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Computer-aided diagnosis of breast cancer from mammogram images using deep learning algorithms

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Abstract

Even though accurate detection of dangerous malignancies from mammogram images is mostly dependent on radiologists' experience, specialists occasionally differ in their assessments. Computer-aided diagnosis provides a better solution for image diagnosis that can help experts make more reliable decisions. In medical applications for diagnosing cancerous growths from mammogram images, computerized and accurate classification of breast cancer mammogram images is critical. The deep learning approach has been widely applied in medical image processing and has had considerable success in biological image classification. The Convolutional Neural Network (CNN), Inception, and EfficientNet are proposed in this paper. The proposed models attain better performance compared to the conventional CNN. The models are used to automatically classify breast cancer mammogram images from Kaggle into benign and malignant. Simulation results demonstrated that EfficientNet, with an accuracy between 97.13 and 99.27%, and overall accuracy of 98.29%, perform better than the other models in this paper.

Keywords: Computer-aided diagnosis (CAD), Deep learning, Breast cancer, Classification, Medical imaging

Introduction

Breast cancer is the biggest global threat to life among women. It has been shown that timely identification of tumors can aid in identifying the ailment and significantly increase the chances of survival [1]. Different methods have been used to detect breast cancer, with mammography being the most effective and widely used by radiologists [2]. X-ray images of the breast typically have poor contrast and are grainy. Bright areas on a breast mammogram suggest cancer. Tumor and normal dense tissues may coexist in some mammography images. The only way to distinguish between malignant and normal dense tissues is to segment the images [3]. Comprehending the information in mass regions of malignant abnormal tissue area in mammography is crucial for identifying and segmenting the tumor. As a result, detecting malignant tumors in mammography images has become an active research area.

Several approaches for breast cancer segmentation in mammography images have been proposed, including computer-aided detection systems and intensity-based

techniques. Unfortunately, no method is most encouraging or capable of successfully meeting the detection criterion of only extracting the malignant spots [4].

Breast cancer at stage 0 is a type of cancer where cancerous cells are discovered in the lining of the breast milk duct. However, the tumors may continue growing and infect the neighboring breast tissue, extending to adjacent lymph nodes (neck and mediastinal lymph nodes) or other vital body organs (cancer that spreads from the primary tumor to distant organs). If a woman dies due to breast cancer, it is due to severe pathogenic agents spread from the prior site to the secondary site in her body [5].

It was projected in 2020 that there would be 2.3 million new cases of breast cancer and 685,000 deaths globally [6]. Except for young women who are below the age of puberty, all the other ones are vulnerable to breast cancer, with sophisticated cases occurring among other women. Breast cancer typically manifests as a harmless growth or swelling of the breast. Even if there is no pain, it is critical that women who discover an atypical lump in their breast visit a medical doctor as soon as possible. Getting medical help at the earliest hint of a suspected illness provides for more effective therapy [7]. Breast lumps can occur for a myriad of purposes, many of which are not malignant. Nearly 90% of growths in the breast are non-cancerous. Nonmalignant tumor such as non-cancerous breast tumor that usually occurs in young women and membranous sacs, in addition to infections, are examples of non-cancerous breast abnormalities [7].

Breast cancers can extend to different arrears of the body, causing added warning signs. The lymphatic tissues beneath the arm are frequently the first detectable site of dissemination, while cancer-bearing lymphatic tissues that cannot be touched are possible. Tumor cells can extend to other organs over time. On getting to such areas, they may cause additional cancer-associated symptoms like rare skeletal disorders or migraine [8].

Mammography has been recognized as the better-known and more straightforward approach to cancer detection in its initial periods. Radiologists have asserted that the accuracy of mammography is higher than 90%. Nevertheless, they might likely fail to detect 10–15% of breast cancer [9]. This problem of a high false-positive rate can be overcome by authenticating and analyzing mammogram images. Authenticating entails the same mammogram images to be scrutinized by two separate radiologists at various periods. At the same time, authentication has proved to enhance detection accuracy by 15% compared to inspection just once over the years. The downside of this approach is that it is time wasting and expensive practice. This cost can be greatly lowered by adopting computer-aided diagnosis (CAD) and computer-aided detection (CAdE) [10]. Another drawback of this approach is how to decrease the false positives in the mammography breast cancer detection process. To surmount this challenge, the use of image processing and machine learning techniques have been proposed to aid in breast cancer diagnosis [11–14]. Several image processing approaches have been applied to mammography by first eliminating the noise, then segmenting the image, and identifying the edges and regions of interest to discover masses. Afterward, essential features are extracted from the images, and detection is done. The downside of this approach is that the accuracy is relatively low.

This paper proposed an approach for identifying breast cancer in breast images. The approach consists of two key phases. In the first phase, image processing methods are applied to get ready images for the feature extraction process. The extracted features

are employed as input to a deep learning algorithm that is used to train the image dataset. Our contributions to this work are summarized below:

1. Design of a new CAD system for early breast cancer detection and diagnosis is presented.
2. A new breast cancer detection system employing a deep learning technique is implemented.
3. Application of Convolutional Neural Network (CNN), Inception, and EfficientNet for improved breast cancer detection system performance is proposed.
4. A novel system with increased accuracy in breast cancer detection is presented. The novelty of our system lies in the combination of specific data augmentation techniques, the use of EfficientNet-B4 as a base model and fine-tuning the model to achieve improved accuracy. This approach results in a more effective and accurate breast cancer detection system compared to previous studies.

The paper is structured into five sections. Section two presents a review of related works. Section three describes deep learning, CNN, Inception, and EfficientNet used in this work. Section four presents experiments that are performed to evaluate the ability of the proposed system to detect breast cancer using a number of images. Finally, section five discusses the research conclusions and a number of recommendations for future work.

Review of related works

Many works have been done in this field. Filipczuk, Kowal, and Obuchowicz [15] applied a segmentation method that incorporates a kind of thresholding that mainstreamed spatial disparities in brightness, clustering, and restricted abrasion for detecting breast cancer. The techniques used produced satisfactory results. The shortcoming of the work is that the size of the dataset used is too small, and the performance of the work was not compared with high-performing machine learning models to evaluate its effectiveness.

Raj et al. [16] presented a thermography approach for capturing cancerous breast images with thermal infrared by finding the discrepancy in temperature between them. The ultimate grouping of cancerous and non-cancerous breast images is generated applying some set of processes. Simulation results showed that the method used achieved contrast improvement for thermography images. The drawback of the work is that the performance of the proposed system is low. Also, the size of the dataset used is very small. Moreover, the proposed system was not benchmarked with other deep learning algorithms to determine its effectiveness.

Araujo et al. [17] used CNN for the categorization of breast cancer images. The classification approach relied on feature extraction meant for a particular problem—the adopted method classified images into four groups. The advantage of the process is that the network design can retrieve relevant features from images irrespective of tissues' scale and general arrangement. The approach permits the expansion proposed model to scan glass slides to generate digital images. The pitfall of the technique is that the accuracy is low.

Rasti et al. [18] employed deep ensemble learning to classify breast cancer into benign and malignant tumors. The proposed approach can randomly segregate image space through concurrent and modest studying of its components. Results of the simulation demonstrated that the method has satisfactory performance compared to other single-classifiers and two convolutional ensemble approaches. The downside of the method is that the size of the dataset used for the experiments is small, and the overall accuracy is low.

Yassin et al. [19] did a systematic review that involved a broad collection of scientific databases. The conditions for the addition and omission of publications were outlined and used to access publications in relevant areas. The scope of the work is restricted to scientific and scholarly publications, while commercial work was not included. ML strategies for breast cancer CAD employing several image formats are the main focus of the research.

Jiang et al. [20] utilized CNN for the categorization of breast cancer mammogram images. The proposed approach makes use of a small SE-ResNet part which is an upgrade of the fusion of residual unit and the component intended to increase the emblematic capability of a network by supporting it to accomplish dynamic channel-wise feature measurement. This enables the system to attain comparable performance using fewer parameters. The proposed system has good performance that is devoid of difficulty in readjusting the learning rate. The study did not include overlay in the cell and imbalanced color distribution in the breast cancer images.

Al-antari et al. [21] used a regional deep learning method for identifying breast cancer. The proposed CNN model is used to identify the tumor and group it as benign or malignant. The model is evaluated using accuracy and other metrics on the annotated INbreast database. Simulation results demonstrated that the novel CAD system performs better than the traditional deep learning approaches. The authors opined that the system would help radiologists identify, segment, and categorize breast cancer. One flaw of the work is that the dataset used for the work is too small as it is inadequate to assert the efficiency of the proposed approach. Also, the overall accuracy of the system still needs improvement. A summary of the related works considered in this paper is presented in Table 1.

The motivation for this work is based on the fact that deep learning algorithms differ substantially from classical ML classifiers in terms of network architecture and learning strategy. A deep learning network has more image processing layers than the traditional ML method for image processing. Every layer is a standard neural network on its own, just like we have in CNN. The deep learning network uses the image as a definite input rather than a collection of image attributes that are generated from the images by hand or automatically. The lower layer networks learn and extract the relevant image features autonomously. As a result, the higher-layer networks classify the images into different intended groups based on the extracted feature patterns. Earlier research has demonstrated that applying a deep learning approach can assist in narrowing the research gap in the field of cancer detection while also providing significantly better classification performance than traditional techniques. This paper used the deep learning technique to determine and evaluate a new CAD strategy for detecting breast cancer. This research aims to see if the proposed strategy can produce better, or identical cancer classification

Table 1 Summary of related works with contribution and research gap

Authors and Year	Technique used	Contribution	Research gap
Filipczuk, Kowal and Obuchowicz [15]	Image segmentation and clustering	Incorporate thresholding that mainstreamed spatial disparities in brightness, clustering and restricted abrasion for detecting breast cancer	The size of the dataset used is too small and the performance of the work was not compared with high-performing machine learning models to evaluate its effectiveness
Raj et al. [16]	Thermography	Outstanding color enhancement of captured images and better classification compared to other approaches. Achieved contrast improvement for thermography images	Poor performance. The size of the dataset used is very inadequate and the proposed system was not benchmarked to determine its effectiveness
Araujo et al. [17]	Convolutional Neural Networks (CNNs)	Ability to extract information from images irrespective of the scale and general arrangement of tissues	The classification accuracy of the approach is low
Rasti et al. [18]	Mixture ensemble of Convolutional Neural Networks (ME-CNN)	Ability to randomly segregate image space through concurrent and modest studying of its components	The size of the dataset used for the experiments is small, and the overall accuracy is low
Yassin et al. [19]	A systematic review that involves a broad collection of scientific databases	The scope of the work is restricted to scientific and scholarly publications while commercial work was not included	Focused mainly on ML strategies for breast cancer computer-aided diagnosis employing several image formats
Jiang et al. [20]	Convolution Neural Network	Used small SE-ResNet part which is an upgrade of the fusion of residual unit to attain comparable performance using fewer parameters	Did not include overlay in the cell, and imbalanced color distribution in the breast cancer images
Al-antari et al. [21]	Regional deep learning method	Detect tumor and group it as benign or malignant to help radiologists inaccurate diagnosis	The size of the dataset used for the work is too small and the overall accuracy of the system still needs improvement

results compared to other techniques reviewed in this work. The subsequent section discusses the specifics of the methodology used in this study.

Methodology

Dataset

The images of breast cancer illness utilized in this paper were obtained from the Kaggle database [22]. The dataset used in this study is MaMaTT2. The original images have a resolution of 2800×2800 pixels with a 24-bit color depth. Due to the high resolution, we resized the images to 224×224 pixels to suit the input requirements of the convolutional neural networks (CNNs) used in this study. The size of the dataset is 408 which is small. The dataset acquired from the database was limited in size and consisted of normal mammograms of benign and malignant breast cancer, as illustrated in Fig. 1. The data augmentation techniques employed in this study include:

Rotation: We applied random rotations to the images to create variability in the dataset.

Scaling: Random scaling was used to modify the size of the images.

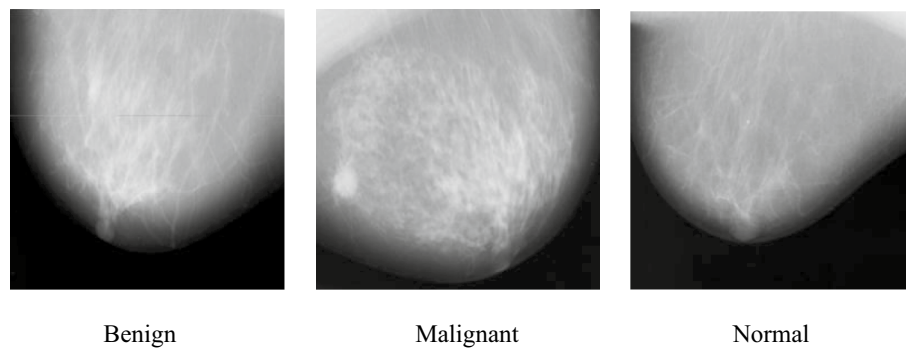


Fig. 1 Images of Benign, Malignant and Normal Tissues in the Breast

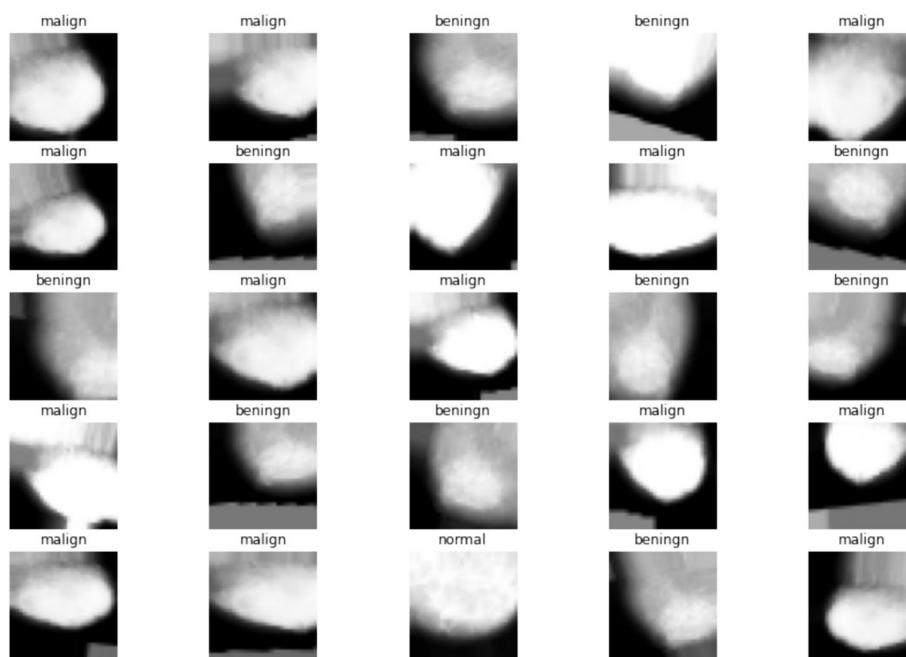


Fig. 2 Random Images generated using Data Augmentation

Flipping: Both horizontal and vertical flips were applied to increase data diversity.

Cropping: Random cropping was used to select portions of the images for training.

Color jittering: Adjustments were made to the brightness, contrast, and saturation of the images.

Gaussian blur: We added a slight blur to some images for additional variability.

These data augmentation techniques help to enhance the robustness of the model by exposing it to a wider range of scenarios and variations within the dataset.

A typical method for increasing the number of images is to use data augmentation by arbitrary disfigurement, cropping, or refining the input, which benefits from lengthening the real size of the training data. Figure 2 depicts a random display of training images for normal, benign, and malignant breast cancer diseases. Figure 3 represent the data augmentation techniques of benign image. Presented in Fig. 4 is the data augmentation

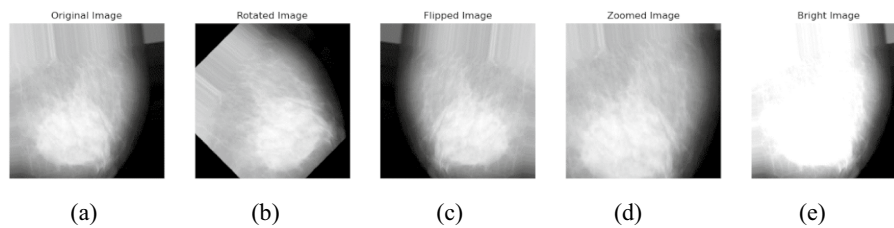


Fig. 3 Data augmentation techniques of Benign Image. **a** Original image, **b** Rotated image, **c** Flipped image, **d** Zoomed image, **e** Adjusted brightness image

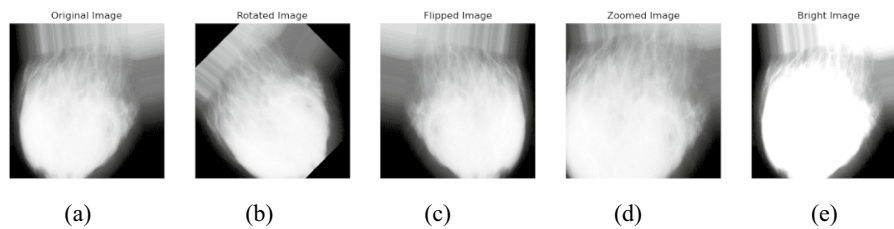


Fig. 4 Data augmentation techniques of Malign Image. **(a)** Original image, **(b)** Rotated image, **(c)** Flipped image, **(d)** Zoomed image, **(e)** Adjusted brightness image

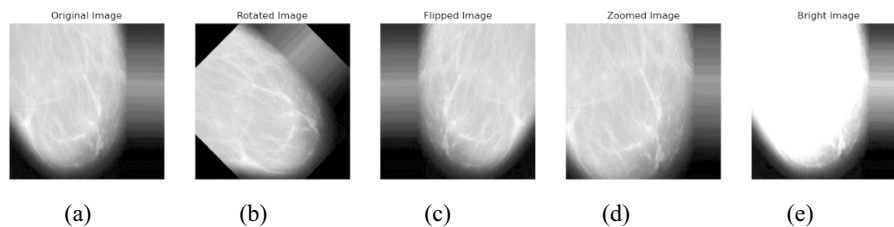


Fig. 5 Data augmentation techniques of Normal Image. **a** Original image, **b** Rotated image, **c** Flipped image, **d** Zoomed image, **e** Adjusted brightness image

techniques of malign image. And Fig. 5 is the data augmentation techniques of normal image. Python 3.7 and Jupyter Notebook are used for our experiment. It is preferred to give examples of the data augmented images for each augmentation type used.

Deep learning

Deep learning is a sort of ML and artificial intelligence that imitates the manner people learn. Deep learning is a subfield of ML, which is effectively a three or more-layer neural network. These neural networks are designed to learn from large amounts of data and simulate human cognitive abilities. Whereas a single-layer neural network may still make reasonable predictions, adding extra hidden layers can help optimize and adjust the network for efficiency. Deep learning differs from conventional ML in the type of data it makes use of and the learning algorithms it uses [23, 24].

Convolutional neural network (CNN)

CNN is the most well-known and often-used algorithm. The ultimate benefit of CNN over its predecessors is that it automatically detects significant elements without the

need for human intervention. CNN has been widely used in various applications, including computer vision, audio processing, and facial recognition [25, 26]. Similar to a traditional neural network, the structure of CNN was inspired by neurons in human and animal brains. Unlike typical fully connected (FC) networks, CNN uses shared weights and local connections to exploit 2D input-data structures such as image signals fully.

This method makes use of a very limited number of parameters, which simplifies the training process while also speeding up the network. This is similar to what happens in visual cortex cells. Each layer input in a CNN model is arranged in three dimensions: height, width, and depth. The depth is also known as the channel number. Several kernels (filters) are accessible in each convolutional layer and have three dimensions comparable to the input images. In a similar manner to NLP, the convolution layer generates a dot product between its input and the weights, but the inputs are undersized portions of the size of the initial image. The convolution layer output is then subjected to non-linearity or an activation function, yielding the following results: Every feature map in the sub-sampling layers is then down-sampled. As a result, the network parameters are reduced, which speeds up the training process and allows the overfitting problem to be addressed.

InceptionV3

The Inception module has three distinct sizes of convolution and one maximum pooling. The channel is aggregated following the convolutional process for the preceding layer network output, and then nonlinear fusion is conducted. In this method, the network expressiveness and adaptation to multiple scales may be increased, and over-fitting can be avoided [27]. Inception v3 is basically a Keras-developed network structure that is pre-trained in Image Net. The image input size is 299×299 with three channels by default.

In comparison to earlier versions such as Inception v1 and v2, the Inception v3 network structure employs a convolution kernel splitting approach to convert huge volume integrals into tiny convolutions. In Inception v3, a 3×3 convolution is divided into 3×1 and 1×3 convolutions. The splitting approach reduces the number of parameters, allowing the network training pace to be expedited while the spatial feature to be retrieved more efficiently. Simultaneously, Inception v3 optimizes the Inception network structure module utilizing three distinct size area grids [28].

EfficientNet

The EfficientNet algorithm was first described by [29] as an excellent way to scale neural network models by increasing depths, breadth, and accuracy. A CNN design and scaling approach use a compounded coefficient to scale all depth, breadth, and resolution variables uniformly. In contrast to traditional practice, which modifies these components arbitrarily, the EfficientNet scaling approach reliably improves network breadth, depth, and resolution with a set of predefined scaling settings [30]. The researchers began by establishing a base network with a technique known as neural architecture search, which automates the construction of neural networks. There are 18 convolution layers in all, each with a 3×3 or 5×5 kernel. The input picture is 224 by 224 pixels in size. The next layers have a lower resolution to minimize the size of the feature map but a higher width

to enhance accuracy. Also, the second convolution layer has $W = 16$ filters, but the following convolution layer has $W = 24$ filters. The completely linked layer was used for the final layer.

The block diagram of the proposed technique is depicted in Fig. 6. Researchers can create a strong breast cancer diagnostic system by using this high-level block diagram, the dataset, cross-validation, and data augmentation approaches, as well as CNN, Inception, and EfficientNet models. This method improves the CNN models' capacity to identify and categorize human breast cancer with more accuracy.

Result and discussion

This section presents the experimental findings of our research on Convolution Neural Networks (CNN), Inception, and EfficientNet-B4. We used the adaptive moment estimate optimization approach throughout the studies. The learning rate and drop factor are both set to 0.5, the minimum learning rate is set to 0.00001, patience is set to 2, and verbose is set to 1. During model training, the hyper-parameters are configured. An early halting strategy was used to avoid overfitting during the training phase. The models were registered at the point where the validation loss value was the best. Data augmentation increased the dataset to 22,500 images divided into 64% Training, 16% Validation, and 20% Test. Equal instances of breast cancer in the training dataset which consists of 4,800 each from the three classes such as malign, benign, and normal mammogram as shown in Fig. 7. Bar Chart of 20% validation set of breast cancer consists of 1200 each for the three classes: benign, malign, and normal, as shown in Fig. 8.

Training a model aims to identify a collection of weights and biases that, on average, have minimal loss across all cases. The greater the loss, the poorer the forecast (for any model). The loss is calculated during training and validation and determines how well the model performs for these two sets. The loss and accuracy curves of Convolutional Neural Network (CNN), Inception, and EfficientNet are shown in Figs. 9, 10, 11, 12, 13 and 14. The loss curves of CNN and EfficientNet are plotted in Figs. 9 and 11, which indicate a decline to the point of stability with a minimum gap between the training and validation loss values. The visualization of the Inception loss curve in Fig. 10 indicates that the training and validation losses have no value. This demonstrates that there is no training or validation loss. As illustrated in Fig. 12, there was a significant disparity between training and validation accuracy. The maximum accuracy on training images

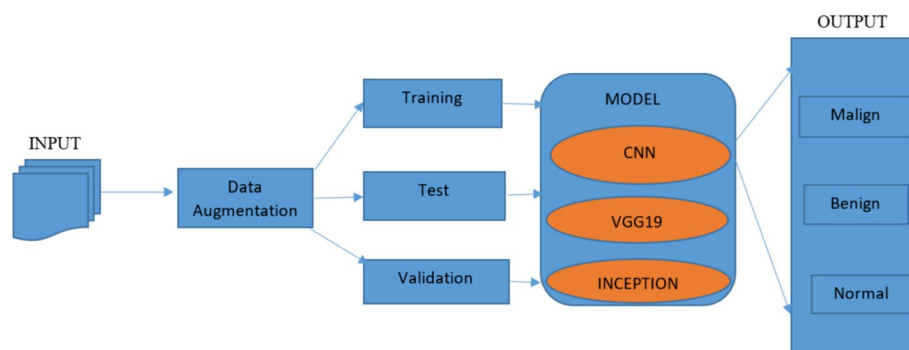


Fig. 6 Block Diagram of breast cancer detection

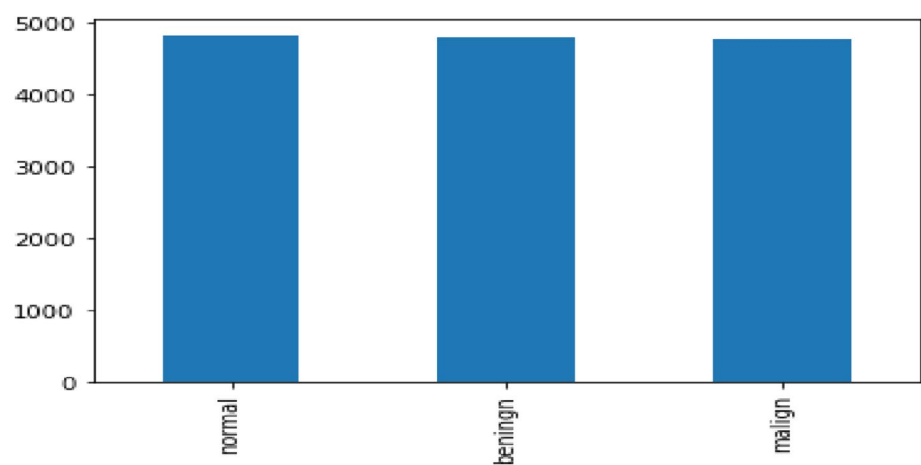


Fig. 7 Bar Chart of 64% Training Dataset

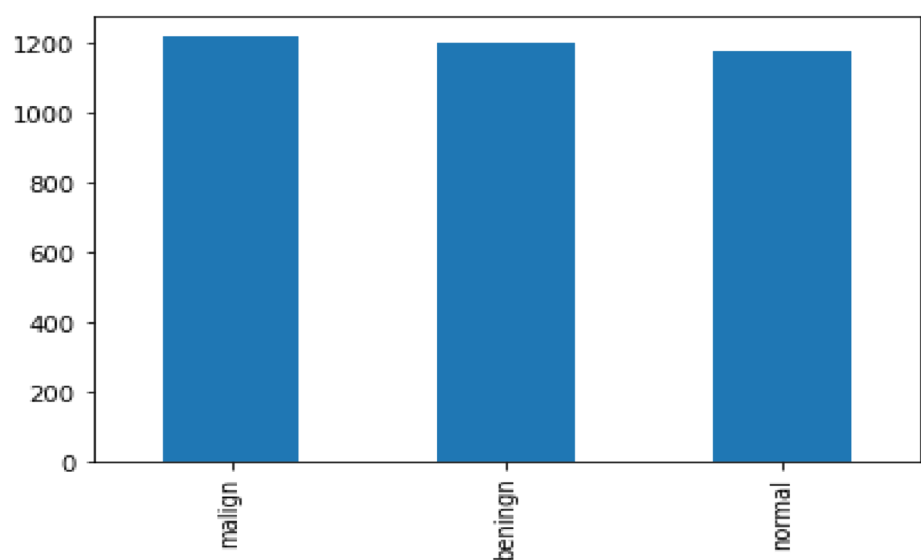


Fig. 8 Bar Chart of Validation Dataset

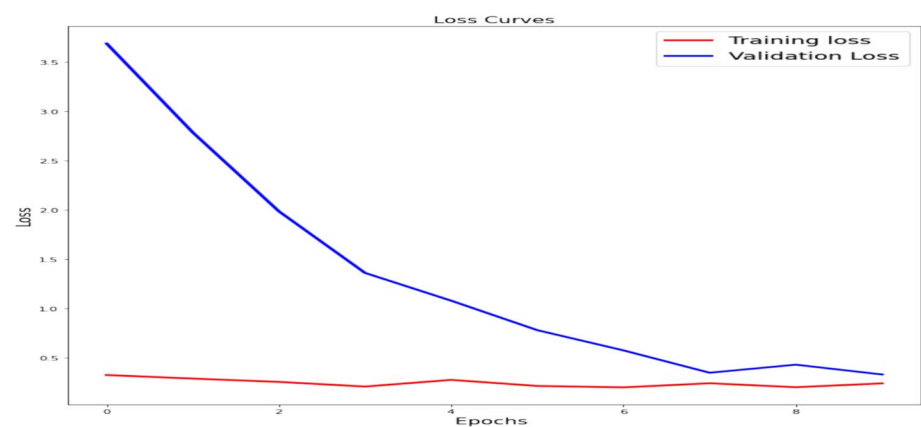


Fig. 9 Loss Curve of Convolutional Neural Network (CNN)

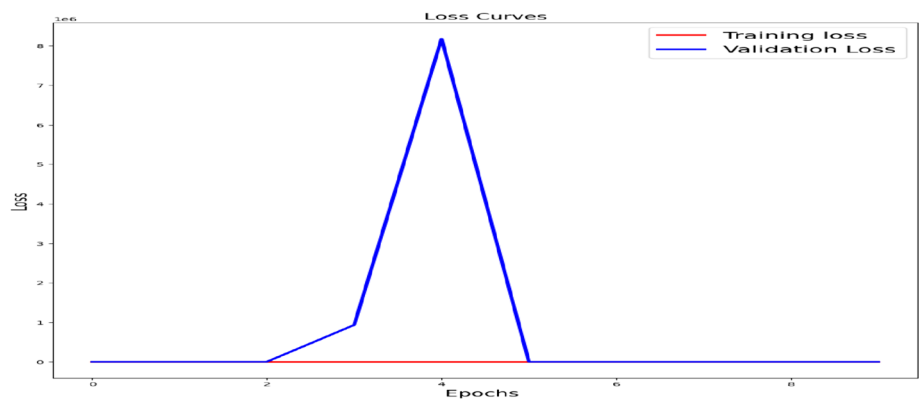


Fig. 10 Loss Curve of Inception

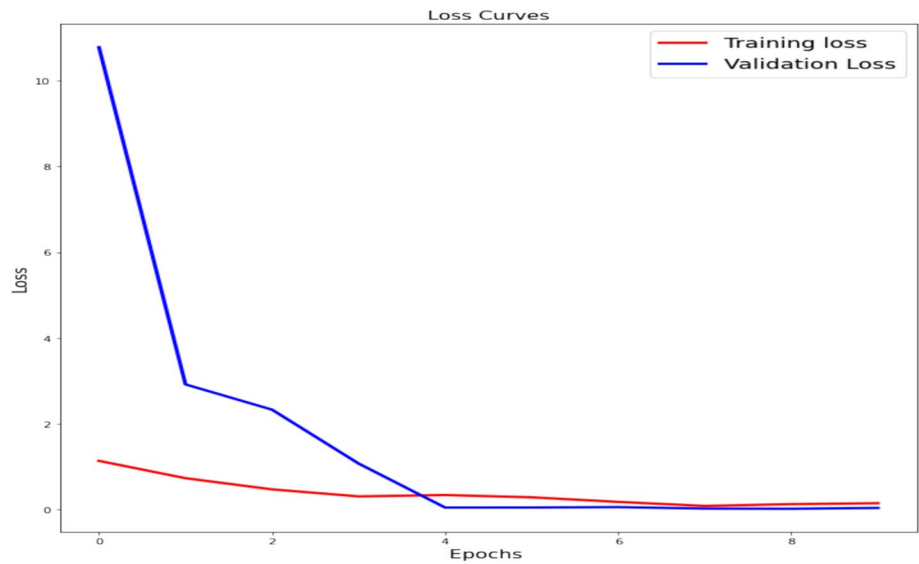


Fig. 11 Loss Curve of EfficientNet

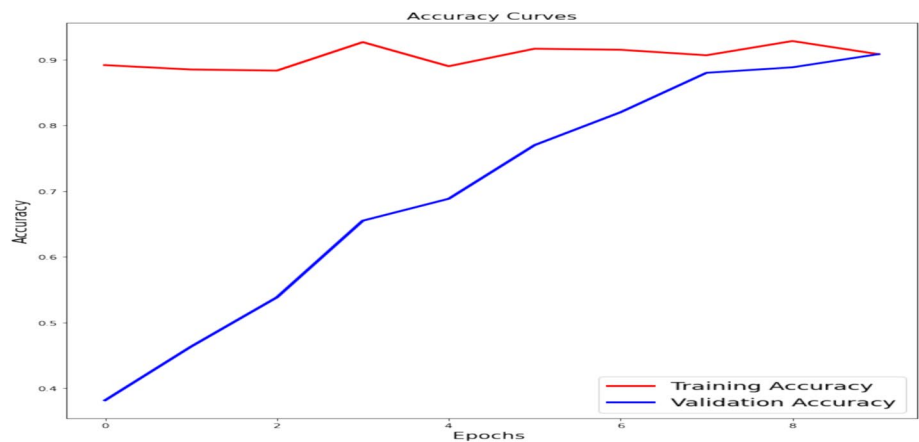


Fig. 12 Accuracy Curve of Convolutional Neural Network (CNN)

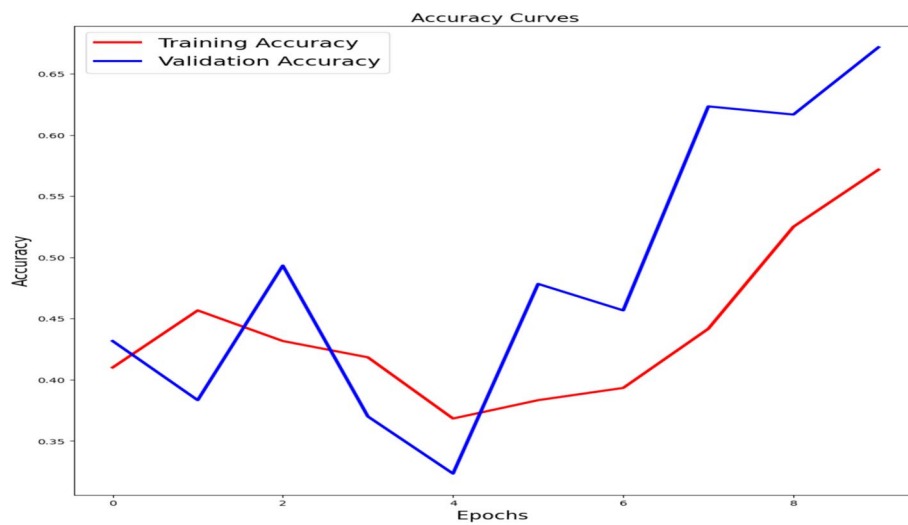


Fig. 13 Accuracy Curve of Inception

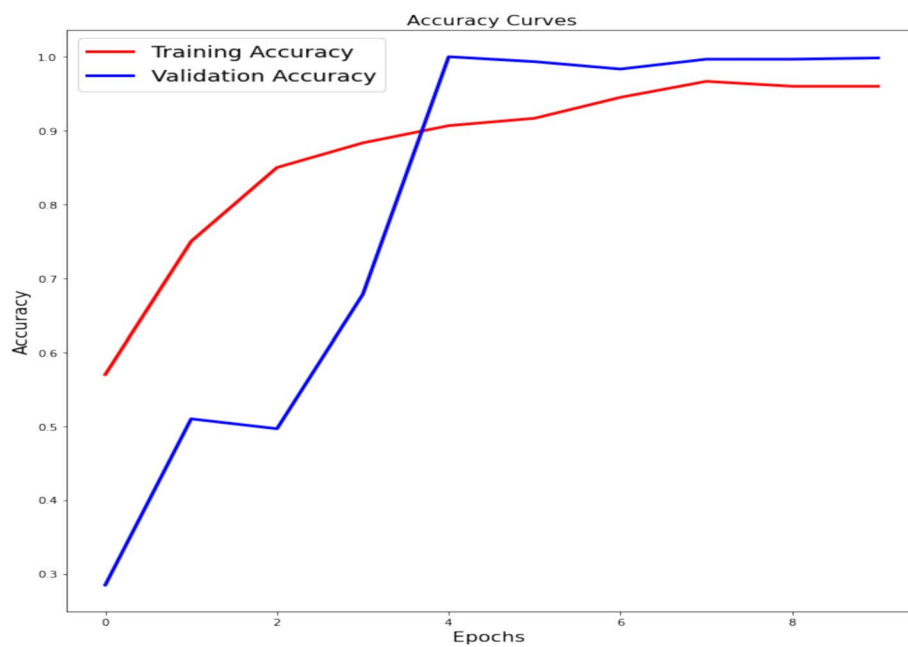


Fig. 14 Accuracy Curve of EfficientNet

was found to be 90%, while the lowest accuracy for both training and validation accuracy was found to be 90% in Fig. 13. Figure 14 depicts a flawless accuracy of 99% for both training and validation accuracy.

Table 2 shows the values of the classification performance of CNN, Inception, and EfficientNet on the image dataset of breast cancer. The CNN model achieved accuracies of 96.05% for normal, 87.89% for malign, and 75.12% for benign images. The Inception model achieved accuracies of 63.75% for normal, 76.32% for malign, and 81.21% for benign images. EfficientNet achieved accuracies of 97.13% for normal, 98.46% for malign, and 99.27% for benign images. Comparing the overall performance

Table 2 Performance Metrics of CNN, INCEPTION and EFFICIENT

Algorithm	Diseases	Sensitivity	Specificity	Prevalence	Balanced Accuracy
CNN	Normal	0.9210	1.0000	0.4276	0.9605
	Malign	1.0000	0.7578	0.2991	0.8789
	Benign	0.5024	1.0000	0.2733	0.7512
INCEPTION	Normal	0.2749	1.0000	0.4276	0.6375
	Malign	1.0000	0.5263	0.2991	0.7632
	Benign	0.7049	0.9193	0.2733	0.8121
EFFICIENT	Normal	0.9496	0.9930	0.4276	0.9713
	Malign	1.0000	0.9692	0.2991	0.9846
	Benign	0.9854	1.0000	0.2693	0.9927

statistics from Table 3, EfficientNet performs excellently well with an overall accuracy of 98.29%. Figure 15 is the ROC curve of CNN, INCEPTION, and EFFICIENT. EFFICIENT classifiers give curves closer to the top-left corner indicating a better performance followed by CNN.

Table 3 Overall performance measures of CNN, INCEPTION and EFFICIENT

Algorithm	Overall Accuracy	95% CI	P-Value
CNN	0.8302	(0.8189, 0.8411)	2.2×10^{-16}
INCEPTION	0.6093	(0.5949, 0.6236)	2.2×10^{-16}
EFFICIENT	0.9744	(0.9694, 0.9789)	2.2×10^{-16}

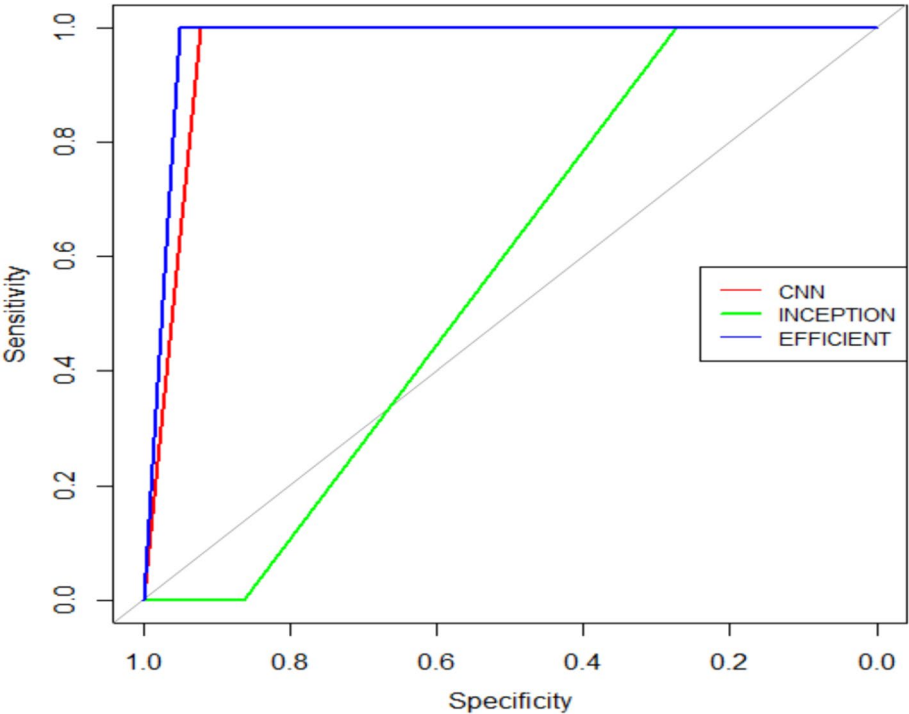


Fig. 15 ROC Curve of CNN, INCEPTION and EFFICIENT

Despite the excellent results achieved in this work, there are still some threats to the validity of the work. Even though deep learning algorithms can effectively extract and classify features and outperform classic ML algorithms, the major obstacle is the timeliness and dependability of access to and use of data. Another problem is legal concerns. Deep learning works best when there is a large quantity of data, which is presently hard to come by in the medical field. The major roadblocks are the challenges of data accessibility and the necessity to resolve legal issues connected to patient confidentiality preservation. For example, developing an algorithm to detect breast cancer will require hundreds of thousands of CT scans from patients who have given their consent; thus, data integrity and privacy will need to be included.

The training of an effective deep learning algorithm is hampered by data imbalance, privacy laws, secrecy, and other ethical issues. Various strategies for artificially increasing the volume of data are available to address the problem of limited data. These augmentation approaches include a variety of ways for increasing the number and quality of data to make deep learning algorithms easier to train. Stretching, spinning, flipping, transcription, and other transformations are used in conventional data augmentation approaches in medical imaging. These modifications are useful to a certain extent, after which they can lessen deep learning's capacity to generalize new data. Conventional augmentation strategies can be used in small amounts and then combined with different sorts of enhancement methods. The performance comparison of some of the approaches used for cancer detection is presented in Table 4.

Conclusion

The study looked at the prediction accuracy of three distinct deep learning models on the most common dataset, which was breast cancer. We concentrated our research on three types of cancer: benign, malignant, and normal. Our primary goal was to determine the accuracy of the various networks on the same datasets and assess the consistency of prediction by each of these deep learning algorithms. We conducted a complete prediction study for evaluating the performance of the networks for different kinds of items. According to the results, EfficientNet networks performed better and had greater rates of accuracy—the multilayer networks correctly identified objects such as benign, malignant, normal images.

Table 4 Performance comparison with other techniques

Technique	Image Type	Classifier	Accuracy (%)
Filipcruk, Kowal and Obuchowicz [15]	Microscopic images of fine needle biopsies	Machine learning models	95.56
Raj et al. [16]	Tumor IR thermography images	SVM	90.00
Araujo et al. [17]	Bioimaging 2015 breast histology classification challenge images	CNN	77.80
Rasti et al. [18]	MRI images	Convolutional ensemble approaches	96.39
Jiang et al. [20]	Histopathological image	CNN, SE-ResNet	99.11
Al-antari et al. [21]	Digital X-ray mammograms	Regional deep-learning method, CAD	95.64
Proposed Method	Digital Mammography images (MaMaTT2 dataset)	CNN, INCEPTION, and EFFICIENT	98.29

The EfficientNet networks achieved accuracy of 97.13% (normal), 98.46% (malign), and 99.27% (benign). The overall accuracy of EfficientNet networks is 98.29%. This proved that the proposed system is a promising one if adopted for automatic breast cancer detection. In the future, this work will be extended by adding more pre-trained networks in breast cancer classification and expanding the block of convolution neural networks and assisting radiologists in accurately authenticating large datasets in a time-liner manner.

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Author contributions

All the authors contributed equally.

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Availability of data and materials

The data is available at <https://www.kaggle.com/tttt2021/mamatt2> also cited the same in the reference list [22].

Declarations

Competing interests

Authors do not have any financial or non-financial interests that are directly or indirectly related to the work submitted for publication.

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