Early Detection of Hepatocellular Carcinoma in PET/CT Images using Improved K-Means Techniques based on Pixel Density

Gamal G.N. Geweid*[1,2,3]
[1]School of Electrical Engineering and Computer Science, University of North Dakota, ND 58202 USA
[2]Electrical Engineering Department, Benha Faculty of Engineering, Benha University, Benha 13511Egypt
[3]Worldwide College of Aeronautics, Worldwide Campus Embry-Riddle Aeronautical University, Daytona Beach, FL 32114, USA
geweidg@erau.edu

Mahmoud A. Abdallah[4]
[4]Manufacturing Engineering Department, Central State University, Wilberforce, Ohio 45384 USA
mabdallah@centralstate.edu

Ayman M. Hassan[2]
[2]Electrical Engineering Department, Benha Faculty of Engineering, Benha University, Benha 13511Egypt
ahassan@aucegypt.edu

ABSTRACT
Hepatocellular carcinoma leads to more human deaths currently. Patient survival rates can be increased by early detection of the tumor which is the main problem. In many cases, the task of early detection in liver grayscale images is very complicated since the intensity values between healthy and abnormal tissues may be very similar. In this paper, a pre-processing step of pixel colors is introduced to determine the pathology that is being observed, then, followed by a robust detection technique for liver PET/CT images using a k-means clustering algorithm based on pixel intensity optimization and evaluation of probability distribution functions. In this method, k cluster centers are changed with the distance between each pixel to each cluster center. This includes three main stages: pre-processing, segmentation, and measuring the percentage of the region having carcinoma. The unwanted regions can be removed from the segmented image by using the median filter. This work consisted of a comparative study of certain segments of medical image techniques in order to determine as accurately as possible when estimating quality segmentation from performance measures, such as Peak Signal-to-Noise Ratio, percentage of tumor detection, segmentation error, and coefficient similarity dice. The algorithm is applied to 60 sets of different real data in the form of liver PET/CT images with and without tumor tissues. The simulation results showed better detection was obtained using the proposed method.

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CCS Concepts
• **Computing methodologies → Machine learning → Machine learning algorithms→Feature selection**

Keywords
Hepatocellular carcinoma; PET/CT images; k-means; early detection.

1. INTRODUCTION
In recent times, medical PET/CT images have been applied in clinical diagnosis widely. This can assist physicians to detect and locate pathological changes with more accuracy. PET/CT images can distinguish different tissues according to their different gray levels. The images, if processed appropriately, can offer a wealth of information which is significant to assist oncologists in medical diagnosis [1]. A patient is subjected to different diagnostic methods to determine the cause of the symptoms mentioned by him [2]. The liver being a vital organ, diseases of the liver is life threatening to human beings [2], [3]. Liver cancer is one of the most difficult cancers to cure and has a high mortality rate overall [2], [4], [5].

There are two types of liver tumor namely Primary Liver tumor and Secondary Liver tumor. Primary liver tumor is the tumor that originates from the liver itself. This type of liver tumor is also known as hepatocellular carcinoma (HCC). It is the fifth most frequent tumor form in the world and third leading cause of tumor death [3]. Secondary liver tumor is the tumor which originates in other organs but then spreads to liver. Secondary liver tumor is also known as Metastatic liver tumor [4].

Experts say that liver tumors, if diagnosed early, are much easier to treat. The only way to know whether one has a liver tumor early on is through screening, because one will have no symptoms.

Currently, only a small percentage of patients with liver tumor or HCC can be cured; according to the National Health Service only about 5% [6]. A medical diagnosis of the liver tumor is based on blood testing, imaging scans (either an PET or CT scan), and biopsy with pathological analysis of the tissue [7].

When oncologists go for tumor removal, they must know the desired tissue extent and exact location of the tumor in the liver based on PET/CT images [2], [4]. The shortage of radiologists and the large volume of PET/CTs to be analyzed make these readings labor intensive and cost expensive. It also depends on the expertise of the technician examining the images [8]. Estimates also indicate that between 10 and 30% of tumors are missed by the radiologists during the routine screening. Segmentation process is the main process in most of the medical image analysis. It is one of the most widely used method to classify the pixels of an image correctly in a decision-oriented application [9].

It divides an image into several discrete regions such that the pixels have high similarity in each region and high contrast between regions. There are different techniques for image segmentation such as threshold based, edge based, cluster based, and neural network based. Clustering methods are one of the most used algorithms in image segmentation [10]. Again, there are different types of clustering: K -means clustering, Fuzzy C-means clustering, Mountain clustering method and Subtractive clustering method [11]. In this paper, a comparative study is applied to four clustering techniques and the proposed technique. The four clustering methods used were: Clustering Analysis of FDG-PET Imaging in Primary Progressive Aphasia (CA-FDG) [10], Segmentation of PET Images for Computer-Aided Functional Quantification of Tuberculosis in Small Animal Models (CAFQ) [13], Fuzzy C-Means (FCM) clustering, and Fuzzy Kernel C-Means (FKCM) clustering [14].

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

2. PRE-PROCESSING

The main target of the pre-processing stage is to improve the tumor detection process. Preprocessing has three steps, noise removal through median filtering, image enhancement through non-linear filter, and image equalization through cumulative histogram equalization as shown in Figure 1.

2.1 Image Noise Removal

In order to detect liver tumor cells early, noise removal technique is used, and it helps to identify tumors, infected and inflamed areas in the image. The patient image is denoised using median filter rather than averaging filter as it removes noise without distorting the edges. This is because in median filtering, the output value is from the neighboring values, new unknown values are not created near the edges, so median filtering is more effective when our main aim is to simultaneously reduce noise and preserve the edges [11], [12].

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

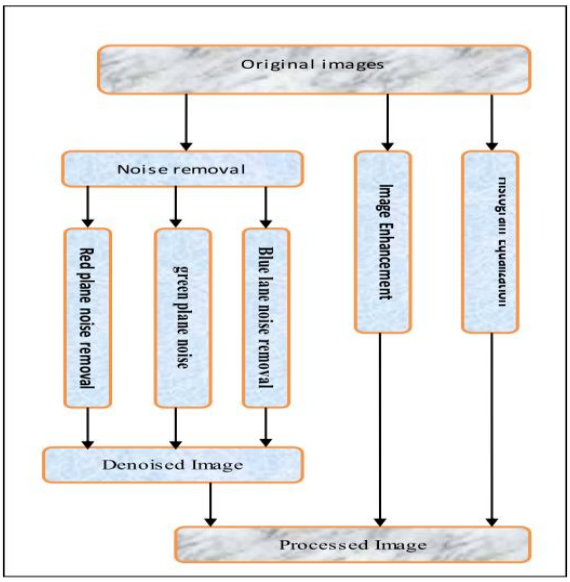


Figure 1. Block diagram of pre-processing stage.

2.2 Image Enhancement

Image enhancement 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) [12].

In this work, image enhancement by using filtering techniques (median filtering used as a non-linear filter) can be processed to get the enhanced image of the tumor. In this filtering the input pixel is replaced by the median of the pixels contained in a window around the pixel, that is [13],

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

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 one of the 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 modifying by using histogram equalization technique so that its histogram has a desired shape [12], [13].

There are several different types of histogram equalization algorithms, for instance cumulative histogram equalization and normalized cumulative histogram techniques which are still the same as it is critical to identify tumor in liver image [14]. 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[13], [14].

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

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

Thus, this technique helps to improve low contrast and uniform histogram in the input image to obtain accurate diagnosis.

3. K-MEANS SEGMENTATION

In this section we introduce some basic concepts of K-means clustering, Mathematical representation, and algorithm.

3.1 Overview of K-Means Clustering

K-means is one of the unsupervised learning algorithms for clusters [16]. Clustering the image is grouping the pixels according to the same characteristics. Color image segmentation uses color as homogeneity criteria for grouping.

In this technique, the processed image is taken as input for the segmentation stage. The proposed segmentation algorithm is based on K-means clustering performed on liver PET/CT images. In this method, on the basis of the color, the clusters of pixels are computed.

The K-means algorithm initially has to define the number of clusters k [12], [13], [14]. Then k-cluster centers are chosen randomly. The distance between each pixel to each cluster centers are calculated. The distance may be of simple Euclidean function. Single pixel is compared to all cluster centers using the distance formula [16], [17]. The pixel is moved to particular cluster which has the shortest distance among all. Then the centroid is re-estimated. Again, each pixel is compared to all centroids. The process continues until the center converges. Figure 2 shows the flowchart of k-means algorithm.

3.2 Mathematical Representation

For a given image, compute the cluster means m:

$$\sum X_{i:()} = X_i / N\,K \quad (2)$$

Now, calculate the distance between the cluster center to each pixel:

$$D(i)=\text{argmin} \left\| Xi - Mk \right\| 2,\ i = 1,.....,N \quad (3)$$

Repeat the above two steps until the mean value convergence.

3.3 K-means Algorithm

a) Give the number of cluster value as k.
b) Randomly choose the k cluster centers
c) Calculate mean or center of the cluster
d) Calculate the distance between each pixel to each cluster center
e) If the distance is near the center, then move to that cluster.
f) Otherwise move to the next cluster.
g) Re-estimate the center.
h) Repeat the process until the center doesn't move

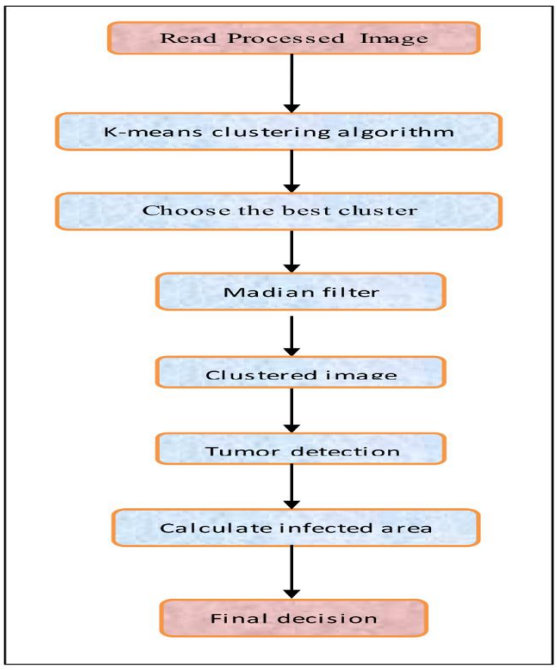


Figure 2. Block diagram of proposed k-means algorithm.

4. Performance Metrics

To estimate the performances studied and test techniques for segmenting PET/CT images, comparisons are calculated using the following parameters between segmented images taken by all evaluated techniques and the proposed algorithm.

4.1 Dice Metric (DM)

A PET/CT images contain set of pixels in two or 3 dimensions. The main target is how to determine which pixels represent a desired area or bad tissue. The parity coefficient of the Dice gives a mathematical solution for the difference [19].

Figure 3 shows two dissimilar areas of R_D and R_S. In this description, the two ROIs have the same borderlines and size and differ only in their location. When R_D and R_S is the area of the reference mask whose spacing between the two images corresponds to the section of the mask area of the processed image, the image segment is specified by a result of the proposed algorithm. The Dice metric can be measured as follows:

$$DM = \frac{2(R_D \cap R_S)}{R_D + R_S} \quad (4)$$

This indicates the relationship between the section of overlap of the two desired regions which is divided into two areas R_D and R_S. Therefore, DM can be represented as a number between zero and one, where one is the full consent and zero does not mean overlap at all.

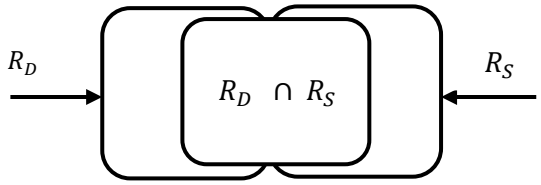


Figure 3. The overlapping between the two ROIs in obtained segmented PET/CT images.

4.2 PSNR Metric

In this paper, Peak Signal-to-Noise Ratio (PSNR) is used to measure the quality of segmentation techniques. The PSNR is an expression of the ratio between the maximum possible value of a signal and the power of the distorting noise which affects the quality of its representation. Since many PET/CT images have an immersive dynamic range, the PSNR is usually expressed in logarithmic decibels [19], [20].

$$SNR = 10\,log_{10}\left(\frac{U}{MSE(R_D\,,R_S)}\right) \quad (5)$$

4.3 Measuring the Tumor Percentage

After the segmentation stage, it is important to calculate the percentage of tumor tissue in the segmented image. In this stage, the region of interest (ROI) and shape feature extraction is performed on the selected cluster to quantify the size of the tumor. ROI is selected using GUI based polygon method which selects a polygonal region of interest within an image [18], [19], [21]. Then shape feature extraction is performed on the selected ROI to calculate the infected area. Area used to calculate the actual number of pixels in the region. Rectangle section is the scalar 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 hepatocellular carcinoma in the patient's images we propose the following equation:

$$\text{HCC } \% = \frac{\text{NP}}{\text{TP}} \times 100 \quad (6)$$

where, HCC is the hepatocellular carcinoma percentage, NP is Number of pixels of rectangle section shown in tumor, and TP is total number of pixels of liver PET/CT image.

5. RESULTS AND DISCUSSION

These results were obtained through using a K-means clustering on a set of liver PET/CT images. The data base here is generated from 60 different patient images with different dimensions, shapes and types. A novel approach is proposed to detect Hepatocellular carcinoma using improved K-means clustering technique based on pixel intensity optimization and evaluation of probability distribution functions. This technique gives a different yet complementary view of the medical images and is used to improve the performance of the segmentation process. The proposed technique started with reading the original (patient) image and applying the preprocessing stage which is to be done to enhance the images and remove noise to increase accuracy of our process. 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 can be used to remove the noise, since it is much more sensitive than other filters. Results are given in Figs. 4 to 6. The resulted image of the pre-processing step is shown in Figure 7 which depicts the salt and pepper noise. The output of first stage, the processed image, is taken as input for the segmentation stage. Then processed image clustering is performed using K-means to segment the image. In this stage, based on color, the clusters of pixels are computed then the third stage is done for calculating the percentage of detected tumor in the segmented image, rectangle section of tumor detected by polygon method as shown in Figure 8. The highest DM, PSNR, and HCC scores yield was obtained from the proposed algorithm as seen in Table I. The changing of k cluster centers with the distance between each pixel to each cluster center lead to a greater than 4% loss in the results. The shortest processing times can be obtained by using the cluster center with rectangular windows, although the times of the algorithm options do not exceed more than a few seconds. Our algorithm is the best option with reasonable processing times and higher accuracy.

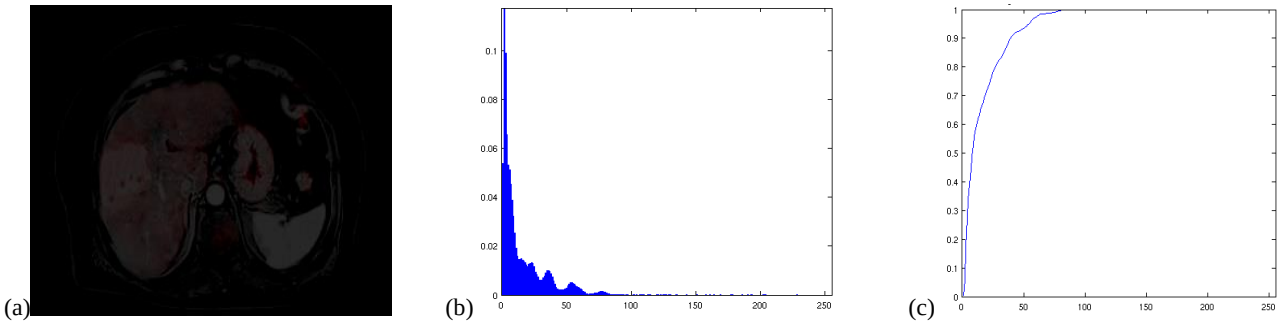


Figure 4. (a) Patient image; (b) histogram of original image before equalization and (c) Original cumulative distribution function.

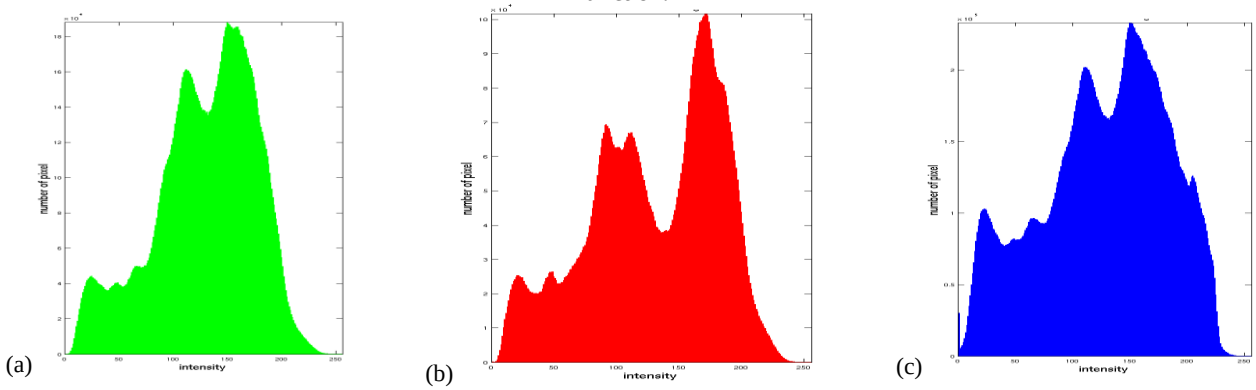


Figure 5. (a) Grean plane histogram; (b) Red plane histogram; (c) Blue plane histogram.

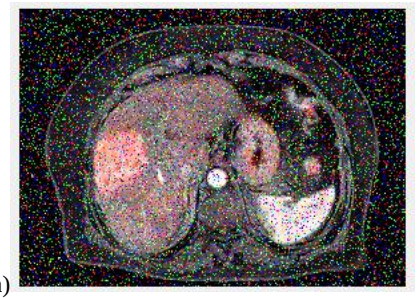
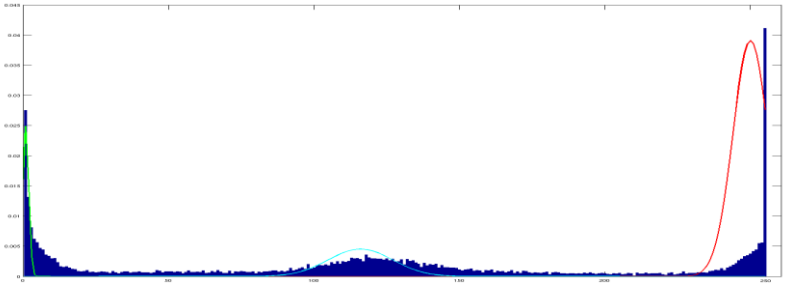
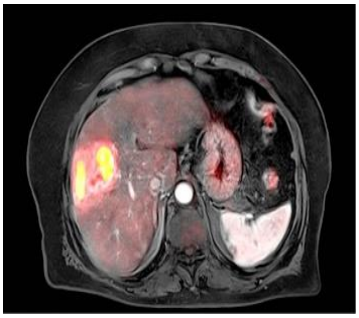
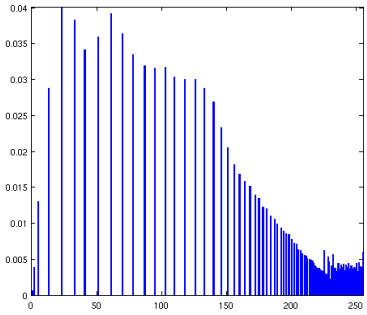
(a)  (b) 

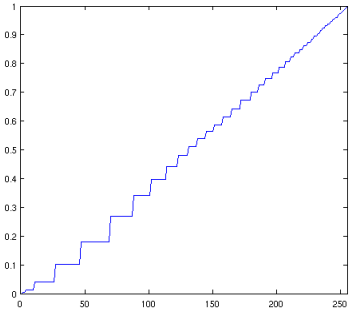
Figure 6. (a) Salt and Pepper Noise in image, (b) Multivariate Gaussian distribution.



(a) Processed image

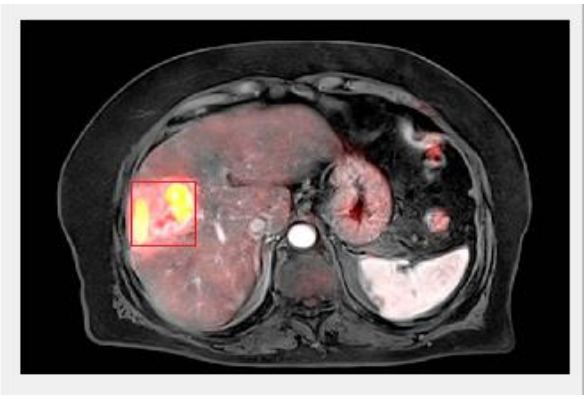


(b) Histogram of processed image after equalizing.

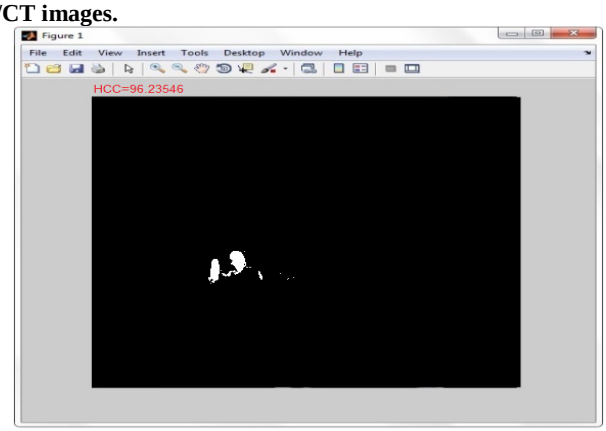


(c) Equalized cumulative distribution function

Figure 7. Shows the results resulted image and the sample cumulative distribution function after applied improved K-Means algorithm to PET/CT images.



(a) Detected tumor with Region of Interest



(b) percentage of tumor tissue

Figure 8. Results of the improved K-means on a PET/CT images for HCC.

Table 1. Comparative results of early detection of hepatocellular carcinoma in PET/CT images using four methods and improved K-means techniques

Clustering technique	DM	PSNR	HCC	Average execution time
CA-FDG	0.79	9.16	81.90%	120.13±1.23
CAFQ	0.63	12.38	83.91%	130.58±1.98
FCM	0.40	19.52	80.96%	179.23±2.01
FKCM	0.23	21.40	85.72%	200.23±8.02
Improved K-means	0.94	25.93	96.30%	90.419±1.98

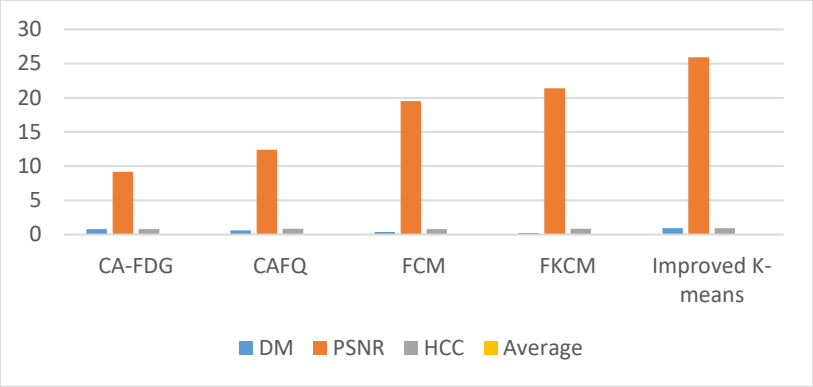


Figure 9. Comparative results of CA-FDG, CAFQ, FCM, and FKCM and Improved K-means clustering techniques.

To ensure that our algorithm is comparable to state of the art, the average DM, PSNR, and HCC scores of our algorithms were compared to reported results in table 1 for the same HCC image dataset using four different clustering methods. The four clustering methods used were: CA-FDG, CAFQ, FCM, and FKCM clustering with comparison shown in Table 1. In this paper, the errors due to changing of k cluster centers with the distance between each pixel to each cluster center and errors due to clustering is combined into the total segmentation error. The identification of the shapes that define the boundaries between the malignant and healthy cells relies on the combined results of the improved K-Means algorithm over the three performance matrixes. In this, the result of a perfect segmentation image arises from the perfect assignment of k-centers to clusters as shown in Figure 9. The available ground truth mask can be used to measure the segmentation error contributed as a result of the Improved K-Means process. A perfect clustering algorithm can be mimicked by comparing each k cluster centers and distances to the matching subset of pixels in the ground truth mask. An example of the improved K-Means evaluation was applied to one of the images in our dataset shown in Figure 8. A calculated average error due to clustering of 1.19% ± 0.48% was found by averaging the measured DM, PSNR, and HCC scores for each mask produced by the improved K-Means evaluation over all 60 PET/CT images. With sufficient accuracy provided by the improved K-Means process, the larger source of segmentation error is clearly caused by the clustering process. Detection of hepatocellular carcinoma in PET/CT images using proposed technique is generating robust early diagnosis for liver images with the actual pathological analysis as obtained from Alexandria Cancer Institute.

6. CONCLUSIONS

This paper presents a robust segmentation technique for liver tumor using K-means clustering. This proposed technique is applied to PET/CT color image for early detection of hepatocellular carcinoma. The validity of the algorithm is carried out for a set of real data under noisy environment. Liver PET/CT images require pre-processing of colors to determine the pathology that is being observed and reach an accurate diagnosis. As early diagnosis of tumor is a complicated task, therefore segmentation accuracy is always assigned much importance. Combination of pre-processing technique with clustering technique can be useful for the process of liver image segmentation. Polygon method is performed on the selected ROI to measure the percentage of cancerous tissue in the segmented images. Clustering accuracy was calculated by can comparing each k-cluster centers and distances between each pixel to each cluster center to the matching subset of pixels in the ground truth mask. Results show good agreement with the actual blood test and biopsy results as obtained from Alexandria Cancer Institute.

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