Improved Malignant Diagnosis Using Fuzzy C-means Based on Histopathological of PET-CT Lung Images

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ABSTRACT

Currently, evaluation of abnormal lesions on lung Computed Tomography (CT) images is an important step, especially in patients who have tumor in the early stages, leading to increased survival rates. In early cases of tumor diagnosis on lung, Positron Emission Tomography (PET-CT) and histology images (colored) are very complicated since the intensity values of healthy and abnormal tissues may be very close. The objective of this paper is to differentiate between healthy and abnormal tissues through an image processing clustering algorithm. Fuzzy c-means clustering algorithm is applied to the lung PET-CT and histology images. The algorithm uses the microscopic examination of malignant and benign tissues to improve clustering process based on minimization of the objective function. This paper introduces a new method for predicting the type of patients with unknown lung cancer from their PET-CT images in early stages. The proposed technique differentiates between normal and abnormal tissues based on histopathological information. This paper develops a membership function based on iterative optimization to find the similarity between any measured data and the center leading to improving the clustering process. This incorporates preprocessing stages of noise removal and image enhancement. The diagnosis stage includes color PET-CT and histology image segmentation to identify the region with abnormal tissue. This leads to improved early diagnosis of lung cancer. Finally, the proposed technique measures the percentage of affected area with cancerous tissue. The algorithm is applied to 40 sets of different real data in the form of lung PET-CT and histology images with normal, abnormal tissue and early tumor. The experimental results show that the proposed algorithm proved effective in detecting tumors on lung PET-CT especially in images having tumors that were undetected by traditional methods

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CCS Concepts

• Computing methodologies→Machine learning→Machine learning algorithms→Feature selection

Keywords

Lung tumor; PET-CT images; Segmentation; Fuzzy c-means; Differentiatation

1. INTRODUCTION

Nowadays, lung cancer is one of the major causes of death in many countries. Lung cancer is a disease of abnormal cells multiplying and growing into a carcinoma [1]. Lung cancer often spreads toward the center of the chest because the natural flow of lymph out of the lungs and toward the center of the chest [2]. Cancer that starts in the lung is called primary lung cancer.

Lung cancer starts when cells of the lung become abnormal and begin to grow out of control. As more cancer cells develop, they can form into a tumor and spread to other areas of the body [1,3]. The two main types are small-cell lung carcinoma (SCLC) and non-small-cell lung carcinoma (NSCLC). The three main subtypes of NSCLC are adenocarcinoma, squamous-cell carcinoma and large-cell carcinoma[1,4] Nearly 40% of lung cancers are adenocarcinoma, which usually originates in peripheral lung tissue. In small-cell lung carcinoma, the cells contain dense neurosecretory granules, which give this tumor an endocrine/paraneoplastic syndrome association [5-7]. Most cases arise in the larger airways (primary and secondary bronchi) [7]. Sixty to seventy percent have extensive disease which cannot be targeted within a single radiation therapy field [1,8]. The most common symptoms are coughing (including coughing up blood), weight loss, shortness of breath, and chest pains [9].

Lung cancer may be seen on chest radiographs and computed tomography (CT) scans[10]. The diagnosis is confirmed by biopsy which is usually performed by bronchoscopy or CT-guidance [11].

Medical PET-CT images have been applied in clinical lung diagnosis widely. This can assist physicians to detect and locate pathological changes with more accuracy. Computed Tomography images can distinguish different tissues according to their different gray levels [10,12]. Although surgeons are using the latest methods in the diagnosis for lung carcinoma, but they say it is difficult to predict or detect a tumor in the early stage.

The images, if processed appropriately can offer a wealth of information which is significant to assist oncologists in the medical diagnosis [9]. A patient is subjected to different diagnostic methods to determine the cause of the symptoms mentioned by the patient [13-14].

Experts say that lung cancer, if diagnosed early, is easier to treat. The only way to know whether a patient has lung cancer early on is through screening, because they will have no obvious symptoms [14].

A medical diagnosis of the lung cancer is based on blood tests, imaging scans, and biopsy. When surgeons go for tumor removal, they must know the abnormal tissue extent and exact location of the tumor on lung PET-CT image. The shortage of radiologists and the large volume of PET-CT images to be analyzed make these readings labor intensive and expensive. It also depends on the expertise of the technician examining the images [15].

Estimates also indicate that 10 to 30% of tumors are missed by the radiologists during routine screening [16].

Clustering methods are one of the most used algorithms in image segmentation. There are different methods of clustering: K - means clustering, Fuzzy C- means clustering, mountain clustering and subtractive clustering [17].

This research uses a pre-processing stage before applying the proposed Fuzzy C-Means (FCM) clustering. In fuzzy clustering, data elements can belong to more than one cluster, and associated with each element is a set of membership levels. These levels indicate the strength of the association between that data element and a particular cluster.

Fuzzy clustering is a process of assigning these membership levels, and then using them to assign data elements to one or more clusters. One of the most widely used fuzzy clustering algorithms is the Fuzzy C-Means Algorithm [13][18].

A new concept is introduced in this paper where the microscopic examination of malignant and benign tissues is used to define the target clusters leading to improving the clustering process. For developing the membership association, a minimization of the objective function is utilized. As a result, no feature extraction is necessary to apply the FCM algorithm. This leads to Increasing reliability and accuracy of identification and diagnosis of lung cancer in the early stages using the proposed algorithm.

This paper focuses on early diagnosis of abnormal tissue on PET-CT lung and histology images, providing systems that detect the tumor and its shape. The proposed algorithm saves the detection time in addition to the improved diagnosis. This paper is organized in six sections. Sections I and II consist of an introduction and pre-processing stage. Fuzzy c-means clustering algorithm is discussed in Section III. Section IV presents measuring the lung carcinoma percentage stage. Section V presents results of the proposed technique with FCM clustering. Finally, the conclusion is presented in Section VI.

2. PRE-PROCESSING

The aim of the preprocessing stage is to eliminate the background noise and improve the image quality for the purpose of determining the affected region in the input image. It performs noise removal through median filtering, image enhancement through non-linear filtering, and image equalization through cumulative histogram equalization as shown in Figure.1.

2.1 Denoising Step

In order to detect and segment the abnormal tissue in the patient image, a noise removal technique is also used, and it helps to identify affected regions in the input image. The original image is denoised using median filter rather than averaging filter as it removes noise without distorting the edges. In median filtering, the output value is generated from the neighboring values. New unknown values are not created near the edges, so median filtering is effective to simultaneously reduce noise and preserve the edges. For better understanding of the median filter function, the salt and pepper noise are artificially added to the image then removed by using median filter [19-20].

In this work, lung PET-CT and histology images are firstly converted into red, green and blue planes, then the median filter is applied on each color separately. Finally, all the denoised RGB plans are combined to get the output (denoised) images as shown in Figure. 1.

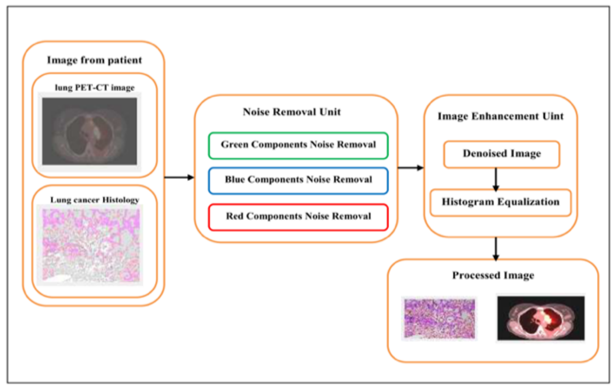


Figure 1. Block diagram of pre-processing stage.

2.2 Image Improvement Step

Image improvement techniques provide a multitude of choices for improving the quality of poor images by reducing the effects of noise, degradations, blurring and distortion of the input image. Color Image Enhancement is divided into two types: linear filtering and non-linear filtering [21-23].

In this work Image enhancement by using filtering techniques (median filtering used as a non-linear filter) is applied to get the enhanced image of the tumor.

In this filtering process the input pixel is replaced by the median of the pixels contained in a window around the pixel, that is [17,24],

$$v(m,n)=\text{median}\{y(m-k,n-l),(k,l) \in W\} \qquad (1)$$

where W is a suitably chosen window. The algorithm for median filtering requires arranging the pixel values in the increasing or decreasing order and picking the middle value. It is useful for removing isolated lines or pixels while preserving spatial resolution.

2.3 Image Equalization

Histogram equalization has been considered one of the most powerful techniques for image enhancement, in order to adjust the contrast of an image by modifying the intensity distribution of the histogram. The image can be modified by using histogram equalization technique so that its histogram has a desired shape [17][25-26].

There are several different types of histogram equalization algorithms. For instance, cumulative histogram equalization and normalized cumulative histogram techniques will lead to the same results in identifying tumors on lung image [18][27-28]. This is attained via the histogram of the image, using a technique that allows the pixels with low contrast to gain higher contrast by spreading out the most frequent intensity values equalization, and localized equalization[17][29-31].

In this work cumulative histogram equalization is proposed for implementation. This algorithm is selected due to its good performance and easy implementation. The cumulative histogram equalization algorithm works as follows:

a. Create the histogram for the image.
b. Calculate the cumulative distribution function histogram.
c. Calculate the new values through the general histogram equalization formula.
d. Assign new values for each gray value in the image

This technique helps to improve low contrast and uniform histograms in the input image to obtain accurate diagnosis.

3. FUZZY C-MEANS CLUSTERING

In this section we introduce some basic concepts of FCM clustering, mathematical representation, and algorithm.

3.1 Overview of Fuzzy C-means Clustering

FCM is an unsupervised clustering algorithm that has been applied to wide range of problems involving feature analysis, clustering and classifier design. The fuzzy logic is a way of processing the data by giving the partial membership value to each pixel in the image [19,21,31]. The membership value of the fuzzy set ranges from 0 to 1. Fuzzy clustering is basically a process that allows intermediate values i.e., member of one fuzzy set to also be a member of other fuzzy sets in the same image.

The clusters are formed according to the distance between data points and cluster centers are formed for each cluster. The FCM algorithm is a method of clustering that allows one piece of data to belong to two or more clusters [22,29,31]. In FCM a dataset is grouped into n clusters with every data point in the dataset belonging to every cluster to a certain degree. For instance, a certain data point that lies close to the center of a cluster will have a high degree of belonging or membership to that cluster and another data point that lies far away from the center of a cluster will have a low degree of belonging or membership to that cluster. It starts with an initial guess for the cluster centers, which are intended to mark the mean location of each cluster. [23-24,31]. The initial guess for these cluster centers is most likely incorrect. Next, FCM assigns every data point a membership grade for each cluster by iteratively updating the cluster centers and the membership grades for each data point. FCM iteratively moves the cluster centers to the right location within a data set [29]. This iteration is based on minimizing an objective function that represents the distance from any given data point to a cluster center weighted by that data point's membership grade.

3.2 Mathematical Model

In this paper, a new approach for implementing FCM is introduced to improve lung cancer identification and diagnosis process. It develops an FCM mathematical model using optimizing of the membership function based on minimization of the objective function. PET-CT and histopathological images are taken as input for FCM clustering algorithm with the specification mentioned above to 40 lung PET-CT color images. The proposed segmentation algorithm is based on FCM clustering performed on lung PET-CT color images. In this method, on the basis of color, the clusters of pixels are computed [30-31]. The process of clustering is to assign the q feature vectors into K clusters, for each kth cluster Ck is its center. A variety of Fuzzy clustering methods have been proposed and most of them are based upon distance criteria [14][25][30]. This algorithm has an input of a predefined number of clusters, k. Means stands for an average location of all the members of a particular cluster and the output is a partitioning of k cluster on a set of objects [15,29-31]:

Fuzzy c-means (FCM) is based on reducing the following function:

$$J = (W^{q^k}, C^{(k)} = \sum_{(q=1,Q)} \sum_{(k=1,K)} (W_{qk})^p \left\| X^{(q)} - C^{(k)} \right\|^2 \qquad (2)$$

where, p is any real number greater than 1, Wqk is a degree of membership of X; in the cluster k, x(q) : data measured in d-dimensional, C(k): dimension center of the cluster.

3.3 Fuzzy C-means Algorithm

The FCM allows each feature vector to belong to multiple clusters with various fuzzy membership values [24-25,29]. Then the final classification will be according to the maximum weight of the feature vector over all clusters. The algorithm uses the Histopathological microscopic examination of both malignant and benign tissues taken from real patients. Membership function to improve the clustering process is based on the minimization of the objective function. FCM partitioning is carried out through an iterative optimization of the objective function shown above equation (2). The update of the membership function is based on iterative optimization to find the similarity between any measured data and the center leading to improving the clustering process.

The algorithm contains the following steps:

a) Initialize random weight for each pixel, it uses fuzz weighting with positive weights W_{qk} between [0, 1].
b) Standardize the initial weights for each qth feature

$$W_{qk} \Big/ \textstyle\sum_{r=1,K} W_{qr} \qquad (3)$$

c) Standardize the weights over k = 1,…,K for each q to obtain W_{qk}, via:

$$W_{qk} = W_{qk} \Big/ \textstyle\sum_{r=1,Q} W_{rk}\,, q = 1, \dots, Q, \qquad (4)$$

d) Calculate new centroids C(k), k = 1,….,K via
$C^{(k)} = \sum_{(q=1,Q)} W_{qk}\, X^{(q)}, k = 1, \dots, K, q = 1, \dots, Q$ (5)

e) Update the weights W_{qk} via

$$W_{qk} = \frac{\left(1 \big/ \left\| X^q - C^k \right\|^2 \right)^{1/(p-1)}}{\sum_{(r=1,K)} \left(1 \big/ \left\| X^q - C^k \right\|^2 \right)^{1/(p-1)}} \qquad (6)$$

For k = 1,....,K , q= 1,....,Q

f) If there is a change in the input image, return to step 3, else terminate.

g) Assign each pixel to a cluster based on the maximum weight. The algorithm is depicted in Figure. 2.

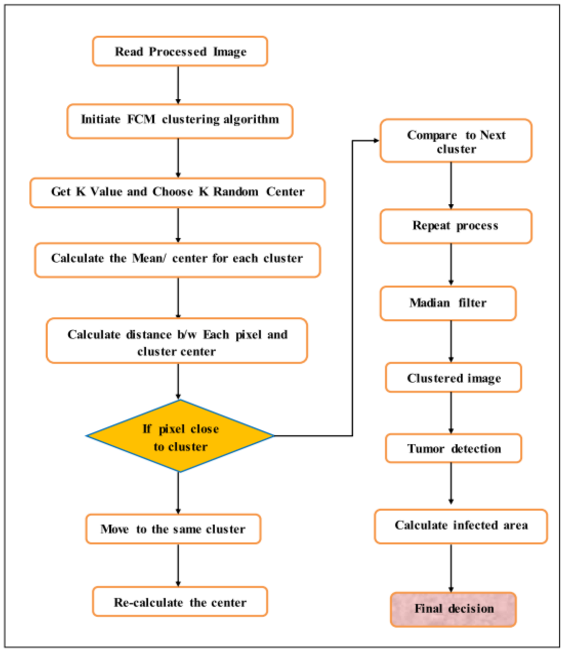


Figure 2. Block diagram of proposed C-means algorithm.

4. MEASURING OF AFFECTED REGIONS

After the segmentation stage, it is important to calculate percentage of tumor in the segmented image. In this stage, the region of interest (ROI), is selected then shape feature extraction is performed on the selected cluster to quantify the size of the tumor. The ROI is selected using GUI based polygon method which selects a polygonal region of interest within an image [26,30-31]. Consequently, shape feature extraction is performed on the selected ROI to calculate the affected area. Area estimation is used to calculate the actual number of pixels in the region. Rectangle section is the scale which specifies the diameter of the region of interest. Perimeter gives the distance between each adjoining pair of pixels around the border of the region.

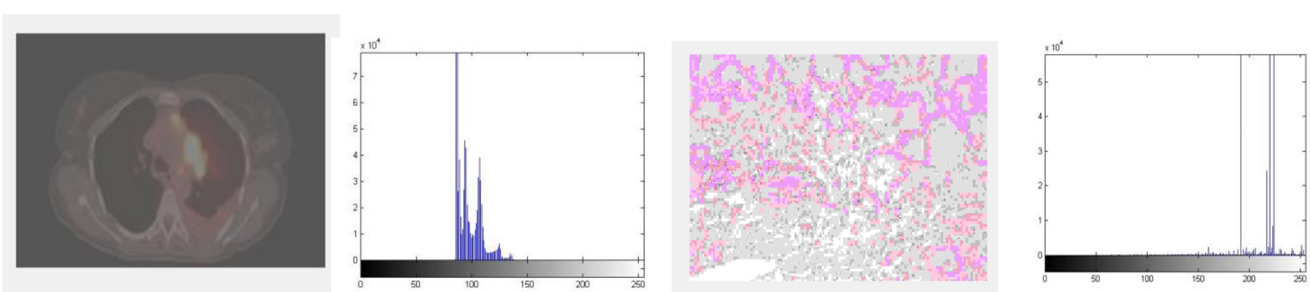
To measure the percentage of cancerous lung tissue in the images, the following equation is proposed:

$$LC\,\% = \frac{NP}{TP} \times 100 \qquad (7)$$

where, LC is the cancerous lung tissue percentage, NP is Number of pixels of rectangle section shown in the tumor, and TP is Total number of pixels of lung PET-CT and histology images.

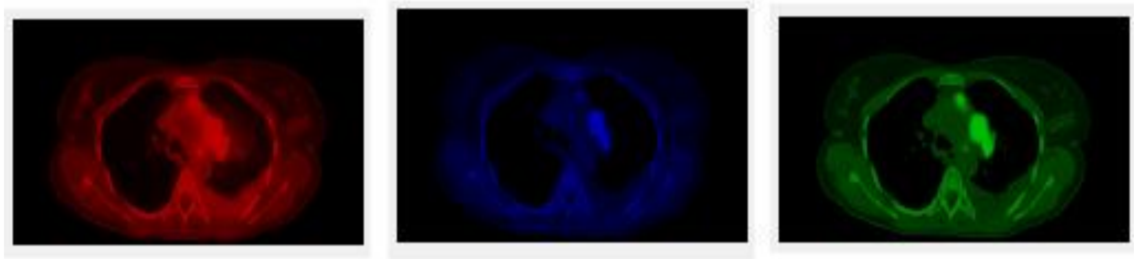
5. RESULTS

The following results were obtained through using Fuzzy c-means algorithm on a set of lung color PET-CT and histology images. The data is generated from 40 different patient images with different dimensions, shapes and types. The proposed technique started with reading the original (patient) image and applying the pre-processing stage which includes image enhancement and noise removal to increase process accuracy. The median filter is applied to the original image to remove the salt and pepper noise to get the smoothed image. Due to occurrence of salt and pepper noise, a median filter has been used to remove it, since the median filter is much more sensitive than other filters. Results are given in Figures.3 and 4. The resulted images of the pre-processing step are shown in Figure. 5 which depicts the salt and pepper noise. The output of the first stage (processed image shown in Figure. 6) is taken as input for the segmentation stage. Hereafter, processed image clustering is performed using FCM to segment the processed images. In this stage, and on the basis of color, the clusters of pixels are computed as shown in Figure.7. Then the third stage is done to calculate the percentage of detected cancerous tissue in the segmented image. Rectangle section of the tumor region is selected by polygon method as shown in Figure. 7, (b), (d). Finally, Figure. 8, shows quantitatively, the learning error waveforms of FCM during the clustering process. Detection of cancerous lung masses on color PET-CT and histology images using the proposed technique resulted in robust early diagnosis for 8 cases in lung images with the actual pathological analysis as obtained from Alexandria/Egypt Cancer Institute. Experiments show that the proposed approach produces good results with increasing reliability and accuracy of prediction, and identification of lung cancer in the early stages from the PET-CT images only.

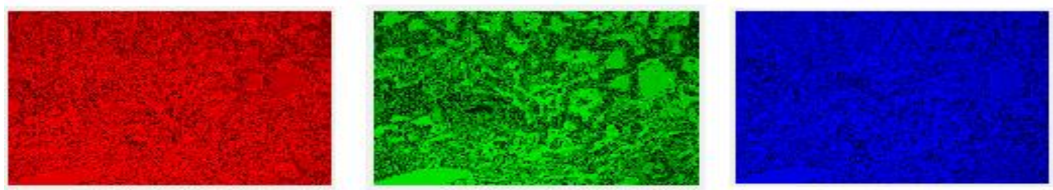


(a) (b) (c) (d)

Figure 3. (a) The original PET-CT image, (b) histogram of original PET-CT image, (c) Input lung histology image, and (d) lung histology image with histogram.



(a)

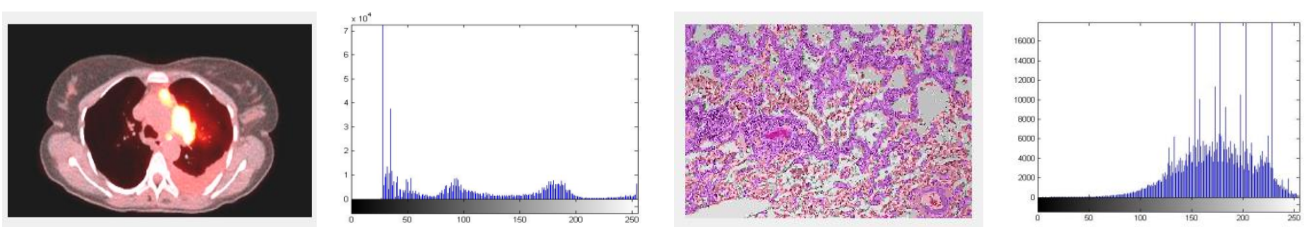


(b)

Figure 4. (a) lung PET-CT image: top left, red plane; top right, green plane; and in-between, blue plane. (b) lung histology image: bottom left, red plane; bottom right, blue plane; and in-between, green plane.

(a) (b)

Figure 5. salt and pepper noise in; (a) lung PET-CT image, (b) lung histology image.



(a) (b) (c) (d)

Figure 6. (a) processed PET-CT image, (b) histogram matching processed PET-CT image, (c) processed histology image and (d) histogram matching processed histology image.

(a) (b) (c) (d)

Figure 7. (a) Processed PET-CT image with identifying the infected region; (b) the segmentation results for processed PET-CT image with percentage of tumor tissue; (c) processed lung histology with identifying the infected tissues. (d) The segmentation results for processed histology image with percentage of infected area.

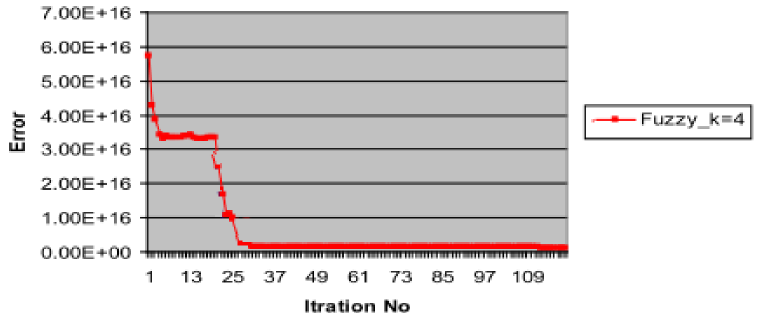


Figure 8. The learning error waveforms of FCM during the segmentation process, for the processed image.

6. CONCLUSIONS

This contribution presents a robust segmentation technique for the detection and analysis of lung tumors using Fuzzy C-mean clustering based on minimization of the objective function. This paper introduces a new method for predicting the type of patients with unknown lung cancer from their PET-CT images in early stages. The proposed technique differentiating differentiates between normal and abnormal tissues based on histopathological information (microscopic examination of both malignant and benign tissues). The proposed technique is applied to lung PET-CT and histology color images to get early detection of cancerous lung tissue. The validity of the algorithm is carried out for a set of real data under noisy environment. Input images require pre-processing of colors to determine the pathology that is being observed and reach an accurate diagnosis. Early diagnosis of lung cancer is a complicated task; therefore, segmentation accuracy is always assigned much importance. The combination of pre-processing technique with clustering technique is useful for the processing of segmented lung images. The polygon method is performed on the selected ROI to calculate the percentage of affected tissue in the clustered images. Results show good agreement with the actual blood test and biopsy results as obtained from Alexandria Cancer Institute, Alexandria city, Egypt.

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