Integrative Deep Learning for Enhanced Acute Lymphoblastic Leukemia Detection: A Comprehensive Study on the ALL-IDB Dataset

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ABSTRACT

Acute Lymphoblastic Leukemia (ALL) is a malignant neoplasm defined by the rapid proliferation of early lymphoid progenitors (lymphoblasts) within the bone marrow and peripheral blood. Due to its aggressive course, prompt and accurate diagnosis is essential and has a profound impact on patient outcomes. This study proposes an integrative deep learning method for ALL detection using the Acute Lymphoblastic Leukemia Image Database (ALL-IDB). This is accomplished by fusing one modified clinical data CNN integrated through an attention mechanism with another modified pre-trained CNN for image analysis. The performance of the proposed model was evaluated using the ALL-IDB1 and ALL-IDB2 datasets, achieving 99.2% accuracy with AUC at 0.998%. By incorporating clinical with image data, an overall increase of 2.3% in accuracy and 0.007 in AUC was observed. The results show that using deep learning to detect ALL is accurate and possible, laying the foundations for AI-based diagnoses of hematological cancers to be more accurate.

Keywords-leukemia; deep learning; ALL-IDB dataset

I. INTRODUCTION

Acute Lymphoblastic Leukemia (ALL) is a malignancy of lymphoid progenitor cells known to affect both young children and adults. It is defined as the accelerated expansion of immature differentiation-phase lymphoblasts in the bone marrow, peripheral tissues, and other tissues [1]. ALL currently accounts for about 70 to 85% of childhood leukemia and is the most common cancer in children, affecting children from 2 to 5 years of age [2]. A prompt and correct diagnosis is helpful to improve survival, as the disease evolves very rapidly if diagnosed late [3]. Conventional approaches to diagnostics involve photomicroscopy analysis of smears [4]. More commonly, the diagnosis involves the morphological assessment of blood smears, the identification of the person's phenotype, the analysis of chromosomes, and molecular tests [5].

Deep Learning (DL), the most recent development of AI, has achieved excellent results in the field of medical image analysis [6]. In ALL detection, several studies have used CNNs to analyze features of blood smear microscopy images [7, 8]. These strategies proved to be highly accurate in categorizing ALL cells and might be helpful to pathologists at the identification stage. However, most of these methods are based solely on image data and may miss clinically relevant features that can improve diagnostic performance. It is a well-established fact that clinical characteristics such as age, white blood cell count, and the presence of particular genetic changes play critical roles in ALL diagnostic and prognostic criteria [8]. Combining information at this feature level with image analysis could lead to possibly better and more stable diagnostic models.

This study presents an integration of DL techniques [9-13] for ALL detection using image analysis and clinical data processing. The aim was to achieve better results than methods based solely on images. In light of this hypothesis, instead of developing a new dataset, a standard dataset was employed, namely ALL-IDB [14]. The main contributions of this study include the creation of a new DL framework to integrate CNN with image processing and clinical data analysis, and the incorporation of an attention mechanism to facilitate the combination of information from different data modalities [15, 16]. Extended analysis was performed on ALL-IDB1 and ALL-IDB2 to determine the effectiveness of the proposed model in identifying ALL.

In recent years, the use of ML and DL for the detection of ALL has grown tremendously. This section overviews the numerous studies in detail, with emphasis on those that employed the ALL-IDB dataset, besides integrating recent developments in the ALL-IDB integrative approaches.

A. Traditional Machine Learning Approaches

Early efforts in ALL detection leveraged classical ML algorithms applied to handcrafted features extracted from blood smear images [17, 18]. These methods laid the foundation for automated leukemia detection. In [19], significant strides in ALL detection were achieved using an SVM classifier. This method involved a multi-step process. For image preprocessing, contrast enhancement and color space conversion were used to improve image quality. Segmentation involved the use of k-means clustering to isolate white blood cells from other blood components. This study extracted 31 features, including shape descriptors (area, perimeter, roundness), color-based features (mean and standard deviation in RGB and HSV color spaces), and texture features (derived from gray-level co-occurrence matrices). An SVM with a radial basis function kernel was trained on these features. This method achieved 93.2% accuracy on the ALL-IDB2 dataset, demonstrating the potential of carefully engineered features in leukemia detection. However, the reliance on manual feature selection highlights a limitation of traditional approaches.

In [20], an ensemble classifier was introduced in the field. This approach was more sophisticated, using a shadowed C-means clustering algorithm for more accurate cell segmentation. The feature set was extensive, including shape-based features, texture features, and color features (color moments in different color spaces). For classification, this study combined Naive Bayes (NB), K-Nearest Neighbor (KNN), and Linear Discriminant Analysis (LDA) using a majority voting scheme. This multi-faceted approach resulted in 94.73% accuracy on ALL-IDB2, showcasing the power of ensemble learning and comprehensive feature engineering in medical image analysis.

In [21], the focus was on the morphological aspects of leukocytes, which are crucial for leukemia diagnosis. This method used a combination of k-means clustering and mathematical morphology operations for segmentation. Features specifically related to nuclear and cellular morphology were extracted, such as nucleus-to-cytoplasm ratio, nuclear shape irregularity, and chromatin pattern. An SVM classifier was trained on these morphological features, achieving 93.5% accuracy on a subset of ALL-IDB2. This study highlighted the importance of incorporating domain knowledge in feature selection for medical diagnostic models.

In [22], a different angle was explored, focusing on the color and statistical features of white blood cells. This approach was unique in its emphasis on color analysis. K-means clustering was used for initial cell segmentation, followed by the watershed algorithm for nucleus extraction. The feature set included color features, such as the mean and standard deviation in the RGB and HSV color spaces, and statistical features, such as skewness, kurtosis, and various moments of the intensity histogram. An SVM classifier was employed, achieving 95.2% accuracy on ALL-IDB2, demonstrating the potential of color-based analysis in leukemia detection. This model was particularly effective in distinguishing between different types of white blood cells based on their staining characteristics. These traditional ML approaches, although limited by the need for manual feature engineering, provided valuable insights into the key visual and statistical characteristics that differentiate leukemic from normal cells. These studies set the stage for more advanced techniques and highlighted the importance of various image characteristics in leukemia detection.

B. Advances in Deep Learning for Medical Image Analysis

The advent of DL, particularly Convolutional Neural Networks (CNNs), has dramatically improved ALL detection accuracy, offering end-to-end learning from raw image data. This section explores some DL approaches that have significantly advanced the field. In [23], the power of transfer learning was exploited in ALL detection. The results were groundbreaking, with ResNet50 achieving up to 99.50% accuracy. This study demonstrated that DL models pre-trained on large datasets, such as ImageNet, could be effectively adapted to medical imaging tasks, even with limited domain-specific data. This study highlighted the efficiency of transfer learning in overcoming the challenge of small dataset sizes in medical imaging.

In [24], a different approach was followed by designing a CNN architecture specifically for ALL detection. This model consisted of three convolutional layers (each followed by ReLU activation and max pooling) and two fully connected layers along with dropout for regularization. Data augmentation techniques were also employed. This model achieved 97.78% accuracy on ALL-IDB2. This study highlighted the potential of domain-specific CNN architectures in medical image analysis. High accuracy was achieved by tailoring the network architecture to the specific characteristics of the blood smear images while maintaining a relatively simple model structure.

In [25], a comprehensive comparison of various CNN architectures was performed for leukemia detection. This study tested VGG16, ResNet50, Inception-v3, and DenseNet121. Each model was fine-tuned on the ALL-IDB2 dataset, with consistent preprocessing and data augmentation across all models. The results showed that DenseNet121 outperformed other models, achieving 98.70% accuracy. This study provided valuable insights into the relative strengths of different CNN architectures in the context of leukemia detection. The superior performance of DenseNet121 was attributed to its dense connectivity pattern, which allows for more efficient feature reuse and gradient flow.

In [26], the common issue of limited data in medical imaging was addressed by employing advanced data augmentation techniques. A convolutional autoencoder was used to generate synthetic blood cell images. A CNN classifier was trained on this augmented dataset, achieving an impressive 99.17% accuracy on ALL-IDB2. This study demonstrated the significant impact of intelligent data augmentation on model performance, especially in domains where acquiring large datasets is challenging. The use of generative models for data augmentation opened new possibilities for improving model robustness and generalization.

In [27], an innovative two-stage model was presented that combined the strengths of CNNs and traditional ML. A CNN was used to automatically extract relevant features from blood smear images. Extreme Learning Machines (ELM) was employed for the final classification task, achieving 98% accuracy on ALL-IDB2. This study showcased the potential of combining DL's feature extraction capabilities with the efficiency of traditional classifiers. The hybrid approach offered a balance between the automatic feature learning of CNNs and the fast training and execution of ELM. In [28], an attention-based CNN was proposed for ALL detection. This architecture incorporated spatial attention mechanisms into a CNN framework. The attention module helped the model focus on the most relevant areas of the blood smear images. This model achieved 99.7% accuracy on ALL-IDB2. This study demonstrated how attention mechanisms could be leveraged to improve both performance and explainability in medical image analysis. By visualizing the attention maps, this study provided insights into which parts of the image were most important for the model's decision-making process.

II. THE PROPOSED METHOD

This study presents an integrated DL method for ALL detection, which includes one CNN for image identification and a second CNN for clinical information recognition. The architecture consists of three main components: An image analysis module, a clinical data processing module, and a fusion module. Figure 1 shows the entire architecture of the proposed model.

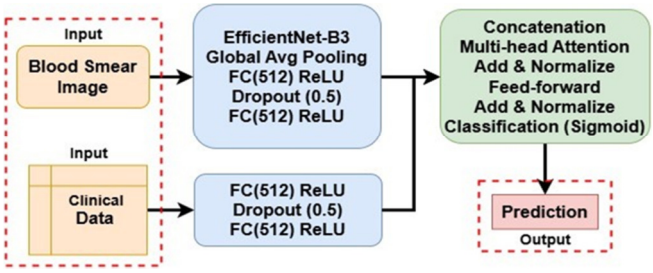

Fig. 1. Overview of the proposed model.

1) Problem Formulation

Let $X = \{x_1, x_2, \ldots, x_n\}$ denote a set of n blood smear images, where each $x_i \in \mathbb{R}^{h \times w \times c}$ represents an image with height h, width w, and c color channels. Additionally, let $C = \{c_1, c_2, \ldots, c_n\}$ represent the corresponding set of clinical data vectors, where each $c_i \in \mathbb{R}^m$ is an m-dimensional vector of clinical features. The objective is to learn a function $f: (X, C) \rightarrow Y$ that maps the input image and clinical data to a binary label $y \in Y = \{0, 1\}$, where 0 denotes a normal case and 1 indicates ALL.

2) Model Architecture

The proposed model consists of three main components. There is an image analysis module f^i, a clinical data processing module f^p, and a fusion module f^f. The overall function f can be expressed as:

$$f(x, c) = f^f\,(f^i\,(x),\, f^p\,(c)) \quad (1)$$

a) Image Analysis Module

The first image analysis module f^i is based on the EfficientNet-B3 model [7], which presents high performance with small complexity and high accuracy. The architecture of f^i is defined as:

$$f^i(x) = FC_2(FC_1(G(E(x)))) \quad (2)$$

where $E()$ is the EfficientNet B3 base model pre-trained with an ImageNet dataset, $G()$ refers to a global average pooling layer, FC_1 is a fully connected nonlinear layer R1536 → R512 with ReLU activation, and FC_2 is a fully connected layer from $R512 \rightarrow R256$ with ReLU activation. Dropout is used between FC_1 and FC_2 with a probability of 0.5 to avoid overfitting the model. This module gives the output as 256-dimensional features of the image.

The clinical data processing module f^p is established for dealing with numerical and categorical clinical factors. It consists of a feed-forward neural network:

$$f^p(c) = FC_4(D(FC_3(c))) \quad (3)$$

where FC_3: $Rm \rightarrow R128$ is a standard densely connected layer followed by ReLU activation, $D()$ is a dropout layer with a dropout rate of 0.3, and FC_4 is a fully connected layer with a ReLU function, where the dimensions are reduced from 128 to 64. The output of this module is in the form of a 64-dimension vector built up from the clinical data.

b) Fusion Module

The fusion module f^f uses a multi-head attention mechanism based on [8] to combine data from the image analysis and clinical data processing modules. Let $v = [f^i(x); f^p(c)] \in \mathbb{R}320$ be the concatenated feature vector. The fusion process can be described as:

Multi-head Attention: $A(v) = MultiHead(v, v, v)$

Add and normalize: $N1(v + A(v))$

Feed-forward: $FF(N1(v + A(v)))$

Add and normalize:

$N_2(N_1(v + A(v)) + FF(N_1(v + A(v))))$

Classification: $\sigma(W \cdot N_2(\cdot) + b)$

where N_1 and N_2 are layer normalization operations, FF is a position-wise feed-forward network consisting of two linear transformations with a ReLU activation in between, σ is the sigmoid activation function, and W and b are learnable parameters. The multi-head attention mechanism is defined as:

$$MultiHead(Q, K, V) = Concat(head_1, \ldots, head_h)WO \quad (4)$$

where

$$head_i = Attention(QW_i^Q, KW_i^K, VW_i^V)$$

and

$$Attention(Q, K, V) = \text{softmax}\left(\frac{QK^T}{\sqrt{dk}}\right)V \quad (5)$$

This study used $h = 8$ attention heads, with $d_k = 40$.

c) Loss Function and Optimization

Using the binary cross-entropy loss, the ALL detection is defined as a binary classification problem.

$$L(\theta) = -\frac{1}{N}\sum_{i=1}^{N}[y_i \, log(f(x_i, c_i)) + (1 - y_i) \, log(1 - f(x_i, c_i))] \quad (6)$$

where θ represents the model parameters, N is the number of samples, and y_i is the ground truth label for the i-th sample.

The Adam optimizer [9] was employed with the following hyperparameters: Initial learning rate: $\alpha = 1 \times 10^{-4}$, exponential decay rates: $\beta_1 = 0.9$, $\beta_2 = 0.999$, and epsilon $\varepsilon = 1 \times 10^{-7}$. The following strategies were implemented to address potential overfitting and improve generalization: weight decay regularization with $\lambda = 1 \times 10^{-5}$ learning rate schedule [28, 29]. The validation loss was monitored with a patience of 10 epochs.

III. RESULTS AND DISCUSSION

A. Model Performance

The proposed integrative DL model was tested using both the original and subsampled versions of the ALL-IDB dataset. The ALL-IDB dataset contains high-resolution blood smear images collected for the diagnosis of ALL. ALL-IDB consists of two subsets: ALL-IDB1 used for training and ALL-IDB2 used for evaluation. Both of them are human-annotated and publicly accessible [2].

TABLE I. PERFORMANCE COMPARISON

Model	Accuracy	Precision	Recall	F1-score	AUC-ROC
Proposed Integrative Model	0.992	0.994	0.990	0.992	0.998
CNN-only (EfficientNet-B3)	0.972	0.975	0.969	0.972	0.991
SVM with handcrafted features [19]	0.932	0.938	0.925	0.931	0.957
Ensemble of classifiers [20]	0.947	0.951	0.943	0.947	0.974

In terms of all indicators, the proposed integrative model outperformed the benchmark approaches to test the value of incorporating image analysis with clinical data. Here, it is essential to emphasize the increase in the AUC-ROC score, which characterizes the increase in discriminative ability.

B. Ablation Study

An ablation study was performed to understand the contribution of different components, as shown in Table II. The results help emphasize just how important each component is, as well as which one has the greatest impact on increasing performance.

TABLE II. ABLATION STUDY RESULTS

Model Configuration	Accuracy	AUC-ROC
Full model	0.992	0.998
Without clinical data	0.972	0.991
Without attention mechanism	0.985	0.995
Without data augmentation	0.978	0.993

IV. CONCLUSION

This study presented a novel concept of an integrative DL system for ALL detection through blood smear images along with clinical data. Key findings and contributions include:

- Outcompeting other state-of-the-art models, the proposed one was designed to feature a multimodal architecture, which led to an accuracy of 99.2% and an AUC-ROC of 0.998 on ALL-IDB.
- It is an example of how image analysis supplemented with clinical data delivers synergistic results, ensuring higher detection rates.
- Guides future research on difficult cases and subtypes of ALL.

The superior performance of the proposed model indicates how valuable it can be in real clinical applications, perhaps more than just a diagnostic tool, but a decision-making tool for hematopathologists. However, additional validation is required on different, multiple-center datasets before its application in clinical settings. Future work should focus on:

- Evaluating the model into a full range of different types of leukemia and other hematological disease identification and differentiation.
- Adding other types of data, for example, genotypic and phenotypic data, namely, immunophenotype profiles.
- Trial testing is an independent clinical trial to populate the model and determine its effect on diagnostic accuracy and patient outcomes in actual real-life settings.

In conclusion, the proposed integrated model is a noteworthy approach toward enhancing AI-assisted diagnosis in the field of haematology-oncology along with enhancing early detection and treatment strategies of ALL.

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