A COMPARATIVE STUDY OF TECHNIQUES FOR LEUKAEMIA DETECTION

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ABSTRACT

Leukaemia is a cancer of blood that causes more deaths than any other cancer. Presently, the diagnosis of blood samples is done through visual examination by doctors. For proper and efficient treatment of leukaemia it is essential to detect it in early stage and proceed with the monitoring and evaluation. Till date many research have been done to design an automated system for detection of leukaemia either through study of microscopic images of blood samples or bone marrow biopsy.

In this paper, a literature review has been done to classify the types of leukaemia and the various methodologies being followed by the researchers to detect it. Also, we have discussed some of the issues faced by the researchers. This paper also describes the various changes on texture, geometry, color and statistical analysis of microscopic images.

Keywords: ALL, AML, Microscopic Imaging, MLP, SFAM.

I INTRODUCTION

Over the past few decades there has been huge growth in the application of image processing techniques in the bio-medical area. Researches are being carried out to develop efficient and cost effective system for solving medical problems. Presently the diagnosis of the blood samples is done through visual examination by the haematologist. However these morphological or biochemical analysis are subjected to various short comings like operators experience, tiredness, fatigue and slowness and these cell images are prone to have errors due to lack of efficiency, difficulties in cell nature and problems related to preparation of staining of blood cell slides [1][2][3]. Also, it has been found that the manual recognition method has an error rate between 30% and 40%. [4].This situation is further gearing up the demand of developing an automated system to provide more accuracy and precision.

One of the most feared disease by the human is cancer. Leukaemia is the cancer of blood, and if not detected in the early stage can even lead to death. Automated systems based on artificial vision can speed up this operation [5].

Most of the symptoms and conditions of a disease are reflected in the blood. Studies have shown that all the techniques developed for medical imaging uses all the information about blood for classifying various diseases like leukaemia, anaemia, cancer, thalassaemia etc. These parameters may be RBC count, haemoglobin level or other parameters such as color, shape, size etc [11].

In general leukaemia detection is done by performing the complete blood count [6]. If the count is found to be abnormal, study of morphological bone marrow smear is done to confirm the leukaemia [4]. From decades basically two main analyses are performed: cell classification and counting. The morphological analysis do not require a blood sample and hence is suitable for low cost accurate and remote screening system, as it just needs an image [5].

Alteration in WBC can be neoplastic and non-neoplastic. Leukaemia is the neoplastic proliferations of hemopoietic cells. It is quite complicated to practically classify leukaemia and it can be categorised on the basis of genetic abnormalities, cell of origin, clinical characteristics and morphologic findings [2].

When there is an abnormal production of white blood cell by the bone marrow, leukaemia is said to occur. Due to increase in WBC count there will be misbalance in the blood system. These blast cells can be either myeloid or lymphoid. Leukaemia can be broadly classified as acute or chronic on the basis of severity of the situation. Further, we can classify acute leukaemia as either Acute Lymphoblastic Leukaemia (ALL) or Acute Myelogenous Leukaemia (AML). During the observation, three types of WBC need to be considered, that are Lymphoblast, Myeloblast and normal WBC [7].

The acute Lymphoblastic leukaemia disease is concerned with lymphocyte formation in bone marrow and into the peripheral blood. In preparation of blood, colorant are used which tend to concentrate only in WBC, particularly at the nuclei centre. Mostly size of white cells is bigger than red cells. One of the most common methods for leukaemia classification is FAB method [8]. Further advanced method is immunologic classification which requires more sophisticated setup for testing [9].

Toure and Basu applied the MLP network by an algorithm called Back Propogation (BP). It predicted the type of leukaemia whether it is ALL or AML, and they succeeded with 58% accuracy on test data [10].

II BACKGROUND

The three principle cells present in the blood are red blood cells, white blood cells and platelets. A microscopic image of a WBC is shown in Fig. 1.

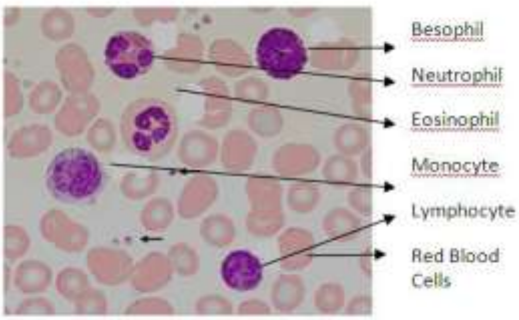

Figure 1: White blood cell [3]

Granules are contained in Leucocyte cells called granulocytes (collected by neutrophil, basophil, eosinophil). Rest of the cells which are without granules are called a granulocytes (composed of monocyte and lymphocyte). The percentage of range of leucocytes in human blood has following values: Eosinophils 1- 5%, neutrophils 50-70%.Basophils 0-1%. monocytes 2-10%, lymphocytes 20.45% [3].

Changes in health and development of specific diseases can be retraced from the information provided from the blood. Variation in the number or appearance of elements that formed will guide health condition of an individual [11].

2.1 Leukaemia

Bone marrow is a soft material found in middle of each bone. Cells in the bone marrow produces blood cells, most of which are called stem cells. On maturing, stem cells become some kind of blood cell. Blood consist of four main components, namely:

a) Red Blood Cell (erythrocytes)

b) White Blood Cell (leukocytes)

c) Platelets

d) Plasma

Old or damaged cells die and are replaced by the new cells [11].

Fig. 2 shows that how stem cells became mature and evolve into several components of blood.

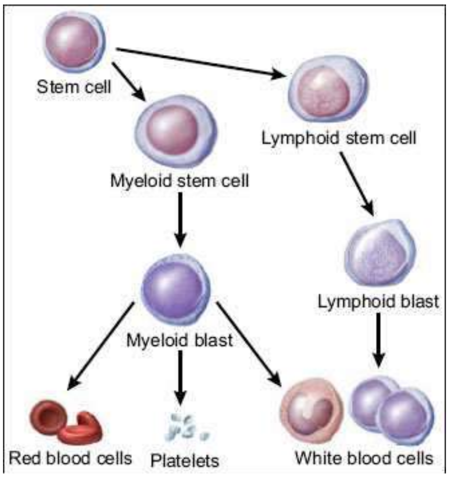

Figure 2: Production of Blood Cell [11]

The stem cell on maturity evolves either into myeloid stem cell or lymphoid stem cells. Lymphoid stem cells eventually become lymphoid blast which will further form several types of WBC. On the other hand, the myeloid cells on maturity become myeloid blast and form RBC, platelet and several type of WBC. The WBC from lymphoid blast and myeloid blast differ.

For a person suffering from leukaemia, the bone marrow will produce abnormal WBC. These abnormal WBC don't die when they should and become numerous. Thus, they interfere with the duties of the normal WBC. This causes imbalance of blood system in human body. In other words, certain abnormalities cause the rapid growth and division of cell which seem to live longer than the normal cells.

One of the basic ways of classifying leukaemia is on the basis of severity and progress of the disease. They are:

a) **ACUTE:** In this type of leukaemia the abnormal cells are the immature blasts which are not capable of carrying out normal work and multiply rapidly. This condition needs to be treated quickly and on time.

b) **CHRONIC:** This type of leukaemia has more mature cells which replicate and accumulate. They can work like normal cells for some period of time. In this case accumulation of abnormal cell is slow and the leukaemia can go undiagnosed for years.

On the basis of type of WBC affected, leukaemia can be classified as:

a) **LYMPHOCYTIC:** In this case lymphoid cells are affected. Lymphoid cells develop lymphatic tissues which makes our immune system.

b) **MYELOGENOUS LEUKEMIA:** This type of leukaemia affects the myeloid cells. Myeloid cells give rise to red blood cells, white blood cells and platelet-producing cells.

2.2 Types of Leukaemia

- **Acute lymphocytic leukaemia (ALL).** This is the most common type of leukaemia in young children. ALL can also occur in adults.

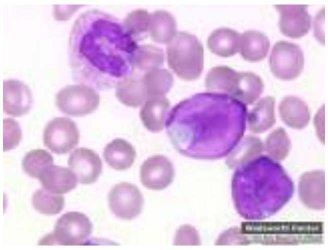

Figure 3: Acute Lymphocytic Leukaemia (ALL) [12]

- **Acute myelogenous leukaemia (AML).** AML is a common type of leukaemia. It occurs in children and adults. AML is the most common type of acute leukaemia in adults.

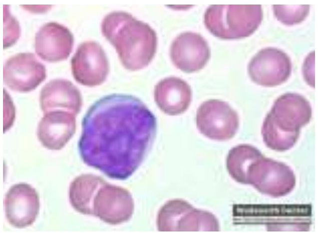

Figure 4: Acute Myeloid Leukaemia (AML) [12]

- **Chronic lymphocytic leukaemia (CLL).** With CLL, the most common chronic adult leukaemia, you may feel well for years without needing treatment.

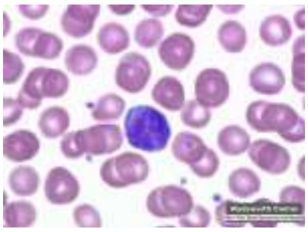

Figure 5: Chronic Lymphocytic Leukaemia (CLL) [12]

- **Chronic myelogenous leukaemia (CML).** This type of leukaemia mainly affects adults. A person with CML may have few or no symptoms for months or years before entering a phase in which the leukaemia cells grow more quickly.

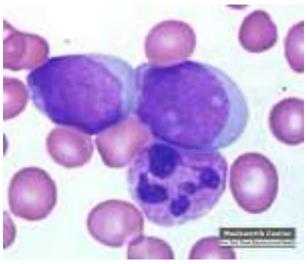

Figure 6: Chronic Myeloid Leukaemia (CML) [12]

III RELATED RESEARCH

For detection of leukaemia disease firstly blood samples are gathered and further studied. The samples are then segmented by using various techniques. The methodologies so used may vary and researches are being carried out to find the most efficient segmentation technique. Researchers have given various methods for image segmentation. When there is good contrast between foreground and background, edge detection can prove to be a meaningful segmentation technique [13]. Automatic thresholding method was used by cseke in 1979. However it does not always produce precise results as during the selection of the segmentation threshold no spatial information is used [14]. Another method that can be used is fuzzy C-mean clustering in which single cell image of WBC in bone marrow is segmented into two regions (nucleus and non-nucleus). However it has been reported in [15] that if the number of clusters is greater than two then the computational time may increase.

From years researches has been done to present an automated leukaemia detection technique which can assist the haematologist to obtain accurate results for mapping the disease. The main objective of these techniques is to allow automatic image segmentation, feature extraction and classification. The various schemes applied may differ in the methodologies employed to study WBC. The segmentation technique may vary, or the parameters used for classifying abnormal blood cells may differ.

Minal D. Joshi et. al. in. [1] represents blood side image segmentation and classification for automatic detection of leukaemia. In this paper, lymphocytes are detected and using feature extraction module, their features such as perimeter, circularity, area etc are calculated. The author emphasizes on the correct segmentation technique used as the subsequent accuracy of feature will depend on it. Pattern recognition is also considered a powerful tool for the differentiation of normal cells and blast cells. The paper mainly concentrates on calculation of features such as area, perimeter, circularity etc and the features were classified using kNN classifier. The technique developed was applied on 108 images and gave an accuracy of 93%.

Subrajeet Mohapatra et. al. in. [2], a comparative approach for the detection of Acute Lymphoblastic Leukaemia (ALL) based on WBC nucleus image segmentation and morphological analysis is introduced. The author suggests that the leukaemia detection process depends on proper WBC nuclear segmentation, feature extraction and classification. The segmentation is done using color based clustering followed by feature characterisation and assessment of lymphoblast. The clustering algorithm used were k-means, k-medoid, FCM, GK and FPCM for microscopic image segmentation. First K-means color based clustering was used to obtain WBC nucleus of the image. Then the image was cropped around each nucleus to obtain the sub-image. Noise detection process employed included incorporation of adaptive threshold to get more reliable detection of noise.

The author suggested that nucleus is sufficient for leukaemia feature extraction and classification. However, cytoplasm obtained in clustering scheme can also be used as an indicator of leukemic conditions. Further, Hausdorff dimension (HD) was measured. The analysis was conducted on 50 samples and it was found that none of the lymphocytes had a HD larger than 1.22. on the other hand, larger percentage of lymphoblast had HD more than this value. Therefore, this was considered to be most suitable method for leukaemia detection [2].

Another parameter used in the paper is contour signature. First, centroid of the nucleus contour is determined and then Euclidean distance between the centre and the boundary was depicted. Then the variance of the distances of the lymphocytes and lymphoblast is measured and is chosen as a hard limiter to identify whether the nucleus is healthy or leukemic. The limit for the feature was fixed as 0.02 .Also shape color and texture were extracted and fed to the SVM classifier for detection of leukaemia. Accuracy of 92% was obtained [2].

Ruggero Donida Labati et. al. in. [5], the authors have proposed a data set of blood samples that provides evaluation and comparison of the performance algorithm of segmentation and image classification. They have also proposed a metric to evaluate the performance of algorithm employed for the detection of ALL in the automatic systems. They have illustrated a need for a system that can work with different structures of module and can identify the presence of blast cells in the input image. They have also proposed a bench mark approach to measure and compare the identification accuracy of different structures of module.

Aimi Salihah. A. N. et. al. in. [16] the author proposed a technique to detect Acute Myelogenous Leukaemia. Employing this technique, any abnormalities in WBC can be detected by the combination between contrast enhancement and segmentation. The contrast enhancement technique includes partial contrast and bright stretching. Here authors have used HSI color space technique instead of RGB as it is observed to yield better results. The results showed that the enhancement technique used reduces the interference of background images to a great extent and allow efficient extraction of morphological images from the blood samples.

Aimi Salihah. A. N. et. al. in. [17] considered contrast enhancement technique at the pre-processing stage to be very useful in diagnosing Acute Myelogenous leukaemia in blood. In this paper the authors suggested two phase methodologies: first was contrast enhancement technique and second was segmentation using HSI technique. Contrast enhancement technique includes bright stretching, dark stretching and partial contrast which enhanced the area of acute leukaemia. After using HSI color space if results so obtained are satisfying then these images are filtered using NxN (N=7) median filter to obtain better results.

Abdul Nasir et. al. in. [18], the authors discussed various problems that haematologist encounter when they try to observe the samples due to its uneven texture and irregularity. Thus in this paper threshold technique is suggested to overcome the problems. In this technique the original blood cell images are firstly converted to greyscale image and then the WBC and RBC threshold count are observed manually. Then the image is converted into binary images. These images may sometimes contain small spots which are considered to be noise. These spots can be eliminated by using two techniques: removing pixels technique and Gaussian filter. They studied 91 microscopic images and found that the ratio range is 0.2 to 2.5 for ALL and 0 to 14 for AML. Therefore, these counts were sufficient for the detection of leukaemia.

N. H. Harun et. al. in. [19], the authors classified the blasts in acute leukaemia samples using artificial neural network. From the blood images a total of six morphological features were extracted and for the classification purpose these were used as neural network inputs. To perform the task of classification Hybrid Multilayer Perceptron (HMLP) neural network was used. The HMLP is trained using RPE (MRPE) training algorithm for 1474 samples. It was observed that HMLP produces an performance accuracy of 97.04%. The results indicated that the HMLP neural network was capable of differentiating the blast cells from acute leukaemia blood samples. HMLP network is said to have high accuracy even in testing of cervical cancer and breast lesions successfully with accurate results. After input being fed to HMLP network, images are captured and finally to ensure the correctness of the results so obtained haematologist or technologists revise those images.

Aimi Abdul Nasir et. al. in. [20], the author have presented the classification of white blood cells inside the acute lymphoblastic leukaemia (ALL) and acute myelogeneous leukaemia (AML) blood samples by using multi-layer perceptron and simplified fuzzy ARTMAP (SFAM) neural networks. The limitation of the ability of computer to perform certain task was overcome by ANN. The segmentation process employed used morphological pre-processing followed by bythe snake –balloon algorithm.In the paper, the author has used several types of features based on intensity, color, shape and texture. It has been evaluated that SBM produce 91.03% accuracy as compared to multi-layer perceptron network using conjugate gradient descent, linear vector quantization and K-nearest neighbour classifier which produce 89.74%, 83.33% and 80.76% of accuracy respectively. This paper utilised the potential use of MLP and SFAM networks for categorising WBC as lymphoblast, myeloblast and normal cell. The methodology used includes image acquisition, image segmentation, feature extraction and classification using ANN. Here identification of blood cell is based on color and features were derived from red, green, blue and intensity components. Total of 12 color features were extracted from cytoplasm of WBC.

Using both MLP and SFAM network have given promising result with testing accuracy of more than 80% for the three categories of features (shape, size and color) [20].

For MLP it was observed that the color based testing accuracy is highest followed by size and shape. For SFAM the size based testing accuracy was found to be highest followed by color and shape based feature. The results provided in the paper using MLP_LM, MLP_BR and SFAM networks with testing accuracy of 95.55%, 95.70% and 92.43% respectively [20].

IV INFERENCES DRAWN AND DISCUSSIONS

From all the literature studies above, it is clear that the detection of Leukaemia involves some basic steps. These are as follows:

- Image Acquisition
- Image Preprocessing
- Image Segmentation
- Feature Extraction

4.1 Classification on the basis of features

The overall efficiency and effectiveness of the technique depends upon the methodology being followed. Image segmentation is a very crucial stage and hence many researches have been made to obtain the proper segmentation technique. This is because the preciseness of the extracted feature will majorly depend on the quality of the segmented image.

a) **Acquisition of Image**: Firstly, all the blood images are gathered. These images can be obtained from the public dataset available.

b) **Preprocessing**: During image acquisition, there are chances of image staining or we could say image gets distorted by noise. These noises may appear as illumination or shadow which blurs the image. To enhance the quality of image contrast enhancement techniques are used.

c) **Segmentation**: After preprocessing, various segmentation techniques are employed such as threshold otsu method, automated histogram thresholding, data clustering such as K-means, fuzzy C- means, etc., snake balloon algorithm, Fluorescence in-situ hybridization (FISH) method, immunophenotyping, cytogenetic analysis and cytochemistry. Fig. 7 shows the flow chart representation of various segmentation techniques used.

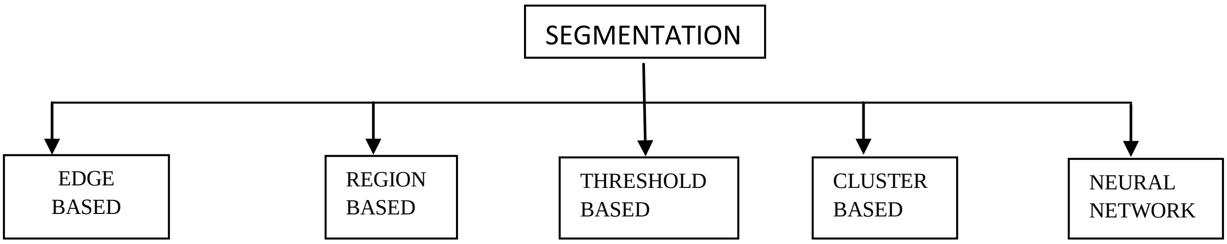

Figure 7: Flow Chart Representation of Segmentation Techniques

d) **Feature extraction**: In this technique, input data is transferred into set of features. Various features of the cells are studied to identify Leukaemia. Some of these features are: geometry, texture, color, contour signature, statistical features, etc.

e) **Classification**: Once the features are extracted from the segmented image, then classification of Leukaemia type is done. This classification can be done by employing one of the mentioned techniques, which are kNN rule, Reinforcement learning algorithm. By classification, Leukaemia can be categorized as AML, ALL, CML, CLL.

From all the literature studies, it was observed that all the authors emphasize on designing a system that can be employed for digital pathology, and at the same time follow the methodology to obtain a robust system. Accuracy and precision is still a problem and more research need to be done in this field.

V CONCLUSION

From the complete literature survey, it can be concluded that no matter whatever methodology is being employed by the author, the main focus is to use a precise and correct segmentation technique. Many techniques have been developed to detect leukaemia namely study of microscopic images using image processing techniques, MLP, SFAM and bone marrow biopsy. Some of the authors have suggested shape and size to be the sufficient parameter to detect Leukaemia, however others have suggested to take into account the features such as Contour signature and HD for more accurate results.

Even after so many techniques, problems are still faced when it comes to staining of the cells, noise detection and segmentation. Researchers are still looking for technique which can help to develop a robust, fully automated detection system which can be efficiently used for medical image mapping.

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