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REVIEW ARTICLE

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RECENT DEVELOPMENTS IN THE DETECTION AND CLASSIFICATION OF LEUKEMIA - A COMPREHENSIVE EVALUATION OF DEEP LEARNING SOLUTIONS

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Abstract: The blood is essential for keeping us alive since it carries oxygen, nutrients, and immune cells around the body. Leukemia is a type of cancer that affects the tissues that make blood. It can be deadly if not caught early. So, finding it early is for getting the right therapy and living longer. Blood smear analysis using a microscope has long been a major way to diagnose diseases. However, looking at these pictures by hand takes a lot of time, is easy to make mistakes, and isn't always consistent. Machine learning (ML) and other automated methods have been used to solve these problems by looking at enormous datasets and finding patterns that are difficult to see by hand. But ML methods frequently need people to choose the right features, and they might not work well with data that is complicated and has a lot of dimensions. Deep learning (DL) solves these problems by automatically learning important aspects from raw medical images. This makes it easier and faster to find leukemia. DL models, notably convolutional neural networks (CNNs), have shown that they can classify different types of leukemia better than other methods with little help from people. This article gives a full picture of the most recent improvements in DL methods for finding leukemia and shows how they could change the way blood tests are done. Also, a comparison of several DL models is shown, along with their pros and cons, to that they can still provide more accurate diagnoses and lower the chance of human error. There is also a discussion of the problems and opportunities in this sector, with a focus on how DL can help find leukemia early and accurately.

Keywords: Deep Learning; Leukemia Detection; Peripheral Blood Smear Samples; Machine Learning; Flow Cytometry

I. INTRODUCTION

Leukemia, a kind of blood cancer, starts in the bone marrow and stops the production of white blood cells (WBCs). It makes aberrant, immature white blood cells called blasts or leukemia cells grow quickly. These cells don't work right and make the immune system weaker [1]. These strange cells crowding the bone marrow make it harder for the body to make healthy red blood cells (RBCs), white blood cells (WBCs), and platelets [2]. Symptoms like tiredness, frequent infections, and easy bruising and bleeding are caused by low oxygen levels, a weakened immune system, and slower blood clotting [3]. Fig. 1 depicts the way normal blood cells and damaged blood cells are different.

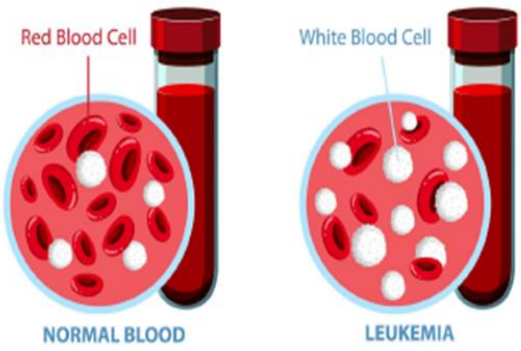

Figure 1. Normal vs Leukemia Blood Cell

A. Different Types of Leukemia

Acute and chronic leukemia are the two primary categories. These are defined as:

1. *Acute leukemia:* It occurs when the number of red blood cells, which are still immature, surges dramatically. These excess cells crowd the bone marrow, preventing it from producing healthy blood cells, which leads to low haemoglobin and platelet levels [4]. Because the disease progresses quickly and the malignant cells can enter into the circulatory system and beyond, urgent treatment is necessary. Among children, acute leukemia is by far the most prevalent form of the disease [5].
2. *Chronic leukemia:* It involves a slow build-up of abnormal, but more mature, WBCs (and sometimes RBCs). The disease usually progresses over months or even years, with these abnormal cells being produced in excess [6]. Unlike acute leukemia, chronic leukemia often doesn't require immediate treatment and may be closely monitored before starting therapy to achieve the best results. Although it can strike anyone at any age, it primarily impacts the elderly [7,8].

There are two subtypes of acute leukemia according to the French American British (FAB) classification: acute lymphoblastic leukemia (ALL) and acute myeloid leukemia (AML). Conversely, Chronic Lymphocytic Leukemia (CLL) and Chronic Myeloid Leukemia (CML) are the two main types of chronic leukemia [9].

1) Acute Leukemia Types

a) Acute Lymphoblastic Leukemia (ALL)- It is a type of acute leukemia that starts in the lymphoid stem cells and affects lymphocytes. Although adults are not immune, it most frequently affects youngsters [10]. Fig. 2 shows the growth of ALL.

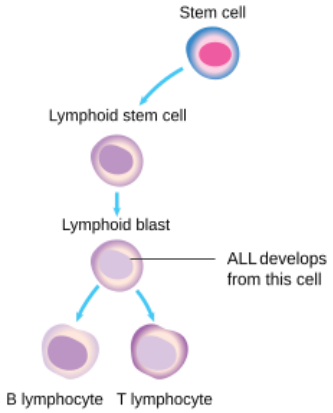

Figure 2. Acute Lymphoblastic Leukemia [11]

b) Acute Myeloid Leukemia (AML)- It also progresses rapidly and begins in the myeloid stem cells, impacting the development of myeloid cells. Unlike ALL, AML is more common in adults and less frequently found in children [12]. Fig. 3 shows the growth of AML.

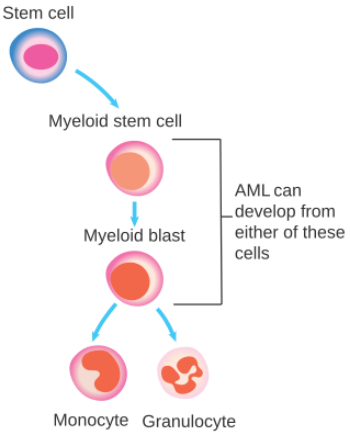

Figure 3. Acute Myeloid Leukemia [13]

2) Chronic Leukemia Types:

The chronic forms of lymphocytic leukemia and myeloid leukemia involve the same cell types but progress much more slowly than the acute forms, with few individuals live longer without treatments.

3) Rare Leukemia Types:

There are few rare types of leukemia exists which are defined as follows.

1. ***B-cell prolymphocytic leukemia (B-PLL)*** It's generated by B cells, which are white blood cells that have a role in the immunological response. Various forms of leukemia and lymphoma, as well as other malignancies of the blood and bone marrow, can make a diagnosis of this illness difficult. Although B-PLL typically progresses rapidly, about 10% of patients show no symptoms at the time of diagnosis [14].
2. ***Blastic plasmacytoid dendritic cell neoplasm (BPDCN)*** is a very aggressive kind of acute leukemia that can strike anyone at any time, however it is more commonly found in more advanced age, with around half of the cases found in individuals aged 70 or older. This cancer arises from plasmacytoid dendritic cells, a rare immune cell typically located in the bone marrow, blood, skin, spleen and lymph nodes. Chemotherapy has long been the standard treatment, but stem cell transplants are an option for younger, healthier individuals.
3. ***Chronic myelomonocytic leukemia (CMML)*** has too many white blood cells (WBCs), which help the immune system fight infections, and too few healthy blood cells (HBCs). One way to treat the condition that can work is stem cell transplantation. Chemotherapy, on the other hand, doesn't cure the condition. It can only kill cancer cells and help the body make healthy blood cells. People with low blood counts can also have blood transfusions and medications that help cells proliferate [15].
4. In ***Hairy cell leukemia (HCL),*** The lymphoid stem cells make too many abnormal B lymphocytes. The disease gets its name from the hair-like projections that are common on the surface of these cancerous cells. Most of the time, the disease progresses slowly, and sometimes it stays stable without causing any visible symptoms. Chemo, immune, and targeted therapies are available for use when treatment is required [16].
5. ***Juvenile myelomonocytic leukemia (JMML)*** primarily affects young children, typically those under the age of 4. In JMML, the cancer originates in monocytes. The disease grows more quickly than chronic leukemia, but less aggressively than acute leukemia. The abnormal cells tend to collect in organs, so children may also experience an enlarged spleen and difficulty breathing due to cancer cells building up in the lungs. The standard treatment for JMML is a stem cell transplant, which offers the best chance for a cure.
6. ***Large granular lymphocytic leukemia (LGLL)*** originates from lymphocytes, specifically mature T cells and natural killer (NK) cells. The aberrant T or NK cells proliferate uncontrollably, displacing normal blood cells. The majority of patients are elderly, and over 20% of those people also suffer from another autoimmune disease, like rheumatoid arthritis. The NK cell version of LGLL can be more aggressive than the T cell type, but in general, the disease advances slowly. Treatment usually involves immunosuppressive drugs to control the overactive immune cells. Chemotherapy may also be used. Additionally, medications are given to manage cytopenias, which means low levels of healthy blood cells [17].
7. ***T-cell prolymphocytic leukemia (T-PLL)*** originates from T-lymphoid stem cells. The exact cause of T-PLL remains unknown, but recent research has identified several genetic and chromosomal abnormalities associated with the disease. Although T-PLL may initially present as slow-growing, it typically progresses to a more aggressive phase. Common symptoms include elevated white blood cell counts, enlarged lymph

nodes, liver and spleen, skin rashes, and fluid build-up around the lungs or heart.

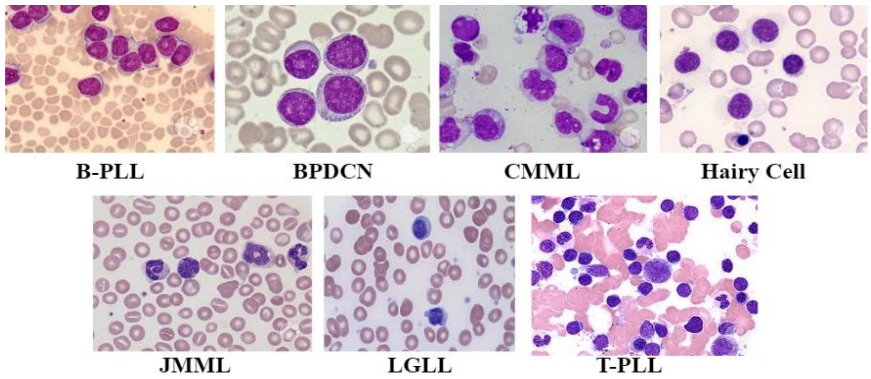

Figure 4. Rare Types of Leukemia

Currently, no therapies are specifically approved for T-PLL. However, monoclonal antibody therapy has shown a high response rate, and stem cell transplantation is recommended for eligible patients who achieve remission. Fig. 4 shows the sample images of these rare type leukemias.

B. *Treatment Options*

Restoring normal blood cell production and eliminating malignant cells are part of leukemia treatment. Bone marrow transplant, radiation therapy, immunotherapy, targeted therapy, and chemotherapy are among the treatment possibilities. The patient's health, the stage of the leukemia, and the kind of leukemia determine the treatment approach. Throughout the course of treatment, imaging and laboratory tests are employed to monitor patient response and adjust therapy as needed.

1) Physical Examination: The initial evaluation often involves a physical examination to assess clinical signs indicative of leukemia. Lymphadenopathy and enlarged liver and spleen can be felt during this test. Additionally, inspection of the eyes, oral mucosa, and skin is conducted to identify signs such as infections, bruising, and bleeding, which are commonly associated with leukemia. A neurological assessment may be performed to evaluate balance, sensation, and reflexes, as neurological involvement can occur in some cases [18].

2) ***Laboratory and Blood Tests:*** Laboratory tests, particularly blood tests, serve as primary diagnostic tools for leukemia. In CLL, blood tests may suffice for diagnosis, whereas in acute lymphocytic leukemia ALL and other subtypes, bone marrow analysis is generally required [19].

- *Complete Blood Count (CBC):* The complete blood count (CBC) is a fundamental hematological test that quantifies the levels of RBCs, WBCs, and platelets in a patient's blood sample. Abnormalities in these parameters often serve as initial indicators of hematologic malignancies such as leukemia.
- *WBC Differential:* The differential count provides a quantitative analysis of the several white blood cell subtypes, such as basophils, eosinophils, monocytes, and lymphocytes. The presence of immature or atypical leukocytes can offer critical diagnostic clues, particularly in acute leukemia where blasts are frequently detected.
- *Peripheral Blood Smear:* A peripheral blood smear is a stained film of blood made from a small sample of peripheral blood that is examined under a microscope. This test enables detailed morphological assessment of blood cells. Abnormalities such as anisocytosis, poikilocytosis, or the presence of blast cells are characteristic findings in various forms of leukemia. The qualitative visual analysis provided by the smear complements the quantitative data from the CBC and differential, thereby enhancing diagnostic accuracy [20].

3) Flow Cytometry: Flow cytometry is utilized to analyze the DNA content and proliferative activity of leukemia cells. This technique involves labeling cells from blood or bone marrow with specific antibodies targeting surface proteins. The presence of a monoclonal population suggests malignancy of leukemia in the blood [21].

4) Biopsy Procedures: Bone marrow biopsy is critical for confirming diagnosis, classifying leukemia type, assessing tumor burden, and detecting disease spread. Bone marrow aspiration retrieves liquid marrow, while a core sample of bone and marrow tissue is obtained during a bone marrow biopsy [22].

5) Imaging Modalities: Imaging studies assist in staging and detecting complications related to leukemia. Chest X-rays evaluate for pulmonary infections.

- *Chest X-ray (CXR):* A chest X-ray is a fast and widely used imaging diagnostic that can detect infections, especially in people with leukemia that have a low white blood cell count and are therefore more susceptible to infections. It is also useful for identifying enlarged lymph nodes in the chest, which may occur in cases of ALL and CLL where cancer cells spread to lymphatic tissues.
- *Computed Tomography (CT):* In a CT scan, X-rays are combined from various angles to provide very detailed cross-sectional pictures of the body. Chest computed tomography (CT) scans are preferred over traditional X-rays for diagnosing enlarged lymph nodes and evaluating lung infections in leukemia patients. CT scans can also evaluate spleen enlargement (splenomegaly), a common complication in many types of leukemia due to the accumulation of cancer cells.
- *Positron Emission Tomography (PET) Scan:*

Functional imaging combining PET and CT scans reveals regions of high metabolic activity, which usually indicate the presence of cancer cells absorb a higher concentration of the radioactive tracer, resulting in them standing out more on the scan, as a tiny quantity of tracer is given into the body. PET scans help locate leukemia cells in different tissues and assess how widespread the disease is.

- *Magnetic Resonance Imaging (MRI):* MRI is a non-invasive imaging technique that creates high-resolution pictures of inside organs and tissues by combining radio waves with strong magnets. In cases of acute myeloid leukemia (AML) and acute lymphoblastic leukemia (ALL), it is extremely helpful in determining whether the cancer has progressed to the central nervous system. It can also reveal abnormalities in organs or swollen lymph nodes.
- *Ultrasound:* Ultrasound imaging captures images of internal organs and lymph nodes in real-time by the use of high-frequency sound waves. It is a radiation-free method used to examine whether leukemia has spread to the liver, spleen, kidneys, or lymph nodes.
- *Two-Dimensional Echocardiography:* This specialized ultrasound shows the heart in motion and is used to monitor cardiac health, particularly in leukemia patients receiving chemotherapy drugs like anthracyclines, which can damage heart tissue. By using sound waves to form images of the beating heart, physicians can assess heart function before, during, and after chemotherapy to manage potential side effects effectively [23].

Depending on the type and stage of leukemia, there are different imaging tests to assess complications, detect organ involvement, and monitor treatment effects. However, human intervention in the diagnosis of blood diseases such acute leukemia, requires highly experienced medical professionals to achieve accurate and early diagnosis. Blood cells' complicated morphology, noise, blurred images, weak edges, intensity changes, and overlapping cells are some of the obstacles that can make this process difficult. These problems make microscopy analysis hard, prone to mistakes, and take a long time. Because of this, Computer Vision and Artificial Intelligence (AI) can help doctors make accurate and early diagnoses of blood illnesses like leukemia [24]. Because of the information these systems give, doctors can better detect ailments and come up with good treatment strategies. This is good for patients. Machine learning (ML) is a popular subject of AI that is already being used in medical research since it focuses on algorithms and mathematical relationships. ML lets computers learn from their mistakes even if they do not know anything about them before [25].

C. *Steps in Image Processing*

To find leukemia using computer vision, a series of steps for analyzing images must be followed in a specific order.

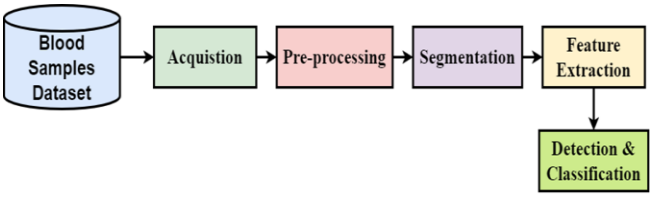

Figure 5. Image processing techniques

Fig. 5 shows that these phases normally include getting the image, processing it, breaking it up into parts, picking out features, and finally, putting it into a category. At each phase, little blood smear images are gradually improved and studied to help with the right diagnosis.

1) Image Acquisition: The first step is to get the images, which are blood smear images taken with a digital microscope. The quality of the picture taken depends on several things, such as the lighting and the camera's resolution. Getting clear pictures of blood cells requires the right amount of light.

2) Pre-processing: Pre-processing procedures improve the image after acquisition and prepare it for further analysis. Before processing, you might need to do things like remove noise, improve contrast, normalize, or change the color space. These techniques help improve the visuals and cut down on data variations that aren't needed.

3) Segmentation: The next important step in the process is segmentation. This stage is all about breaking the image up into several areas that have similar traits. When it comes to finding leukemia, segmentation mostly means separating white blood cells (WBCs) from red blood cells (RBCs), platelets, and the background. The main goal is to get the nucleus out of the WBCs since looking at the shape of the nucleus is very important for advising normal cells from cancer cells.

4) Feature Extraction: Feature extraction turns the different parts of an image into a set of numbers that describe them in a way that is useful for classification. Some of these features are shape descriptors (like perimeter, area, and roundness), color features (like mean intensity and histogram values), and texture features (like entropy, contrast, and homogeneity). By reducing the visual input to relevant parameters, feature extraction simplifies the subsequent classification work while keeping diagnostic information.

5) Detection and Classification: During the detection phase, the retrieved features are used to identify the difference between normal and pathological white blood cells. This means figuring out if the WBCs that appear have signs of leukemia, like changes in the shape of the nucleus, the texture of the cytoplasm, or the structure of the cell as an entirety. The categorization stage occurs after the discovered WBCs are placed into groups that have already been set up. This step means being able to recognize the difference between healthy cells and cancerous cells, like lymphoblasts (which are linked to acute lymphoblastic leukemia) or myeloblasts (which are linked to acute myeloid leukemia). Supervised learning techniques or neural networks trained on labeled datasets are usually used to do classification. The results of this step give important diagnostic information on the type and presence of leukemia [26].

Using these technologies to handle medical data has produced amazing results, and they have been quite useful in finding out exactly is wrong with people. ML approaches make it easier to extract and evaluate image features in medical image processing. This, in turn, makes the complicated medical decision-making procedures better.

However, ML methods depend on manually created features and rely a lot on the quality of those features, which could make it difficult for them to find complex patterns in the data. On the other hand, DL models can automatically learn hierarchical features from raw images. This makes it

easier to represent and categorize the images. On the other hand, DL methods can automatically learn features from images that haven't been processed. Without having to manually extract features, models like CNNs can find precise patterns and changes in blood test images [27]. This makes DL models better at diagnosing leukemia and more accurate.

The goal of this research is to give a full evaluation of different DL classification methods for diagnosing leukemia using blood test analysis. It also examines their techniques used, advantages, and limitations. A comparison of these methods is also provided to show their relative performance and to highlight areas for future research. The following is the paper's structure: Leukemia prediction and classification using blood test data is covered in Section II, which examines DL frameworks. Section III compares the reviewed methods in terms of architecture, datasets, and evaluation metrics. Section IV evaluates the performance of existing approaches, including accuracy and efficiency. Section V provides a concise overview of the results and recommendations for further study to round up the work.

II. Survey on Leukemia Detection and Classification using Deep Learning Models

Bukhari et al. [28] created a convolutional neural network (CNN) model to detect leukemia cancer in very little blood samples. At first, the dataset was expanded by rotating and randomly shifting samples to increase its size. These samples were then processed through a series of convolutional and max pooling layers, which extract and condense important spatial features. To further enhance the network's focus on the most informative channels, squeeze-and-excitation blocks are integrated into the CNN architecture. These blocks recalibrate feature maps by modeling channel-wise dependencies, emphasizing crucial patterns relating to leukemia. Finally, the processed features are passed through FC layers to predict leukemia.

Ahmad et al. [29] suggested an enhanced framework for the subtype classification of WBCs to detect leukemia by integrating transfer learning with a feature selection method based on a customized Quantum-Inspired Evolutionary Algorithm (QIEA). This approach leverages deep convolutional neural networks (CNNs), specifically Darknet53 and Densenet201, to extract deep features from WBC images, utilizing a large-scale synthetic dataset encompassing five WBC subtypes. The extracted features from both models are subsequently fused to form an ensemble feature vector. To optimize the feature set, feature selection was formulated as an optimization problem. This algorithm, grounded in quantum computing principles, performs individual quantum rotations for each variable in the candidate solutions, thereby improving the selection process by eliminating redundant and noisy features. The reduced feature vector is then evaluated using various baseline classifiers with different kernel configurations.

Batool & Byun [30] introduced a lightweight CNN based EfficientNet-B3 model which incorporates depthwise separable convolutions for binary as well as multi-class classification of ALL. Initially, the images and annotations were pre-processed using Min-Max normalization approach and later on, supplemented to further expand the dataset using rotation, flipping etc. Finally, EfficientNet-B3 model was employed for classification. It made use of a compound scaling technique that scales breadth, resolution, and depth all at simultaneously, enabling improved performance on high-resolution medical images with minimal computational overhead. Depthwise separable convolutions are used to make the model more efficient at finding useful features and to lower the number of trainable parameters. This technique makes the model more efficient at finding valuable features.

Genovese et al. [31] suggested using a multi-task cross-dataset transfer learning technique framework to improve the accuracy of detecting acute lymphoblastic leukemia (DL4ALL). It used a pre-trained DL model and replaced the last fully connected layer with two parallel output layers: one for multi-label classification in the source domain and one for single-label classification in the target domain. The learning phase employed a cross-dataset transfer learning method. This method combined the source and target domains at the same time. Next, we applied three different algorithms to the cross-dataset transfer learning: regular, greedy, and self-supervised. These techniques made it easier to generalize the ALL-detection task.

Lewis et al. [32] developed with attention-based multi-instance learning models (ABMILMs) to help find leukemia in different ways, like predicting acute leukemia, advising the difference between AML and ALL, and using flow cytometry data to find certain cytogenetic abnormalities and genetic mutations. The process begins with data from two-tube leukemia panels, which are fed into neural networks that learn to extract meaningful features from each tube. Attention modules then evaluate how important each flow cytometry event is for diagnosing a case, assigning weights accordingly. These weighted features are used to create a summary of the information from each tube. The summaries are then combined and passed through a final neural network, which makes a prediction at the sample level.

Manescu et al. [33] developed a customizable annotation-free DL based Multiple Instance Learning for Leukocyte Identification (MILLIE). This model can differentiate between healthy bone marrow aspirates and those with Acute Promyelocytic Leukemia (APL), as well as identify certain subtypes of white blood cells, lymphoblasts, and immature myeloid cells in pictures taken with a phosphobotic smear. At first, the high-resolution images were processed to extract individual white blood cell patches, which were grouped into "bags" representing positive (diseased) and negative (healthy) samples. The CNN was then trained to classify these bags based on overarching diagnostic labels, allowing it to implicitly learn disease-specific features with weakly supervision technique.

Sulaiman et al. [34] developed ResRandSVM, a method for detecting ALL in blood smear images that relies on deep feature selection. For deep feature extraction from blood smear images, the technique utilized seven DL models: ResNet152, VGG16, DenseNet121, MobileNetV2, InceptionV3, EfficientNetB0, and ResNet50. After that, three feature selection methods were used to extract insightful and statistically significant features: ANOVA, PCA, and Random Forest (RF). The four classifiers used to determine if the images were normal or leukemia were AdaBoost, SVM, Artificial Neural Network (ANN), and Naïve Bayes (NB).

Asar and Ragab [35] developed an optimization algorithm called FOADCNN-LDC that uses a deep convolutional neural network to detect and classify leukemia. At first, the input photos were successfully noise-filtered using Median Filtering (MF). The FOADCNN-LDC method used the ShuffleNetv2 model for feature extraction, which allowed for fast and light processing. The next step was to perform the detection and classification tasks using the CDAE model. The Falcon Optimization Algorithm (FOA)

was used to fine-tune the hyper parameters of the CDAE model to improve its performance.

Awad & Aly [36] created a technique for detecting ALL using the YOLOv8 and YOLOv11 DL models. Initially, the blood smear images were preprocessed to remove irrelevant elements such as background noise and unrelated blood components. Image segmentation was performed by converting images into HSV color space and applying binary masks to isolate WBCs. To enhance robustness and prevent overfitting, data augmentation techniques like mosaic augmentation, random rotation were employed. Then, both the YOLOv8 and YOLOv11s model were selected for evaluation.

Awais et al. [37] developed a way to sort ALL into two groups and subtypes. Initially, they used a Greedy Differential Evolution (GDE) method to strengthen the visual contrast. This method used local neighborhood pixel values to better preserve edges and improve contrast adaptively. Next, a hybrid feature extraction approach was used, incorporating transfer learning with deep neural networks—InceptionV3 and DenseNet201—to obtain comprehensive feature sets. Then, the feature vectors from the two CNNs were combined using horizontal concatenation. It used the binary Grey Wolf Optimization (GWO) method to choose the features and lower the number of dimensions of the combined features. It used the selected features to train several classifiers, which made the classification more accurate by catching a wider range of patterns.

Himel et al. [38] developed a dual-phase ensemble DL based Computer Aided Diagnosis (CAD) model to diagnose acute leukemia by analyzing images of blood smears under a microscope. At first, the images were augmented using rotation and flipping and then image enhancement techniques were applied. Two stages make up the detecting framework. Two pretrained and fine-tuned base models, EfficientNetB7 and MobileNetV3Large, were used at first. To get feature maps, the last dense layers of these models were extracted. These maps were then put together and sent to a fully linked meta-classifier in the second phase, which classified the different forms of leukemia.

Mahesh et al. [39] introduced a hybrid optimization technique combining to improve feature selection for leukemia prediction using microarray gene expression data, the Ant Lion Optimizer (ALO) with Particle Swarm Optimization (PSO) was used. The algorithm was based on the ALO antlion hunting method. At first, the placements of the ants and antlions are random, and their performance is measured by fitness functions. During the process, an elite antlion, which is the best-performing solution, is found and upgraded over and over again. Ants change their places according to their fitness values while they interact with antlions in each iteration. If an ant's fitness is higher than the fitness of the current position, its placement is changed. At the same time, the elite antlion is changed anytime a better solution is found during the optimization cycle. We combine ALO with PSO to leverage the strengths of both methods. This strategy combines the exploration and exploitation skills of these algorithms to make feature selection more accurate and faster to converge.

Shree et al. [40] created a DL-based Optimized Deep Recurrent Neural Network (ODRNN) to help diagnose leukemia by observing blood smear images under a microscope. The method used deep recurrent neural networks (DRNNs) to extract features and classify them during the diagnosis process. The Red Deer Optimization Algorithm (RDOA) was used to improve the performance of the DRNN by improving its weights. The optimization process was based on the way red deer behave, especially the number of times they declare. This helped to fine-tune the weight parameters of the DRNN, which made the model better at learning and classifying issues.

Almahdawi et al. [41] suggested a DL-based way to use microscope pictures to diagnose leukemia cells by combining Particle Swarm Optimization (PSO) and Ant Colony Optimization (ACO) to choose one feature at a time. Initially, we used DL models to extract features from leukemia images. Then, PSO and ACO were used to find the most important features for classification, which makes the classification more accurate. It used three machine learning classifiers K-Nearest Neighbors (K-NN), Support Vector Machine (SVM), and Decision Tree (DT) to look at the chosen features.

Dutta et al. [42] created a multi-class classification approach for ALL using peripheral blood smear (PBS) images and an attention-based CNN model called LEU3. These images were prepared for normalization and then changed in size, height, and rotation to improve them. LEU3 used convolutional layers to process the input images and gradually pull out spatial and feature hierarchies. The attention module then boosted important characteristics to make classification more accurate. We then flattened the extracted characteristics and added a dropout layer to help prevent overfitting. Finally, a softmax algorithm was utilized to classify the ALL subtypes into more than one class.

Muduli et al. [43] investigated using a range of pre-trained DL models for ALL detection and classification. These models include VGG16, VGG19, ResNet50, Xception, ResNet152, EfficientNet-B0, NASNetMobile, DenseNet169, DenseNet121, and EfficientNetV2B0. At first, the PBS images were preprocessed using augmentation and then classified with the pre-trained models. Explainable AI (XAI) components, including Gradient-weighted Class Activation Mapping (Grad-CAM), Grad-CAM++, and Score-CAM, were added to the system to make it even better at finding things. The XAI methods created heat maps that highlight the important areas that affect the decisions on classification.

Rejula et al. [44] developed an automated way to find, categorize, and diagnose leukemia cells utilizing advanced approaches for segmentation, feature extraction, and classification. Initially, an enhanced dual threshold segmentation technique, which improves the segmentation of leukocyte cell images by effectively distinguishing both the nucleus and cytoplasm regions was employed. Then, a hybrid Discrete Wavelet Transform (DWT) feature extraction method is applied to capture both spatial and frequency information from the segmented images. For the classification task, an improved Adaptive Neuro-Fuzzy Inference System (I-ANFIS) is employed, by integrating neural networks' capacity for learning with the decision-making ability of fuzzy logic.

Thiriveedhi et al. [45] an individualized convolutional neural network (CNN) model called ALL-Net for the purpose of dividing PBS pictures of ALL into benign (hematogones) and malignant (Early-B, Pre-B, and Pro-B) categories. To correct for class imbalance, these photos were preprocessed by downsizing and normalizing. Then, data augmentation was done to the benign class only. In order to classify the photos, the ALL-Net model first retrieved complicated features from them. We used explainable artificial intelligence (XAI) techniques, namely the Local Interpretable Model-Agnostic Explanations (LIME)

algorithm, to improve the model's interpretability and fix ALL-Net's block box difficulties. LIME identified key image regions influencing classification outcomes, promoting transparency, trust, and error detection in medical diagnostics.

Prakash et al. [46] introduced a lightweight and enhanced YOLOv8 model for accurately detecting and categorizing leukemia. Initially, the blood smear images were augmented using techniques like rotation and flipping to reduce overfitting. Then, pre-processing was done using Gamma Correction to normalize and improve the images. The actual YOLOv8 model is integrated with Depthwise Separable Convolution (DWSCNN) and Residual Convolution Block Attention Mechanism (RCBAM) layers. The backbone structure in YOLOv8 model incorporated DWSCNN layer whereas the neckbone structure includes RCBAM layer which in turn integrates attention mechanisms, both ensures efficient feature extraction and contextual information gathering. Finally, the head of the model was designed for multi-scale object detection, with dedicated blocks for identifying large, medium, and small feature maps.

III. COMPARATIVE ANALYSIS

This section compares the above-mentioned DL models for leukemia detection and classification. Table 1 highlights the comparison by showing its merits, demerits, techniques used, dataset used and performance evaluation.

Table I. Comparison of DL models for leukemia detection

Ref No.	***Techniques***	***Merits***	***Demerits***	***Dataset Used***	***Performance Evaluation***
[28]	Deep CNN	This model has fewer layers and trainable parameters, making it computationally less expensive.	Due to a lack of training, the model might have trouble generalizing to uncommon or undetected forms of leukemia.	ALL-IDB1, ALL-IDB2	Accuracy= 98.3%; Precision = 98.16%; Recall= 98.16%; F1-Score = 98.43%
[29]	QIEA, Darknet53, Densenet-201	The model effectively reduces the feature vector size, which minimizes computational load.	The model is trained on specific data, which may struggle to generalize to rare or unseen leukemia variants without retraining.	Publicly Available unknown dataset	Accuracy= 99.8 %
[30]	EfficientNet B3	The model utilized fewer trainable parameters due to depthwise separable convolutions, making it more efficient and lightweight.	The performance was slightly lower on multi-class classification compared to binary, indicating a need for further refinement in more complex tasks.	C_NMC_2019, ALL datasets	Accuracy= 97.50%; Precision= 91.63%; Recall= 97%; F1-score = 92.89%
[31]	DL4ALL	The self-supervised variation achieves strong performance without the need for manually labeled source data, reducing annotation costs.	It requires ~36 hours for 100 epochs due to model complexity and additional computation in the greedy learning algorithm.	C_NMC_2019, ALL datasets	Accuracy= 97.85%; Specificity= 98.79%; Sensitivity = 95.81%
[32]	ABMILM	This method Offers visual output that supports clinical decision-making.	The model does not distinguish between new and recurrent AML cases, limiting its use in longitudinal monitoring.	Flow cytometry data	Accuracy = 96.1%
[33]	MILLIE	Binary and multi-class classification jobs are both handled well by the package.	The models id trained only with diagnosis-level labels that may reduce the model's ability to handle complex features.	ALL Image Database (ALL-IDB)	AUC = 0.935
[34]	ResRandSVM, ANOVA, PCA, RF, AdaBoost, SVM, ANN and NB	This method works well even without extensive manual annotations or large expert-labeled datasets, useful when labeled data is scarce	This method uses multi-stage pipeline which increases complexity	C_NMC_2019 dataset	Accuracy= 90% F1-score= 0.929
[35]	FOADCNN-LDC, MF, CDAE	The model enables efficient deployment in resource-constrained environments without sacrificing feature quality.	The model may hinder real-time or embedded deployment unless optimized.	Unknown Medical Dataset	Accuracy = 99.62%, Computation time =3.88s
[36]	YOLO-v8, YOLO-v11	The training and validation curves showed smoother convergence, indicating better	Imbalanced dataset slightly impacted the model's ability to correctly classify normal	Kaggle and ALL-IDB1 datasets	YOLO-v11 (best performed): Accuracy= 98.2%, F1-score= 99.2%,

		generalization	cells.		Precision= 98.6%, Recall= 99.8%, Specificity = 93%
[37]	GDE, InceptionV3 and DenseNet201, GWO	GWO not only reduces feature dimensions but selects semantically meaningful features	Training used fixed parameters which may not be optimal across all datasets or tasks.	ALL-IDB2 dataset	Accuracy = 98.14%
[38]	EfficientNet-B7, MobileNet-V3Large	It required less training time and used fewer computational resources	The ensemble structure increases memory usage during deployment.	ALL-IDB1, ALL-IDB2, and American Society of Hematology (ASH) datasets	Precision = 99.3 %, Recall= 99.3%, Accuracy = 99.3%, F1-score = 99.3%, AUC= 0.99
[39]	ALO-PSO	The model demonstrated improved capability in correctly identifying both positive and negative cases.	The model relies on fine-tuning multiple parameters, which are time-consuming and sensitive to initial settings.	Leukaemia dataset	Accuracy= 87.88%, Average Sensitivity= 0.8733, Average Specificity= 0.9344, Average F-Measure= 0.8755
[40]	ODRNN, RDOA	The model performed well on partly covered, blurred, and fuzzy images, indicating strong robustness to typical real-world image imperfections	The model exhibits high computational complexity	C_NMC_2019, AML, and ALL database	For blurred Images, Accuracy= 91.23%, Precision = 90.48%, Specificity= 90.21%, Recall = 91.1%, F1-score= 91.23%
[41]	PSO-ACO, SVM, K-NN, DT	This model shows reduced complexity and computational cost while maintaining diagnostic accuracy	Small dataset size restricts the generalizability and robustness of the conclusions, limiting confidence in performance	ALL-IDB2 dataset	For ResNet-50: Accuracy= 91.02%, Sensitivity= 93.15%, Specificity= 88.89%, Precision= 92.75%
[42]	LEU3	It showed strong generalization, involving robustness to slight variations in input data.	The model relies heavily on high-quality datasets, which may not always reflect real-world data variability.	Customized blood cells cancer dataset	Precision =99%, Recall= 99%, F1-score = 99%
[43]	ResNet152, EfficientNet- B0, NASNet-Mobile, DenseNet169, DenseNet121, and EfficientNet-V2B0, Grad-CAM, Grad-CAM++, Score-CAM VGG16, VGG19, ResNet50, Xception,	The model exhibits lower training times	The training set was so tiny, the model might still be overfitting.	Publicly available leukemia dataset	Accuracy= 100%
[44]	I-ANFIS, DWT	The approach successfully distinguishes between multiple cell types, showing its suitability for complex, multi-class medical problems	It may require extensive manual tuning and domain knowledge for hyperparameter selection and segmentation thresholding.	Microscopic blood cell dataset	Accuracy = 95.67%, Sensitivity= 96%, Specificity= 90%
[45]	Customized CNN, LIME	This model used significantly fewer layers which reduces the memory requirements	Performance may degrade if trained or deployed on low-quality or limited datasets	Kaggle ALL dataset	Accuracy = 99.32%
[46]	Enhanced YOLOv8, DWSCNN, RCBAM	The model results in less inference time making it more powerful	The fine-tuning process was done manually, which is time-consuming.	Publicly accessible RoboFlow dataset	Accuracy = 98.4%

IV. Performance Evaluation

This section evaluates the DL models compared in the prior section using benchmark datasets. The basic metric used for the comparison of these models is accuracy as it is the numerical measure for assessing a model's performance. Fig. 6 represents the performance analysis of different DL models for leukemia detection utilizing benchmark datasets.

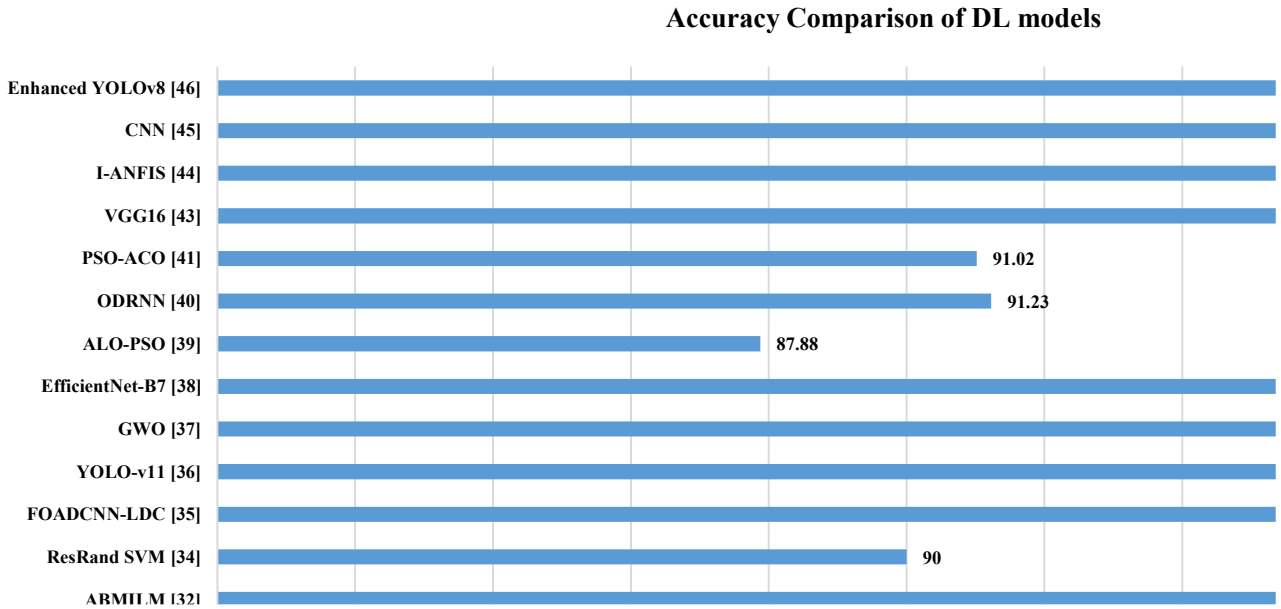

Figure 6. Evaluation of DL techniques for leukemia prediction on benchmark datasets

From this comparative analysis, it is evident that VGG16 [43], QIEA [29], and FOADCNN-LDC [35] achieved superior accuracy, with VGG16 reaching a perfect accuracy of 100%. These models demonstrate strong learning capabilities, efficient feature extraction, and high generalization performance across datasets. However, they are prone to overfitting due to a small training dataset, which may hinder its generalization in diverse clinical settings. Then, Enhanced YOLOv8 [46] has shown promise by achieving 98.4% accuracy respectively, while also optimizing speed and memory efficiency. This model balance accuracy and performance, making them more suitable for practical deployment in clinical settings. On the other hand, models like ALO-PSO [39] and PSO-ACO [41] had lower accuracies of 87.88% and 91.02%, mostly because they were difficult to compute.The Enhanced YOLOv8 [46] model is thought to be the best model based on the analyses. The model strikes a good balance between accuracy and speed, making it the best and most practical method among those compared, even if it still needs manual fine-tuning throughout training.

V. Conclusion

Leukemia is a deadly disease that necessitates prompt and careful attention to find out exactly what is wrong with the development of white blood cells. Early detection of leukemia is important to lower the death rate. Deep learning (DL) methods have gotten a lot of interest in the last several years because they are effective at finding leukemia in its early stages. This study looks at different DL algorithms to see if they can use medical imaging and blood smear data to correctly diagnose leukemia. They look closely at the pros and cons of different models, as well as the way they work. By understanding the limitations of existing methods, researchers can develop better and more effective models that assist in accurate diagnosis and informed clinical decision-making. Future research will aim to create more advanced deep learning structures that can work with a broader variety of leukemia data, improve the analysis of microscopic images, and assist in creating better diagnosis and treatment plans for leukemia.

VI. References

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