A New Image Segmentation of Leptomeningeal Metastasis in Leukemia Patients

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Abstract. Leptomeningeal metastasis is an indication of the malignancy that occurs in leukemia patients. Although it only has a 5-10% portion caused the leukemia patient to relapse, the abnormality is the basis in determining the best treatment given to them. Leptomeningeal metastasis are better detected by using Magnetic Resonance Imaging (MRI) because of their high sensitivity in neuraxis images. High ability to see and analyze is needed for a radiologist in reading the Brain MRI results of leukemia patients with suspect leptomeningeal metastasis. Therefore, the classification will take a long time and allow for the misreading of the results. In this experiment, we used a dataset from the Brain MRI of leukemia patients of Dharmais Cancer Hospital. We implemented the proposed method in performing the leptomeningeal metastasis segmentation. The preprocessing image applied for sharpening and removing unwanted noises in the image using the Median Filter. A hybrid semi-automated skull stripping was also developed to improve the accuracy of the segmentation. Then Fuzzy C-Means is used to segment the abnormalities and reach an average evaluation performance at 49.1% Jaccard Index.

1. Introduction

Leukemia is a type of cancer that starts (starts) in blood stem cells (stem cells), which are stem cells where many types of cells in the body develop. Therefore, Leukemia is also known as blood cancer. Each blood stem cell will later develop into lymphoid stem cells or myeloid stem cells that have the characteristics of each function [1]. Normally these blast cells can develop into mature blood cells (blood cells). In the case of Leukemia, there will be an overproduction of blast cells that accumulate in the bone marrow resulting in a reduction in normal blood cells. Over time, these healthy blood cells cannot do their "work" optimally. In addition to accumulating, these blast cells can spread to other body organs such as the spine, lymph glands, liver, kidneys, lungs, even to the brain [1]. After Leukemia diagnosed clinically, the blast cell is also called a leukemia cell.

A series of tests are usually done to diagnose and determine the type of leukemia cells. The accuracy of the diagnosis is essential in estimating how quickly the disease will develop and determine
the effectiveness of the treatment. A series of tests carried out include blood and bone marrow tests, genetic tests, spinal fluid tests, and imaging tests [2]. Determination of the appropriate treatment is also done by considering the spread of malignant cells in the central nervous system (CNS) / leptomeningeal metastasis through lumbar puncture (LP) and combined with the Magnetic Resonance Imaging (MRI) scan. Leptomeningeal metastasis can be said to be the beginning of Leukemia occurring [3]. Therefore, early diagnosis of leptomeningeal metastasis is crucial information for doctors to provide the best treatment in order to get a high chance of successful treatment [4]. The occurrence of leptomeningeal metastasis in leukemia patients often missing due to the absence of signs or symptoms at the onset spread of the malignancy. Moreover, these events often occur during remission, where the patient is in a stable condition (no systemic symptoms). The incidence of CNS relapse is 3-8% in leukemia patients and accounts for 30-40% of overall relapse [5].

Appropriate treatment needs to be carried out quickly to slow the progression of leptomeningeal metastasis. If left untreated, it would reduce the patient’s chance of survival by up to 3 months. Imaging plays a vital role in identifying this because it becomes the first clue of the re-emergence of the disease (relapse). CSF Cytology, which done through LP, often gets falsely negative results. T1-weighted MR images with paramagnetic contrast have been the right choice for assessing leptomeningeal metastasis quickly with a sizable sensitivity of 71% [6].

A Dharmais Cancer Hospital radiologist also said that LP sensitivity is only around 25% in the first puncture, 25% -50% in the second puncture, and only reaches 60-75% in the third puncture. Due to its small sensitivity, the MRI brain results that will determine the treatment protocol that will be given. If the MRI brain results have shown positive results, then the treatment protocol can be given while walking the LP examination (there is certainly a spread of malignancy in the brain). Conversely, if the LP results are positive, the brain MRI results will have to come out to decide on the treatment protocol that will be given. Although not the primary protocol, the MRI brain results determine what treatment will be given to the patient.

The complexity of the structure of the human brain makes analysis difficult and requires much time. Moreover, some cases of metastatic leptomeningeal have many similarities with other cases of infections with or without signs and symptoms. Although an MRI reading can be done with the naked eye by a radiologist, a reading error could be found. High ability to see and analyze is needed in reading the MRI results of brain leukemia patients with suspect leptomeningeal metastasis. Because it requires a very high concentration at the time of classification and a long time, it gives an increased chance of misreading results. A computer-based automated system or Computer-Aided Diagnosis (CAD) can be one solution for reading and analyzing MRI results [7].

Recent studies of MRI Brain, have produced almost perfect accuracy, especially in the classification of brain tumors. The most recent research is classification using SVM, which is combined with DWT and BoW extraction features resulting in an accuracy of nearly 100% [7]. High accuracy is also shown in the classification using the K-means segmentation method [10] and Fuzzy C-Means [8], with results close to 97%. Still, with SVM, previous studies have also managed to get an accuracy of 95.7% in the classification of brain tumors [9]. Similar to research on the classification of brain tumors, deep learning methods are used to do this work with an accuracy of 96.97 for DNN [10]. The feature extraction supports the high accuracy in the image and the segmentation technique that is done. Some of the segmentation methods are K-Means Clustering [11] and Fuzzy C-Means [8] [12] [10] [13].

Our contribution in this study focused on unsupervised method on the image segmentation algorithm based on fuzzy c-means clustering. The method was considered a significant segmentation tool for brain MR images. Further, several authors [8] [12] [10] [13] used segmentation methods, mainly the Fuzzy C-Means in order to segment the brain very well. The rest of the paper constructed as follows: Section 2 describes the proposed method. Section 3 presents the result and explores the analysis of the experiments by the proposed method — finally, conclusions and future directions drawn in Section 4.
2. Proposed Method

Fuzzy C-Means Clustering technique has been proven as a good segmentation method on the Brain MRI datasets, especially Brain tumor. Therefore, we applied the most accurate segmentation method in leptomeningeal metastasis using Fuzzy C-Means Clustering on the Brain MRI results of leukemia patients. Proposed methodology in segmenting leptomeningeal metastasis is as follows:

a. Step 1: Brain MRIs Dataset Acquisition and determine ground truth.

b. Step 2: Image preprocessing by increasing the sharpness of the pixel image (sharpen), changing the image from RGB to grayscale, as well as eliminating noise by applying a median filter noise remover.

c. Step 3: Skull stripping by removing the lightbox that surrounds the image and setting the threshold to get the binary image.

d. Step 4: Image segmentation using Fuzzy C-means.

e. Step 5: Evaluate the comparison of segmentation results with Ground Truth using the Jaccard Index.

2.1. Data Acquisition and Ground Truth

In this paper, our research focuses on leptomeningeal metastasis, which is a secondary cancer of leukemia patients that spreads to the brain through the spinal cord.

The dataset is a non-public dataset that consisted of 50 leukemia patients Brain MRI results from the Dharmais Cancer Hospital with axial and coronal planes, T2-weighted with contrast. All datasets are 17 patients’ images with leptomeningeal metastasis and ground truth, 22 patients with normal images, and 11 patients with excludes images because they do not use contrast, and there is a hemorrhagic stroke in the brain. An example of the dataset is illustrated in Fig. 2. Due to this study focused on malignant segmentation based on leptomeningeal metastasis, we only used data images from 17 patients with leptomeningeal metastasis suspects.

2.2. Image Preprocessing

In the collection and capturing of the Brain MRI dataset, noise can occur due to many external transmission systems and environmental factors, namely the presence of Gaussian noise, salt and

![Fig. 1. Steps in Proposed Method](image1.png)

![Fig. 2. From left to right sample of Brain MRI dataset (a) Abnormal, (b) Normal, (c) Exclude, and (d) Ground truth](image2.png)
pepper noise, speckles, Poisson, and blurred which will interfere with the experimental results [14] [15]. In this research, the image quality is sharpened to reduce the blur that occurs. The median noise removal filter is also applied to reduce the noise value of an image by replacing it with the value of the neighborhood (mask). The working principle is to collect the pixels of the mask sorted by its gray level, which is then the median of the set of values stored to replace the noisy value [16]. Noise removal is an important thing to implement because not only to enhance image quality, but it also increases efficiency and improves the robustness of the next method to be performed [17].

The results of the median filtering formulated as 
\[ g(x, y) = \text{med}(f(x_i, y_i), i, j \in W) \]
where \( f(x, y) \) and \( g(x, y) \) are the original image and output image respectively. \( W \) is the two-dimensional mask with a matrix size \( n \times n \); the size of the mask can be linear, circular, square, cross, etc.

Median filter is a non-linear filter, image with some random noise has a complex mathematical analysis. For an image with zero mean noise distribution, the variance of the median filter is approximately [16].

\[ \sigma_{med}^2 = \frac{1}{4n^2 f^2(n)} \approx \frac{\sigma_i^2}{n^2 + \frac{\pi}{4}} \]

Where \( \sigma_i^2 \) is the input power noise variance, \( n \) is the size of the median filtering mask matrix, \( f(n) \) is a function of noise density. Then, for the average noise variance, compute as.

\[ \sigma_0^2 = \frac{1}{n} \sigma_1^2 \]

The size of the mask and the distribution of the noise are necessary in the median filtering technique. The performance of median filtering for random noise is better than the performance when applied to average noise variance [16]. The improved median filter in the proposed method is also by taking the green channel. The green channel can show brightness well compared to the other two. Furthermore, the human eye is more sensitive to brightness compared to chromaticity [17]. For this reason, it would be appropriate to apply an improved median filter removal by taking the green channel on the results of Brain MRI so that the gray colors that look very similar to each other could be adequately extracted.

2.3. Skull Stripping

Skull stripping is one of the crucial algorithms in biomedical image analysis. It is effectively applied to brain images [12] [18] and commonly referred to as whole-brain segmentation due to the separation process of noncerebral regions such as skin, fat, muscle, connective tissues, and undesired tissues (skull), which are not regions of interest in this study. It can also impact on the quality of subsequent processes and lead to diagnostic confusion [19] [20]. Many methods and approaches are used for automated or semi-automated skull stripping [20]. In this study, we developed a hybrid algorithm semi-automated skull stripping that combines cropping unneeded images with thresholding. The stages of the skull stripping algorithm in this study are given in Fig. 3.
2.4. Image Segmentation

Image segmentation is an essential step in image processing used by radiologists to understand the information presented by an MRI result. The result of segmentation manually depends on the knowledge and experience possessed by the radiologist and requires a very long processing time. Therefore, in Computer Aid Diagnosis (CAD), many image segmentation has been applied automatically using several methods [21] [22].

In this study, the focus of image segmentation using fuzzy c-means method. Fuzzy C-Means Clustering is divided into some specific parts of the image into clusters. This algorithm is better than K-means because of the additional membership function (value) for measuring additional accuracy achievement. FCM is unsupervised algorithm that used in reducing the dimensions of a dataset by setting boundary values for the features of each predefined cluster [11]. In Fuzzy C-Means sample data is assigned with a membership value with a range of 0 to 1 based on the cluster center, the more similarity, the higher the membership value too [23]. The Fuzzy C-Means method could deal with some inaccuracy issues related to membership value. The Fuzzy C-Means method has been widely implemented in image analysis cases where the datasets have uncertain boundaries among regions [11] [24]. As an example, Brain MRI results typically contain fuzzy regions and unclear boundaries.

Fuzzy C-Means clustering algorithm is grouping a set of "fuzzy" data on n-elements (i.e., Pixels), where each element is $X_i \in \mathbb{R}^d$, a vector that has d real-valued dimensions that represent the $X_i$ element. A fuzzy membership matrix formulated as in Eq 3.

$$M_{fcn} = \{U \in \mathbb{R}^{cn}|\sum_{j=1}^{c} u_{ij} = 1.0 < \sum_{i=1}^{n} u_{ij} < n, and u_{ij} \in [0,1]; 1 \leq j \leq c; 1 \leq i \leq n\}$$

That equation represents the number of c clusters in fuzzy for n-elements, which signifies fuzzy membership of the $i^{th}$ elements to the $j^{th}$ cluster (fuzzy cluster). Each element of the data is part of a fuzzy cluster, in N data samples, to minimize the subsequent cost function for decreasing dimensional feature features as

$$J = \sum_{i=1}^{N} \sum_{j=1}^{m} u_{ij}^m \|x_i - v_j\|^2$$

$u_{ij}^m$ shows the membership value of the $x_i$ data in the $j^{th}$ cluster, $v_j$ is the $j^{th}$ cluster center, $m$ is a constant, and $\|\|$ represents the norm metric.
When converging data to group according to membership value as 0 or 1, it will create crisp partitions in the data. Although Fuzzy C-Means works by reducing the dimensions of the feature set, a threshold value is determined by selecting a random healthy brain MRI and calculating the feature value of the image. In his study, we set a threshold on taking each RGB color channel, which on average, is used as a feature threshold value. The matrix then becomes the initial center of the fuzzy centroid cluster. The overview of this process shows in Fig. 4.

Fig. 4. Diagram of the Fuzzy C-Means Method

2.5. Segmentation Evaluation

Subsequent to Brain MRI segmentation based on leptomeningeal metastasis, we evaluate the performance qualitatively using the manual segmented images by the expert (ground truth), and quantitatively using the Jaccard index. The value of Jaccard index always lies between 0 and 1 [25][26]. Jaccard index is given by

$$J = \frac{|A \cap B|}{|A \cup B|}$$  \hspace{1cm} (5)

A represents the labeled regions by the expert (ground truth), and B represents the regions by the Fuzzy C-Means segmentation method. If the value near 0 indicates a lesser amount of segmented image and its corresponding ground truth images. The higher measure Jaccard index near to 1, indicates more accurate segmentation (similar).

3. Result and Analysis

The experiments performed on the processor Intel® Core™ i5-8265U @1.8GHz CPU and 8GB memory running under Windows 10 OS. Implementation and testing of the proposed algorithm was developed in MATLAB R2017a environment.
Preprocessing applied for dataset images by sharpening to fix the quality of small pixel images and removed noise with Median Filtering Noise Removal. Leptomeningeal metastasis is an abnormality in the brain that often occurs in patients with solid cancer or blood cancer. This study more focused on leptomeningeal metastasis that occurs in leukemia patients. The obstacle that is often encountered in reading the results of Brain MRI with leptomeningeal metastasis is the similarity of the number of colors that are vague with healthy cells. The next step in the proposed method described in Fig. 1, is doing whole-brain segmentation based on skull stripping.

In this step, we separated the connected tissue and lightbox in the brain to minimize segmentation errors. The only resulting segmented whole-brain part would be used in the next step. Fig. 5 shows the results of a sample skull strip segmenting images.

Fig. 5. Brain MRI Image leukemia patients of Dharmais Cancer Hospital Dataset. (a)-(d) Original Image; (e)-(h) Image preprocessing using sharpen and median filter noise removal; (i)-(l) A whole-brain segmentation based on skull stripping results.

Only part of the whole-brain segmented is used in the next process, namely leptomeningeal metastasis segmentation using Fuzzy C-Means. Before segmenting, the image is changed first from grayscale to HSV to show better the differences of the colors of the brain parts that resemble. Leptomeningeal metastasis is a secondary cancer that affects treatment, healing, and even the symptoms of malignant relapse of leukemia patients. Even the color range is difficult to distinguish from healthy brain parts. Therefore, we changed the color to HSV to make the color range of leptomeningeal metastasis more clearly visible. From these experiments, it found that the color range for the leptomeningeal metastasis has threshold more than 200. This information can be used as feature information for each dataset.

The implementation of the Fuzzy C-Means segmentation algorithm was by setting the initial cluster center in this study determined through the threshold of the RGB channel. If the threshold value of a dataset feature is less than the maximum of cluster centers, so the dataset is selected as a member cluster (scored as 1). The similarity color between lesion (leptomeningeal metastasis) and the other healthy brain region is one of the significant challenges to do. The Fuzzy C-Means segmentation performance evaluation using the Jaccard Index is 49.1%. It measures the intersection over the union of the Fuzzy C-Means segmentation result and labeled region by the expert (ground truth).
segment regions that are recognized as abnormalities (leptomeningeal metastasis). The color similarity between leptomeningeal metastasis tissue and other parts of the healthy brain is very high, so it still segmented as noises. That high number of values of the union rather than the intersection between segmentation and ground truth results so that the Jaccard Index was small. In Table 1, the immense Jaccard Index value is in image 3, with a score of 0.66, which means that the results of segmentation are similar to ground truth.

| Dataset | Jaccard Index |
|---------|---------------|
| Image 1 | 0.34          |
| Image 2 | 0.48          |
| Image 3 | 0.66          |
| Image 4 | 0.43          |

4. Conclusions and Future Work

Leptomeningeal metastasis is an abnormality in the brain and potentially life-threatening conditions, even a disease relapse, especially for leukemia patients. MR imaging is the best tool for the detection and localization of treatment planning. This work proposed in automatic segmentation of leptomeningeal metastasis using Fuzzy C-Means. It shows several advantages to assist the doctor in deciding treatment in less time and easy to operate.

In this study, we proposed an automatic segmentation method to detect leptomeningeal metastasis in leukemia patients. We used a preprocessing method to improve the quality of images and to eliminate the unwanted noises. A hybrid semi-automated skull stripping algorithm that combines cropping unneeded images and thresholding is also applied. Furthermore, we used the Fuzzy C-Means segmentation method to segment the leptomeningeal metastasis. The segmentation performance evaluation only produces 49.1% Jaccard index. It is possible because the leptomeningeal metastasis is difficult to observe even for an expert; the similarity of colors between abnormalities and healthy tissue is very high. Besides that, we need to improve the preprocessing method to define the threshold between normal and abnormal tissue further so that it can reduce unwanted noise segmentation, which also reduces segmentation accuracy.

In future works, we will investigate the effect of implementation of some feature extraction techniques or combining more than one segmentation methods for improving the performance evaluation. Maybe we even need to find out whether by doing the classification process directly, whether it can improve the accuracy obtained.

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