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Original Article

Integration of Convolutional Features and Residual Neural Network for the Detection and Classification of Leukemia from Blood Smear Images

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Abstract *- Malignant Acute Lymphoblastic Leukemia (ALL) attacks blood and bone marrow. Leukemia mostly affects both youngsters and older people all over the world. It is critical to detect leukaemia slightly earlier to offer patients the best possible therapy, specifically in the case of youngsters. As a result, computational methods for medical image processing are in high demand and have been the focus of medical image processing research. The major goal of this study is to use image processing and artificial intelligence approaches to forecast ALL cells. Computer Aided Diagnosis (CAD) has quickly grown in popularity over the last few years. Early-stage leukemia detection that is swift, safe, and precise is critical for treating and preserving patients' lives. A residual Neural Network (RNN) can be identified as a variant of a neural network that is again modified as ResNet-50. The max-pooling and convolutional layers were utilized to extract the maximum features present in the source image. The completely linked layer differentiates between malignant and healthy cell images. ResNet50 was used to detect leukemic cells with 99.61% accuracy. The findings showed that the proposed model outperformed other famous algorithms in detecting healthy vs leukemia patients.*

Keywords *- Acute lymphoblastic leukemia, Computer-aided diagnosis, Convolutional layer, Medical image processing, ResNet-50.*

1. Introduction

The leukemia would be distinguished by the impaired emergence of leukocytes in the bloodstream and bone marrow. A huge proportion of malignant immature white blood cells (WBCs), recognized as blast cells or blasts, decrease the number of blood cells. The actual cause of leukemia is unidentified, possibly due to inherited and genetic factors. In the U. S. in 2019, nearly 61,790 cases of leukemia have been recognized. [1] Every year, approximately 9990 new occurrences of leukemia are diagnosed in the United Kingdom [2].

Over 10,000 cases of pediatric cancer have been discovered in India each year. Based on image processing, methodologies are indeed being employed to detect diseases such as leukemia through automatic detection of blood smears of blood plasma and marrow of the bone smear image data. Much study has been conducted inside this region, with various techniques employed for identifying and classifying leukemia. Classification is an important step throughout these identification systems, including imaging techniques, extraction of features, and categorization. The quality of classified images influences the effectiveness of image processing and analysis. Depending upon the image classification technique used, the proposed paper examines the existing research in this area [3].

As shown in Table 1, blood includes 3 kinds of cells: erythrocytes (red blood cells), leukocytes (white blood cells), and platelets (thrombocytes). These cells have been reprimanded in plasma, a fluid medium [4].

Table 1. Blood cells and their roles

Blood cells	Functions
Red blood cells	Transporting oxygenated blood to a human body
White blood cells	Defending role for preventing infection
Platelets	Support in blood clotting

Platelets and cells comprise approximately 45% of blood and plasma 55%. WBC seem to be generally below 1% of the total. Leukocytes are categorized into granulocytes and agranulocytes based on the cell morphological features.

Leukemia, also usually referred to as leukaemia, is a leukocyte cancer. Leukemia is categorized as myeloid or lymphoid according to the origin of the cell line and chronic or acute according to the clinical curriculum. It tends to result in four distinct types of cancer [1-3]: Acute Myeloid Leukemia (AML), Chronic Myeloid Leukemia (CML), Acute Lymphoblastic Leukemia (ALL), and Chronic Lymphocytic Leukemia (CLL). Compared to leukemia, the proliferation of tumor tissue in acute leukemia is extremely rapid.

1.1. Acute lymphoblastic leukemia (ALL)

ALL mainly affects kids between the ages of 2 and 10. Also, it affects the centre and senior citizens. ALL is characterized by the emergence of premature cells known as lymphoblast in the bone marrow and blood. Persons who suffer from this condition usually show symptoms such as fever, lack of energy, losing blood, knee pain, migraine, dizziness, and so on.

ALL is split into three sections: L1, L2, and L3. The nuclei are frequent, and the chromosomal pattern has been perfect and uniform in L1 type ALL, while the color of the cytoplasm is generally sparse, blue, and uniform. The lymphoblast in L1 does have a rising nucleii-cytoplasm proportion. L2 would be distinguished by larger cell types and much more variability in biological data between and within cases. L3 cells are huge and consistent, having a cylindrical or roundish nucleolus and notable nucleus, and the cytoplasm has been intensely basophilic with vacuoles. In kids, roughly 71% of ALL cases seem to be L1, 27% are L2, and 2% are L3. The most popular ALL version in adults is L2 [5].

An enhanced Convolutional neural network and optimization to develop an effective classification approach for white blood cell leukemia. The dataset holds 207 images with only a comparable quantity of benign and cancerous diseases, and they were capable of achieving a 90% accuracy. Our article's objective is to create an automatic leukemia classification system that could be expanded for evaluating time-critical advancement and distinctions the type of cancer or phase [6].

The RESNet50 was used to establish a leukaemia detection module in this article. Max-pooling and a convolution layer were employed to obtain most characteristics from input images. The completely linked layer is employed to distinguish between images of cancerous and good cells. In this study, ResNet50 was employed to detect leukemic cells with high accuracy.

The remainder of the article is organized as follows: Section 1 provides a brief overview of the study. Section 2 discusses the recent works. Section 3 illustrates the suggested methodology. Section 4 deals with outcomes and performance evaluation. Section 5 conclusion is stated.

2. Related works

White blood cells (WBC) are important in protecting the body from sickness. Leukemia, often known as blood cancer, a pathologist will detect various it by examining a blood smear under a microscope. Blood counting is done using both conventional and automated methods. Traditional approaches rely on technicians' abilities to perform diagnostic procedures to attain higher accuracy. Most hospitals and laboratories cannot afford automated procedures because they are exceedingly expensive [7]. As a result, deep learning algorithms are used to overcome these challenges and diagnose problems quickly. Acute Lymphoblastic Leukemia (ALL) can be described as WBC malignancy which is caused due to the continual growth and increased generation of undeveloped WBC in the bone marrow. It is most commonly found in youngsters. ALL have highly identical symptoms to fever and other infectious symptoms, such as tiredness, weakness, and joint and bone pain, making diagnosis extremely challenging [8].

The kind of treatment (radiation, medicine, and chemo) and planning depends on a correct diagnosis. All the procedures for diagnosing leukemia are manual and rely only on qualified and experienced medical personnel. Blood cell microscopic examinations are an important part of the diagnosing process. For this evaluation, a skilled pathologist is needed to spot aberrant structures in blood cells. In the realm of medicine, medical pictures are among the most significant diagnostic tools. The images cannot be utilized without interpretation and analysis since the information is concealed in the pixels; consequently, they must be processed [23].

An automated technique for diagnosing acute leukemia. WBCs were segmented using a mix of k-means with color space representation in CIELAB. The linear interpolation approach was used to separate overlapping cells [10]. For classification, a binary classifier with simple majority voting was utilized. Their investigation used a dataset of 633 bone marrow leukemia cell images with various color stains. The average accuracy of classification and segmentation was about 95%. In addition, the categorization of leukemia subtypes was revealed to have a 90% accuracy rate [11]. Fatichah suggested a strategy for classifying leukemia subtypes. WBCs were segmented using a fuzzy morphology-based technique, and categorization was done using a fuzzy decision tree method. There were 120 photos of acute leukemia in the collection. The average categorization accuracy was found to be about 84%. Tosta et al. [12] demonstrated a technique for detecting WBCs in CLL patients. Wavelet transform, optimized genetic algorithm, and morphological operations were used to create the suggested segmentation approach. In this work, the algorithm was tested on 12 histology pictures. The separation of CLL cells had an average Dice value of 0.89.

A CNN [30] transfer learning strategy to diagnose leukemia. Pre-trained networks such as CafeNet and VGGNet were employed for feature extraction. Furthermore, the gain ratio approach was used to identify the characteristics, and the classifiers were utilized to detect leukemic WBCs. An identification of leukemic WBCs was found to have a 99 percent accuracy rate. A piece of color information including R and B of images and morphological procedures to segment WBCs. Using handmade characteristics to train the SVM classifier, basophils and eosinophils were recognized. Additionally, features from CNN were retrieved for training the Random Forest that can categorize neutrophils, monocytes and lymphocytes with a claimed accuracy between 75% and 96% [14].

Algorithms and procedures for medical diagnosis and evaluation have been created due to recent pathologic and microscopy image processing breakthroughs. Due to the fast development of advanced machine learning algorithms, artificial intelligence has recently demonstrated amazing effectiveness in evaluating medical images. These achievements have boosted the ability to address complicated real-world issues and perform picture analysis [25]. Machine learning is an important area in medicine because of its importance in increasing diagnosis and specificity in illness classification; yet, some researchers believe feature engineering is a major flaw in machine learning [16]. Simply put, feature extraction algorithms are frequently created by hand and precisely applied to images. Deep Learning (DL) can be considered a subclass of Machine Learning (ML). Using specific data retrieval characteristics of images and boosting the device's efficiency makes DL feasible for handling complicated issues to a great extent. On the other hand, these networks instantly learn characteristics from the source data. As a result, suggested networks evaluate and compare other networks depending on their design and parameters.

Classifying ALL lymphoblast cells are normal or abnormal. The framework had two stages: the first separated white blood cells from those other lymphocytes, and the second extracted lymphocytes. The system detected haematological disabilities using Gray Level Co-occurrenceMatrix (GLCM) and then categorized a feature extraction map using SVM [11]. The author of [18] concentrated on cell segmentation using conventional methods to split red blood cells. The automated process calculated the image limit and utilized a canny filter to retrieve the edge using thresholding. The author in [19] employed the Gram-Schmidt approach and parametric deformable designs to split the cytoplasm from the nucleus. In addition, the novel pre-processing method is utilized to portion white blood cells (WBC) based on Hue Saturation Intensity (HSI). [20] The classical methods are utilized to extract objects from pictures and machine learning for categorization. To begin, the images were transformed into binary image data to split the foreground (objects) from the background. Instead, the threshold was chosen as the value of the density of the background and object.

This paper's contributions are summarized below.

- ResNet50 was used to detect leukemic cells from Blood Smear Images
- To extract maximum features present in the source image, the max-pooling along with the convolutional layer was utilized
- Comparing the performance of the proposed method to that of recently developed techniques.
- Experiment results show that the proposed technique surpasses existing techniques.

3. Proposed Methodology

Many radiological images with good health and ALL cells were chosen. Preprocessing processes, including scalability, augmentation, and normalization techniques, are utilized to prepare the selected data set. The proposed pre-trained network uses convolution and max pooling layers to extract important information necessary to identify ALL and healthy cells (ResNet-50). The suggested network's design is simpler than that of existing pre-trained networks. It is also used to provide parameters to train pre-trained networks. In this network, no stored weights were used. Figure 1 illustrates a schematic block of the DL-based leukemia categorization framework.

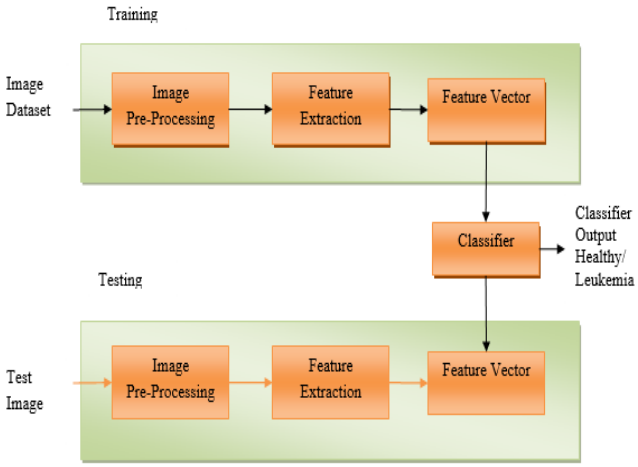
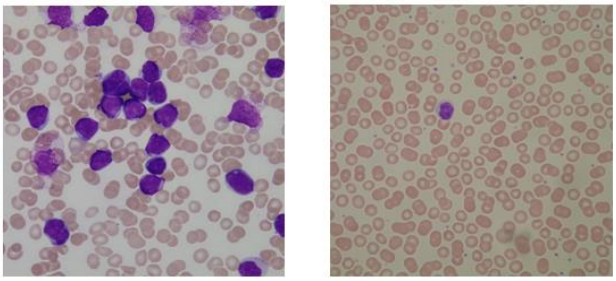


Fig. 1 DL-based leukemia categorization framework

3.1. Leukemia Dataset

The ALL-IDB database [21] contains microscopic pictures of ALL and normal blood cells. This image library is free on the website and provides an ample assortment of photographs covering various hematologic subjects. This work utilized all annotated images having blood leukemia, including 4 subareas. The ALL collection contains illustrated blood cell images obtained using the microscopic camera. These images are used for classification, assessment, and

segmentation. Only normal and ALL forms of leukemia samples are found in the ALL-IDB database. The ALLIDB dataset does not contain the additional leukemia subtypes indicated. Because expert oncologists gave the ALL categorization for each picture in the dataset, the ALL-IDB is thought to be more trustworthy. Figure 2 shows a few input images from sets of data.



(a) (b)

Fig. 2 Sample images fromALL-IDB dataset (a) Sample with ALL, (b) Healthy sample

The samples within the data set have been taken with an optical research lab microscope and a Canon PowerShot G5 camera. All the images appear in JPG format, with rgb values of 24 bits and pixel resolution of 2592×1944. The images were taken using various optical microscopy high resolutions varying from 300µm to 500µm. The above subset is composed of 108 images that were gathered. It includes roughly 39000 plasma components, with the lymphocytes labelled by specialist doctors.

3.2. Preprocessing

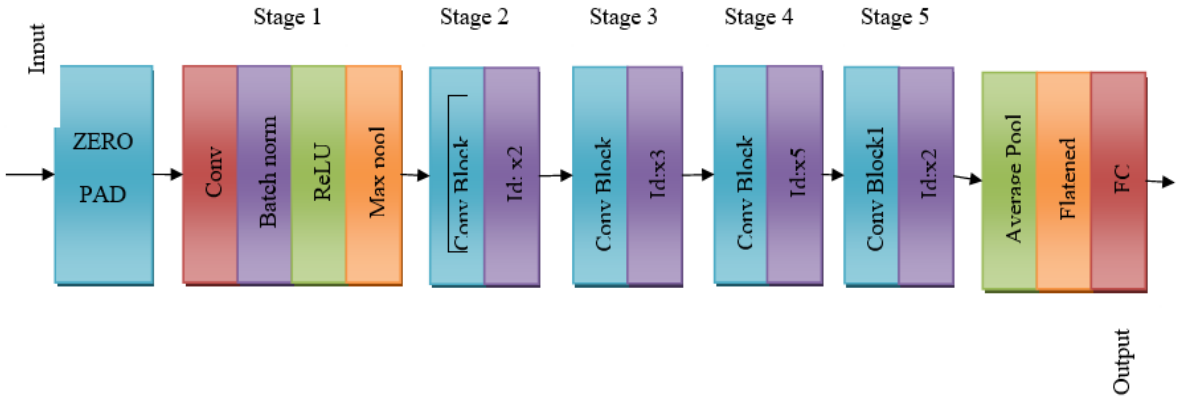
Consider the dataset holds images of blood smears. The images in the set of data are pre-processed to improve classification outcomes. The image samples must be of the correct size to regulate these same classification tasks, so the pictures are resized during pre-processing. Image resizing simplifies the process of segmentation.

3.3. Data Augmentation

Data augmentation strategies are frequently employed in deep learning to improve the number of datasets and reduce overfitting. Several image alteration strategies, such as rotate, flip, and shift, were applied to create different pictures from the source image. Deep learning methods would be much more generally applicable if they were trained to utilize both the actual images and their sub-versions. Multiple methods of data reproduction have also reduced modelling erroneous rates by providing superior speculation in automated segmentation studies to CNNs. In this case, the recovered datasets give a wider range of microscopic images, although both datasets comprise samples from a small number of ALL subtypes. Since the datasets for DL algorithms are so small, overfitting is possible. Pictures modification or data augmentation techniques such as rotation, length shifting, breadth transition, horizontal flipping, zooming, and shear are utilized to maximise the dataset. Both datasets raise the sample size after applying image processing algorithms. The ALL-IDB dataset's sample size increased to 2470 after data augmentation.

3.4. Feature Extraction and Classification

The major building block of proposed ResNet 50 is the convolutional layer. Convolution is described as a systematic procedure for combining two sources of data. In this case convolution filter is applied to the input data for generating a feature map. The architecture of the proposed ResNet 50 neural network is depicted in Figure 3.



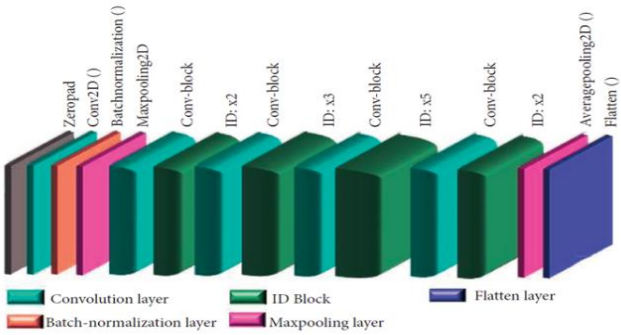


Fig. 3 ResNet50 architecture

This design is considered to be the deepest network with 152 levels. The network comprises many residual modules that are layered on top of one another to create the ResNet50 design's fundamental building component. The residual module can perform a sequence of actions on input data or skip them completely. These layered leftover modules may be used to build a whole network [16-19]. ID BLOCK stands for identification blocks, and three are piled together here.

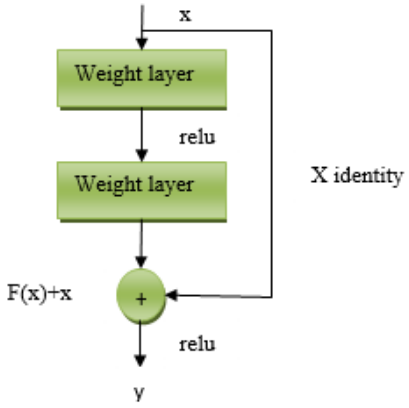


Fig. 4 Residual block of ResNet 50

The Residual Block Unit (RBU) [22] is the core structure of the ResNet-50 network, and the residual block's framework is depicted in Figure 4. The convolution layer, batch normalization, and ReLU are all part of anRBU.$H(x)$ is seen as an essential mapping for being fit through minimum convolution layers in residual learning, with x representing the opening of these layers' inputs as displayed in Figure 4. If one assumes that several regressive layers can approximate complex functions asymptotically, one can compute the residual function as given in Equation1.

$$F(x) = H(x) - x \tag{1}$$

After considering the weights, the building blocks' output is mentioned in Eqn. (1). Provided $W_i$is with the weight and $F(x, W_i)$ is the residual mapping expected to be trained.

$$y = F(x, W_i) + x \tag{2}$$

Shortcut connections introduce no extra parameters or computational complexity. In Equation2, the dimensions of x and F have to be the same. For matching the dimensions, execute a linear projection $W_s$using the shortcut connections as expressed in Equation3.

$$y = F(x, W_i) + W_i x \tag{3}$$

It commonly applies max pooling after the convolutions to minimize the dimension. It allows us to limit the parameter count, reducing training time and preventing overfitting. Downsampling layers samples each feature map individually, lowering the length and breadth while maintaining the depths. The most frequent pooling is max pooling, which simply takes the pooling window's maximum value. In contrast to convolution, pooling has no constraints.

So far, the data has yielded several useful characteristics thanks to the convolution layer. The fully linked layer receives this information and creates the final output. The classic neural network is the completely linked layer in a CNN. The convolution layer produced a 2D matrix as its output [27-28]. Each row should, ideally, reflect a single image as input. The completely linked layer, in reality, can only cope with 1D data. As a result, the results of the preceding operation are first transformed into a 1D representation. A linear transformation itself can catch complex interactions. As a result, the system acquires a new element that provides added nonlinear behavior to data. This innovative design component is referred to as the activation function. In this research *softmax* activation function ($\sigma(x_i)$) is used to categorize images into leukemia and healthy. $\sigma(x_i)$for binary classification (N=2) is given in Equation4. The input vector to the softmax layer is the feature vector (x_i).

$$\sigma(x_i) = \frac{e^{x_i}}{\sum_{i=1}^{N} e^{x_i}} \tag{4}$$

Classification is validating or allocating an unlabelled variable to a known class. The provided sample set could be categorized into the healthy or cancerous classes utilizing a classifier.

4. Results and Discussion

4.1. Experimental setup

The proposed method employs a CNN classifier integrated with the MATLAB tool, as well, as the following configurations are supposed for testing: a PC with the Windows 10 operating system, 4Gb Of ram, and an Intel I3 processor.

As stated previously, the study's primary objective would have been to categorising pictures into normal and leukemic classifications. There were 2470 pictures in the collection, with 1235 healthy plus 1235 leukemic cells. Network classification accuracy is one of the most important metrics for assessing artificial neural networks. The receiver operating characteristic (ROC) for the pre-trained ResNet50 model is shown in Figure 5. The ResNet-50 model's ROC area for the healthy category is 0.91, whereas the class for leukemia is 0.90.

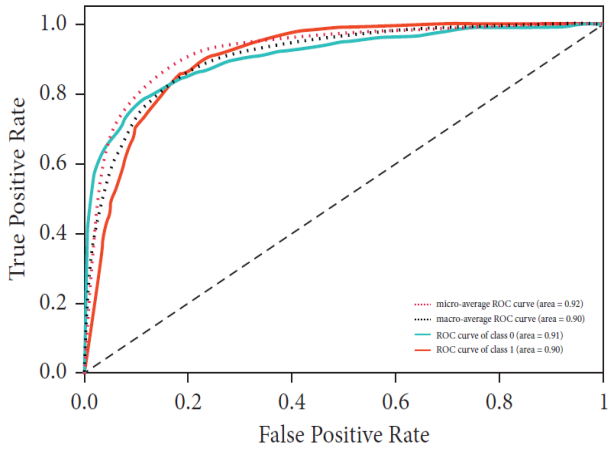


Fig. 5 ROC of proposed ResNet50 classifier

Each cycle achieves accuracy for train and test data by splitting the data between training and test images. For the assessment of this network in terms of validation accuracy, the average accuracy for 100 epochs in categorizing 2 classes, such as ALL and healthy, is computed. Common assessment metrics such as accuracy, recall, and F-measure were computed for three networks. The findings of the networks presented in this paper are summarized in Table 1. TheResNet-50's training accuracy is 100 percent, and its validation accuracy is 99.6154 percent. Other classifiers reported poorer train and test accuracy when contrasted to the suggested ResNet50 classifier. Other characteristics for these classifiers were computed, including specificity, sensitivity, Negative Prediction Value (NPV) and Positive Prediction Value (PPV), for which the suggested classifiers provided the best results. Performance metrics are shown in Figures 6a to 6e.

4.2. Performance Evaluation

The performance of the suggested system is measured using the following metrics [26]: Accuracy, Specificity and Sensitivity. These performance metrics are explained as follows.

4.2.1. Accuracy

The accuracy of image classification is a percentage representing the total number of correctly identified pixels divided by the total number of pixels in the image. It calculates the number of properly pixeled pixels in an image.

$$\text{Accuracy} = \frac{TP+TN}{(TP+TN+FP+FN)}$$

Where TN is True Negative, TP is True Positive, FN is False Negative, and FP is False Positive

4.2.2. Sensitivity or recall

The size of accurately average data is divided by the overall size of correct data.

$$\text{Sensitivity or recall} = \frac{TP}{TP+FN}$$

4.2.3. Specificity or Precision

It is calculated by dividing the amount of correct negative values by the total number of negative values.

$$\text{Specificity or Precision} = \frac{TN}{TN+FP}$$

4.2.4. F-measure

F-measure is computed by using precision and recall value

$$\text{F-measure} = \frac{2*Precision*Recall}{Precision+Recall}$$

4.2.5. FalsePositiveRate(FPR)

$$\text{FPR} = \frac{FP}{FP+TN}$$

4.2.6. FalseNegativeRate (FDR)

$$\text{FDR} = \frac{FN}{FN+TP}$$

Table 2 summarizes the overall accuracy, specificity, sensitivity, PPV and NPV for various existing methods like GoogleNet, ResNet101, Resnet152, VGG16 and VGG19, which is visually represented in Fig 6. Compared to previous techniques, the suggested technique outperforms in terms of results.

Table 2. The performance metric for various classifiers

Performance Metrics	GoogleNet	ResNet101	Resnet152	VGG16	VGG19	Proposed ResNet50
Accuracy(%)	95.3846	96.9231	97.3077	98.0769	98.8462	99.6154
Sensitivity (%)	96.1538	95.3846	96.9231	100	98.4615	100
Specificity (%)	94.6154	98.4615	97.6923	96.1538	99.2308	99.2308
PPV (%)	94.697	98.4127	97.6744	96.2963	99.2248	99.2366
NPV (%)	96.0938	95.5224	96.9466	100	98.4733	100

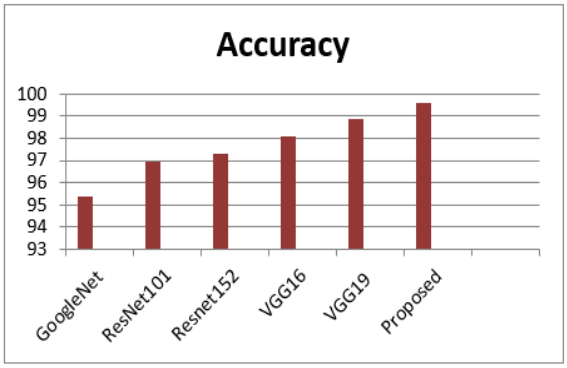


Fig. 6a Accuracy

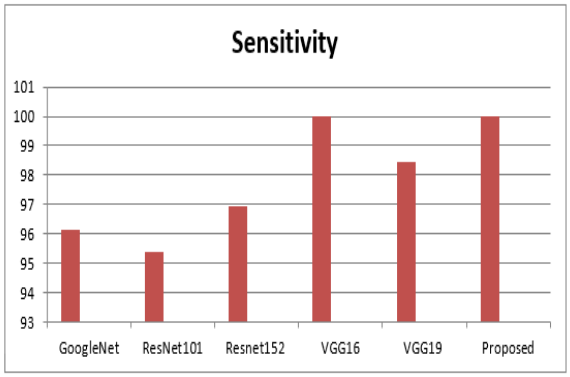


Fig. 6b Sensitivity

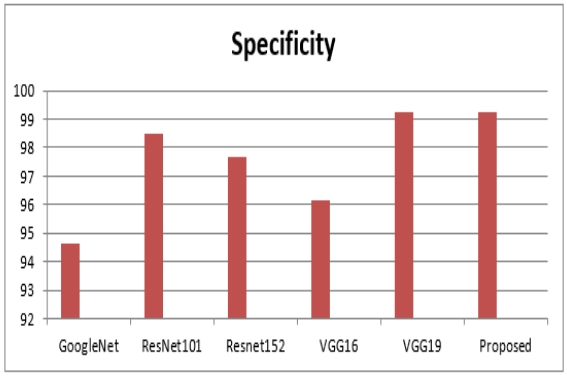


Fig. 6c Specificity

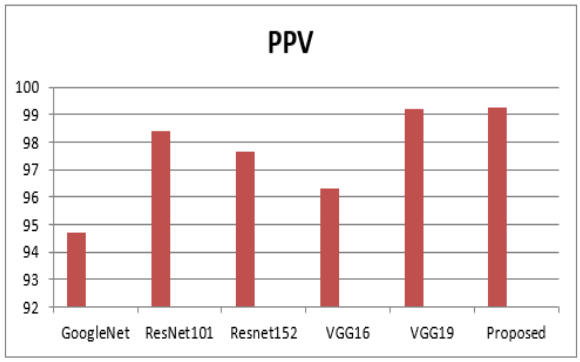


Fig. 6d PPV

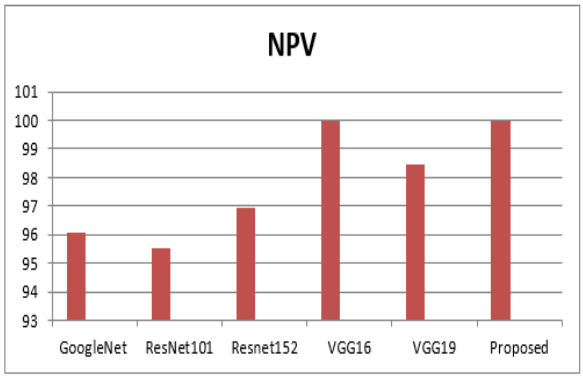


Fig. 6e NPV

This study concentrated on the categorization of leukemia, specifically ALL. Moreover, this work achieved better accuracy in classification and diagnosis.

Table 3. Comparison of accuracy with existing methodologies

Classifier	Features	Dataset Images	Accuracy (%)
7LayerCNN [22]	Morphological	356	96.6014
6 Layer CNN [23]	Morphological	510	88.2536
8Layer AlexNet[24]	Color	306	99.4512
DCNN [25]	Morphological	2200	96.3254
ResNet 50 (Proposed)	Convolutional	2740	99.6154

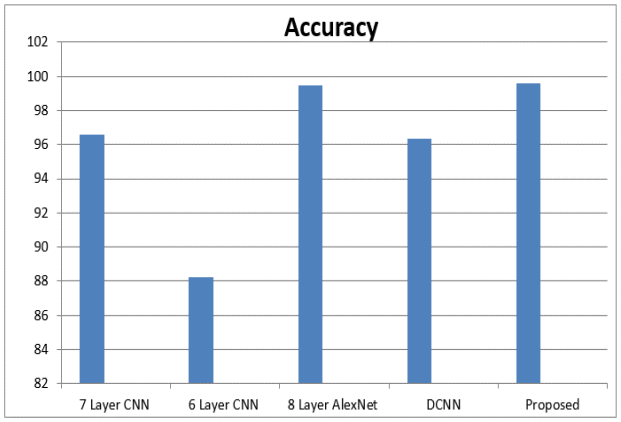


Fig. 7 Comparison of leukemia classifiers

As mentioned in Table 3, the accuracy of the ResNET 50 classifier is contrasted with existing classifiers for leukemia classification.7-layer CNN and 6-layer CNN with morphological features provided an accuracy of 99.6014% and 88.2536%, respectively. 8-layer AlexNet with color features provides the second-best accuracy of 99.4512%. Deep CNN (DCNN) with morphological features provided an accuracy of 96.3254%. The proposed ResNet50 classifier provides the best accuracy of 99.6154% and is the best leukaemia classification classifier. The comparison of proposed methods with existing methods is depicted in Figure7.

5. Conclusion

The healthcare business is among the fields where AI and ML are used. This study looked at ResNet applications and designed ResNet50 to diagnose and classify ALL and differentiate between healthy and cancerous cells. In addition, a new ResNet50 was set up for the previously indicated aim. It achieved a training accuracy of 100 percent and test accuracy of 99.6154% for ResNet50 using image processing techniques. The study's ultimate purpose was to evaluate the results of networks that may use to categorize depending on factors like complexity, architecture, accuracy and runtime. Because trained networks are more resilient and have a unique design, better outcomes are likely. Pre-trained networks are notorious for taking a long time to execute, yet suggested ResNet 50 has been quick, and regardless of its design, the outcomes were encouraging. The proposed method provides support to laboratory professionals and oncologists. This approach will significantly influence leukemia patients from a clinical standpoint. This work employed a little quantity of training and assessment data, which may have influenced the training phase of ResNet 50. As a result, setup DL to understand from the start with bigger image datasets. These computational approaches can be applied in real-life situations to assist specialists and oncologists in accurately detecting leukemia.

Acknowledgement

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