ISSN 2278-3091
Volume 9, No.5, September - October 2020
International Journal of Advanced Trends in Computer Science and Engineering
Available Online at http://www.warse.org/IJATCSE/static/pdf/file/ijatcse161952020.pdf
https://doi.org/10.30534/ijatcse/2020/161952020

Automated Leukemia Detection with Image Processing and Machine Learning: A Review

Suchitra N Shenoy[1], Dr. Ganesh V Bhat[2], H Nagesh Shenoy[3], Dr. Dattatray Prabhu[4]
[1]Dept. of Electronics and Communication, Canara Engineering College, India, suchiprab_16@yahoo.co.in
[2]Principal, Canara Engineering College, India, 2ganeshvbhat@gmail.com
[3]Dept. of Computer Science, Canara Engineering College, India, h.nagesh.shenoy@gmail.com
[4]Dept. of Anaesthesiology, Kasturba Medical College, India, da.prabhu@manipal.edu

ABSTRACT

Leukemia is the cancer that impacts the blood-forming tissues of the body (bone marrow and lymphatic system), especially affecting white blood cells, and hindering the ability of the body to fight infections. While a routine pathological blood test may suggest leukemia, hematologists use microscopic study of human blood samples for blood cell examination, checking for type and shape of blood cells to aid the diagnosis. Manual inspection of microscopic images is time consuming, with a questionable accuracy at times. Hence, it is at this stage that automation would come in handy, perhaps even for an early detection of leukemia. The use of image processing techniques, including microscopic color imaging, segmentation, feature extraction, classification, and clustering allows identification of leukemia in patients. The coupling of image processing and machine learning for automation of leukemia detection could facilitate the early detection of leukemia in patients, leading to administering the required treatment and a higher chance of survival. This paper reviews some of the significant work in automating the detection of leukemia over the years.

Key words : Image Processing, Machine Learning, Segmentation, White blood cell detection

1. INTRODUCTION

Blood is classified as a highly specialized connective tissue, accounting for approximately 8% of the adult body weight, and is composed of four main components, namely erythrocytes (RBC), leucocytes (WBC), thrombocytes (platelets), and plasma. Leucocytes are comprised of neutrophils, eosinophils, basophils, lymphocytes (B, T), and monocytes. One microliter of blood contains 4.2-6.1 million RBCs, 4,000-11,000 leucocytes, and 200,000-500,000 thrombocytes. A routine pathological blood test reports these numbers from the blood sample, in addition to several other component values. Leukemia, being a cancer affecting WBCs generated from the bone marrow, gets diagnosed by primary physical examination and blood tests, followed by the bone marrow tests and scans [1] [2]. Leucocytes comprise the vital part of the immune system, and owing to the complex nature of the cell, the segmentation of these cells from the background and automatic counting remains challenging. The absence of a nucleus in RBCs contribute to the ease of segmenting RBCs and WBCs on the basis of presence of nucleus (WBCs are nucleated cells), while platelets can be separated by its size factor. Pathologists observe size and shape, along with other features of WBCs in blood samples, classifying them as normal mature cells or immature cells (the most immature cells are lymphoblasts and don't account for more than 5% of bone marrow cells). However, variations in slide preparation techniques [15], unclear images, complexity of blood smear images, coupled with the range of features render a certain degree of difficulty and uncertainty in manual detection of leukemia.

Figure 1 shows the development of blood cells, wherein a blood stem cell passes through multiple steps to emerge as a RBC, WBC, or platelet.

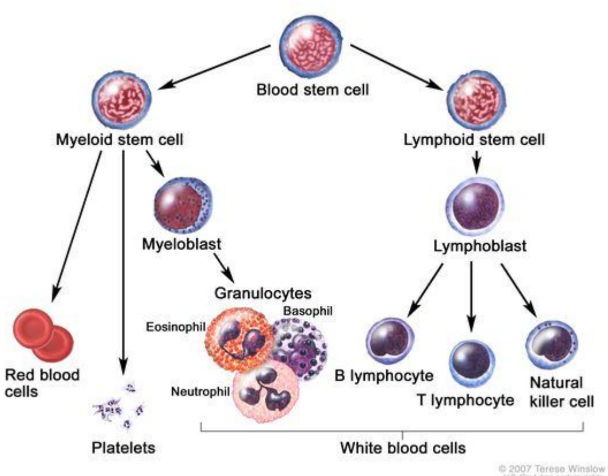

Figure 1: Development of blood cells

Based on the type of cells being affected (myeloid cells or lymphocytes), and the onset of leukemia - acute (sudden) or chronic (slow) [12] - there are four main types of leukemia as shown in Figure 2.

Type of Cells being affected	Type of Onset	
	ACUTE	**CHRONIC**
LYMPHOCYTES	Acute Lymphocytic Leukemia (ALL) • occurs mostly in children • ~6,000 new cases diagnosed annually* • five-year survival rate - 68.2%	Chronic Lymphocytic Leukemia (CLL) • affects people over 55 years mostly • rarely seen in children • ~20,000 new cases diagnosed annually* • five-year survival rate - 83.2%
MYELOID CELLS	Acute Myelogenous Leukemia (AML) • can occur in children and adults • ~21,000 new cases diagnosed annually* • most common form of leukemia • five-year survival rate - 26.9%	Chronic Myelogenous Leukemia (CML) • affects mostly adults • ~9,000 new cases diagnosed annually* • five-year survival rate is 66.9%

* - statistics based on Surveillance, Epidemiology, and End Results Program of National Cancer Institute (NCI), US

Figure 2: Main Types of Leukemia

The need to detect leukemic cells in a short duration of time, to aid in administering of required treatment at the earliest possible stage, leads to the ever expanding research that integrates techniques of image processing along with machine learning. The process flow generally followed for automated detection of leukemia is shown in Figure 3.

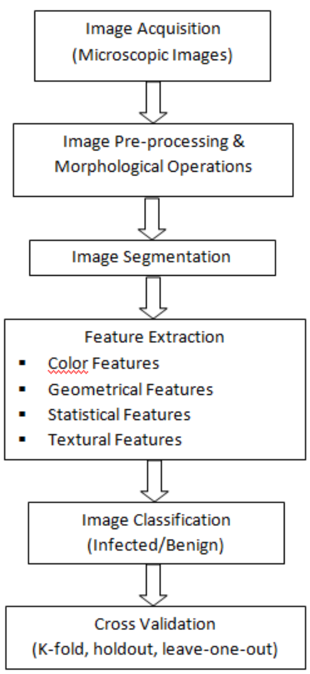

Figure 3: Process Flow for Automated Leukemia Detection

As can be seen from the literature survey following this section, different researchers adopt different techniques at each step of the process flow, the general flow being more or less the same. The major difference, however, lies in the segmentation techniques used, owing to the fact that the effectiveness of the segmentation step determines the effectiveness of the following steps of feature extraction and classification. The process of segmentation aims at achieving the following:

a. segregation of leucocytes (WBCs) from other blood components such as RBCs and platelets
b. segmentation of nucleus [14] and cytoplasm of the WBCs (followed by the next step that extracts features of the nucleus that ultimately help in detecting leukemia).

The following sections comprise of: (i) the literature survey that discusses some of the relevant research conducted over the past years in automating leukemia detection, (ii) the fundamentals of segmentation, (iii) a discussion on the outcome of the review conducted on the past research, and (iv) the conclusion drawn from the review.

2. LITERATURE SURVEY

This section reviews techniques utilized in various researches to automate leukemia detection with the use of image processing and different classification algorithms. The general approach for leukemia detection using microscopic images of a blood sample comprises of three main steps:

i. Image Segmentation to segregate the leucocytes
ii. Feature Extraction of the segregated leucocytes
iii. Detection and Classification of leukemic cells based on the extracted features.

As quantitative microscopy aids in the diagnosis of dreaded diseases including leukemia, [4] proposes an approach for ALL detection wherein investigation of texture features of WBC nucleus is performed. K-means clustering is utilized to segment the image into 4 segments: nucleus, cytoplasm, RBC, and background stain. This is followed by the bounding box technique that provides with sub images, and the sub images containing lymphocytes are selected with image morphology. The feature extraction uses Gray Level Co-occurrence Matrices (GLCM), shape features, and color features. With the extracted features, any classification technique could be applied to automate the detection of ALL. [5] mentions how the standard technique of diagnosis for leukemia primarily remains the microscopic examination of blood sample images, despite the availability of advanced techniques like molecular probing, flow cytometry, immunophenotyping, etc. The need for automated screening arises due to several drawbacks involved in manual inspection of blood images. After the initial pre-processing of microscopic blood images containing multiple nuclei, the segmentation of WBCs is done with k-means clustering. Primarily, five features are used: cell size, shape, color, granularity, and density. The classification is done using Support Vector Machine (SVM) followed by validation using the hold-out cross validation technique. Around 93.5% of the AML blood smear images were classified correctly using this system.

While discussing the drawbacks involved in manual analysis of microscopic blood images, [6] presents a comparative approach that aids in ALL detection. The use of color based clustering (such as K-means, Fuzzy Possibilistic C-Means (FPCM), Fuzzy C-Means (FCM), and Gustafson Kessel (GK), all used for comparative analysis) segregates the multiple blood components in addition to segmenting the WBC nucleus. This is followed by the feature extraction step that employs texture based techniques, along with the use of Haudroff Dimension (HD) and contour signature to measure boundary irregularities of the nucleus. The classification is achieved using SVM classifier, resulting in 92% accuracy on the test images utilized.

[7] proposes a comparatively simple approach to automatically detect AML from blood smears that classifies entire blood smear images (instead of sub-images). In order to segment the nuclei, k-means clustering is utilized. For feature extraction, HD, Local Binary Pattern (LBP), GLCM, shape and color features are extracted. For classification, a linear SVM two-class classifier is utilized. In order to evaluate and compare learning algorithms, three kinds of cross-validation techniques (K-fold, hold-out, and leave-one-out) are used. The system efficiency without LBP was 93.5%, while the use of LBP improved the classifier efficiency by 4%. This resulted in 98% accuracy for the overall algorithm.

The design of a novel CAD system to detect leukemia on the basis of GLCM and shape based features has been presented in [8]. The design comprises of 4 modules: a) pre-processing to remove outlines, b) segmentation, c) feature extraction of nucleus and cytoplasm, and d) classification of select features by using auto SVM binary. The system accuracy is computed for GLCM texture feature and shape features for nucleus and cytoplasm. The combined accuracy is 89.8%, with the conclusion that nucleus shape is more important than cytoplasm shape to detect immature lymphocytes.

In order to ease the detection of leukemia owing to various complexities and drawbacks, [10] proposes the use of Fuzzy C-means clustering combined with contour segmentation and morphological processing. The approach consists of a) highlighting the nuclei by using contrast enhancement, b) morphological contour segmentation, and c) classification of leukemic cells by Fuzzy C means. By attempting to exclude the influence due to subjective factors, in addition to increasing the ability to accurately detect early stage of leukemia, an accuracy of 98% is achieved.

The use of Fuzzy C-means clustering for segmentation of WBCs is achieved in [11], which is basically a modified form of the k-means clustering method. Marker based watershed segmentation is used to segregate adjacent WBCs, which in turn eases up the process of feature extraction wherein area, energy, and entropy are some of the features considered. Finally, the classification is performed by a neuro-fuzzy classifier - Adaptive Neuro Fuzzy System (ANFIS) that incorporates the beneficial characteristics of fuzzy systems as well as neural networks.

In what appears to be a commonly used segmentation technique (to segregate WBCs for automated leukemia detection) across several researches, k-means clustering is used in the system proposed by [13] as well. The grouping of WBCs is done using histogram equalization and Zack algorithm. For feature extraction, features such as mean, compactness, elongation, solidity, entropy, variance, etc. are calculated. This is followed by classification by using SVM that resulted in 93.57% accuracy. The proposed system claims to be effective in calculating the percentage of leukemic infection from the microscopic images as well.

The automation technique proposed in [16] utilizes some filtering techniques in the image pre-processing step, followed by k-means clustering approach for segmentation. Prior to feature extraction, an automated counting algorithm counts WBCs for detection of leukemia. Features such as centroid, solidity, concavity, entropy, SD, compactness, rectangularity, etc. are calculated. The image classification uses SVM classifier along with probabilistic neural network (PNN) to classify cells as infected or not. The accuracy achieved with the proposed method is 94.11%.

While the segmentation of nucleus from the cytoplasm is done using k-means clustering in [17], the performance of this is compared with other segmentation techniques like texture based, and color based segmentation. Performance measures such as Probability Random Index (PRI), Variance of Information (VOI), and Global Consistency Error (GCE) have been used for the qualitative analysis of the segmentation approaches. Classification using k-Nearest Neighbor and Naïve Bayes Classifier on a dataset of 60 pretested samples provided an accuracy of 92.8%.

With an aim of complete images rather than sub-images, [18] presents a system that considers complete peripheral blood smear images to automate ALL classification. The commonly considered features from other systems have been tested in order to take into consideration the most relevant features for this system. K-means clustering has been used for image segmentation, in addition to morphological filtering steps. The additional feature of "cell energy" has been used in this system. The classification technique is supervised SVM. In order to cross-validate the classifier output and derive accuracy measures like F-measure, precision, sensitivity, and specificity, the techniques of k-fold, hold-out, and leave-one-out have been used. The accuracy attained by this system is 94%.

A combination of contrast enhancement, local binary pattern detection, and Fuzzy C-means clustering has been used by [19] for automated AML detection. A fuzzy based strategy based on two stage color segmentation is employed to segregate WBCs from the other blood components. The final detection of leukemia uses discriminative features such as shape of the nucleus, and texture.

A considerably different approach has been presented by [20] to increase the accuracy of leukemia detection by using object wise approaches. The extraction of the cell count from a blood sample's microscopic image is done module by module. The detection of WBCs uses k-means clustering, while the grouping of WBCs is done using histogram equalization along with Zack algorithm. Features like mean, SD, area, color, perimeter, etc. are computed in the feature extraction process. This is followed by classification using SVM. There are 5 distinct modules used in this system: Image module, the 3 color space modules -RGB, CMYK, and YCbCr, and result calculation module.

3. FUNDAMENTALS OF SEGMENTATION

As can be observed from the past researches, it is evident that image segmentation is a vital step for detection of leukemia, while the choice of the segmentation technique varies considerably. Figure 4 displays the different image segmentation techniques [30].

3.1 Region based segmentation

This method partitions an image into regions. The outcome is homogenous areas with connected pixels by applying homogeneity criteria within candidate pixel sets. The pixels in each region will be similar in terms of certain characteristics or numerical values like color, intensity, or texture. A few region based segmentation techniques [23] are as follows:

3.1.1 Region growing

This is a bottom-up method of segmentation [29] in which an initial set of smaller areas (pixels or sub-regions) are grouped on the basis of some similarity constraints. With the initial selection of a seed pixel, the neighboring pixels are compared with it. Those neighboring pixels that are similar to the seed pixel in terms of variance, texture, color, shape, average intensity, etc. are added into the region, thereby increasing the region's size. If one region's growth stops, another seed pixel is chosen that doesn't belong to any region yet, and the process is repeated all over, until all pixels of the image are added into some region.

3.1.2 Region split and merge

Contrary to the region growing technique, the region split and merge technique works on complete images. The process of region splitting works in a top-down approach. A whole image is divided up till each sub region is uniform. The splitting process continues till the properties of a newly split pair are not different from those of the original region by more than a threshold. Merely splitting is insufficient for the process of segmentation owing to the limits in the shapes of segments. Hence, the process of splitting is followed by merging.

The merging process begins from a uniform seed region, which could also be a single pixel. Upon establishing a seed, the neighbors are merged till the uniformity criterion conformity is not met by the neighboring regions. At this point, the region gets extracted from the image, while a further seed is extracted to merge another region.

3.1.3 Threshold

Considered as the simplest technique for segmenting images, thresholding is utilized to create binary images from grayscale images [21]. The three main types of thresholding

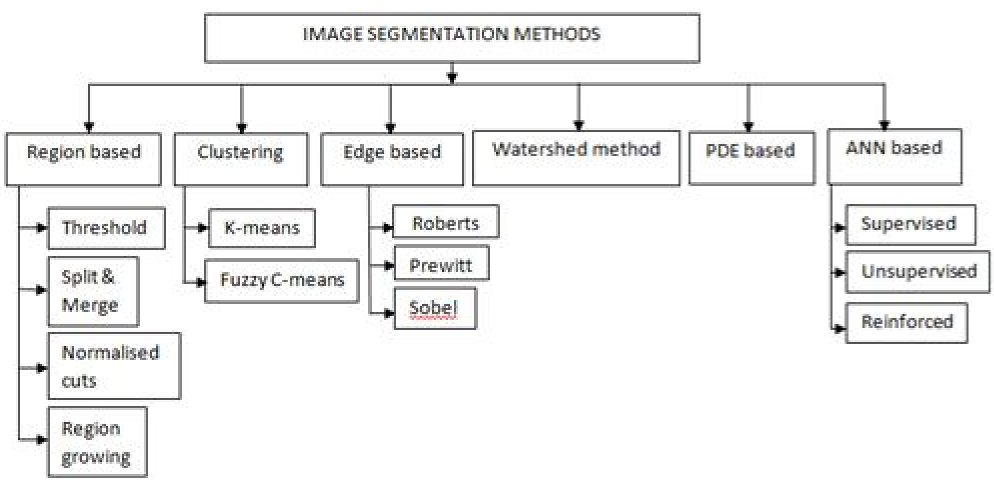

Figure 4: Various techniques of image segmentation

are global thresholding, local thresholding, and dynamic/adaptive thresholding [25].

Global threshold - Utilized for images with sufficiently distinct distribution of intensity of objects and background pixels, and works on the whole image [28] with a single threshold value. A few techniques classified under global thresholding are histogram based, Otsu's method, multithresholding, clustering based, etc.

Local threshold - The presence of shadows or uneven illumination requires more than a single threshold for segmentation. This technique works by partitioning the image into sub-images with a threshold being selected per sub-image.

Adaptive/Dynamic threshold - While global thresholding cannot be used for images with uneven illumination, each pixel within the image is assigned a threshold with adaptive thresholding technique. While pixels with values less than the threshold are set as background value, the rest are assumed as foreground value. Different local areas use different threshold values in this technique.

3.1.4 Normalised cuts

The image segmentation problem can be formulated as a graph partitioning problem that partitions the vertex set into subsets, wherein based on some measure, vertices in any subset have high similarity, while vertices in two different subsets have low similarity.

3.2 Clustering

In order to group similar objects within an image into a cluster, and dissimilar objects into other clusters, the process of clustering is utilized. The two main clustering techniques utilized for segmentation of images are k-means and fuzzy c-means [24].

3.2.1 K-means

Being a very widely used clustering technique, k-means clustering divides the images into k segments by using thresholds, while minimizing the overall inter-segment variance (exclusive clustering algorithm).

3.2.2 Fuzzy C-means

An unsupervised clustering technique, fuzzy c-means clustering groups the dataset into n clusters wherein each data point within the dataset can belong to multiple clusters (overlapping clustering algorithm).

3.3 Edge based

Edges in images provide the topology and structural information of the objects within an image. The use of edge detection to segment an image characterizes the changes in intensity in terms of the physical processes that originated them. In the derivative approach of edge detection, edges can be detected by taking a derivative (Robert operator) followed by thresholding, and can incorporate noise cleaning scheme (Prewitt and Sobel operator). In order to generate an edge map, some of the approaches include noise smoothing, edge localization, edge enhancement, edge linking, edge following, and edge extraction.

3.4 Watershed method

The watershed is basically the transformation of grayscale images; wherein an image is segmented usually when two regions of interest are close enough for their edges to touch. The image to be segmented is treated as a topographic map in this technique, and the brightness of each point corresponds to its height.

3.5 PDE based

Image segmentation by coupling level set methods and fast marching methods comprise of PDE based techniques. These methods extract boundaries from the image quickly and accurately. There is no requirement for apriori knowledge about the number of objects or object topology in the image.

3.6 ANN based

Neural-oriented approaches segment the image on the basis of pixel data obtained from a convolution window or from information on local features provided to the neural classifier. The three different approaches to ANN learning [22] are:

i) The supervised methods of ANN based segmentation that require human intervention; wherein the training data is carefully selected by human experts that are used to segment the images. Examples of supervised methods include Naïve Bayes, SVM, and Random Decision Forest.

ii) Unsupervised methods of ANN based segmentation that are either semi- or fully automatic and partitions the images without human intervention. Examples of unsupervised methods include K-means and KNN.

iii) Reinforced learning, which divides the image to multiple sub-images with each object being assigned a suitable value by each RL agent. A Q-matrix is used to store the valuable information that is used for segmentation of further similar images. Examples of reinforced learning includes Markov decision process and Brute force.

The choice of segmentation techniques is vast. Based on the advantages and disadvantages of each technique, as well as the accuracy of the outcome, any of these techniques could be selected in the segmentation process for leukemia detection. Figure 5 lists out the merits and demerits of the segmentation techniques discussed above.

Segmentation Method	Technique	Advantages	Disadvantages
Region based	Region Growing	• Separates the ROI correctly as defined. • Provides well segmented results with clear edges. • Small number of seed points required to define the property of interest.	• .It's a local method with no global view of the problem. • Sensitive to noise. • Requires prior knowledge. • Computationally expensive.
	Split & Merge	• Connected regions are guaranteed. • Limited (some) possibility to incorporate geometric knowledge.	• It is difficult to find point of splitting. • No unique solution is available.
	Normalised cuts	• Addresses segmentation in a global optimization framework with a guarantee of globally optimal solution for a wide class of energy functions. • Uses both regional and boundary properties if required.	• Has issues with segmentation of thin elongated objects.
	Threshold	• Simplest segmentation technique. • Previous information not required.	• Object coherency not guaranteed. • Sensitive to noise. • Difficult to set threshold.
Clustering	K-means	• Ease of implementation. • High speed performance. • Measurable and efficient in large data collection. • Relatively efficient.	• Selection of optimal number of clusters is difficult. • Selection of initial centroids is random. • No guarantee of global optimum, only local optimum reached. • Difficult to produce different size clusters.
	Fuzzy C-means	• Unsupervised - no human intervention needed. • Always converges. • Best result for overlapped data set.	• Long computation time. • Sensitivity to initial guess (speed, local minima). • Sensitive to noise. • Apriori specification of number of clusters.
Edge based		• Works well when edges are prominent. • Works well for images with good contrast. • Easy to extract edges.	• Not suitable for images with too many edges. • Not suitable for images with smooth images. • Sensitive to noise. • Edge information is often unreliable and often broken.
Watershed method		• High computational speed. • Incorporating prior knowledge about object of interest. • Very accurate segmentation results that matches the object boundaries precisely.	• Sensitive to noise. • Possibility of over-segmentation is more.
PDE based		• Fastest segmentation method. Great for time critical applications. • Works well for images having good contrast between regions.	• High computational complexity. • Operator size and computational complexity are proportional to each other.
ANN based		• Easy model building with less formal statistical knowledge required. • Non parametric classifier. • It is a data driven, self-adaptive technique that efficiently handles noisy inputs. • High computation rate .	• ANN training is time taking. • Semantically poor. • Difficult to choose the type of network architecture. • Prone to over-fitting due to model structure complexity.

Figure 5: Merits and demerits of different segmentation techniques

4. DISCUSSION

On the basis of the review of some of the prominent work done for automation of leukemia detection over the years, it is evident that although considerable progress has been achieved, the need for earliest possible detection of leukemia continues to motivate researchers to explore different techniques. Table 1 summarizes the review conducted for automated leukemia detection.

Table 1: Review Summary

Ref. No.	Type of Leukemia	Segmentation approach	Classification approach	Accuracy %
[4]	ALL	K-means	-	-
[5]	AML	K-means	SVM	93.5
[6]	ALL	K-means	SVM	92
[7]	AML	K-means	SVM	93
[8]	ALL	-	SVM	89.8
[10]	ALL	Curve & corner detection	Fuzzy C-means	98
[11]	ALL	Fuzzy C-means + Watershed	Adaptive Neuro Fuzzy system	-
[13]	ALL	K-means + Zack algorithm	SVM	93.57
[16]	-	K-means + Zack algorithm	SVM + PNN	94.11
[17]	ALL	K-means	kNN + Naïve Bayes classifier	92.8
[18]	ALL	K-means + morphological filtering	SVM	94
[19]	AML	Fuzzy C-means	-	-
[20]	ALL	K-means + Zack algorithm	SVM	-

As can be seen from table 1, the work done for automated detection of ALL is considerably greater than that for AML or any other chronic leukemia. While the choice of pre-processing steps is dependent on the type of image procured, the shortcomings in the image that need refinement, and the segmentation technique that follows, most research shows that segmenting of WBCs from the other blood cells, as well as nuclei separation from the cytoplasm is performed using K-means clustering approach more commonly [9]. The features to be extracted range over color, geometrical, statistical, and textural features. Yet another commonly used technique for classification over most of the research is the SVM technique. A decent accuracy has been achieved for various researches conducted, however, the requirement for a well-developed early leukemia detection system for various leukemia types (acute and chronic) has not subsided. A hybrid of techniques for each step of the leukemia detection process with most accurate results is the need of the hour.

5. CONCLUSION

Owing to the various drawbacks of manual inspection of blood smear images to detect leukemia, such as being time-consuming, variance in accuracy, error prone (owing to several human factors like stress, fatigue) etc., there is an ever-increasing need for automating the process of leukemia detection. The purpose of automating leukemia detection contributes to earlier and more accurate detection, hence aiding in administering the required treatment, leading to increased chances of survival. The use of image processing techniques like pre-processing, segmentation, and feature extraction, coupled with machine learning techniques (classification), facilitate the automated detection.

REFERENCES

1. https://www.cancer.org/cancer/acute-lymphocytic-leukemia/detection-diagnosis-staging/how-diagnosed.html
2. https://www.mayoclinic.org/diseases-conditions/leukemia/diagnosis-treatment/drc-20374378
3. J Toedling, P Rhein, R Ratei, L Karawajew, and R Spang. **Automated in-silico detection of cell populations in flow cytometry readouts and its application to leukemia disease monitoring**, *BMC Bioinformatics* 7:282, 2006.
4. S Mohapatra, D Patra, and S Satpathy. **Automated Leukemia Detection in Blood Microscopic Images using Statistical Texture Analysis**, *ICCCS'11, Proceedings of the 2011 International Conference on Communication, Computing, & Security*, February 2011, Pages 184-187.
5. M. Madhukar, S. Agaian and A. T. Chronopoulos. **Deterministic model for Acute Myelogenous Leukemia classification**, 2012 *IEEE International Conference on Systems, Man, and Cybernetics (SMC)*, Seoul, 2012, pp. 433-438.
6. S Mohapatra, D Patra, and S Satpathy. **Unsupervised Blood Microscopic Image Segmentation and Leukemia Detection using Color based Clustering**, *International Journal of Computer Information Systems and Industrial Management Applications*, Volume 4, pp. 477-485, 2012.
7. Sos Agaian, Monica Madhukar, and Anthony T. Chronopoulos. **Automated Screening System for Acute Myelogenous Leukemia Detection in Blood Microscopic Images**, *IEEE Systems Journal*, Vol. 8, Issue: 3, Sept. 2014, Pages 995-1004.
8. J Rawat, A Singh, HS Bhadauria, and J Virmani. **Computer Aided Diagnostic System for Detection of Leukemia using Microscopic Images**, Procedia Computer Science 70 (2015) 748-756, Published by Elsevier B.V., *4th International Conference on Eco-friendly Computing and Communication Systems*, 2015.
9. S Sanal. **Automated Detection of Acute Lymphocytic Leukemia-A survey**, *International Journal of Engineering Research and General Science*, Volume 3, Issue 3, May-June 2015.
10. P Viswanathan. **Fuzzy C Means Detection of Leukemia based on Morphological Contour Segmentation**, Procedia Computer Science 58 (2015) 84-90, Published by Elsevier B.V., *Second International Symposium on Computer Vision and the Internet* (VisionNet'15), 2015.
11. S Sanal, K Lashma and V Balakrishnan. **Acute Lymphocytic Leukemia Detection from Blood Microscopic Images**, *International Journal of*

Engineering Research & Technology (IJERT), Vol. 4, Issue 09, September 2015.

12. HP Vaghela, H Modi, M Pandya, and MB Potdar. **Leukemia Detection using Digital Image Processing Techniques**, *International Journal of Applied Information Systems (IJAIS)*, Volume 10, No. 1, November 2015.
13. N Patel and A Mishra. **Automated Leukemia Detection using Microscopic Images**, Procedia Computer Science 58 (2015) 635-642, Published by Elsevier B.V., *Second International Symposium on Computer Vision and the Internet* (VisionNet'15), 2015.
14. R. G. Bagasjvara, I. Candradewi, S. Hartati and A. Harjoko. **Automated detection and classification techniques of Acute leukemia using image processing: A review**, *2nd International Conference on Science and Technology-Computer (ICST)*, Yogyakarta, 2016, pp. 35-43.
15. S Bhole. A **Survey on Acute Myelogenous Leukemia Detection in Blood Microscopic Images**, *International Journal of Scientific & Engineering Research*, Volume 7, Issue 5, May-2016.
16. T Hazra, M Kumar, and Dr. SS Tripathy. **Automatic Leukemia Detection Using Image Processing Technique**, *International Journal of Latest Technology in Engineering, Management, & Applied Science (ILJTEMAS)*, Volume 6, Issue 4, April 2017.
17. Kumar S., Mishra S., Asthana P., and Pragya. **Automated Detection of Acute Leukemia Using K-mean Clustering Algorithm**, In: Bhatia S., Mishra K., Tiwari S., Singh V. (eds) *Advances in Computer and Computational Sciences. Advances in Intelligent Systems and Computing*, vol 554. Springer, Singapore, 2018.
18. Sos Agaian, Monica Madhukar and Anthony T. Chronopoulos. **A new Acute Leukemia Automated Classification system**, *Computer Methods in Biomechanics and Biomedical Engineering: Imaging & Visualization*, 2018.
19. P Chitra, Jebarani M R Ebenezer, P Kavipriya, K Srilatha, M Sumathi, and S Lakshmi. **Detection of AML in Blood Microscopic Images using Local Binary Pattern and Supervised Classifier**, *Research Journal of Pharmacy and Technology*, Vol. 12, Issue 4, 2019.
20. Sai Sreeja Alapati and Dr. M. Rama Bai. **Leukemia Detection using Object Oriented Method**, *International Journal of Engineering Research & Technology (IJERT)* Volume 09, Issue 05, May 2020.
21. M Fatma and Jaya Sharma. **A Survey on Image Segmentation Techniques used in Leukemia Detection**, *International Journal of Engineering Research and Applications (IJERA)*, Volume 4, Issue 5, May 2014, pp. 66-71.
22. A Kaur and Dr. Yogeshwar Radhawa. **Image Segmentation using Artificial Neural Networks Alongwith Updated Jseg Algorithm**, *IOSR Journal of Electronics and Communications Engineering*, Volume 9, Issue 4, Jul-Aug 2014, pp. 1-13.
23. N. M. Zaitoun and Musbah J Aqel. **Survey on Image Segmentation Techniques**, *International Conference on Communication, Management, and Information Technology (ICCMIT 2015*), 797-806.
24. M.S. Abirami and Dr. T. Sheela. **Analysis of Image Segmentation Techniques for Medical Images**, *Proceedings of International Conference on Emerging Research in Computing, Information, Communication, and Applications (ERCICA-14).*
25. K. Bhargavi and S. Jyothi. **A Survey on Threshold Based Segmentation Techniques in Image Processing**, *International Journal of Innovative Research & Development*, Volume 3, Issue 12, November 2014.
26. Aldrin K. and Om Prakash. **Automatic Segmentation of Leukocytes for the Detection of Leukemia using a new computing algorithm**, *International Journal of Advancements in Technology*, Volume 9, Issue 2, 2018.
27. S. Ravikumar. **Image Segmentation and Classification of White Blood Cells with the extreme learning machine and the fast relevance vector machine**, *Artificial Cells, Nanomedicine, and Biotechnology*, 2015. 985-989.
28. B. Baral, S. Gonnade, and T. Verma. **Image Segmentation and Various Segmentation Techniques - A Review**, *International Journal of Soft Computing and Engineering (IJSCE)*, Volume 4, Issue 1, March 2014.
29. D. Karungan and Dr. N. Sujatha. **Survey on various Image Segmentation Techniques**, *Journal of Emerging Technologies and Innovative Research*, Volume 4, Issue 2, February 2017.
30. D. Kaur and Y Kaur. **Various Image Segmentation Techniques: A Review**, *International Journal of Computer Science and Mobile Computing*, Volume 3, Issue 5, May 2014, pg. 809-814.
31. Rao A S,D'Mello D A, Anand R, and Nayak S. **Clinical Significance of Measles and its Prediction Using Data Mining Techniques: A Systematic Review**, In: Chiplunkar N, Fukao T (eds), *Advances in Artificial Intelligence and Data Engineering. Advances in Intelligent Systems and Computing*, vol 1133. Springer, Singapore, August 2020.
32. A Rao and S Bhat. **Development of an application for better online shopping using computer vision**, *International Conference on Energy, Communication, Data Analytics and Soft Computing (ICECDS-2017).*