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Follow-up of patients Using Artificial Intelligence During The Pandemic and Its Application In The Diagnosis of Leukemia

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A B S T R A C T

The prestige of the recent technologies such as “deep learning”, “internet of things (IoT)”, “cloud technology”, “big data”, “machine learning” are increasing day by day, and “artificial intelligence (AI)” is one of the most important components that pave the way for the development and transformation of those technologies. Recently, the use of artificial intelligence in medicine has become gradually widespread, and “artificial intelligence technologies” can be used in various fields of medicine today. Similarly, computer aided diagnosis (CAD) methods have been employed more and more extensively in medicine. A variety of “machine learning algorithms” have also been generated to diagnose several diseases such as “leukaemia”. As it is well-known, a fast, safe and accurate early-stage diagnosis of leukaemia is a crucial factor in healing patients and saving their lives. The current study, which is based on a method of artificial intelligence, aimed to investigate the use of internet of medical things (IoMT) to enable and improve a rapid and safe diagnosis of leukaemia. In the proposed IoMT system, medical devices and tools are connected to network with the help of cloud computing. In this system, the techniques used to identify the subtypes of leukaemia were “residual convolutional neural network” (ResNet-34) and “dense convolutional neural network” (DenseNet-121). By means of data magnification techniques, ResNet-34 and DenseNet-121 were both put into service to process multiple image patterns. For all healthy cases, the estimation accuracy of ResNet-34 and DenseNet-121 was measured as 100% and the precision rate was found to be 100%.

1. Introduction

The use of information and communication technologies in the field of health has brought health transformation processes to very high levels. Artificial intelligence was termed for the first time by John McCarthy as "intelligent machines, especially, the science of making intelligent computer software and engineering," as has been described [1]. Deep learning, the Internet of Things (IoT), cloud technology, big data, machine learning, cyber security and artificial intelligence technologies enable dramatic improvements in the health field. Major disease areas that use AI tools include cancer, neurology and cardiology.

Leukemia is a disease of the white blood cells (WBC) that affects the bone marrow and / or blood. There are two major forms of leukemia, acute and chronic. There are therefore four leukemia subtypes. Each form is subdivided into myeloid and lymphoid. There are therefore four leukemia subtypes.

Various methods have been developed to describe leukemia with its subtypes. This work provides an application based on the Internet of Things (IoMT) to develop and enable early and uncritical identification of leukemia. In this system, clinical tools are connected to network resources with the help of cloud computing. The system allows synchronous communication between patients and healthcare professionals for the testing, diagnosis and treatment of leukemia. In this way, the transmission of medical data over a secure network to facilitate health systems [3]. With the rapid develpoment of IoMT, making the health of the patient primary, secure and correct diagnosis and treatment of different diseases opens the door also to remote diagnostics applications [4].

The present study could be very useful for solving the problems of critically ill patients in pandemics such as COVID-19. The methods used to define leukemia subtypes in this study as recommended by the study group are the Dense Convolutional Neural Network (DenseNet-121) and the Residual Convolutional Neural Network (ResNet-34). In this study, two public data sets, ALL-IDB and ASH image bank, were used for leukemia. The results obtained show that the model proposed in this study is an effective method that can be used to determine leukemia subtypes. In the proposed IoMT system, clinical tools are connected to network resources with the help of cloud computing.

2. Definition of Leukemia

Leukemias are a heterogeneous group of neoplastic diseases that develop as a result of transformation of hematopoietic cells. During the developmental stages of bone marrow cells in leukemia, the rate of cell proliferation increases and neoplastic clones proliferate in the bone marrow and begin to replace other bone marrow cells. An increase in the number of cell lines is seen to replace blood cells in the peripheral blood [6,7].

Leukemia of white blood cells (WBC) is a disease associated with production of mature WBC. There are two main types of leukemia based on progression, acute and chronic leukemia. Infected WBC grow rapidly and do not perform normally in acute leukemia, while in chronic leukemia they can migrate normally and grow less rapidly. In this case, the cells may not be easily differentiated from healthy WBC [2]. Leukemia cells proliferate primarily in the bone marrow and lymphoid tissues, then pass into the peripheral blood and spread to other tissues. They originate from myeloid and lymphoid cells that proliferate in the bone marrow [8]. There are 2 types of leukemia, lymphoid and myeloid, depending on the size and shape of the WBC, and they can be divided into two subspecies, as acute lymphocytic leukemia (ALL), chronic lymphocytic leukemia (CLL), acute myeloid leukemia (AML) and chronic myeloid leukemia (CML).

2. 1. Acute Lymphocytic Leukemia

Acute lymphocytic leukemia (ALL) is a type of leukemia arising from lymphoid precursor cells in the bone marrow [12]. Blast cells in the peripheral blood and the bone marrow proliferate and accumulate [38]. ALL has mostly immature bone marrow WBC and is a cancer caused by the overproduction and continuous multiplication of the cells. It usually occurs between 2-5 years of age in children. ALL shows flu-like symptoms, with fatigue in the joints and bones, and weakness and pain symptoms, quite similar to other common diseases. It can be very difficult to diagnose the disease. To diagnose ALL, hematologists perform an examination of the blood and bone marrow. Manual blood testing techniques that have been in use for a long time are often slower and more difficult to use for diagnosis. It is known that the morphological similarity of these cells makes the diagnosis of the disease problematic, which can lead to death if undetected and the treatment process is not initiated.

2. 2. Acute Myeloid Leukemia

Acute Myeloid Leukemia (AML) is an acute non- lymphocytic leukemia characterized by replacement of normal myeloid cells by undifferentiated blasts as a result of acquired genetic changes [10]. Malignancy develops with the ability of the cells to proliferate and block differentiation processes or deviate from normal mechanisms [2]. In the most common type of acute leukemia, bone marrow blasts begin to produce immature WBC. They can also create red blood cells and platelets that are abnormal. Common symptoms of early-stage AML can be similar to symptoms of the flu or other common illnesses. AML develops in 25% of patients. It is frequently observed in men and in middle age [11].

2. 3. Chronic Lymphocytic Leukemia

Chronic Lymphocytic Leukemia (CLL) is the most insidious and slow leukemia type among all leukemias. It is characterized by the accumulation of small, mature appearing lymphocytes and is a clonal disease mostly of B cells, rarely T cells [12]. Briefly, CLL is characterized by the accumulation of dysfunctional B cells and their infiltration into bone marrow, blood, lymph nodes and other tissues. CLL is a hematological disease that gradually worsens. Generally, adults are affected [2].

2. 4. Chronic Myeloid leukemia

Chronic Myeloid Leukemia (CML) is also known as chronic myeloblastic leukemia or chronic granulocytic leukemia [13]. CML is a slowly growing type of leukemia. CML has three-phases. It starts with chronic phase myeloid and proceeds to excessive growth of cells and blasts, ending with crisis. In the chronic stage, the leukemia is at its strongest and grows slowly. In the second stage, the blood cells are immature and this is often referred to as the extended stage. The third stage is the explosion stage, also known as the acute stage or transformation stage. Chronic myeloid leukemia often occurs between the ages of 25-50 [14]. The blood structure and types of leukemia are shown below, Figure 1.

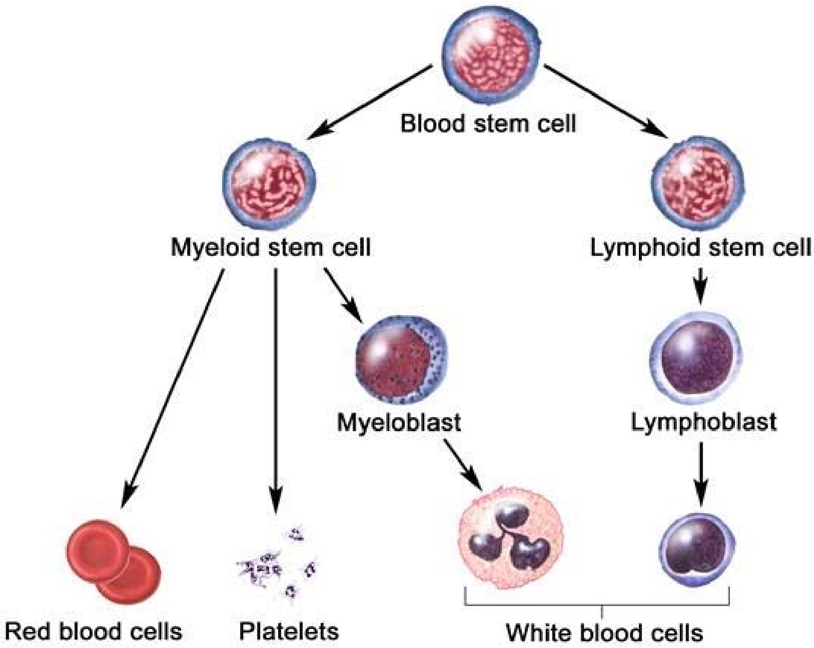

Figure 1: Blood and leukemia types.

3. Use of Deep Learning Algorithms to Identify Leukemia

It is very difficult for hematologists to detect the presence of leukemia and to determine the correct leukemia treatment. Use of specialized optical blood analysis followed by sample inspection in defining the leukemia is an important and time-consuming process. Many CAD methods using machine learning and deep learning methods have been developed for the quantitative analysis of peripheral blood samples. These methods also have disadvantages in obtaining the correct diagnosis.

In this study, an IoMT-based construct was used to automatically identify leukemia subtypes. In the build used, an IoT-enabled microscope uploads blood smear images to the leukemia cloud. It is applied by using resnet-34 or dendennet-121 as a deep learning model according to the leukemia type. Thanks to the high predictive power of deep learning algorithms, their areas of use have expanded. In this study, microscopic images of blood were used to identify ALL, AML, CLL, and CML.

According to the proposed model, Leukemia types predicted diagnostic results can be viewed on the clinician's computer and leukemia patients can be offered medical care accordingly. As shown by work in 2019 on coronavirus disease (Covid-19), for both patients and doctors, significant benefits were provided. Despite the Restriction in most countries due to the rapid spread of COVID-19, patients with chronic illness have had to leave their homes for disease control. Although there is a threat with restriction, patients with chronic illnesses have had to leave their homes for disease control. Therefore, this application could be applied to the current crisis in order to provide adequate medical care in the homes of patients as a facility would provide. Diagnosis of subtypes or support of oncologists would also reduce the need to travel to a facility [2].

4. Studies Conducted Using Deep Learning Methods

Various studies have been conducted for the diagnosis of computer-aided (CAD) leukemia. In these studies, different machine and deep learning algorithms have been used to define leukemia.

S. H. Rezatofighi and H. Soltanian-Zadeh carried out the segmentation of cells with Gram-Schmidt orthogonalization in the first stage of their study for the recognition of WBCs in peripheral smear images, and in the next stage, they performed feature extraction using morphological and structural features. In the last stage, they questioned the success of the proposed method on SVM and ANN by using the obtained feature vectors. At the end of the study, they saw that SVM produced better results [15].

In 2012, N. Ramesh et al. proposed a method for the segmentation of cells that uses the color and morphological characteristics of the cells. The authors, who tested their methods on 1938 images, stated that they could correctly distinguish 1804 of them. The authors who performed Linear Discriminant Analysis using the feature inferences they obtained after segmentation achieved a total accuracy of 93.9% [16].

In 2013, M. Habibzadeh et al. They proposed a model for the detection and classification of low resolution WBCs. The authors, who performed the first segmentation of 140 images in their data sets, worked with 115 of these images in SVM, kernel PCA SVM and CNN. They tested the classifier models on 25 samples and stated that they achieved the highest success in CNN [17].

In 2017, X. Li et al. They performed blood cell classification on hyperspectral images using CNN. They performed feature extraction with PCA and then compared their results using an 8-layer architecture with a trained SVM. They showed that CNN is 30% more successful than SVM [18].

D. Mundhra et al. proposed a method for automatically segmentation and sorting of WBC, red blood cells (RBC) and platelets in preferic smear images. First of all, the authors, who increased the number of samples by means of data enhancement techniques, were able to provide WBC extraction with an accuracy of 99.5% with the method they suggested [19].

Again in 2017, J. W. Choi et al. In the study carried out by, the existing 2174 images were increased to 48000 levels with data enhancement techniques. They stated that the CNN architecture they created after some transformation and normalization processes they performed in color channels reached 95.68% accuracy. A. I. Shahin et al. They proposed a two-step classification model in their study where they used 2551 images. Comparing success rates with a standard CNN, the authors showed that their proposed model produced better results [20].

J. Zhao et al. first they transformed the color channels of the images into grayscale, then they used a pre-treatment process to remove the noises. An SVM was arranged with the features they extracted from the cells, thus providing a separation of three classes as basophil, eosinophil and other cells. Subsequently, feature extraction of CNN and other cells was performed and they performed neutrophil, lymphocyte and monocyte classification by means of RF algorithm. At the end of their studies, they achieved classification success ranging from 70% to 100% [21].

In 2018, M. Habibzadeh et al. They performed a classification for four WBC subtypes. The researchers, who passed their samples through pre-processing (data enhancement, color channel transformations, etc.), trained ResNet and Inception architectures using 11200 images, and used 1244 images in the test process. At the end of the study, the authors who achieved success of up to 100% stated that they achieved the highest success with the ResNET 50 architecture [22].

5. Experimental Phase

The deep learning models are used to classify the subtypes of leukemia.

5. 1. Leukemia Database

In leukemia diagnosis, the data set was collected from two different sources: the ASH image bank [2, 26] and ALL-IDB [2, 27,28].

Experienced oncologists provide full classification for each image in the data set.

5. 2. Data enlargement

In proposed mode l, rotation is used to acquire images from different sources and various image conversion and shift schemes are then used. In different image splitting studies using CNN, a large number of information copying methods gave better results, reducing the error rate. Image transformation or data enlargement techniques were used to maximize the data set. After applying the image transformation methods, the sample size was increased in both data sets [2].

6. Deep Learning Models Used in the Study

After performing magnification of the data set, a deep learning model convolutional neural network CNN (convolutional neural network) was created.

Advanced CNN models such as ResNet and DenseNet are deeper, more complex and capable of better learning. Therefore, in the present study, the ResNet-34 and DenseNet-121 models were used in supervised learning to define and classify leukemia according to type [2].

6. 1. ResNet-34

ResNet-34 is a 34-tier model of Microsoft ResNet architecture. The cause of this problem involves gradients. The use of ResNet solves this problem since gradients flow from the starting layers to the last layers, skipping some layers.

ResNet-34 consists of a total of 34 layers, one of which is convolutional and has the same pattern, in addition to the other four layers. Each layer is surrounded by a 3 × 3 convolution with a feature map of 64, 128, 256 and 512, respectively [2, 29].

6. 2. DenseNet-121

DenseNet architecture uses dense connections like ResNet architecture. DenseNet-121 consists of 121 layers. DenseNet architecture uses fewer parameters than ResNet to operate the network [2].

6.3. Experimental results

In order to evaluate the proposed models, the performance measures used are precision, recall, F1 score, and accuracy. Recall is the accuracy of prediction for the known leukemia subtype class. Accuracy is the prediction for the known leukemia and non-leukemia subtype classes [2,31].

Table 1: Performance of the ResNet-34 / DenseNet- 121 model for leukemia subtype classification [2].

ResNet-34					DenseNet-121				
Leukemia type	**Accuracy**	**Precision**	**Recall**	**F1 score**	**Leukemia type**	**Accuracy**	**Precision**	**Recall**	**F1 score**
ALL	100	1.0	1.0	1.0	**ALL**	100	1.0	1.0	1.0
AML	99.65	1.0	0.99	0.99	**AML**	99.91	1.0	1.0	1.0
CLL	99.73	0.99	0.99	0.99	**CLL**	99.91	1.0	0.99	1.0
CML	99.73	0.99	1.0	0.99	**CML**	100	1.0	1.0	1.0
Healthy	100	1.0	1.0	1.0	**Healthy**	100	1.0	1.0	1.0

It is exhibited from Tables Tables1 and 2 that the ResNet-34 and DenseNet-121 prediction accuracy for All and healthy cases is 100%, while precision, recall, and F1 score are also 100% to demonstrate its efficiency, the proposed models were compared with the previous approaches GA, SVM and CNN as shown Figure 2 [2]. It is depicted from Table 2 that the proposed models outperform the previous approaches with average accuracy for ResNet-34 and DenseNet-121, respectively.

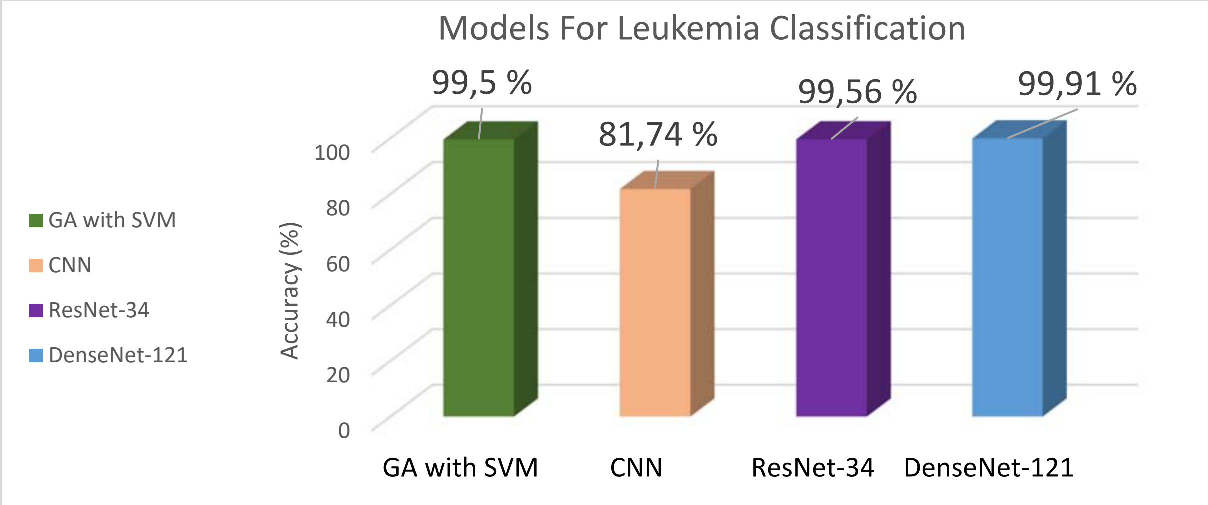

Figure 2: Comparision of the studies detection of subtypes of leukemia [2].

Table 2: Comparison of studies detection of leukemia subtypes [2].

Reference	**Dataset**	**Classification**	**Classifier**	**Accuracy (%)**
Ahmed et al.	ALL-IDB	Leukemia vs healthy	CNN	88.25
			Naive Bayes	69.69
			Decision tree	62.94
			KNN	58.57
			SVM	50.09
	ALL-IDB, ASH image bank	Leukemia subtypes classification	CNN	81.74
			Naive Bayes	52.68
			Decision tree	45.92
			KNN	43.51
			SVM	20.84
		Subtypes of acute lymphoblastic leukemia	AlexNet	96.06

Reference	Dataset	Classification	Classifier	Accuracy (%)
Jothi et al.	ALL-IDB	Acute lymphoblastic leukemia detection	Jaya, SVM	99.00
			Jaya, decision tree	98.00
Acharya et al.	ALL-IDB	White blood cells	K-medoids algorithm	98.60
Al-jaboriy et al.	ALL-IDB1	Acute lymphoblastic leukemia detection	GA and ANN	97.07
Pansombut et al.	ASH image bank, ALL-IDB1	Lymphoblast cells	CNN-based convnet	81.74
Moshavash et al.	ALL-IDB1, ALL-IDB2, Dr. Juan Bruno Zayas Alfonso Hospital, Santiago de Cuba	Acute lymphoblastic leukemia detection	Two ensemble classifiers with SVM	89.81

7. Conclusion and Evaluation

The study group appeared to use an IoMT-based model for automatic identification and detection of leukemia subtypes. In this model, the IoT- enabled microscope uploads the blood smear images to the leukemia cloud. In the model design, leukemia is diagnosed according to its types using ResNet-34 or DenseNet-121 deep learning models. As a result of the study, when compared with previous trials, it was seen that the diagnostic power of ResNet-34 and DenseNet-121 surpassed all previous approaches [2]. Using data magnification techniques, ResNet-34 and DenseNet-121 both can process multiple image patterns. After the diagnosis is made, the result is sent over the cloud to the doctor's computer where medical care is provided. This model facilitates the lives of patients and physicians in pandemics such as the current COVID-19 pandemic [2].

This study has been tested to show it can be used to find other blood abnormalities. Diagnostic results predicted according to the types of leukemia can be displayed on the clinician's computer. The system also allows real-time coordination between patients and healthcare professionals for testing, diagnosis and treatment of leukemia.

The biggest help for doctors in any field could be algorithms, machine learning systems and skilled robots. Artificial intelligence has revolutionized health, as in every aspect of our lives. Healthcare services around the world are significantly affected by this change. Machine learning and artificial intelligence affect doctors, hospitals and all health-related areas. The use of this technology in healthcare is an important factor that increases the enthusiasm for artificial intelligence and robotics in the speed and accuracy of diagnosis and treatment, however, trust in the technology is critical for its greater use and acceptance [2].

In recent years, very successful results have been obtained in image processing and machine learning-based studies on the classification of digital blood images. The high accuracy values obtained show that machine learning-based systems in the field of digital hematology can be used as auxiliary systems for physicians in clinics. In the coming years, it is predicted that artificial intelligence and machine learning-based solutions will be used at a much higher rate in the field of hematology.

Results obtained from this study showed that the proposed model could replace other machine learning algorithms used to identify leukemia subtypes [2].

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