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Classification of Acute Leukemia Using CD Markers

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Abstract— **This paper presents characteristics of morphology, immunophenotype, molecular and cytogenetic of bone marrow samples were analyzed. Leukemia is divided into two categories which are acute leukemia and chronic leukemia and other types. Our work focuses on classification of Foil of Bretagne (Lymphoid) and Almeida Lloyd (Myeloid).The features are extracted from the segmented images and classified using the Support Vector Machine (SVM).The method has been evaluated using a set of 200 images with 100 abnormal samples and 100 normal samples obtained. The classification proposed 3 subtypes of ALL and 8 subtypes of AML that are characterized by unique morphologic, immunologic, and cytogenetic features Immunologic (MIC group) markers cluster of differentiation (CD). The computer simulations show that the proposed system robustly segments and classifies Acute Myelogenous Leukemia based on complete microscopic blood images. We have obtained accuracy 93.89 %.**

Keywords- cluster of differentiation (CD), immunophenotyping, flow cytometry, Support Vector Machine (SVM), Morphologic immunologic cytogenetic (MIC).

I. INTRODUCTION

Leukemia is a blood cancer originated from abnormality blood cell in the bone marrow. The differential diagnosis may be associated with an elevated leukocyte count and a left shift. So, patients with acute leukemia may also present with low leukocyte counts together with anemia and thrombocytopenia. It is critical to distinguish these malignant diseases, which require rapid therapeutic intervention, from benign hematologic disorders.

For this problem, this paper provides the research of the classification of acute leukemia by using image processing to identify the types of acute leukemia. The values pattern of Leukemia cells image after processing will be compared to the values pattern of standard Leukemia cells image automatically and then classify them. Our techniques will help medical practitioners to diagnose the types of Acute Leukemia to be faster and more efficiency. This paper presents a method for classifying leukemia. Leukemia is divided into two categories.

II. LITERATURE REVIEW

A. Leukemia

Acute Leukemia is the cancer that is the most common malignant disease affecting children. Acute Leukemia has a peak bimodal age distribution in children between 2 and 5 years old and again in people who older than 65 years old. In the United States, the approximate acute leukemia ratio in children is 1:25,000. In Thailand (2003), the approximate acute leukemia is 53% of all childhood cancers. The development of acute leukemia has been associated with potential etiologic factors such as Genetic syndromes, Medications (Topoisomerase inhibitors and Alkylating agents) and Viruses (Epstein-Barr virus, HTLV-1) [1].

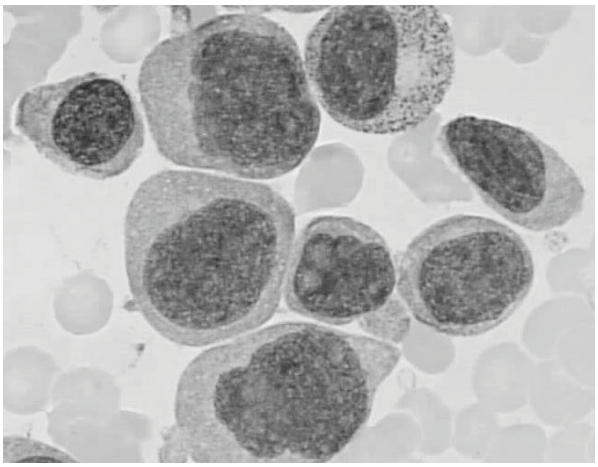

Fig 1. Acute leukemia cells

In most cases, the leukemia starts in the bone marrow. Then, it will produces blood cell uncommonly and may spread to other places and invades the blood fairly quickly. Moreover, It can spread to other parts of the body, which included the lymph nodes, liver, spleen, central nervous. [2].

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III. PRE-PROCESSING : Digital Microscope

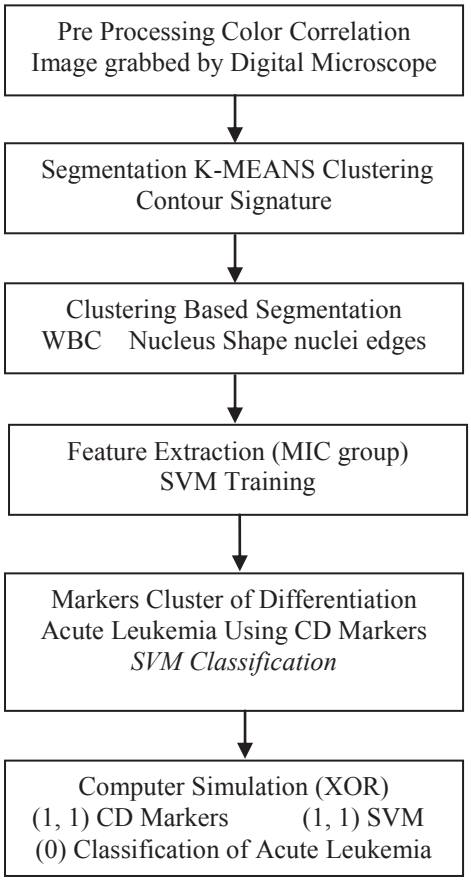


Fig 2. System Over view

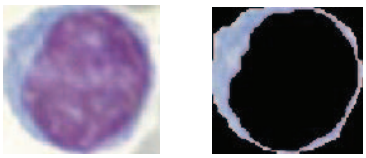
IV. SEGMENTATON K-MEANS CLUSTERING

In this paper, at first, nuclei are extracted by clustering the microscopic images into three color clusters in Luv color system using K-means method [3]. The K-means clustering has been used for image segmentation

To consider an objective function of the method, it can rewrite as Equation (1).

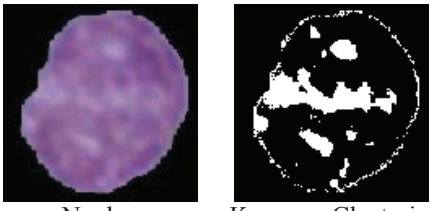
$$J = \sum_{j=1}^{k} \sum_{i=1}^{n} \left\| x_i^{(j)} - C_j \right\|^2 \qquad (1)$$

Where, J is the distance between the pixel (x) and the cluster center(c),k is the number of cluster and n is the number of data



Lymphocyte Cytoplasm

Fig 3 segmented cytoplasm and nucleus images



Nucleus K-means Clustering

Fig 4. Examples of Segmentation using K-means Clustering

While performing K-means segmentation, it was observed that in some of the segmented images, we obtained only the nuclei edges (refer Figure 4:) as opposed to the whole nuclei. Hence to make the system more robust, all segmented images were made to undergo morphological filtering [5]. Texture based features were then extracted from the resultant images.

V. FEATURE EXTRACTION

The FAB classification of ALL and AML is based on morphology and Cytochemical staining of blasts. Those are differentiated based on morphology, including cell size, prominence of nucleoli, color of cell and the amount and appearance of cytoplasm. The FAB classification is shown in the Table1. Table2. Pattern recognition is selecting the proper diagnostic features, describing the image by the numerical values, and enabling the automatic system to perform the recognition. Usually many of the features using texture, geometrical and statistical analyses of the image .The classification of acute leukemia by FAB system. FAB (French-American-British Corporative group) is the original classification scheme proposed which divides AML into 8 subtypes (M0 to M7) and ALL into3 subtypes (L1 to L3) [5].

TABLE I. TABLE TYPE MIC GROUP

MIC group	*FAB Classification*		
	Based Using CD Markers	***(ALL)***	***(AML)***
(XOR)	(1, 1) CD Markers (1, 1) SVM	(0) L1-L3	(0) M0-M7

VI. COMPUTER SIMULATION

Among all the features the most relevant features are selected and used to train the SVM [6] such as number of nuclei lobes it differentiate the nucleus of each type, ratio of nuclei to cell, ratio of perimeter to nuclei and entropy. The number and structure of nucleus lobes is one of the prominent features used to identify the class of the WBC. [7] SVM is a powerful tool for data classification based on hyper plane classifier. This classification is achieved by a separating surface (linear or nonlinear) in the input space of the data set. [4] They are basically two class classifiers that optimize the margin between the classes. The classifier training algorithm is a procedure to find the support vectors. Shape and texture based features are extracted for the image nucleus sample and recorded. In Table 1

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TABLE II The FAB classification

FAB Classification	
Acute lymphocytic leukemia Cancer Set (ALL)	Descriptive Term SVM Training
L1	Small monotonous lymphocytes
L2	Mixed L1- and L3-type lymphocytes
L3	Large homogeneous blast cells
Acute myeloid leukemia Cancer Set (AML)	Descriptive Term
M0	Acute myeloblastic leukemia, undifferentiated
M1	Acute myeloblastic leukemia, without maturation
M2	Acute Myeloblasts with maturation (best AML prognosis)
M3	Acute promyelocytic leukemia
M4	Acute myelomonocytic leukemia
M5	Acute monocytic leukemia
M6	Erythroleukemia/DiGuglielmo syndrome
M7	Acute megakaryoblastic leukemia

VII. PERFORMANCE EVALUATION

Precision, Specificity, Sensitivity and F-Measure are all defined in relation to the possible outcomes of the classifier system. *True Positive* (cancerous cell correctly identified), *False Positive* (non -cancerous cells identified as cancerous), *True Negatives* (non-cancerous correctly identified), *False Negatives* (Cancerous cells identified as non-cancerous).

TABLE I. PERFORMANCE EVALUATION PARAMETERS

No.	Evaluation parameters		
	Parameters	***Formulae***	***Value***
1	***Sensitivity***	TP/(TP+FN)	93.89%
2	***Specificity***	TN/(TN+FP)	92.17%
3	***Precision***	TP/(TP+FP)	91.35%
4	***F-Measure***	$\frac{2 \times \text{Precision} \times \text{Sensitive}}{\text{Precision} + \text{Sensitivity}}$	90.62%

TABLE III Performance Evaluation Statistics

Measure	**Value**
Sensitivity	93.89%
Specificity	92.17%
Precision	91.35%
F-Measure	90.62%

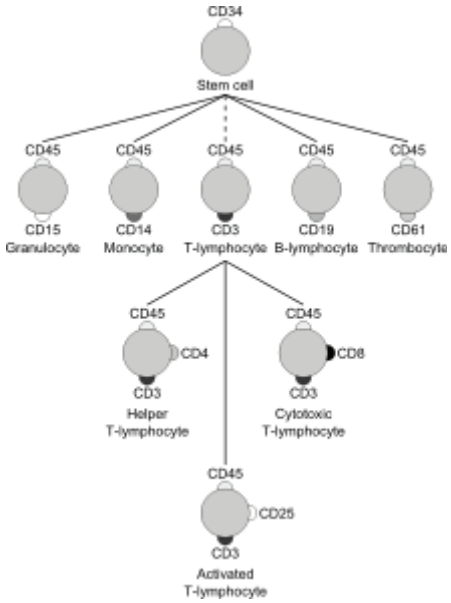
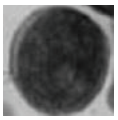
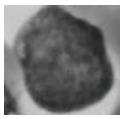
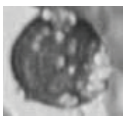


Fig 3. The Acute leukemia cells and Cluster of Differentia

FAB (French-American-British Corporative group)	
Cancer Set Acute lymphocytic leukemia (ALL)	Descriptive Term Training Set
 L1	Small monotonous lymphocytes Small cell CD33 and CD13
 L2	Mixed L1- and L3-type lymphocytes Large cells CD19 and CD4
 L3	Large homogeneous blast cells CD56 and CD20

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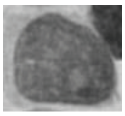
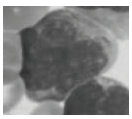
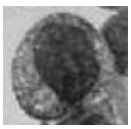
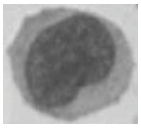
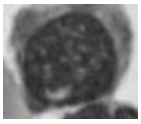
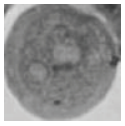
Cancer Set Acute myeloid leukemia (AML)	Descriptive Term Training Set
 M0	Acute myeloblastic leukemia, undifferentiated CD13, 14, CD15
 M1	Acute myeloblastic leukemia, without maturation CD13, 14, 15, 33 and CD34
 M2	Acute Myeloblasts with maturation (best AML prognosis) CD13 and CD15
 M3	Acute promyelocytic leukemia CD13, CD15, CD1 and CD33
 M4	Acute myelomonocytic leukemia CD13, CD33, CD11b and CD14.
 M5	Acute monocytic leukemia CD11b and CD14
 M6	Erythroleukemia/DiGuglielmo syndrome CD13, CD33
 M7	Acute megakaryoblastic leukemia CD41, CD42 and CD61

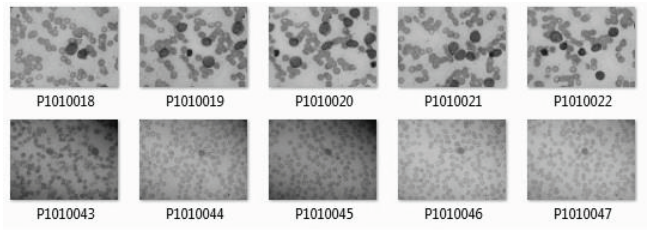


Fig 4. AML-ALL data set using different size of feature set [7]

VIII. CONCLUSION

In this work our method for classifying leukemia. Leukemia is divided into two categories which are acute leukemia and chronic leukemia and other subordinate types. The method has been evaluated Classification of Acute Leukemia Based Using CD Markers. Features extracted from the segmented cytoplasm and nucleus, are motivated by the visual cues of shape and texture. The classification proposed 3 subtypes of ALL and 8 subtypes of AML that are characterized by unique morphologic, immunologic, and cytogenetic features Immunologic (MIC group) markers cluster of differentiation (CD). Our work focuses on classification of Foil of Bretagne (Lymphoid) and Almeida Lloyd (Myeloid). The features are extracted from the segmented images and classified using the Support Vector Machine (SVM). The method has been evaluated using a set of 200 images with 100 abnormal samples and 100 normal samples obtained. Classification of Acute Myelogenous Leukemia based on complete microscopic blood images. We have obtained accuracy 93.89 %.

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