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Transfer Learning for the Medical Diagnosis of Acute Leukemia Cancer

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Abstract—Leukemia is a cancer that starts in the blood cells due to the excessive production of immature leukocytes that replace the cells with the normal blood cells. Physicians rely on their experience to determine the type and sub-type of Leukemia from the blood sample. Most people are misdiagnosed when it comes to its sub-types. The error rates can be up to 40% during the classification process and that too depends on the expertise of the physician. Leukemia-caused death

is in the top ten most dangerous mortality cause for human being. Among many reasons, is the slow decision-making process costing a lot of time before getting diagnosed. Therefore, it has become a necessity to have a reliable clinical decision support system for acute leukemia classification. This gives us the motive to automate the classification process so that that a physician can get help in decision making and can get another opinion.

In this paper, a medical image classifier that classifies acute leukemia and its five sub-types using state of the art pre-trained neural network architectures and deep learning techniques, namely, Transfer Learning and Fine Tuning is proposed. The proposed methodology results in better accuracy and more time effectual as compared to a hematologist visual classification.

Index Terms—Acute Leukemia, Convolutional Neural Networks, Fine Tuning, Feature Extraction.

I. Introduction

Leukemia the most common cancer worldwide with 250,000-300,000 new cases every year. The percentage of death caused by Leukemia is 74 % which is typically caused by poor identification of types, sub-types of Leukemia, and delay in diagnosis. According to statistics stated by INEGI in 2006, leukemia was the fifth and sixth cause of death in men (7%) and women (5.8%) with cancer, and it was the first cause of death in children with cancer between 1–4 and 5–14 years old, with 48.5% and 52.2% of deceases, respectively [1]. Leukemia begins in the bone marrow and bone marrow cells (See Figure 1) start to produce abnormal white blood cells that are substituted by normal blood cells in our body. Because of this, our body starts losing its fight against all sorts of infections and diseases due to the absence of defenses and normal white blood cells [2]. Early diagnosis of the disease can result in quick recovery in the case of children. Leukemia has two types, namely, acute (fast-growing) & chronic (slow-growing).

Acute leukemia grows fast and invades the body in about few weeks or months, whereas chronic leukemia's are slowgrowing but worsen over the time.

The French–American–British (FAB) classification categorizes Acute Lymphocytic Leukemia (ALL) into three sub-types (L1L2-L3) [3, 4, 5] and Acute Myeloid Leukemia (AML) into eight different sub-types (M0, M1, M2, M3, M4, M5, M6, M7) respectively [6, 7, 8]. There are main three cell types whose percentages specify AML sub-types M1, M2 and M3, namely: myeloblast, promyelocyte, and monoblast [9].

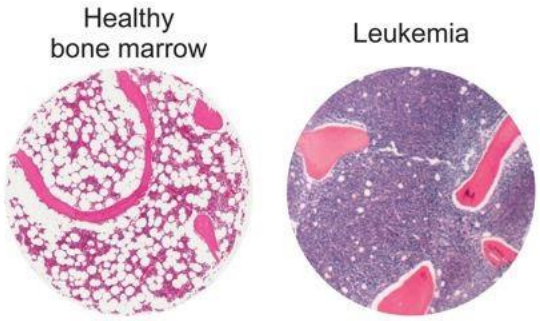

Fig. 1. Healthy Bone Marrow and Leukemia. Source: leukemia research foundation

A. Acute Lymphocytic Leukemia (ALL)

Acute Lymphocytic Leukemia (ALL), additionally called acute lymphoblastic leukemia and acute lymphoid leukemia is a type of blood cancer that results when unusual white blood cells (leukemia cells) aggregate in the bone marrow. ALL advances quickly, supplanting solid cells that produce healthy lymphocytes with leukemia cells that can't develop appropriately. leukemia cells are carried in the bloodstream to different organs, cells and tissues, where they proceed to mature and separate. Overproduction and spreading of these leukemia cells may result in various conceivable side effects (See Figure 2). ALL is predictably linking to having more B lymphatic cells than T cells. T and B cells undertake dynamic jobs in keeping the body from contaminations and germs and decimating cells that have just turned out to be tainted. B cells especially help keep germs from contaminating the body, however, T cells eliminate infected blood cells.

ALL can strike at any age; however acute lymphocytic leukemia occurrences happen most often in individuals younger than 15

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or beyond 45 years old, albeit ALL makes up the biggest level of leukemia analyze in youngsters younger than 15 (mostly amid in the age of 2-4 years), it is uncommon for grown-ups to have this ailment [10].

ALL Treatments may incorporate radiation/chemotherapy, chemotherapy with undeveloped cell transplant, radiation therapy. The incorporated group of leukemia specialists will answer the inquiries and suggest treatment options reliant on his specialization in findings. chemotherapy for ALL typically starts with enlistment chemotherapy, in which a blend of medications is utilized to destroy the malignant cells. This is followed by combination chemotherapy, to destroy any outstanding leukemia cells that can't be found in the blood or bone marrow. Patients with ALL may likewise get support chemotherapy. This less escalated course of chemotherapy is utilized to decline the risk of the disease and repeating the process until cured.

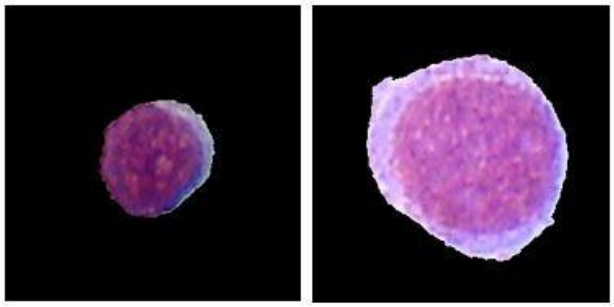

Fig. 2. L1 and L2 type Cell

B. Acute Myeloid Leukemia (AML)

Acute Myeloid Leukemia (AML) is the deadliest type of Leukemia as it progresses quickly and gives us a very small window to its cure. It is also the highest acknowledged type of leukemia [11]. It happens when the bone marrow starts to make cells that have not yet totally developed, the cells are abnormal and affect the normal cells. And the body loses its defense mechanism. In AML, the bone marrow may likewise make anomalous red blood cells and platelets. The quantity of these abnormal cells increments quickly, and the anomalous (leukemia) cells start to swarm out the ordinary white blood cells, red blood cells and platelets that the body needs (See Figure 3). One of the fundamental things that separate AML from the other principle types of leukemia is that it has eight diverse sub-types

Myeloblastic (M0) - on special analysis, Myeloblastic (M1) - without maturation, Myeloblastic (M2) - with maturation, Promyeloctic (M3), Myelomonocytic (M4), Monocytic (M5), Erythroleukemia (M6), Megakaryocytic (M7)

AML Treatment might incorporate chemotherapy, radiation treatment, or stem cell transplant. Pathologists will prescribe treatment options depending on the sub-types of Leukemia according to his expertise. Which may also we wrong and time taking, which will lead to a very ill-timed treatment [12].

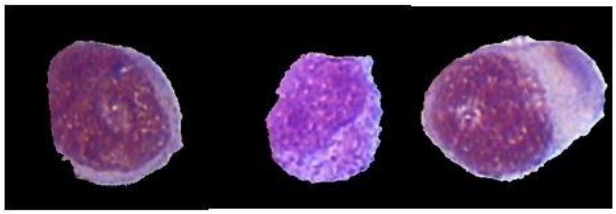

Fig. 3. sub-types of AML according to FAB, (a) M2 type ALL, (b) M3 Type ALL, (c) M5 Type

C. Leukemia Prognosis

There is an adequate need to set up a quick diagnosis because the classification process only depends upon the expertise of the hematologist and his experience, which can lead to many problems like misdiagnosis or delay in the diagnosis. Our proposed system will give the hematologist another ML-based opinion which will give him an insight into the classification problem.

The accompanying disadvantages may fundamentally hamper manual morphological examination of bone marrow cells:

- Poorly arranged or recolored blood smears.
- Time utilization is an important aspect. Even though an accomplished master plays out the PB spread examination, it can't be considered as a quick procedure, where the administrator needs to complete a watchful report on the impact cells morphology (estimate, shape, core chromatin structure) with the end goal to turn out with right diagnosis and guarantee that the correct treatment will be given.
- The technique is available to human mistakes.
- Bone Marrow Aspirate Morphological Examination

Bone Marrow is an extraordinary greasy tissue containing immature microorganisms situated inside a couple of vast bones. These foundational microorganisms can change into WBCs, RBCs and platelets that have different jobs. Inside this uncommon tissue, youthful stems cells dwell, alongside additional iron. Undeveloped cells stay undifferentiated until irregular, debilitated, or harmed cells should be supplanted. This is the main procedure through which cells get supplanted to keep up a solid body. Doctors normally utilize 5-year survival rates to quantify illness results. Survival rates incorporate

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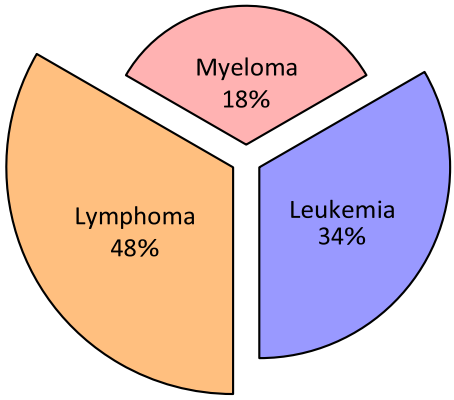
patients who survive 5 years after diagnosis, whether disappearing, i.e. in a state amid which the symptoms of the infection are lessened.



Unlike most of the studies, work has been limited to the detection of Leukemia or classifying just one type or sub-type. The proposed techniques are focused on the classification of ALL and AML including their respective sub-types, using state of the art pre-trained neural network models. Key contributions of the proposed study are as follows:

- To classify the acute leukemia and its sub-types using the features extracted from state-of-the-art CNN architectures.
- To validate the proposed approach using a hospital provided dataset.
- To perform a thorough breakdown of transfer learning using the finest techniques is presented.

II. Literature Review

This section is solely dedicated to the conclusions of the literature reviews conducted. Some of the most prevalent and significant transfer learning techniques are presented and reviewed which have been previously used for classification purposes. We have listed some notable work from previous studies to get an insight into the research problem.

A. Analysis and Discussion

In this section, we present a basic overview of machine learning methods that are used for the acute lymphoblastic leukemia detection and classification of bone marrow cells. An overview is presented on the findings of literature review on classification of acute leukemia and its sub-types using machine learning algorithms and their comparison. A summary of the existing techniques and methods are presented in Table I. The comparison is done on the basis of dataset, preprocessing, classifier and accuracy as evaluating parameters.

Previously, pre-processing and hand-crafted feature extraction techniques were employed which were then followed by a classifier, most notably Support Vector Machine (SVM), for classifying into normal and blast cells as depicted in the works of [1], [32], [25], [28], [33]. Histogram equalization and morphological filtering of ALL images combined with fuzzy c-means for segmentation of white blood cells followed by Gabor texture extraction for feature extraction yielded an accuracy of 90% by SVM classifier [1]. This work was further enhanced by using a combination of histogram equalization and median filter combined with WBC segmentation for cancer cells followed by geometrical features and an SVM classifier to achieve an accuracy of 93.57% [32]. Some works targeted the same feature extraction techniques, i.e., geometrical features and SVM classifier but with different segmentation techniques, namely separation of saturation component of HSI color space and a combination of k means clustering algorithm, Marker controlled watershed algorithm and HSV color-based segmentation algorithm to achieve an accuracy of 97.55%, 92.00%, 93.70 and 98.00%, respectively [25], [28], [33], [20].

The authors in [26] used image-processing techniques to detect AML cancer. The approach used Zack algorithm for background removal, Hough transform for feature extraction and distance transformation of watershed algorithm for separating grouped cells. The authors claimed that their proposed approach resulted in inaccurate results in some scenarios. Also in the work of [34], the authors used morphological analysis to detect leukemia cells.

In some works, the authors extracted boundaries of objects of interest from microscopic images [35], [4], [3] using region and edge based detection techniques. The problem faced by these works suffer from the presence of noise that results in level from pixel to pixel random variation.

A review of various techniques for leukemia detection and prevention is presented in [36] targeting ANN (Artificial Neural Network), image processing, LDA (Linear Dependent Analysis) and SOM (Self Organizing Map). The authors concluded that for detection of leukemia Support Vector Machines should be chosen as a classifier for higher accuracy rates. The overall accuracy of 91.00% is achieved in the work of [21] where the authors have used different classifiers, namely ANNs, LDAs and SVMs and in another work [25], the authors achieved 96.43% by using clinical decision support classifiers. The Authors in [37] studied the effectiveness of transfer learning in four different applications across three imaging modalities. They used pre-trained weights from [38] to either a few or many layers in a CNN. Overall,they concluded a pretrained model results in better accuracy than training one from scratch.

After investigating the prior approaches, we have deducted that there is room available for increasing the accuracy. The detection and diagnosis of ALL are very sensitive issues. A sophisticated evolution in health care informatics has made feasible to diagnose leukemia cancer in a short period. This is a very challenging task due to highly overlapping blood cells which makes them difficult to separate. It is also been found

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out that classification of ALL and AML sub-types is ignored in the literature. Most of the researchers have neglected the identification of sub-types of acute lymphoblastic leukemia because of their inter-class similarity. These sub-types are difficult to classify but play a vital role in the precise diagnosis of disease and are very crucial for the medical treatment of the disease. Few works have targeted the sub-types of AML subtypes. The authors in [21] classified between M3 and other sub-types using genetic algorithms, simulated annealing and hill-climbing and concluded that simulated annealing is the best for the detection of leukemia by achieving an accuracy of 97.22%. EPMs for two types of leukemia resulted in 97.68% [29] and machine learning algorithms for the segmentation and classification for types and sub-types of leukemia resulted in 95% accuracy [30]. An ALL sub-types work is proposed in [39] where authors used segmentation and CNNs to achieve an accuracy of 97.78%.

We present a performance of the proposed classification techniques with state-of-the-art transfer learning techniques evaluated on the database we have used. As discussed earlier, most of the work has been done on individual type of leukemia detection or on red blood cells. And in rare cases where transfer learning is used, it is only limited to one type of leukemia. The results have been good but the dataset used contained fewer images. It is also analyzed that classification of ALL & AML sub-types are not present in the literature. Most researchers have neglected the identification of sub-types of acute lymphoblastic leukemia because of their inter-class similarity and intra-class variability.

TABLE I

COMPARISON OF DIFFERENT ALL AND AML CLASSIFICATION TECHNIQUES

Study	Year	Dataset	Preprocessing	Classifier	Accuracy
[13]	2009	L2 Type ALL Blood Images	Canny Edge Detection technique, zack algorithm	-	92.00%
[14]	2010	Lab Images	Selective median filtering, Unsharp Masking	SVM	95.00%
[15]	2010	Lab Images	K-means Clustering	SVM	95.00%
[16]	2010	Digital Images	Morphological filtering	RF	97.52%
[17]	2011	Lab Images	Selective median filtering, Unsharp Masking	SVM	93.00%
[18]	2011	Public ALL-IDB 1	Scale-space filtering	RF	97.00%
[19]	2012	Cell Images	Morphological filtering	EPSMS	97.68%
[20]	2014	AmericanSociety of Hematology (ASH)	-	SVM	98.00%
[21]	2014	Online Images	Histogram Equilization, Median Filter	ANN	91.00%
[22]	2014	Lab Images	Shadowed Cmeans clustering	MLP, SVM, KNN	94.73%
[1]	2015	Public ALL-IDB 1	Histogram Equilization, Morphological Filters	SVM	97.70%
[23]	2015	-	Median Filtering, Wiener Filtering	SVM	93.57%
[24]	2015	Lab Images	Fuzzy C- mean, Watershed algorithm	SVM	96.33%
[25]	2016	Sample Images	Histogram Equilization, Median Filter	SVM	97.55%
[26]	2016	ALL-IDB 1	Hough Transform	-	90.00%
[27]	2016	Lab Images	Histogram Equilization	SVM	97.50%
[28]	2017	Images	-	SVM	92.00%
[29]	2017	Public ALL-IDB 1	Morphological filtering	-	96.43%
[30]	2017	Public ALL 1	Morphological filtering	SVM	90.00%
[31]	2017	Public ALL-IDB 1	Zack algorithm	SVM	92.00%
[32]	2018	Public ALL-IDB 1	Histogram Equilization, Median Filter	ANN	93.57%
[33]	2019	ALL-IDB 1	-	SVM	93.70%

III. METHODOLOGY

In current years, manual classification of leukaemia has been done by a haematologist based on their expertise. Modern machine learning algorithms like Support Vector Machines (SVMs), Random Forests (RFs) have been practised in the process of classification. The hand-crafted features are now substituted by machine-learned features utilizing convolutional neural networks (CNNs). This segment exhibits in detail the recommended technique for the classification of leukaemia and its sub-types. In the following areas, we first provide an overview of CNNs supported by a discussion to accommodate our problem. Hence the suggested classification framework is executed in MATLAB. Multiform pre-trained models are practised in our study as feature extractors and fine-tuned to our custom made dataset. Since we have targeted the classification either than detecting leukaemia, the features are derived from images (in our curated dataset) with the help of ground truth information. Segmented images are labelled with the guidance of a haematologist, which is moreover used for system training and evaluation. In the next

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section, we will first confer the details of the database, attended by the data preparation and recognition.

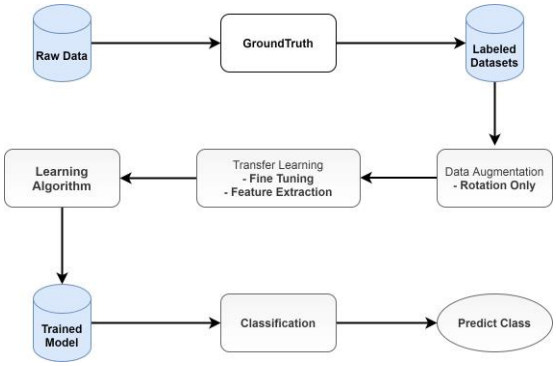

Fig. 4. The Architecture of the Proposed Approach

A. Overview of system

The comprehensive architecture is demonstrated in Figure 4. In this research, we have deployed the pre-trained CNN's for the classification of acute lymphocytic leukaemia, acute myeloid leukaemia, and its sub-types. In the past years, the manual features extraction (usually perceived as handcrafted features) is superseded by machine-learned features with the help of convolutional neural networks (CNNs). We additionally employ CNNs in our study. In the following sections, we first impersonate a survey of CNNs, followed by a discussion on adapting them to our problem. Our study expands transfer learning techniques to distinguish cellular elements nucleus cellula and then leukaemia and its sub-types. We have applied remarkable well-known pre-trained CNNs for our problem by using the transfer learning methods. The employed networks are temporarily outlined in this section following the system overview. Training the classifiers to identify images needs labelled images, so we have been manually producing and identifying the training data under the surveillance of a haematologist. The suggested architecture has two convolutional layers with 24 (9 9) and 48 (7 7) filters. The convolutional layers are followed by the ReLu activation function and the max-pooling layers, while the last fully connected layer performs classification. The networks are trained by using medical images of the bone marrow cells. The scholar has utilized Alex Net, VGG-16, initiation V3 and a hybrid architecture of inception V3 & ResNets 101 as pretrained networks. Network parameters for system training are set as follows:

- Batch size 30
- Number of Epochs 20
- Momentum 0.9
- Base learning rate 0.001

B. Dataset

The images from the dataset used in this study are formulated in collaboration with the haematologist and the Mexican Social Security Institute (MSSI) to execute a system for the programmed morphological identification of acute leukaemia from bone marrow cell images. The dataset comprises 633 bone marrow leukaemia cell images with contrasting colour staining. All photos were digitalized by Carl Zeiss optical microscope resulting in the exact image resolution for all images. For the classification of subtypes of ALL and AML, these images were labelled to L1, L2 and M2, M3, M5 by an expert oncologist who marked each appearance into ALL and AML sub-types manually. When importing the labelled dataset, 75% and 25% are made between the training data and validation data. This means that 75% of the data is used to train the network, and 25% of the information is used to test the network. Our main objective was to classify the subtypes of acute lymphoblastic leukaemia, which were primarily neglected in the previous literature because they are difficult to classify due to their inter-class similarity and intraclass variability.

C. Data Augmentation

Neural Networks struggle from overfitting caused by either a smaller number of training samples or many complex features. Due to a limited number of training data in our dataset, we used data augmentation techniques by utilizing image manipulation. The authors applied image rotation and mirroring to increase our training data. We rotated these images by 90,

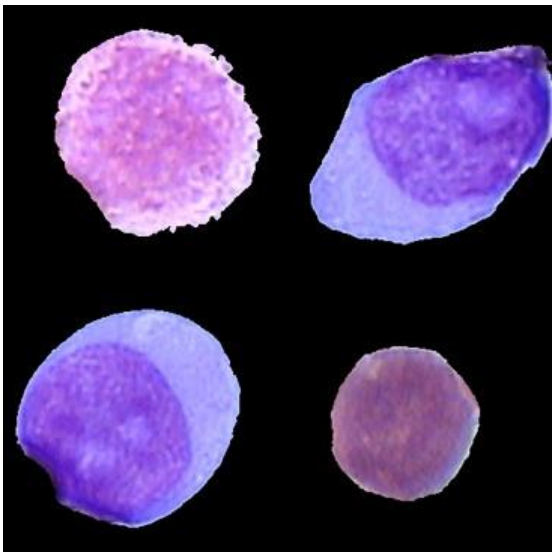

Fig. 5. Different Sub-type Cells of Leukemia

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180 & 270 degrees. Without data augmentation, our network may suffer from considerable overfitting. After applying data augmentation, the total number of images increased to 2532.

D. Convolutional Neural Networks

Convolutional Neural Networks (CNNs) are profound artificial neural systems that are utilized principally to group pictures, cluster them by comparability, and perform object recognition inside scenes. These are the algorithms that can be used to distinguish among road signs, people, faces and numerous different parts of visual information. CNNs detect patterns to arrange or classify pictures and wiping out the requirement for manual feature extraction [40]. The adequacy of CNNs in image recognition is one of the major causes of why the universe has turned out the viability of deep learning. They are changing significant priors in CV (computer vision) that have the evident operations for mechanical technology, drones, self-driving cars, medications, drones, and security for visually debilitated.

A CNN (convolutional neural network) can have many layers in which every layer figures out how to expose or identify distinctive components or attributes of a picture. Convolutional neural network (CNN) have filters in each layer except the last MLP part, and an output of every layer is utilized for contribution with the upcoming layer.

A CNN is made up of an output layer, an input layer, and many invisible layers in between input and output layers. These layers perform tasks that adjust the data to learn features particular to the data. Three of the most widely recognized layers are:

Convolution: Convolution inputs the image through an arrangement of convolutional filters, every one of which initiates certain features from the pictures.

Rectified Linear Unit (ReLu): ReLu takes into account quicker and more powerful training by mapping negative qualities to zero and keeping up positive qualities. This is in some cases alluded to as activation, because just the activated features are conveyed forward into the following layer.

Pooling: Pooling is use to rearrange an output through executing nonlinear downsampling, and lessening the parameter's quantity which is required to learn by the network.

These layers are stacked on top of each other, with each layer figuring out how to distinguish diverse features.

E. CNNs and Transfer Learning

Training a network from scratch requires a huge amount of data to be given to the network for a particular task. This requires a lot of time and resources considering the number of parameters a network learns. At times we may not have enough data available to train our classifier from scratch. This is where transfer learning comes in with techniques, namely Feature Extraction and Fine-Tuning to help transfer knowledge gained on one dataset to be transferred to another dataset. This saves a lot of time and resources by just applying the gained knowledge from one problem to another. The two techniques are as follows:

1) Fine Tuning: One way to deal with getting around time and resources issues is to first pre-train a deep neural net on a huge scale dataset, such as ImageNet. At that point, given another dataset, we can begin with these pre-trained weights when training on our new task. This procedure is generally called fine-tuning. There are various varieties of fine-tuning. Now and then, the underlying neural network is utilized just as a feature extractor. That implies that we solidify each layer preceding the output layer and essentially learn another output layer [40]. To fine-tune a network, we should initially replace the last completely output layer with another one that performs the desired classification. We introduce its weights arbitrarily. At that point, we keep training the last layers. Now and then it's normal to utilize a smaller learning rate dependent on the instinct that we may already be close to a good outcome. The task of fine-tuning a network is to change the parameters of an officially prepared network with the goal that it adjusts to the new task at hand. The starting layers learn extremely broad features and as we go higher up the network, the layers tend to learn patterns more particular to the task it is being prepared/trained on. In this way, for fine-tuning, we need to keep the underlying layers flawless (or freeze them) and retrain the later layers for our task.

2) Feature Extraction: Feature extraction uses a CNN that is already trained on a dataset so that the features can be computed for a given image. The features extracted at the start of the network are all basic and are same for all tasks. It is not until the last few layers of the network that it learns domainspecific features. Features learned by a trained classifier can accomplish aggressive outcomes, in some cases leaving behind the features that are engineered by humans. However, the examinations demonstrate the hyper-parameters, ought to be chosen for better execution. In feature extraction, we chop off the last classification part and use the network as a feature extractor for our given images using the knowledge gained on another problem relating to the one at hand. However, the features extracted are not particularly assigned for the new task and can be repeatedly enhanced using the fine-tuning of the last layers.

IV. Experiments and Results

In this section, we discuss the results of the experiments performed in the study. First, results of fine-tuning and feature extraction will be presented. Finally, we will discuss system evaluation and comparing our results with the other work. The evaluation parameters used are precision, recall and accuracy.

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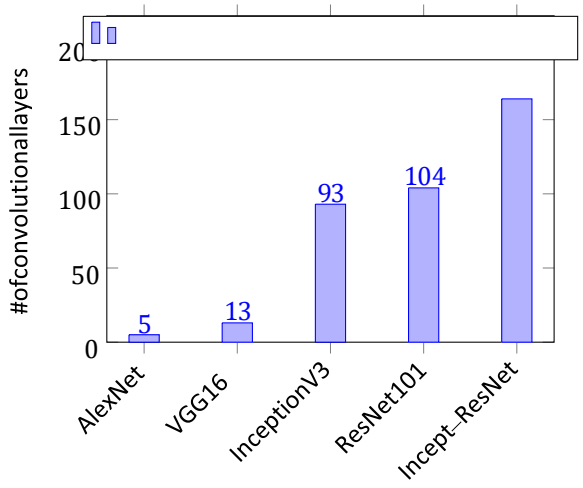
The authors have used five pre-trained CNN models, namely AlexNet [40], VGG16 [41], InceptionV3 [42], ResNet101 [43] and InceptionResNet [44]. The convolutional complexity of the



The authors used Support Vector Machine (SVM) as a these models are presented in bellow bar graph.

Complexity level of convolutional layers

164

classifier in all feature extraction transfer learning experiments. For fine-tuning, the authors have used the default MLP of the pre-trained neural network by only modifying the last layer for our desired number of classes.

For all experiments, 75% of images are used for training and 25% for testing. Results are reported using k-Fold CrossValidation, where *k = 10*. Performance is measured in terms of accuracy as an evaluation measure.

A. Results for Classification of cellular elements.

Pre-trained CNN models are used for the classification of acute lymphoblastic leukemia, acute myeloblastic leukemia and its sub-types. The authors analyzed different training results obtained from the dataset in which the input image was segmented. For the dataset ALL & AML, detection accuracy was comparative to other techniques. Classification accuracy of sub-types are higher than the previously reported techniques. Table II and Table III present the accuracy using transfer learning techniques of ALL & AML and sub-types, respectively.

In the first experiment, the authors classified two main types of leukemia cancer, namely ALL & AML. When using fine-tuning, we truncated the weights of the last layer according to our problem with the same network parameters discussed in Section. Mixed architecture had 825 layers, we froze 822 and used the last three layers using the same network parameters. The classification was carried out using convolution neural networks, we were able to obtain the best results of the classification with Inception-V3. We achieved a result of 87.50% for fine-tuning and 77.70% for feature extraction.

TABLE II
CLASSIFICATION RESULTS FOR ALL & AML

Technique	Model	Classifier	Result
Feature Extraction	AlexNet	SVM	92.09%
	Inception V3	SVM	97.73%
	VGG 16	SVM	87.76%
	ResNet 101	SVM	89.09%
	Inception V3 & Resnet101	SVM	86.40%
Fine Tuning	AlexNet	CNN	61.00%
	Inception V3	CNN	77.70%
	VGG 16	CNN	67.26%
	ResNet 101	CNN	69.04%
	Inception V3 & Resnet101	CNN	56.20%

Classification results for Leukemia and its sub-types are presented in Table III.

TABLE III
CLASSIFICATION RESULTS FOR LUKEMIA AND ITS SUB-TYPES

Technique	Model	Classifier	Result
Feature Extraction	AlexNet	SVM	78.04%
	Inception V3	SVM	87.50%
	VGG 16	SVM	81.03%
	ResNet 101	SVM	79.05%
	Inception V3 & Resnet101	SVM	81.10%
Fine Tuning	AlexNet	CNN	71.00%
	Inception V3	CNN	77.70%
	VGG 16	CNN	65.20%
	ResNet 101	CNN	69.00%
	Inception V3 & Resnet101	CNN	76.10%

Alex Net & VGG 16 has three fully connected layers, i.e.,FC 6, FC 7 & FC 8. The authors employed these for feature extraction. Both classifiers reported higher classification results for feature extraction on FC 6 layer. This shows that CNNs can classify more accurately over the other machine learning classifiers, i.e., LDAs, Na¨ıve Bayes, RFs, etc. It is also

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worth mentioning that to the best of our knowledge, this is the first time these experiments are carried out on five subtypes of leukemia altogether with a large dataset. We have also computed precision and recall for the five sub-types of leukemia and are presented in the Table IV.

B. Effect of Learning Rates on Transfer Learning Experiments

In this section, we discuss the impact of learning rates on feature extraction and fine-tuning for both ALL & AML and their sub-types. Figure 6 shows the effect of learning rates on ALL & AML detection. The authors checked various learning rates starting from 0.01. The classification accuracy increase as we reduce the learning rates until up-to 0.0001 where accuracy slopes down. This conclusion is true for both feature extraction and fine-tuning. Among the both, feature extraction results in higher accuracy.

TABLE IV
PRECISION, RECALL AND ACCURACY FOR ALL & AML SUB-TYPES

Study	Model	Precision	Recall	Accuracy
Feature Extraction	AlexNet	0.80	0.71	78.04%
	InceptionV3	0.84	0.94	87.05%
	VGG 16	0.85	0.89	81.00%
	Incep Resnet101	0.83	0.88	82.70%
	Resnet101	0.81	0.72	79.50%
Fine Tuning	AlexNet	0.72	0.84	71.00%
	Inception V3	0.74	0.82	77.70%
	VGG 16	0.62	0.85	65.20%
	ResNet 101	0.66	0.72	69.00%
	Incep Resnet101	0.77	0.84	76.10%

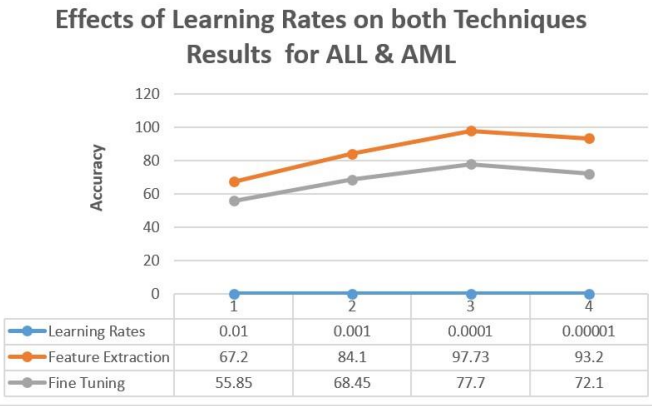

Fig. 6. Effect of Learning Rates on ALL & AML Types

Figure 7 shows the effect of learning rates on sub-types detection. The authors checked various learning rates starting from 0.01. The graph shows the same trends as in basic types detection. Again, among the both types, feature extraction results in higher accuracy than fine-tuning.

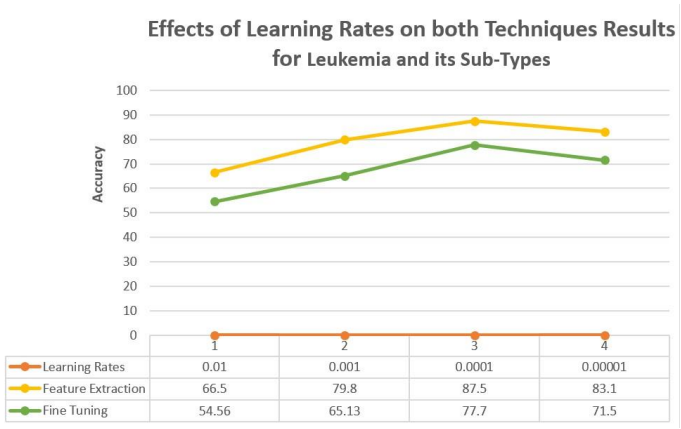

Fig. 7. Effect of Learning Rates on Sub-Types

C. System Evaluation

In this section, the evaluation of the proposed technique is presented. The authors performed a total of twenty experiments, ten experiments for the basic types of leukemia cancer and ten for its sub-types. In all experiments regardless of the transfer learning techniques used, the InceptionV3 outperformed all other pre-trained models. This may be because InceptionV3 uses batch normalization and factorizing n×n convolutions into asymmetric convolutions: 1×n and n×1 convolutions. The other obvious fact about experiments is that feature extraction resulted in better results than finetuning. This may be due to the fact that dataset has a specific characteristic, i.e., inter-class similarity and inta-class variance and feature extraction technique extracted all the relevant features to accurately represent all types and sub-types. While fine-tuning resulted lower because last layers could not capture the necessary details to capture distinction between classes. An aside reason would be the complexity of InceptionV3, as shown in yellow bar graph in the paper. The complexity of InceptionV3 is niether too complex nor to simple and maybe this is cause for its high classification accuracy. Another important factor is that the authors used SVM as a classifier for all feature extraction experiments. The SVM accurately separated all classes by a hyper-plane. The major advantage of the SVM classifier is that it can be paired with the kernel trick. We have used Gaussian kernel for our experiments.

D. Comparison of Results with Notable Studies

The literature review presented detection for acute leukemia and its sub-types using bone marrow cells. The classification process was carried out by extracting the descriptive features such as shape geometry, eigenvalues, mean, standard deviation, etc from nucleus and cellula and classified based on machine learning classifiers such as RFs, LDAs, SMOs, SVMs, etc. The classification process was carried

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out after cell segmentation techniques. They also came up with a diagnostic algorithm that diagnosed leukemia and its sub-types. The studies of literature achieved 97.68% [29] for the lymphoblastic sub-types, and 97.22% [21] for the myeloblastic sub-types. But the catch is they have used two-class or three-class problems like L1 Vs L2 they achieved an accuracy of 81% by using Simple Logistic classifier, and for a three-class problem like M2 vs M3 vs M5 they achieved an accuracy of 78% by using Random Forest as a classifier. Our work was less time consuming and it classified five classes simultaneously instead of classifying two or three classes. It can be concluded that CNNs are more successful in classifying problems more efficiently than just machine learning algorithms.

V. Conclusion

Despite technology innovation, the microscopic examination of blood remains the standard and hence economical method for leukemia diagnosis. But it's not an adequate solution to efficiently be the only factor deciding the diagnosis of leukemia. Also, fewer advances have been made to classify the sub-types of leukemia as it is equally important to classify the sub-types of leukemia. All these approaches of manually identifying the disease depend on the expertise of hematologists. So, there should be some efficient and robust automated system for classification of leukemia through which accuracy of classification is increased hence the diagnosis results can be considerably enhanced without the effect of human intervention. Furthermore, automated systems as compare to manual diagnosis can increase the accuracy and quick diagnosis. This will help the doctors to treat leukemia in more efficient manners. These methods can also play a vigorous role in rural areas, where medical experts are not available. A lot of acute leukemia cases are discovered in low-income people, who have remote access to hospitals, which allows the disease to progress where it is hard to diagnose. The main purpose of our work is that we will be able to provide a method for detecting leukemia fast and with high accuracy and precision, our research focused on the classification of leukemia and its sub-types. This method provides pathologists with a second opinion which will lead to a lesser chance of error and a quick tool to determine the type of disease, which will help suggest a proper diagnostic, as before the treatment dangled on the experience of the pathologist and had a greater chance of error rate of 30-40%, Which lead to the cause of high morality.

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