Detection of Acute Lymphoblastic Leukemia in Microscopic images using Image Processing Techniques

Arun Tom Philip¹, S. Shifaana², Stelin Sunny³, Dr. P. Manimegalai, Associate Professor⁴
Department of Biomedical Engineering, Karunya Institute of Technology and Sciences, Coimbatore, Tamil Nadu, India.
Email: aruntomphilip007@gmail.com

Abstract: Leukemia is a form of blood cancer that affects the body’s ability to fight against infection. Every year, about 1 million cases of leukemia are reported with an increased mortality rate that can cause a delay in diagnosis and treatment of leukemia. Conventionally, Acute Lymphoblastic Leukemia is identified by manual counting of cells from a peripheral blood smear or by bone marrow aspiration. However, this method is time consuming and prone to human errors. To prevail over this, various automated techniques were introduced which are faster, reliable and cheaper than the manual methods. This paper focuses on how image processing techniques can be used to identify Acute Lymphoblastic Leukemia (ALL) from the peripheral blood smear images.

1. INTRODUCTION:
Acute leukemia is a cancer in blood forming cells, which is characterized by the uncontrolled and immature production of leukocytes (WBCs). According to Global Cancer Statistics 2020, there were 19.3 million new patients diagnosed with malignant tumors and among that, 2.5% of patients were diagnosed with leukemia and 3.1% of the tumor deaths were reported to be caused by leukemia with the mortality rate ranked 10 with respect to other malignant tumor deaths globally.

Acute Lymphoblastic Leukemia (ALL) affects the lymphocytic cell of the White Blood Cells (WBCs). Almost 85% of the ALL originates from B lymphocytes and about 15% comes from T lymphocytes. It primarily occurs in children of age group 1-12 and adults aged 40 above. If left untreated, ALL can be severely fatal as it can easily spread through the blood stream and other vital organs of the human body. Hence, accurate diagnosis and classification is imperative for an effective treatment and a fast recovery. But it’s tough to identify at an early stage as the symptoms are not distinct as it can vary from fever and weakness to breathlessness and enlarged spleen or lymph nodes.
1.1. Leukemia Classification

The morphological classification of leukemia is based on the identification of leuke mia cell line and cell differentiation stage. Acute Lymphoblastic Leukemia is classified into three types according to French-American-British (FAB) classification as given below:

i. **L1 - Lymphoblastic leukemia with homogeneous structure:** This is more prevalent among children with 85% of cases in children and about 25 – 30% in adults. Here, the blasts or immature cells are homogeneous with regular nucleus that maybe small or absent. Cytoplasm will be scanty with homogeneous chromatin structure.

ii. **L2 - Lymphoblastic leukemia with varied structure:** This is found more in adults with a frequency of 70% cases and around 14% cases in children. It is characterized by irregular and large nuclei with heterogeneous chromatin structure.

iii. **L3 - Burkitt’s Leukemia:** It is a very rare subtype of ALL with less than 1-2% reported cases. It can be identified by large blast cells with prominent nuclei and abundant cytoplasm. Stippled homogeneous chromatin structure will be present. Nucleus will be surrounded by vacuoles abundantly.
FAB classification of ALL focuses more on the morphology of the blast cells i.e., size, shape and structure of the blast cells. This is considered to be an older technique as doctors are commonly using World Health Organization (WHO) classification of ALL since it is considered to be the most accurate method to classify blast cells. WHO classification uses immunophenotype of the blast cell to classify ALL. The immune phenotype of a blast cell can be easily determined by certain lab tests like cytometry and cytogenetic tests. WHO classifies ALL into three different types:

i. Precursor B cell ALL: This is the most common type of ALL in elder people. This is further divided into two types:
   a) B lymphoblastic leukemia or lymphoma, otherwise not specified.
   b) B lymphoblastic leukemia or lymphoma with recurrent cytogenetic abnormalities

ii. Precursor T cell ALL: T lymphoblastic leukemia or lymphoma. This is more frequent in young people and common in men.

iii. Mature B cell: Mature B lymphoblastic leukemia or Lymphoma Burkitt. This type is identified by particular genetic changes.

1.2. Existing Methods of Diagnosis:

a) Physical Examinations and Medical History: Medical history of the patient and of patient’s family history along with present symptoms of the patients can be used for ALL diagnosis.

b) Complete Blood cell Count (CBC): Counting the number of WBC is the most commonly used technique as leukemia causes uncontrolled production of cells.

c) Bone Marrow Aspiration: Bone marrow sample is observed under microscope for any abnormality in cells.

d) Cytogenetic analysis: Chromosome structure is observed in a blood or bone marrow sample. In case of a leukemic patients, the chromosomes may possess abnormalities.

e) Immunohistochemistry: Special type of antibodies are used to identify the type of cells based on the change in color.

2. LITERATURE SURVEY

There are several methods for ALL detection using image processing, but the core methodology of almost all processes remains the same. The basic working of any automated method for ALL detection is given below,
Detection of ALL from microscopic images can be generally divided into 3 main steps:

a. Image Segmentation
b. Feature Extraction
c. Detection & Classification

The table given below compares the various techniques used by various researchers to successfully create a system that can detect and classify ALL from a microscopic image of a peripheral blood smear. These variations in the methodology contribute to the overall accuracy, precision and reliability of the proposed system.

Table 2.1. Comparison of various methods for ALL detection

| Author, Year | Work | Method used | Strength | Weakness |
|--------------|------|-------------|----------|----------|
| R.G Bagasjvara Mehmood et al-2016 [1] | Automated Detection and Classification Techniques of Acute Leukemia using Image Processing | Pre-processing | | |
| | | Segmentation | Fuzzy C-means and K-means clustering, Thresholding and Watershed segmentation | Segmentatio n methods used yielded great results. SVM classifier showed a greater degree of accuracy | |
| | | Feature extraction | Fisher’s Discrimination ratio | |
| | | Detection | | |
| | | Classifier | SVM Classifier | |
| Prasidhi G. Fal Desai et al-2018[2] | Detection of leukemia using image processing | Pre-processing | HSI model to differentiate colours | Graphical user interface to make it user friendly | |
| | | Segmentation | K means clustering with K=4 | Less number of images used | |
| Feature extraction | Energy Correlation, sum entropy, Difference entropy, Information measure of correlation, contrast & correlation, etc |
|--------------------|--------------------------------------------------------------------------------------------------|
| Detection          | PSNR comparison                                                                                  |
| Classifier         | Neural network                                                                                    |

**Amjad Rehman et al-2018[3]**
- **Classification**: Detection of acute lymphoblastic leukemia using deep learning.
- **Pre-processing**: Converted to HSV colour space
- **Segmentation**: Thresholding method
- **Feature extraction**: Using k-fold cross-validation technique where k = 10
- **Detection**: Fully automated detection of leukemia cells
- **Classifier**: Convolutional neural network
- **Accuracy**: Less accuracy in segmented overlapped cells

**Fabio Scotti-2005[4]**
- **Automatic Morphological Analysis for Acute Leukemia Identification in Peripheral Blood Microscope Images**
- **Pre-processing**: Sobel edge enhancing, Adaptive Canny edge detection, Structured image dilation, Hole filling, Structured image erosion
- **Segmentation**: Otsu’s threshold level method
- **Feature extraction**: Morphological features such as the perimeter, the area, the momentum of the image, etc.
- **Detection**: Fully automated detection of leukemia cells
- **Classifier**: Feed-forward Neural Network
- **Specification**: Limited specificaiton or clarity
| Authors                  | Title                                                                 | Pre-processing | Conversion of RGB image to grayscale image | Feature extraction | Detection | Classifier | Comparison                                                                 |
|-------------------------|-----------------------------------------------------------------------|----------------|-------------------------------------------|--------------------|-----------|------------|-------------------------------|
| Chaitali Raje-2014[5]    | Detection of Leukemia in Microscopic Images Using Image Processing   | Pre-processing | Conversion of RGB image to grayscale image | Feature extraction | Detection | Classifier | Less sensitive to input image variations |
|                         |                                                                       |                | Otsu’s threshold method                   | Geometrical features | Shape features of nuclei | Conversion of RGB image to grayscale image |                          |
| Shubhangi Khobragade et al-2015[6] | Detection of Leukemia in Microscopic White Blood Cell images        | Pre-processing | Linear contrast enhancement technique.    | Segmentation        | Detection | Classifier | Results are processed in good detail |
|                         |                                                                       |                | Otsu’s Thresholding, Edge Detection by Sobel operator |                   | Statistical features such as mean and standard deviation | | Limited application, can’t classify leukemia types |
| J. Rodellar et al-2018[7] | Image processing and machine learning in the morphological analysis of blood cells | Pre-processing | Grey to binary                            | Feature extraction  | Detection | Classifier | Provides good accuracy           |
|                         |                                                                       |                |                                          | Granulometry and the Gray-level co-occurrence matrix (GLCM) | Normal leukocytes and Blast lymphoid cells | SVM | Some of the Follicular lymphoma images have been misclassified in other cell groups |
| Lorenzo Putzu et al-     | Leucocyte classification                                             | Pre-processing | Histogram equalization                    |                    |           |            |                               |


| Year | Authors | Methodology | Pre-processing | Segmentation | Feature extraction | Detection | Classifier | Performance | Complexity |
|------|---------|-------------|----------------|--------------|--------------------|-----------|------------|-------------|------------|
| 2015 | Rohit Agrawal et al. | Detection of White Blood Cell Cancer using Image Processing | Weiner filtering, Histogram equalization and Intensity transformation | Gaussian Distribution, Otsu Adaptive Thresholding, K means clustering, Marker based watershed transformation | Gray Level Co-occurrence Matrix (GLCM) | Co-occurrence matrix | Convolutional Neural Network (CNN) | Simple and efficient | Number of images trained are very less |
| 2015 | Ashikur Rahman et al. | Automatic Detection of White Blood Cells from Microscopic Images for Malignancy Classification of Acute Lymphoblastic Leukemia | RGB to HSV color image | Triangular algorithm, watershed segmentation | Morphological, Textural and Colour features | Color Thresholding | Ensemble of classifier (EOC) | Output values are very dependable due to the complex nature | System has technological drawbacks |
Ivan Vincent et al-2015 [11] Acute lymphoid leukemia classification using two-step neural network classifier

| Pre-processing | Contrast enhancement, Otsu threshold, Morphological filtering | Both Contrast and Hausdorff dimensional features are used. Use of sequential neural network gives improved results | Can’t identify the subtypes of ALL. Number of samples used is less.
| --- | --- | --- | --- |
| Segmentation | Mask building technique, K means clustering | | |
| Feature extraction | GLCM & Fractal features | | |
| Detection | L*a*b color space, K means clustering | | |
| classifier | Sequential Neural Network | | |

3. DISCUSSION:

From the table and other research papers, it’s clearly evident that in the detection of ALL using image processing methods, pre-processing of blood smear image followed by segmentation is a fundamental technique in all the researches. The heart of the ALL detection remains same in all the processes and it consist of segmentation, feature extraction and classification.

For segmentation, methods like K-means clustering, Watershed transform and Otsu’s threshold method were the most commonly used methods by the researchers which produced good results. Methods like Zack’s algorithm, Distance transform and Fuzzy-C-means clustering were also used which yielded satisfactory results.

For feature extraction, features such as geometrical, statistical, color and texture have been used. The researchers have most commonly made use of the Granulometry and Gray Level Co-occurrence Matrix approach which are used to detect the texture. The Fisher’s Discrimination Ratio has been used to acquire the best features.

At the stage of classification, using the SVM classifier the results were found to be highly accurate compared to the other methods.

4. CONCLUSION:

This paper primarily focuses on various methods for automated detection of acute lymphoblastic leukemia using image processing techniques. An automated system can significantly reduce the time required for the analysis and also reduce the human errors which might occur in a manual examination as it depends completely on the examiner’s experience, attentiveness and state of mind. Automated systems provide a simple, robust and precise technique with minimal time and errors.

However, as promising as all this technique may seem, further research is required for a practical application of these techniques so that examiner can easily diagnose the disorder and classify ALL. Techniques need to be more accurate and precise for a practical application. There is a lot of areas yet to be covered like technique to properly classify all the subtypes of ALL, which is still a major challenge.

Further research into this may reveal more efficient methods to identify ALL and its subtypes to better help the medical practitioners so that ALL could be identified at an early stage and help people with their fast recovery.
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