity in the literature due to their ability to handle enormous amounts of data (Albawi, Mohammed, and Al-Zawi 2017). Convolutional Neural Network (CNN) is considered one of the most popular deep neural networks. It has shown excellent performance in various machine learning problems (Wu 2017). DenseNet is one of many types of CNN models, that replace the convolution non-linear and pooling layers with dense blocks and transition layers except for the first convolutional layer (Nawaz, Sewissy, and Soliman 2018). Following the same approach as (Nawaz, Sewissy, and Soliman 2018), using a transfer learning approach, the DenseNet architecture was modified to deal with histopathology images to build a breast cancer multi-class image classifier.

Transfer learning aims to achieve high performance on target tasks by using knowledge learned from another similar task learned in advance, in other words, knowledge is transferred to enhance the performance new task, thus saving time and hardware resources.(Kim et al. 2022).

Following a similar approach as (Nawaz, Sewissy, and Soliman 2018), the DenseNet model with ImageNet weights was used as the pre-trained model. However, this experiment used DenseNet169 and modified the last 10 layers of the original model to be fine-turned, while preserving the pre-trained weights of ImageNet on the rest. Four custom dense blocks were added and three transition layers as (Nawaz, Sewissy, and Soliman 2018) to classify breast cancer tumors. Each dense block is implemented with four convolutional layers and a 3x3 kernel size is used instead of the reference implementation. Following each dense block is the transition layer with a reduced kernel size of 1x1 and an average pooling layer. Finally, a final dense layer is added with the desired number of classification classes, which was 8 in this case. Figure 2 displays the modified DenseNet architecture that was taken as a reference for this implementation

During the training, a list of callbacks is used as they are useful for performing certain actions at various training stages. Three callbacks were implemented, EarlyStopping, ModelCheckpoint, and TensorBoard. EarlyStopping monitors the validation loss and stops the training process if the loss does not improve for a certain number of epochs (specified by patience). ModelCheckpoint saves the best model weights based on the validation loss. And TensorBoard allows model visualization during the training by saving the logs.

Machine Learning Approach

The concept of machine learning refers to various types of algorithms that use a dataset to make intelligent predictions (Nichols and Baker 2019). The present work relies on Deep Learning techniques to extract features from the image dataset. The objective is to conduct a comparative analysis of the classification outcomes between Machine Learning and Deep Learning. This approach uses 3 different algorithms for the multiple class classification of the dataset: Random Forest, Support Vector Machines, and K-Nearest Neighbor.

The support vector machine (SVM) is employed due to its robustness in handling high variable-to-sample ratios and

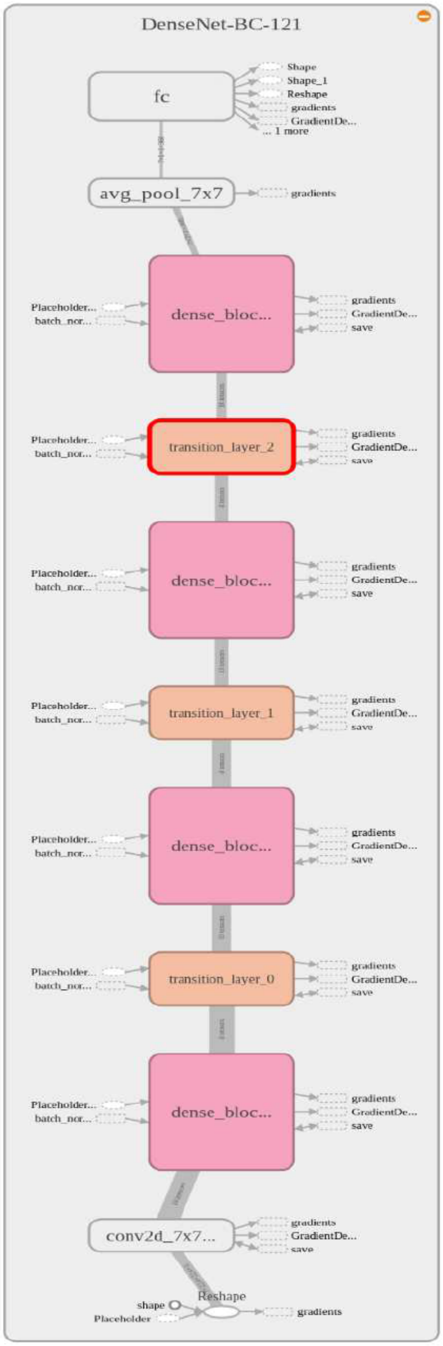

Figure 2: Modified DenseNet Model displaying the dense and transition blocks flow as in (Nawaz, Sewissy, and Soliman 2018).

a large number of variables. SVMs are capable of efficiently learning complex classification functions since they employ powerful regularization principles to prevent overfitting. The Random Forest algorithm is employed due to its construction through a bootstrap approach that utilizes a randomly chosen subset of variables. This approach ensures optimal classification performance within the sample limit. The K-Nearest Neighbors (KNN) algorithm is a non-parametric method utilized for classification. Its efficacy and simplicity are widely recognized. (Statnikov and Aliferis 2007)

In this work, a 10-fold cross-validation approach was employed for each candidate to optimize the three selected machine learning algorithms. The chosen measure for optimization was accuracy. On the other hand, given that this is a classifier with multiple classes, the one-vs-all approach is employed to create a binary classifier for each class.

Upon completion of the fitting process, the optimal classifier is preserved for both the training and validation datasets. The test dataset is utilized to assess the performance of the machine-learning model. The utilization of ROC curve computation is employed, and identical metrics are utilized in the deep learning methodology.

Results and Discussion

The code is publicly available at: https://github.com/abdalrhmanu/magnification-specific-breast-histopathology-image-classification-using-machine-and-deep-learning. The model is tested in a magnification-dependent way. The data was rearranged as explained previously. The magnification used for this experiment is 40X. Furthermore, each class is assigned a number as Table 2 shows.

Name of Class	Name Assigned
Adenosis	Class 0
Ductal carcinoma	Class 1
Fibroadenoma	Class 2
Lobular Carcinoma	Class 3
Mucinous Carcinoma	Class 4
Papillary Carcinoma	Class 5
Phyllodes tumor	Class 6
Tubular Adenoma	Class 7

Table 2: Classes' names for Classification Experiments.

ML Approach results

The Receiver Operating Characteristic (ROC) curve is generated for individual classes by utilizing the actual labels and forecasted scores. In order to compute the false positive rate (FPR), true positive rate (TPR), and thresholds for each class, it is necessary to transform the authentic labels from categorical labels into numerical values using a label encoder. The computation of the area under the receiver operating characteristic (ROC) curve, commonly referred to as AUC, is performed for every individual class. The outcomes of the cross-validation fitting for the selected models in this machine learning methodology are presented in the subsequent table, which displays the Area Under the Curve (AUC) of the OneVsAllClassifier as Table 3.

In addition to the area under the curve (AUC) metric, an analysis of the receiver operating characteristic (ROC) curves is conducted for each class across various algorithms. The outcomes pertaining to the Random Forest model are depicted in Figure 3. Classes 0, 1, and 4-7 in these findings

ML algorithm	**AUC**
Random Forest	0.52
SVM	0.56
K-Nearest Neighbors	0.48

Table 3: Accuracy result for the Multiple Class Classifier.

exhibit an AUC of 1, implying that the RF model attained a complete true positive rate, thereby emulating the class prediction. Classes exhibiting an AUC value of less than 1 suggest that the Random Forest (RF) model may have a comparatively higher rate of false positives or a lower rate of true positives, which in turn indicates challenges in the classification process.

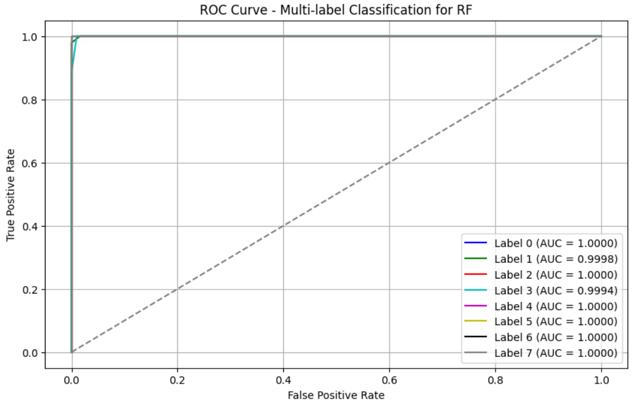

Figure 3: ROC curve Obtained from Random Forest.

The Receiver Operating Characteristic (ROC) table presented in Figure 4 indicates that the classification of Class 1 is challenging. On the other hand, the remaining classes demonstrate similar behavior to that of the RF. The present findings indicate that the performance of SVM is comparatively inferior due to its regularization principles which effectively mitigate the issue of overfitting that may arise from data errors.

The results depicted in Figure 5 indicate that the K-Nearest Neighbors (KNN) algorithm exhibits a high degree of accuracy in classifying the data. Specifically, a majority of the classes demonstrate a perfect classification accuracy of 1, while the remaining classes exhibit near-perfect accuracy.

In summary, the AUC values (see Table 3) indicate moderate performance. In contrast, another study (Naji et al. 2021) also reported that SVM achieved higher efficiency (97.2%), precision (97.5%), and AUC (96.6%) on the Wisconsin Breast Cancer Diagnostic dataset (WBCD), outperforming other algorithms. The authors concluded that SVM demonstrates the best performance in terms of accuracy and precision.

The features fed to the machine-learning algorithms could have been further enhanced using more feature engineering techniques. For instance, Karthiga & Narasimhan (2018) reported higher accuracy values for the SVM classifiers, ranging from 91.3% to 93.3% suggesting better performance in predicting breast cancer using the wavelet-based entropy features and SVM classifiers.

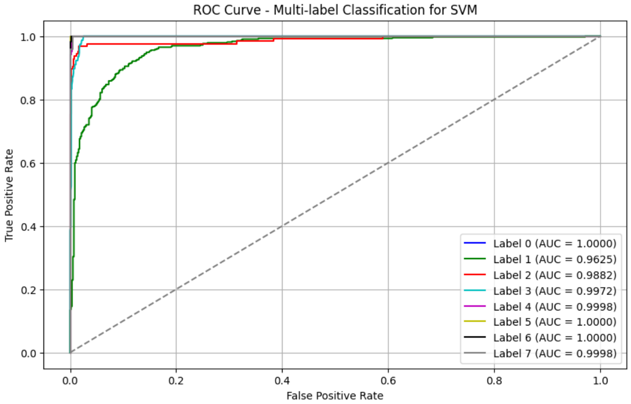

Figure 4: ROC curve Obtained from Support Vector Machines.

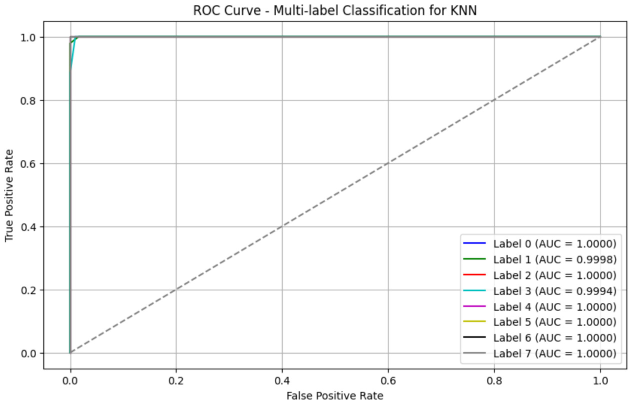

Figure 5: ROC curve Obtained from K-Nearest Neighbor.

DL Approach results

In this study, DenseNet transfer learning is used to perform a classification task. The evaluation of the model on the test dataset yielded a test loss value of 0.0168, which indicates the average discrepancy between the predicted labels and the actual labels in the test dataset. Furthermore, the test accuracy value of 0.7150 means the proportion of correctly predicted labels in the test dataset. Overall, the model is correctly classifying the samples 71% of the time.

In addition to the test accuracy and loss, the performance of the DenseNet transfer learning algorithm using ROC curves for each classification class is also analyzed(see Fig. 6). The ROC curve is a graphical representation that illustrates the trade-off between the true positive rate (TPR) and the false positive rate (FPR) for different classification thresholds.

The class with an AUC of 0.98, like Class 0 and Class 7 in these results, indicates that the DL approach achieved a high true positive rate while maintaining a low false positive

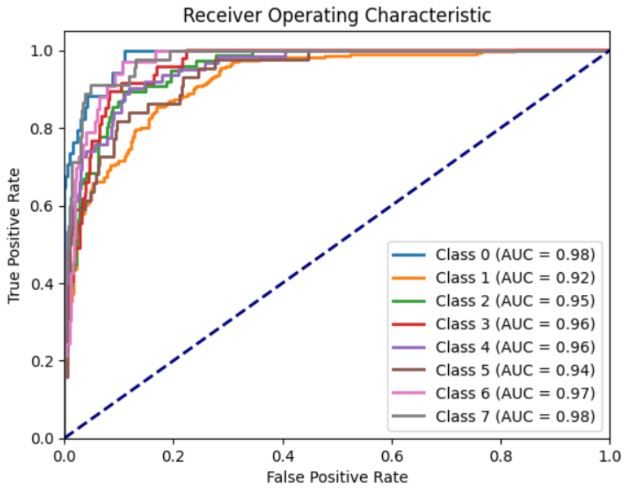

Figure 6: ROC curve Obtained from DL DenseNet Classifier

rate, resulting in accurate predictions for that class. On the other hand, a class with a lower AUC, such as Class 1 with an AUC of 0.92, suggests that the DenseNet may have a relatively higher false positive rate or lower true positive rate, indicating some difficulty in correctly classifying instances of that class.

In this approach, the classification is done with the images at a magnification of 40X. These results show AUC values ranging from 0.92 to 0.98 for different classes. In contrast, (Yari, Nguyen, and Nguyen 2020) performed magnification-dependent binary and multiclass classification at various magnifications, including 40X, 100X, 200X, and 400X. They achieved high accuracies ranging from 97.40% to 100% for binary and multiclass classification. Furthermore, (Yari, Nguyen, and Nguyen 2020) in a magnification-independent experiment, they achieved high accuracies of 99.50% and 97.72% for binary and multiclass classification, respectively. It implies that their model's performance remains consistent across different magnifications, indicating robustness and generalizability.

Regarding the use of DenseNet, in (Vulli et al. 2022), authors compared the performance of the model before and after fine-tuning by analyzing the ROC curves. The authors observed that the model covered 83% of the area under the ROC curve (AUC) before fine-tuning. However, after fine-tuning, the performance of the model significantly improved, with it covering 99% of the area under the ROC curve. This implies that the model's performance became optimal, as it achieved a high AUC value. However, the authors used a filtered version of the pcam dataset that consists of H&E-stained images of sentinel lymph node zones. The pcam dataset also applies under-sampling to expand the field of view. Notably, the pcam dataset focuses on metastasis prediction, while BreakHis provides a broader classification of various types of tumors.

Furthermore, while only transfer learning is used using DenseNet, in another study (Liew, Hameed, and Clos 2021), authors proposed a combination of deep learning with the pre-trained DenseNet201 model and extreme gradient boosting (XGBoost) for classification. They also incorporate pre-processing techniques such as data augmentation and stain normalization. In contrast to this experiment, the focal loss function is used to address the class imbalance issue. However, Liew et al. (2021) claim to improve upon existing work using the BreaKHis dataset by achieving a higher accuracy of 97% for both binary and multi-class classification tasks. This suggests that the machine learning algorithm together with the Deep Learning algorithms algorithm provides a powerful prediction capability for breast cancer image classification.

Conclusions and Future work

This article explores the use of machine intelligence and transfer learning to improve the accuracy, efficiency, and generalization ability of breast cancer classification models using histopathological images.

The study utilizes the BreaKHis dataset, which is a comprehensive collection of biopsy images depicting both benign and malignant breast tumors.

The article uses data splitting, data augmentation, feature extraction, and selection, as well as the implementation of deep learning and machine learning approaches for breast cancer classification.

The deep learning approach employs a modified DenseNet model, which is pre-trained on the ImageNet dataset and fine-tuned for breast cancer classification. The model architecture includes custom dense blocks and transition layers for multi-class classification.

The machine learning approach compares the performance of three algorithms: Random Forest, Support Vector Machines (SVM), and K-Nearest Neighbors (KNN) for multi-class classification of breast cancer. The models are optimized using a 10-fold cross-validation approach.

The results and discussion section of the article presents the performance metrics of the machine learning models. The Area Under the Curve (AUC) is computed for each class, and the values obtained for the Random Forest, SVM, and KNN algorithms are provided

The ML approach achieved moderate performance with AUC values ranging from 0.48 to 0.56, while the DL approach using DenseNet transfer learning achieved an overall test accuracy of 0.7150. Additionally, the DL approach showed varying AUC values for different classes, ranging from 0.92 to 0.98.

Comparing the results to other studies, it appears that the ML and DL approaches in this study may have achieved lower performance metrics compared to some previous works. For example, a study on the Wisconsin Breast Cancer Diagnostic dataset (WBCD) reported higher efficiency, precision, and AUC for SVM. Another study using wavelet-based entropy features and SVM classifiers achieved higher accuracy values ranging from 91.3% to 93.3%. Similarly, other studies on the pcam and BreaKHis datasets reported higher accuracies for binary and multi-class classification tasks using different DL models and techniques.

These comparisons suggest that there is room for improvement in the performance of the ML and DL approaches used in this study. Further experimentation with feature engineering, hyperparameter tuning, different DL models, and additional preprocessing techniques could potentially enhance the accuracy and performance of the classification system for breast cancer detection and diagnosis.

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