Research Paper

A Pre-Trained Ensemble Model for Breast Cancer Grade Detection Based on Small Datasets

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A B S T R A C T

Background and Purpose: Nowadays, breast cancer is reported as one of the most common cancers among women. Early detection of the cancer type is essential to help inform subsequent treatments. The newest proposed breast cancer detectors are based on deep learning. Most of these works focus on large datasets and are not developed for small datasets. Although large datasets may lead to more reliable results, their collecting and processing are challenging.

Materials and Methods: This paper proposes a new ensemble deep learning model for breast cancer grade detection based on small datasets. Our model uses some basic deep-learning classifiers to grade the breast tumors, including grades I, II, and III. Since none of the previous works focus on the datasets, including breast cancer grades, we have used a new dataset called Databiox to grade the breast cancers in the three grades. Databiox includes histopathological microscopy images from patients with invasive ductal carcinoma (IDC).

Results: The performance of the model is evaluated based on the small dataset. We compare the proposed three-layer ensemble classifier with the most common single deep learning classifiers in terms of accuracy and loss. The experimental results show that the proposed model can improve the classification accuracy of the breast cancer grade compared to the other state-of-the-art single classifiers.

Conclusion: The ensemble model can be also used for small datasets. In addition, they can improve the accuracy compared to the other models. This achievement is fundamental for the design of classification-based systems in computer-aided diagnosis.

Keywords: Breast cancer, Neural network models, Deep learning classifier, Image classification

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1. Introduction

Cancer is one of the significant global public health issues and the second leading cause of death [1]. The institute for health metrics and evaluation (IHME) reports that cancer caused an estimated 9.6 million deaths in 2017, as shown in Figure 1 [2].

Figure 2 shows the total number of deaths caused by various cancers across all ages and genders [3]. The leading reason for death is stomach cancer, while breast cancer ranks as the fifth cause of death.

Invasive ductal carcinoma (IDC) is recognized as one of the most widespread phenotypic sub-classification of all breast cancers since nearly 80% of identified breast cancers are IDC [4]. It develops in milk ducts and conquers the fibrous tissue of the breast outside the duct. As Figure 3 shows, pathologists recognize the cancer type and grade through visual investigation of tissue stained by hematoxylin and eosin (H&E) [5].

The precise detection of IDC grade has a significant effect on determining a proper treatment plan. The histologic grade is a prognostic factor and an indicator of response to chemotherapy. It is closely related to the frequency of recurrence and death due to IDC, disease-free interval, and longer life after mastectomy. Several studies show that patients with a high-grade IDC treated with a mastectomy had a remarkably higher frequency of auxiliary lymph node (ALN) and mortality rate than the patients with a lower-grade IDC. The high-grade carcinomas result in early treatment failures, while subsequent recurrences are more often observed among low-grade tumors [6, 7].

The emphasis on early detection of breast cancer is due to the significant impact on the survival rate. According to acute coronary syndrome (ACS), the 5-year survival rate for localized breast cancer (cancer that has not spread beyond the breast) is 99%. For patients with regional breast cancer (cancer that has spread to nearby lymph nodes), that number falls to 86%; for cancer that has spread to more distant parts of the body, the 5-year survival rate is only 29%.

The latest proposed breast cancer detectors are based on machine learning (ML) techniques, such as deep learning (DL). DL is a form of ML that can utilize supervised [4, 8], or unsupervised algorithms [8-10]. DL supports multi-layer hybrid models to gather data [11]. AlexNet [12], VGG net [13], ResNet [7], ResNeXt [14],

and RCNN (region-based convolutional neural network) [15-17] are considered as DL's advanced models. Most previous works in the field of cancer detection focus on large datasets and are not developed for small datasets. Although large datasets may lead to more reliable results, their collecting and processing are challenging. This paper proposes a new ensemble deep-learning model for breast cancer grade detection based on small datasets. Our model uses MobileNetV2, VGG16, and EfficientNet-B0 as pretrained basic transfer learning classifiers to grade the breast tumors, including grades I, II, and III. The features learned from the deep models make the deep network very effective in problems with small-sized datasets.

The rest of the paper is organized as follows, section 2 reviews related works on breast cancer diagnosis. Section 3 introduces the proposed ensemble model. We present the experimental results in section 4. Section 5 indicates the discussion, and finally, the paper concludes with our future work in section 6.

Related Works

Recently, various efforts have been conducted to detect and protect various types of cancer by applying different artificial intelligence methods [13, 18-20]. The effective usage of multiple data features and the assortment of acceptable classification techniques [19, 21] is significant for image classification. Table 1 summarizes the previous breast cancer diagnosis models based on ML. As the table shows, most works focus on large datasets. Moreover, augmentation techniques have not been used in previous models. In this paper, we propose a new ensemble model for breast cancer detection focusing on small datasets and using augmentation techniques.

2. Materials and Methods

Proposed Model

In this paper, we use ImageNet as a pre-trained model on a large-scale dataset. The model is modified to distinguish different images. The trained features of deep models can lead to a deep network that solves problems with limited-size datasets. The VGG16, Inception V3, and Inception-ResNetV2 models are applied to small-sized breast cancer datasets. The EfficientNet-B0 model is considered a standard model for image classification of the limited-size dataset with acceptable performance. Weights trained on ImageNet are used for VGG16, Inception V3, and ResNet 50 deep models. For
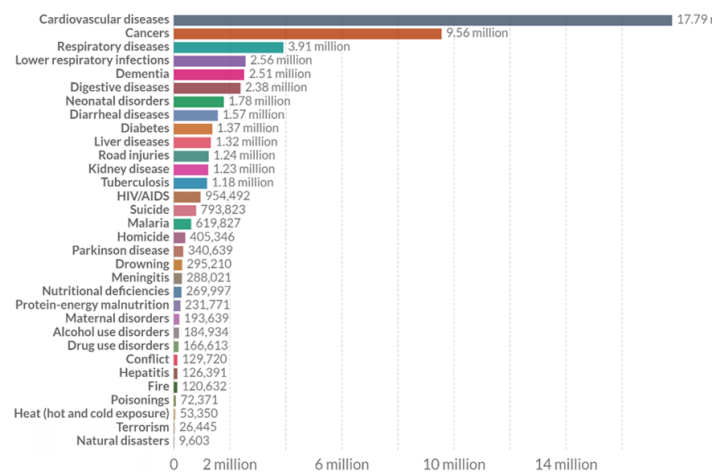
Figure 1. The number of deaths by cause, world, 2020. Source. Institute for Health Metrics and Evaluation (IHME), Global Burden of Disease [2]
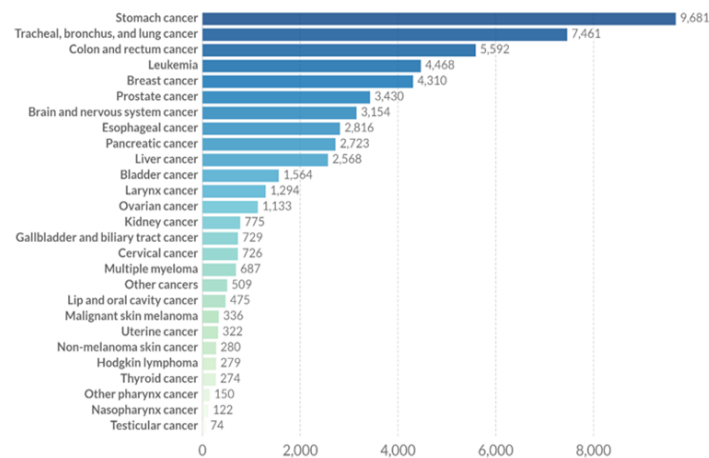

Figure 2. Cancer deaths by type, Iran, 2017. Source. Institute for Health Metrics and Evaluation (IHME), Global Burden of Disease [3]
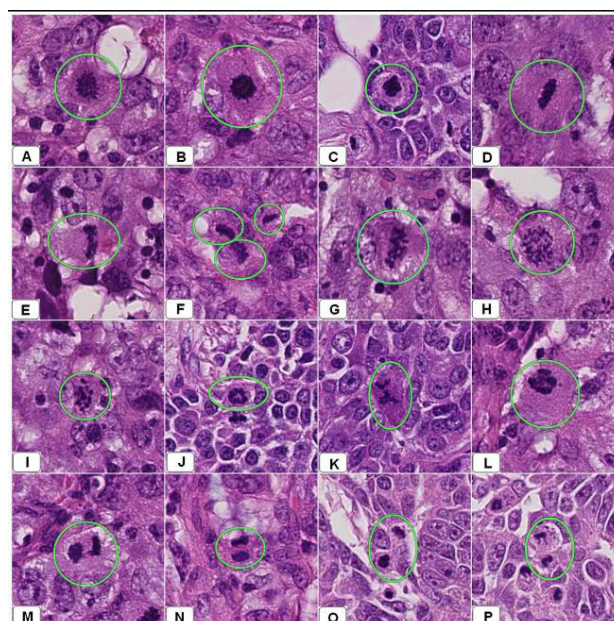

Figure 3. The identification of invasive ductal carcinoma (IDC) grade through visual investigation of tissue [5]

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Table 1. The summary of the previous works on breast cancer detection

Study	Method	Dataset	No. of Images	Purpose	Result-Measure
[22]	DeCaf model	BreaKHis for breast cancer histopathological image categorizations.	7909	Deep Features for Breast Cancer Histopathological Image categorizations	80% to 85%- accuracy
[23]	SVM, LVQ, PNN, MLP	6 different datasets	7273	Detection and diagnosis system	99.7 % -sensitivity and specificity
[24]	Convolutional neural net-work (CNN)	Needle biopsy microscopy images	500	Computer-aided diagnosis of breast cancer	96% -100% accuracy
[25]	Deep learning	Pretrained convolutional neural network	927	Deep transfer learning computer-aided diagnosis (CADx) methodology to diagnose breast cancer using mpMRI.	95%-AUC
[26]	CNN-based model	BreakHis dataset, and the Breast Cancer Classification Challenge 2015 dataset	7909 + 43707	Classify H&E stained breast biopsy images	77.8% and 83.3%- accuracy
[27]	CSDCNN-based approach	BreakHis dataset	7909	Both image- and patient-level classifications	93.2% -accuracy

Abbreviations: SVM, support vector machines; LVQ, learning vector quantization; PNN, probabilistic neural network; MLP, multilayer perceptron; CNN, convolutional neural network; CSDCNN, class structure-based deep convolutional network

the baseline, EfficientNet-B0 is rum directly with the binary classifier as an optimizer without any data dropout or augmentation.

While the training time of the pre-trained networks is relatively low, their accuracy is high. Therefore, the use of pre-trained deep learning methods can increase prediction accuracy and improve image classification. Furthermore, applying well-tuned ensemble models can significantly improve the model's performance. In the following subsections, the proposed model is considered in detail.

Dataset

In this paper, a new dataset, Databiox[1] [4], is used. The Databiox dataset has been chosen to grade breast cancers in three different classes named grades I, II, and III. Databiox is a dataset for histopathological microscopy images of patients with IDC containing 922 images. All images are in RGB format with JPEG type. The resolution of the images is 2100 × 1574 or 1276 × 956 pixels. Table 2 presents the technical specifications of the dataset in detail.

The specimens are breast tissues stained with H&E, obtained from 124 patients diagnosed between 2014 and 2019 in the PourSina Hakim research center of Isfahan University of Medical Sciences in Iran. Each speci-

men is provided with four magnification levels: 4x,10x, 20x, and 40x as shown in Figure 4.

The labeling of all images in the dataset based on their diagnosed grade can be used to train machine learning algorithms to recognize IDC grades. This dataset uses the same grading method as previous datasets but differs from others in that it contains an equal number of samples from each of the three IDC grades, resulting in approximately 50 samples for each grade [28].

Based on the pathologist's opinion, more than one image from a specific magnification level is presented in some cases. For example, four 40x images exist for almost all of the specimens. A score of 1, 2, or 3 is assigned to each, and scores are added to produce a grade. Table 3 presents how the Databiox images have been categorized in each grade and zoom.

Dataset modification

According to section 2, none of the previous works provide breast cancer classification based on the grades. In this paper, breast cancer classification is performed on the Databiox dataset, which is based on the grades. As mentioned, this paper aims to work on small datasets, such as Databiox. For small datasets, it seems a hierarchical augmentation method can generate a larger dataset that is more reliable for the testing and validation process. To generate an augmented image, a series of
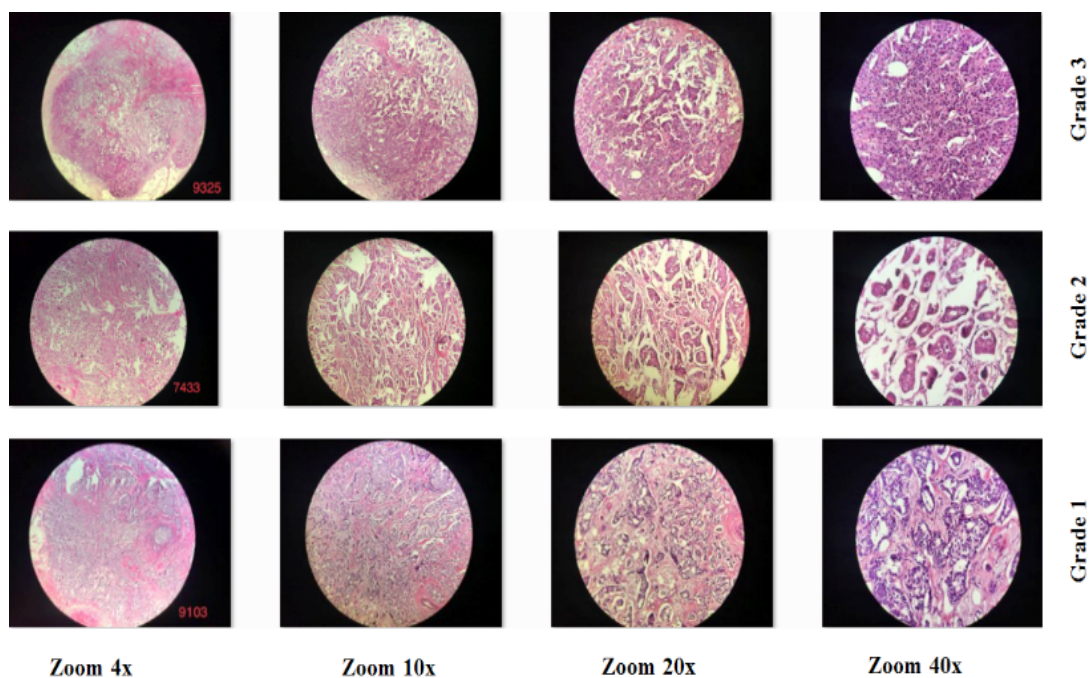
1. http://databiox.com/datasets

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Table 2. The technical specifications of Databiox

No.	Dataset Guidlines	Value
1	Qty of images	922
2	Image format	RGB
3	File	JPEG
4	Resolution	2100×1574 -1276×956
5	DPI (dot per inch)	72
6	Bit depth	24
7	Focal length	4 mm
8	ISO aped	ISO-20
9	Model of camera	Apple iPhone 7 PLUS
10	Size	119KB-2,114KB

Abbreviations: RGB, red, green, and blue; JPEG, joint photographic experts group

Figure 4. Three sample images selected from Databiox in the different grades with different zoom

Table 3. The number of images of Databiox in each grade and zoom

Grade Type		No.	4x	10x	20x	40x
	I	37	45	40	43	131
Grade	II	43	59	64	63	180
	III	44	56	49	49	143
Total		124	160	153	155	454

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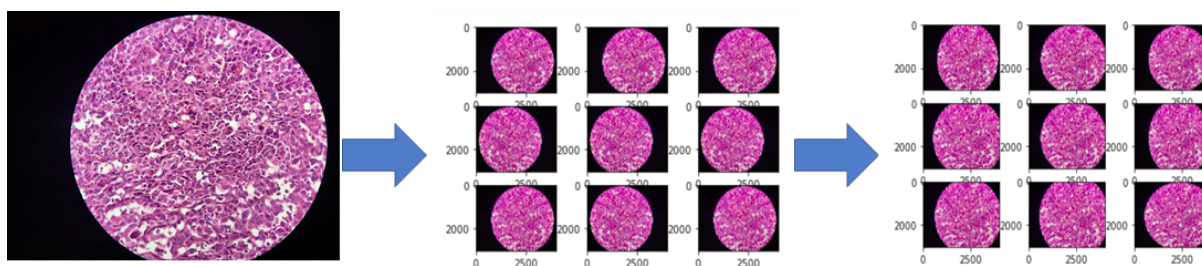
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Figure 5. The steps of the flipping and zooming augmentation for a sample image selected from Databiox
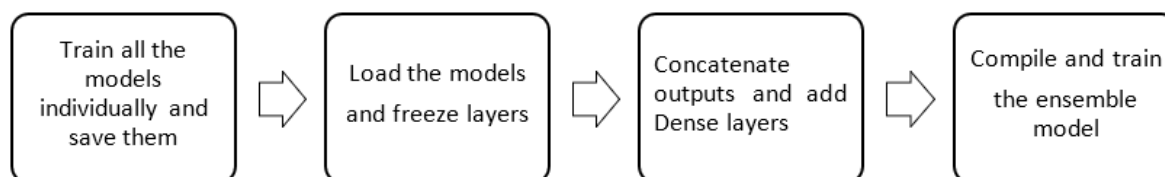

Figure 6. The main steps of the proposed ensemble model

pre-processing transformations, including horizontal and vertical flipping, skewing, cropping, rotating, and zooming is performed on the original image. Indeed, the augmented images can reproduce different data points. It is opposed to just duplicating the same data. The subtle differences of these "additional" images should be enough to train a more robust model. Two horizontal and vertical flipping are employed to zoom the dataset images from 80% to 100%. Figure 5 shows the augmentation methods for a sample image selected from Databiox with both the flipping and zooming augmentation applied to this sample image. The total number of images after applying the augmentation methods is .

The success of image classification depends on the quality and quantity of the training dataset. With a larger dataset, we will have a more effective deep-learning model for image processing. Data augmentation increases the size and diversity of datasets without manually collecting new images.

3. Results

Proposed ensemble model

The goal of the proposed model is to create an efficient ensemble trainer for the diagnosis of breast cancer grades I, II, and III. Ensemble methods employ several machine learning algorithms to reach acceptable performance more than each of the individual methods. Figure 6 shows the main steps of the proposed ensemble model. The steps are explained in the following subsections.

Step 1: Training individual models and saving them

First, all individual models are created by applying three different models MobileNetV2, VGG16, and efficientNEtb0. Then, the weights are loaded, it chooses to freeze or unfreeze loaded weights, and finally, a dens layer is added to the outputs. In the next step, the accuracy and loss of the individual models are compared.
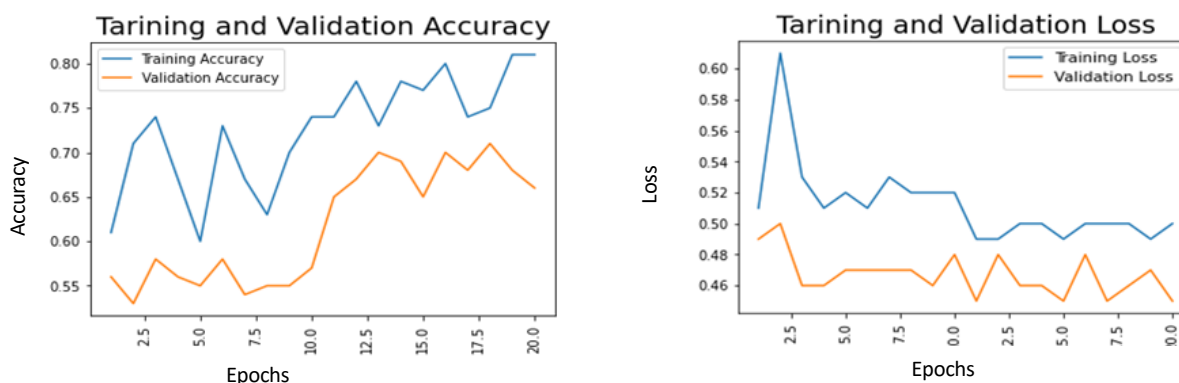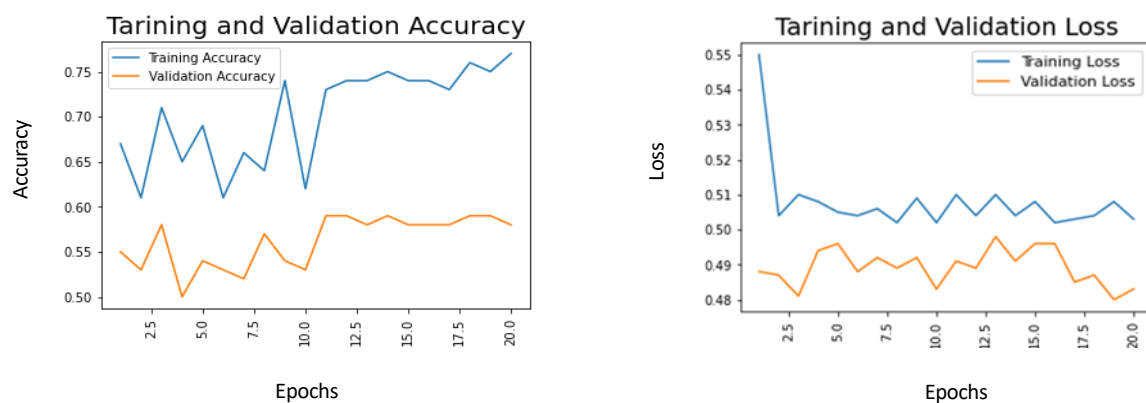

Figure 7. Accuracy and loss of MobileNetv2

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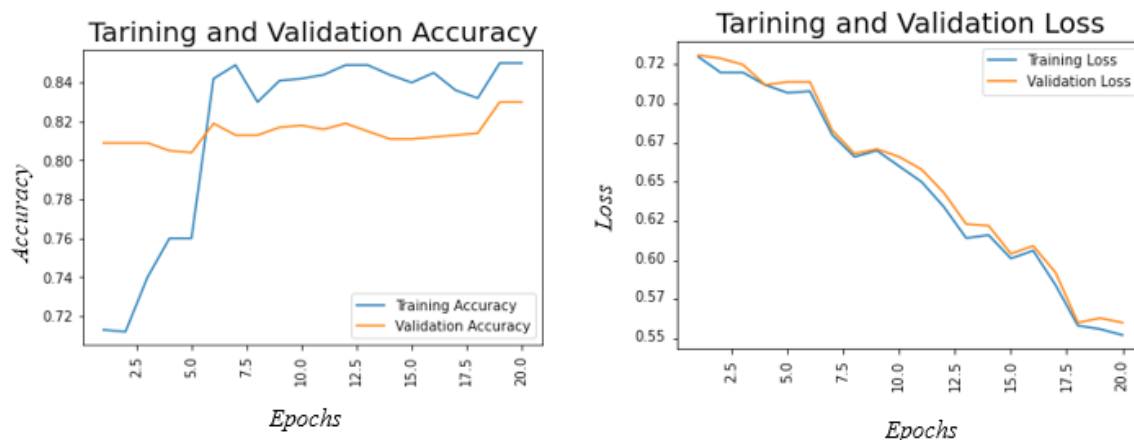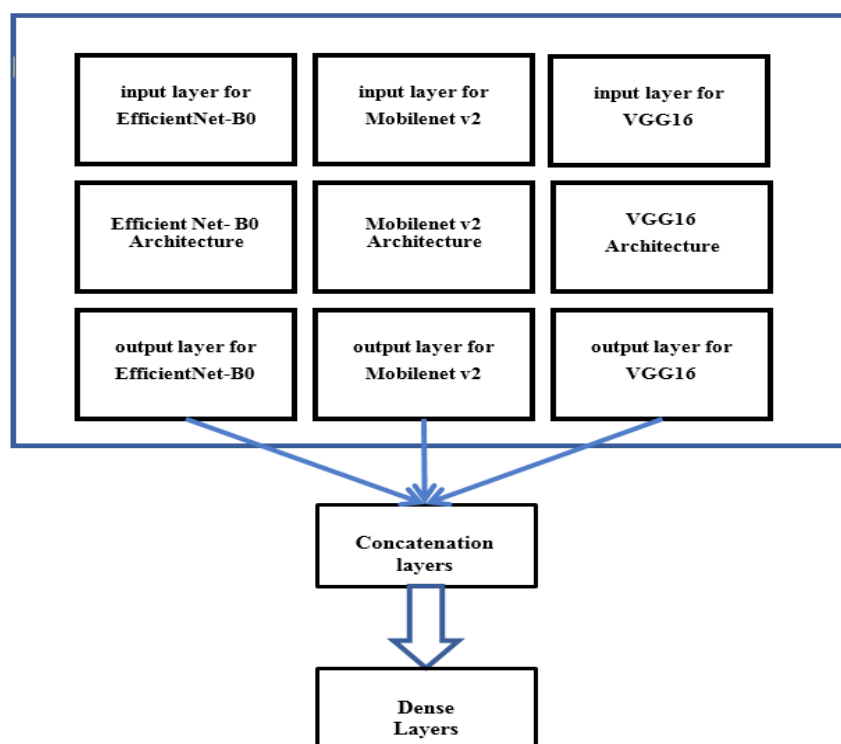**Figure 8.** Accuracy and loss of EfficinetNetB0

Figure 9. Accuracy and loss of VGG16

Figure 7 illustrates accuracy and loss in the training and validation phases for MobileNetv2 in 20 training epochs. The maximum training accuracy for MobileNetv2 is around 81%, and the minimum training loss is about 50%, which occurs after 20 epochs. Additionally, the best validation accuracy after 20 epochs is about 70%, which can be seen in epoch 18.

In a similar way to MobileNetv2, Figure 8 shows training and validation loss and accuracy for efficinetNetB0 in 20 training epochs. The best training accuracy for efficinetNetB0 is around 77%, and the minimum training loss is 50%, which occurs after 20 epochs. Moreover, the maximum validation accuracy after 20 epochs is about 70% Figure 9 shows the accuracy and loss of the training and validation for VGG16 in 20 training epochs. The maximum training accuracy for VGG16 is 76%, and the minimum training loss is 50%, which occurs after 20 epochs. In addition, the best validation accuracy after 20 epochs is 57%.

Steps 2 to 4: The final ensemble model

Figure 10 shows the proposed ensemble framework for breast cancer classification. The framework consists of three different classification models, including EfficientNet-B0, MobileNet v2, and VGG16. EfficientNet-B0 is a new scaling method called hybrid scaling. It suggests that we will get much better performance if we simultaneously scale the dimensions by a fixed amount and do it uniformly. The scaling coefficients can be set by the user. The VGG16 is one of the most popular pretrained models for image classification. VGG-16 broke the AlexNet standards and was quickly adopted by researchers and the industry for their image classification tasks. The MobileNet-v2 architecture is based on an inverted residual structure where the input and output of the residual block are thin bottleneck layers opposite to traditional residual models that use expanded representations in the input. MobileNet v2 uses lightweight depth-wise convolutions to filter features in the intermediate expansion layer.

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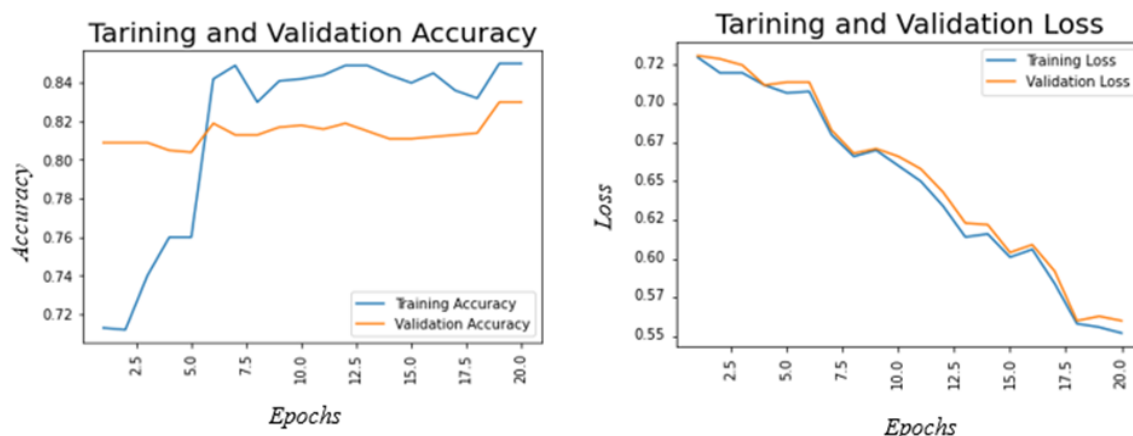
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Figure 10. The architecture of the proposed ensemble model

The individual models and their freeze layers are loaded in the next step so that their weight does not change when the ensemble model is fitted on them. Then we concatenate their outputs and add dense layers. As shown in Figure 10, the proposed model takes the outputs of all the models and puts them in a concatenated layer. Since the proposed method is a multiclass classifier, a dense layer with a sigmoid activation function is used. This procedure is similar to neural networks, where the predictions of all the models are taken as inputs and an output is provided.

Evaluation

To evaluate the proposed model, both individual models and the ensemble models are trained for 20 epochs. Figure 11 shows the accuracy and loss of the ensemble model in the training and validation phases. Table 4 presents the validation accuracy of the models on their final epochs. As the Table shows, the ensemble model improves validation accuracy compared to the individual models. In other words, data augmentation and powerful dropout on a pre-trained deep model lead to very high accuracy. Furthermore, it shows that small datasets can also use the power of depth. Creating an ensemble

Figure 11. Accuracy and loss of the ensemble model

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Table 4. The accuracy of each individual model and the proposed ensemble model on validation set

Model	Accuracy
MobileNet v2	0.66
VGG16	0.57
EfficientNet-B0	0.70
Ensemble	0.81

model is a very long procedure that requires putting more effort and perseverance into a model. However, achieving this accuracy would be valuable, especially utilizing small datasets that were initially unlikely.

The accuracy of the proposed ensemble model is increased by almost 11%, which is remarkable considering that the previous best accuracy was 70% obtained with EfficientNet-B0. However, building an ensemble model in this way is a time-consuming process. It is three times the effort of a single model but can contribute to accuracy that is difficult to achieve in small data sets.

4. Discussion

Few similar studies have been conducted in this area, e.g., Faisal et al. in [29] used the technology of "gradient boosting tree (GBT) with majority voting and radio frequency (RF)-based ensembles" and its accuracy rate was 90%. Bhowal et al. in [30] also used the technology "Choquet integral-based deep CNN models with coalition game and information theory". They achieved 95% accuracy in determining breast cancer grade. These two models show better accuracy than our proposed model because they use large datasets for training. In contrast, our dataset is a small dataset collected from Iranian patients.

Few works train the entire model from the beginning since a significant dataset is rarely provided. Moreover, for feature extraction, most researchers are interested in using a model pre-trained on a widespread dataset, such as ImageNet. Subsequently, researchers introduce transfer learning to optimize time and achieve performance improvement simultaneously.

Recently, several considerable attempts have been made to detect and predict all types of cancer. Artificial intelligence (AI) and its subdomains including machine learning and deep learning are widely used for breast cancer detection. Reviewing several related works conducted in recent years [10-14] validates the importance of machine learning (ML) methods for the classification of the histopathological microscopic image dataset to upgrade IDC. Hence, an ensemble model is proposed for image classification on the Databiox dataset. Table 5 compares our proposed model with the above-tested deep learning models.

The critical limitation of this study occurs when a transformed sample differs significantly from the original sample in terms of pixels. So, the network may not be able to classify it correctly. However, we can train the model for a particular transformation on the transformed data to achieve high accuracy.

An important question is whether deep models, such as region-based CNN (RCNN) [14], and you only look once (YOLO) [31] can be fitted to a very small dataset or not. We plan to qualify more models on very small datasets and compare their performance in our future work.

Table 5. The comparison of the proposed ensemble mode With the other deep learning models on the validation set

Model	Input Size (Pixels)	Top-1 Accuracy
EfficientNet-B0	224×224	70
MobileNet v2:	224×224	66
VGG16	224×224	57
Inception Resnet V2	299×299	75
Resnet 50	224×224	78
Proposed model	400×400	81

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5. Conclusion

In this study, Databiox, a new small dataset, was used to grade breast cancer in three different grades I, II, and III. Since the Databiox is very small and only includes images taken from 124 patients with a total of 924 images, we have applied the augmentation techniques to extend the dataset and consequently improve the accuracy of the proposed methods.

The proposed ensemble model is constructed based on the single models MobileNetV2, VGG16, and EfficientNet-B0Seven, and its performance is compared to these single models. In this paper, we pre-trained the proposed model based on large-scale datasets and applied these qualified models to small-size datasets with great performance. The experiments confirm that the ensemble model can be used for small datasets with precise modifications by applying the proper augmentation techniques. In addition, the findings indicate that the proposed method achieves the best accuracy among all the models. This achievement is essential to design future classification-based systems in computer-aided diagnosis since it shows that the use of ensemble models can improve the accuracy of breast cancer diagnosis, especially for small datasets.

In future work, we work on increasing the classification accuracy. In addition, we plan to consider the impact of the other single deep models on the performance of the ensemble model on small datasets and lower-resolution images.

Availability of Data and Materials:

The dataset used in this study can be found at http://databiox.com/datasets. The codes can be provided, upon reasonable request. They may be available from the corresponding author.

Ethical Considerations

Compliance with ethical guidelines

There were no ethical considerations to be considered in this research.

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Authors contributions

Proposing the model and developing the proposed model, drafting and editing the manuscript, drafting and editing the figures: Farhang Jaryani; Initiating and coordinating the project, interpreting the data, editing the manuscript, and editing the figures: Maryam Amiri.

Conflict of interest

The authors declared no conflict of interest.

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