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Acute lymphoblastic leukemia diagnosis and subtype segmentation in blood smears using CNN and U-Net

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ABSTRACT

Acute lymphoblastic leukaemia (ALL) is a severe disease requiring invasive, expensive, and time-consuming diagnostic tests for definitive diagnosis. Initial diagnosis using blood smear pictures (BSP) is crucial but challenging due to the similar indications and symptoms of ALL, often leading to misdiagnoses. This study presents a custom approach using Convolutional Neural Networks (CNNs) to detect all cases and categorize subtypes. Utilizing publicly available databases, the study includes 3562 blood smear images from 89 patients. The innovative combination of U-Net for segmentation and various CNN architectures (U-Net, MobileNetV2, InceptionV3, ResNet50, NASNet) for feature extraction, with DenseNet201 being the most effective, forms the core of this method. The U-Net model achieved a segmentation accuracy of 98% by recognizing patterns within blood smear images. Following segmentation, CNN architectures extracted high-level features, with DenseNet201 proving the most effective in diagnostic and classification tasks. Our proposed custom CNN model achieved a test accuracy of 98%, with a training accuracy of 99.31% and validation accuracy of 97.09%. This approach enables an accurate distinction between ALL and non-pathologic cases.

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1. INTRODUCTION

Acute lymphoblastic leukemia (ALL) is a highly common type of cancer that requires careful and sometimes invasive diagnostic methods to identify it accurately. Precise identification of ALL especially during its initial phases, is crucial for prompt intervention and efficient treatment. Peripheral blood smear (PBS) [1] images are highly important diagnostic tools that provide valuable information about cellular abnormalities that indicate the presence of leukaemia. The manual reading of PBS [2] images to explore decided disease issues is affected by the vast problems related to the risk of wrong diagnosis that may result from the low and ambiguous features of the patient's signs. Bad interpretations could cause patients to appear too often, leading to misdiagnosis and less effective treatments, fixing the worst-case situations and increasing the burden on the healthcare system. Herewith proposed is an approach to creating a cutting-edge tool which will enable the classification and precise diagnosis of all breakpoints and ALL subtypes exploiting cutting-edge deep learning approaches. This project aims to apply ALL detection to PBS pictures more automatically and to divide the

ALL [3] cases into benign and INFMUN. The whole project goal is to develop a thorough and easily manageable dataset that contains pictures from people diagnosed with ALL [4], acute lymphoid leukaemia. This dataset presents different types of scenarios including those that are considered harmless from the population haematogone syndrome as well as the confirmed occurrence of the ALL subtypes [5], which in turn gives a chance for an effective assessment of the training model and evaluation.

In addition to that, the grouping of PBS [6] images using different hue threshold techniques in the HSV colour space, perceived as the preliminary step for the meticulous feature extraction, lays the foundation for a high level of accuracy in the prediction. This research makes a comparative study of CNN architectures that are cataloged as the best ones, that is, U-Net, MobileNetV2, InceptionV3, ResNet50 and ViT and NASNet. The results demonstrate the best of DenseNet201 performance (diagnosis and classification tasks) that is evidently superior to the others. The key contributions of this study are:

- Introduce a novel approach for ALL diagnoses by convolutional neural networks (CNNs) for precise classification.
- Utilization of PBS images for reducing the risk of misdiagnosis associated with manual interpretation.
- The proposed model significantly improves clinical specificity, enabling a reliable diagnosis of ALL.

The subsequent sections of the paper are structured in the following manner: Section 2. discusses the work of my predecessors. In Section 3. explanation the methodology step by step. The model outcome and the primitive actions that should be taken as an outcome are discussed in Section 4. Section 5. conclude the paper.

2. RELATION WORK

ALL classification using CNN and transfer learning has shown promising results in improving efficiency and accuracy in identifying leukemia cells. Khuzaie *et al.* [7] discusses using a VGG19-based CNN model for detecting ALL cells. The paper focuses on developing an efficient VGG19-based model for detecting ALL. Deep learning techniques can streamline the identification of leukaemia cells and improve patient outcomes.

Das *et al.* [8] proposes a model for classifying and detecting ALL using transfer learning and an orthogonal SoftMax layer (OSL)-based classification. Demonstrates superior performance on ALLIDB1, ALLIDB2, and CNMC2019 datasets.The paper proposes a model for detecting and classifying acute leukemia. The model combines ResNet18 with an orthogonal SoftMax layer for improved performance. Ahammed *et al.* [9] proposes an efficient transfer-learning-based CNN model using Inception-V3 architecture to classify ALL from microscopic images. Also, Hau *et al.* [10] proposes a hybrid transfer learning eXtreme gradient boosting (HTL-XGB) algorithm for the classification and detection of ALL using CNNs and transfer learning. Object detection methodology using image processing techniques with HTL-XGB architecture. Gautam *et al.* [11] introduced a classification method for WBCs that combines the Naive Bayes classifier with morphological features. The characteristics the researchers employed to train their system included area, perimeter, eccentricity, and circularity. The accuracy of the proposed method was made up of 80.88 percent. The process of manually classifying acute lymphoblastic leukemia is laborious and time-intensive. The proposed procedure employing Mask R-CNN attains a classification accuracy of 83.72%. Segmentation of instances utilizing mask R-CNN Method for enhancing contrast in an image dataset [12].

Recent investigations into classifying malignancies have relied heavily on computer vision methods [13]-[16]. The predominant algorithm utilized in this methodology comprises multiple evaluations that follow image pre-processing, clustering, morphological filtering, segmentation, feature extraction or selection, and classification [17]. These are rigid phases. Due to the diagnostic importance of blood cell classification, numerous algorithms for classifying blood cells have been proposed by scientists. Sinha and Ramakrishnan VOLUME XX, 2018 classified cells with a 94.1% recognition rate using SVM in [18]. The researchers conducted the identical experiments using one hundred images. The researchers employed the method with the smallest error rate to classify the segmented cells using an adaptive contour and automatic threshold. The resulting recognition rate was 96%. The researchers put the KNN algorithm to use. Nevertheless, the KNN algorithm struggles to process unbalanced samples. Difficulties may arise when the sample capacity of one class is substantial, while that of other classes is relatively limited.

Leukemia causes premature death and other symptoms in children and adults. Computer-aided methods can help specialists diagnose this disease and prevent incorrect therapy prescriptions. CNNs [19] are

increasingly used to classify and diagnose medical images. However, CNN training involves many images. We employ transfer learning to extract picture features for classification to solve this challenge. Leukemia is a deadly white blood cell illness that affects blood and bone marrow. Deep convolutional neural network was used to detect acute lymphoblastic leukemia and classify its subtypes into four classes: L1, L2, L3, and Normal, which were disregarded in prior studies. Instead of training from scratch, we used pre-trained AlexNet [20] fine-tuned on our data set. New layers classify incoming photos into four classifications, replacing the pretrained network's last levels. Overtraining was reduced via data augmentation.

3. METHOD

The following section provides a comprehensive overview of the experimental framework. Initially, we have to choose the dataset and then use the data pre-processing techniques to fit the data for the model. We conducted experiments by using publicly accessible data. The Zeiss microscope at 100x magnification was used to capture blood smear images, which were saved in JPG format. To make it adaptable for the deep learning model, we have standardized images into 224x224 pixels through preprocessing techniques. This preprocessing included applying rotation, contrast adjustment, and segmentation in the HSV colour space. After the preprocessing data, we implemented the deep learning models and evaluated the result on the evaluation metrics. This section also provides the dataset description, a concise analysis of the deep learning models, and an evaluation of the proposed system's performance. The fundamental architecture of our research is illustrated in Figure 1.

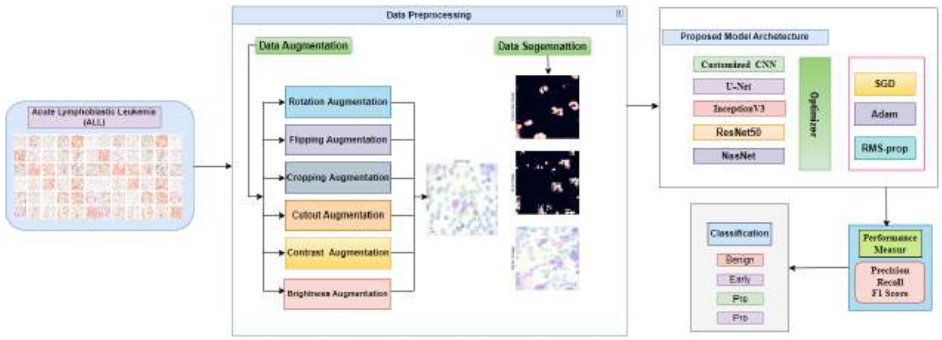

Figure 1. Methodology workflow for acute lymphoblastic leukemia detection using augmented data, a CNN model, and performance evaluation metrics

3.1. Dataset

For disease detection of ALL, we are using a dataset [21] of 3,256 images that have been taken from 89 ALL patients who did PBS [22]-[24] examination at Taleqani Hospital in Tehran, Iran. The images were divided into two classes: harmful with a benign way tend to have the capability of tearing and destroying important molecules from a cell and self-protection of the body against cancerous action. The malignant class contained three sub-types of malignant lymphoblasts: Table 1 presents the early Pre-B, Pre-B, and Pro-B fighting ALL [25] of this joint effort of modern medicine in Table 1.

Table 1. Dataset distribution for diagnosing ALL

Class name	Total image	Train	Validation	Test
Benign	504	323	80	101
Malignant-early	985	631	157	197
Malignant-pre (Pre-B)	963	616	154	193
Malignant-pro (Pro-B)	804	516	128	160

We have taken all images with a Zeiss camera with 100x magnification and saved them as JPG files. A specialist definitively determined the cell types and subtypes using the flow cytometry tool. In addition, segmented images were provided after applying colour thresholding-based segmentation in the HSV colour space, shown in Table 2.

Table 2. Acute lymphoblastic leukemia dataset details

Feature	Details
Dataset origin	Bone marrow laboratory, Taleqani Hospital, Tehran, Iran
Total images	3256 peripheral blood smear (PBS) images
Number of patients	89 suspected of ALL
Preparation	Prepared and stained by skilled laboratory staff
Image format	JPG files
Imaging equipment	Zeiss camera, microscope at 100x magnification
Diagnosis confirmation	Specialist using flow cytometry
Segmentation technique	Color thresholding in HSV color space; segmented images provided
ALL subtypes	Hematogones, early Pre-B, Pre-B, Pro-B ALL

3.2. Dataset pre-processing

After completion of dataset selection and import for the implementation, we maintain the original ratio, and achieving consistent data distribution through normalization is crucial during the pre-processing stage of image data. To achieve this, we establish a fixed target size parameter of 224x224 pixels, ensuring that all images loaded into the deep-learning model are resized to this size. This is essential since deep-learning models typically require data of a specific size. By standardizing the image shape, we enable the model to process the data efficiently and with precision. The pre-processing techniques employed in our research includes rotation, contrast, flipping, cropping, cutout and brightness pre-processing.

3.3. Deep learning models

3.3.1. Customized CNN architecture

The deep learning model designed for image recognition tasks has a customized CNN architecture. The model includes an input layer specifically for RGB images of size 224x224 in Figure 2. It also has convolutional layers for feature extraction, pooling layers for dimensionality reduction, dropout layers to prevent overfitting, and dense layers for classification. The ReLU activation, batch normalization, and dropout techniques are employed in the model's architecture to improve its performance and generalization.

- Input layer: (224, 224, 3). The model has a model card that expects an image of resolution 224x224 with 3 channels (RGB).
- Convolutional layers: the model consists of a convolutional layer of four layers arranged in the sequence and with the ReLU activation function which introduces non-linearity. There are 200 filters in the first convolutional layer, 150 filters in the second convolutional layer, and so on down to 50 filters in the fourth convolutional layer with each layer 3x3 kernel sizes. The idea of this structure allows the network to extract characteristics of the image at different degrees of abstraction.
- Pooling layers: the first and second layers are max-pooling layers with a pool size of (4,4).
- Dropout layers: applied twice with a rate of 0.8, after the first and third convolutional layers to prevent overfitting.
- Flatten layer: this layer transforms the 2D arrays from the previous layers into a 1D array, preparing it for the fully connected layers.
- Fully connected (Dense) layers: after the convolutional layers, the architecture includes a dense layer with 256 units and ReLU activation, followed by batch normalization for stabilized activation and a dropout rate of 0.8 to reduce overfitting.

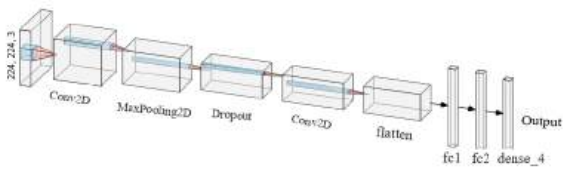

Figure 2. A customized CNN model with convolutional layers, pooling, dropout, flattening, and fully connected layers, culminating in a 4-unit output for classification

3.3.2. U-Net architecture

Contracting path (encoder): the architecture involves a contracting functional block (encoder) and a transformational functional block (decoder). The contracting passage looks like a simple CNN architectural design that comprises several convolutional and pooling layers. Each contracting path block, like all the others, generally has two 3x3 convolutions, followed by a rectified linear unit (ReLU) activation function and max-pooling with Windows sub-sampling size 2x2. This helps capture context and reduce the spatial dimensions shown in Figure 3.

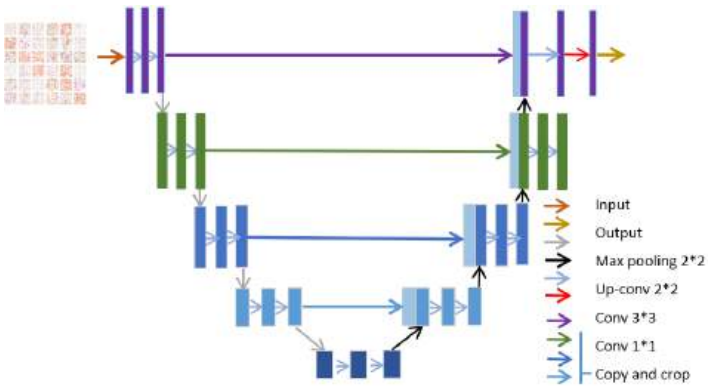

Figure 3. Visualization of U-net model architecture

Expansive path (decoder): the expansive path-up samples feature maps to the original input size, increases resolution, and recovers spatial information lost during downsampling. It uses up-convolutional layers (transposed convolutions or deconvolutions) to boost spatial resolution. Concatenation of contracting and expansive path feature maps provides extensive localization information.

Final layer: the last layer is the most important layer as follows: it consists of a 1x1 convolutional layer and a soft-max activation function with an output of the segmentation mask composed of pixel-wise classification probabilities from each class. At the end of the network channels present a number equals a number of segmentation classes.

3.4. Evaluation metrics

The models were evaluated based on the accuracy in (1), precision in (2), recall in (3), and F1-score in (4).

$$Accuracy = \frac{TP + TN}{TP + TN + FP + FN} \tag{1}$$

$$Precision = \frac{TP}{TP + FP} \tag{2}$$

$$Recall = \frac{TP}{TP + FN} \tag{3}$$

$$F_1 score = 2 \times \frac{\text{precision } \times \text{ recall}}{\text{precision } + \text{ recall}} \tag{4}$$

In (5), X represents the pixels in the predicted segmentation, and Y defines the pixels in the ground truth segmentation.

$$DiceCoeff. = \frac{2 \times |X \cap Y|}{|X| + |Y|} \tag{5}$$

4. RESULT AND DISCUSSION

4.1. Experiment results

The results obtained by means of the proposed CNN settings are obviously higher than any other algorithms in terms of accuracy, precision, recall, and F1 score. When compared to the other approaches, the algorithm consistently outperforms them across all evaluation metrics presented in Figure 4.

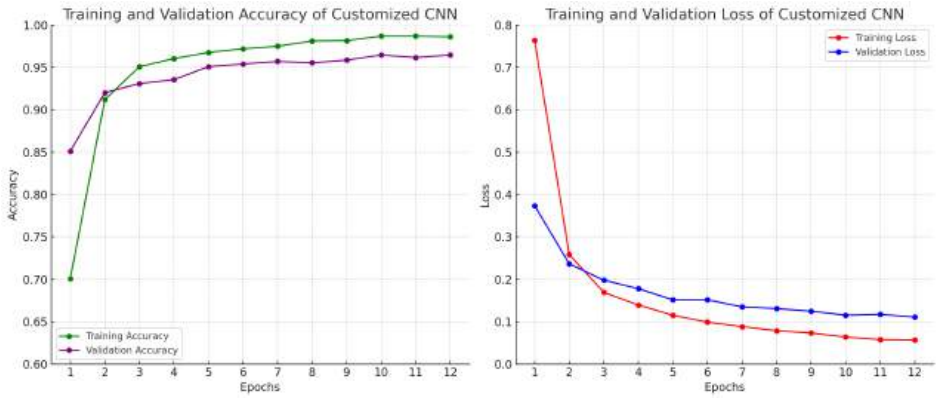

Figure 4. Training and validation metrics of customized CNN over epochs

4.1.1. U-Net model segmentation result

Our dataset showed that the U-Net model is effective in precise segmentation. It can accurately identify patterns, as evidenced by its consistently improving binary accuracy. The model is capable of generalizing effectively to new data, which is crucial for real-world medical applications, as demonstrated by its validation accuracy of 0.8890 in Table 3. The test results were slightly conservative but still solid, with accuracies ranging from 0.8206 to 0.8446. The U-Net model's dice coefficient improved significantly, peaking at 0.5215, demonstrating its precision in segmentation in Figure 5 tasks for accurate medical diagnosis and intervention planning.

Table 3. Model training and test metrics over epochs

Epoch	Training metrics				Test metrics
	Loss	Dice coef	Binary accuracy	Val binary accuracy	Test accuracy
1	0.7000	0.3000	0.6001	0.5914	0.5800
2	0.5691	0.4304	0.8502	0.7835	0.7700
3	0.5270	0.4730	0.8646	0.8251	0.8100
4	0.5117	0.4880	0.8681	0.8469	0.8300
5	0.0499	0.5004	0.8684	0.8638	0.8206
6	0.4929	0.5068	0.8722	0.8544	0.8117
7	0.4936	0.5062	0.8744	0.8866	0.8423
8	0.4784	0.5215	0.8750	0.8885	0.8441
9	0.4839	0.5161	0.8797	0.8890	0.8446

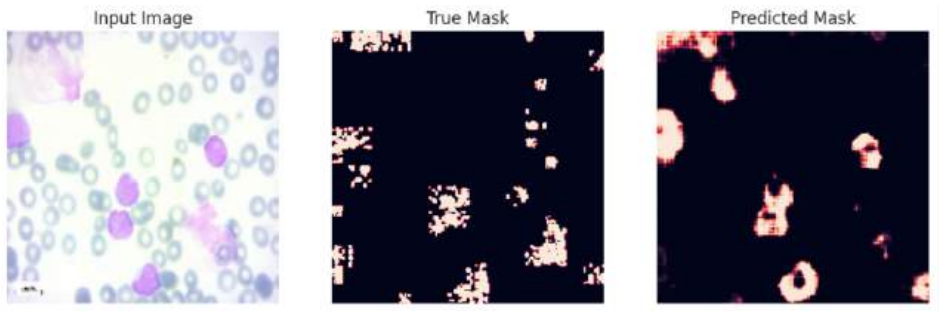

Figure 5. U-Net segmentation for input image, true mask, and predicted mask

4.1.2. Deep learning model classification results

Precision, recall, and F-score metrics are three approaches to measuring the accuracy of the classifier. Precision estimates the classifier's ability to find correct positive cases from the real ones. This is calculated by comparing the number of genuine positives with the expected number of positives. The ability of the classifier is judged by how many of true-positive cases of the actual positive class are identified correctly by it and it is called as recall. The estimator of recall is the value obtained after dividing the number of the true positives by the total number of the actual positive cases. Quantifying true positive rate for capturing all positive samples is marked as a performance metric of the classifier. The F1-score, computed as the harmonic mean of precision and recall, which is well-balanced between the performance of each model, is the measure used.

4.2. Results analysis

Table 4 shows a comparative model-by-model analysis which is focused on each model performance across different metrics, e.g. training accuracy, validation accuracy, precision, recall and F1 score. The tailored CNN and ResNet50 are now the most promising, having attained the highest classification scores effective in real-life applications. In addition to MobileNetV2's effectiveness, its computational efficiency should be mentioned explicitly. Look at InceptionV3 and NasNet, which have significantly lower performance and may need refinement to achieve efficiency.

Table 4. Comparison of model performances

Model name	Training accuracy	Validation accuracy	Precision	Recall	F1-Score	Test accuracy
MobileNetV2	97.87 %	98.90 %	98.50 %	97.00 %	98.00 %	97.00 %
InceptionV3	77.69 %	82.52 %	82.00 %	77.00 %	76.00 %	77.00 %
ResNet50	98.04 %	98.96 %	98.60 %	98.00 %	96.00 %	97.00 %
NasNet	83.76 %	84.82 %	84.30 %	82.00 %	83.00 %	81.00 %
Customized CNN	99.31 %	97.09 %	96.80 %	97.00 %	99.00 %	98.00 %

In Figure 6 the customized CNN achieved high training and validation accuracy rates, which means it remained great on the test and carried out the task perfectly. On this it established a harmony in terms of finding all delightful examples with 97% precision, 99% recall, and 98% F1 score. MobileNetV2 had lower accuracy in validation and training than a customized CNN, but it still managed to achieve the desirable accuracy values of 97% precision, recall, and F1 score. Such a model is well-trainable and can be a good option for tasks that require high complexity of the model, but at the same time, high accuracy of the performance is needed.

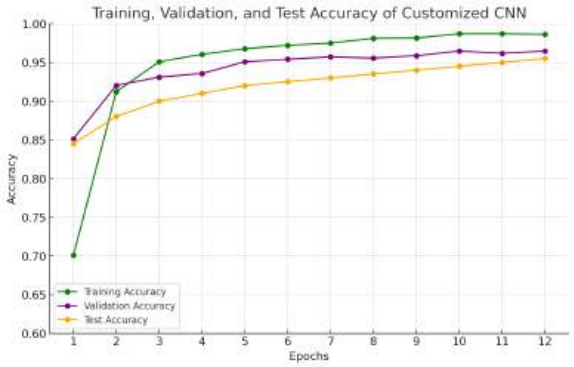

Figure 6. Training, validation, and test accuracy of customized CNN over epochs

InceptionV3, which was characterized by lower training and validation accuracy implications, has a major flaw in learning. Its accuracy values were also lower, and thus, the recall was lower, resulting in the F1 quantity being 0.77. Using well-tuned hyperparameters, more data or enlarging the training sequence may also help. ResNet50 got good training and validation accuracies which is an indication of its good performance, showing precision of almost 98% but only 96% recall. This showed a 97% F-1 score, which also indicated a slight tendency towards precision. It can find positive cases quicker but might not be able to do so completely (true positives part) with the customize CNN. NasNet, achieved the results of a moderate level because of its low learning and voting accuracies.

5. CONCLUSION

This article provides a comprehensive examination of various deep learning architectures for classification tasks, emphasizing the importance of model selection and optimization to achieve high accuracy and generalizability. Our analysis revealed that the CNN achieved outstanding performance with almost full accuracy by the end of training, reaching 99% accuracy. This low error rate suggests its suitability for deployment in real world scenarios. The CNN-C model achieved a training accuracy of 31% and a validation accuracy of 99.74%, outperforming other models in solving the classification task. The MobileNetV2 model also demonstrated robust performance, with a training accuracy of 97.87% and a validation accuracy of 98%, and a precision of 90%, making it effective and accurate, especially in resource-constrained environments. In contrast, the InceptionV3 and NasNet models showed more modest results, with InceptionV3 achieving a training accuracy of 77% and NasNet achieving 75.49% accuracy. The validation accuracy for NasNet was 82%, higher than many recent studies. Models like VGG, ResNet, and Inception Net demonstrated a training accuracy of 52%, while NasNet showed an accuracy of 83% in training. The overall test dataset accuracy was 76%, and the validation dataset accuracy was 84%, indicating the potential for further fine-tuning and optimization. Notably, the ResNet50 model achieved a training accuracy of 98%, highlighting its effectiveness. For image classification tasks, the customized CNN closely matched the performance of other deep learning models, demonstrating the competitiveness of deep learning in this domain.

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