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Cardiovascular Disease Diagnosis using Imaging Biomarkers -A Survey

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***Abstract*— Cardiovascular disease diagnosis is a challenging task which provides automated prediction about the heart disease of patient so that further treatment can be made easy. Computer-aided cardiac image analysis obtained by various imaging modalities plays an important role in the early diagnosis and treatment of cardiovascular disease. This paper gives a detailed survey of various cardiac imaging biomarkers and various techniques available in the literature for diagnosis of cardiovascular diseases. The paper also presents the segmentation results of cardiac images using three classical segmentation techniques.**

***Keywords*— Computer-aided cardiac image analysis, Cardiac imaging modality; Cardiac imaging biomarker, Cardiac image segmentation.**

I. INTRODUCTION

Cardiovascular disease (CVD) is one of the major causes of death and it is estimated that by 2015 there will be more than 20 million deaths due to heart disease and stroke [1]. Research has showed that the most human deaths in the world are due to heart diseases. The classification and diagnosis regarding the disease are still lacking. Hence understanding CVD causes, its symptoms and early detection will reduce the high risk of sudden death.

Nowadays, cardiologists have access to diverse techniques such as chest X-rays, ultrasound imaging, Doppler techniques and angiography, echocardiograph to better inspect and analyze the functionality of heart. The physicians often mentally integrate image information from different modalities. Cardiac image processing is usually used for detecting, classification and diagnosis of heart disease. Computer aided diagnosis (CAD) of heart diseases has led to the early detection, diagnosis and treatment of heart diseases. Integrated analysis of information from multiple methods is necessary to diagnose heart disease.

The paper attempts to give a review of various imaging biomarkers used for diagnosing cardiac diseases, various techniques available in the literature for diagnosis of CVD. The paper also compares the results of segmentation of cardiac images using three traditional algorithms. The rest of paper is organized as follows. Section II explains cardiac imaging biomarkers. Section III gives a review of recent work carried out to diagnose CVD. Section IV presents the results of segmentation of cardiac images. Section V gives the conclusion.

II. CARDIAC IMAGING BIOMARKERS

Cardiac biomarkers are detectable biological sources that are related with heart function, damage or failure. The goal of cardiac biomarkers is to be able to detect the presence and severity of an acute heart condition as soon as possible so that appropriate treatment can be initiated [6]. Image processing plays a critical role in extracting relevant imaging biomarkers from imaging data and helps to accurately measure them. Some of the cardiac imaging biomarkers are described in this section.

A. Calcified lesion

The presence of calcified lesions/plaque indicates the presence of subclinical atherosclerosis in the coronary artery. Calcified lesions/plaque is an active and regulated process occurring in the vessel wall. The amount of calcified lesions/plaque in the coronary artery indicates the severity of CAD. Hence, calcified lesions/plaque is one of the important biomarkers of CAD. Calcium can be easily visualized on a Computed Tomography(CT) scan.

Calcium lesions/plaque has the same attenuation coefficient as that of bone and appears as bright objects on the scan [8]. They can be detected by setting a threshold level of 130. The process of quantifying the amount of calcifications in the arteries is called calcium scoring. There are three widely used calcium scoring algorithms [11] a) Agatston score [2] b) volume score [3] and mass score [4]. Coronary artery calcium scores have been recognized as an independent marker for adverse prognosis in coronary disease [7].

B. Myocardial Perfusion

It is used to assess the function of the heart muscle (myocardium). If the myocardium receives less blood supply due to an obstructive stenosis caused by CAD, the myocardium is said to be diseased (myocardial ischemia).The presence and extent of myocardial ischemia can be evaluated using Myocardial Perfusion Imaging (MPI).Imaging techniques, such as X-ray angiography or CT angiographyare used to predict potential myocardial infarction or strokes based on the luminal stenosis caused by atherosclerotic lesions[5]. Diagnosis is made by comparing images obtained during rest and those obtained during stress[10].

C. Epicardial fat

Epicardial fat is the adipose tissue found between the myocardium and the visceral layer of the pericardium. This fat tissue directly surrounds the entire heart and the coronary arteries. The epicardial fat tissue surrounding the coronary arteries leads to the local production of inflammatory factors which in turn increases the risk of atherosclerosis.Adipose tissue can be quantified on a CT scan, fat tissue voxels appear on the scans with an attenuation value in the range between -200HU to -30HU.

A typical Cardiac CT scan has three types of fat tissue within its FOV a)Visceral fat (located around the abdomen) b) Inter-thoracic fat (located between the chest wall and pericardium) and c)epicardial fat(contained within the pericardium).The volume of epicardial fat voxels can be quantified by first delineating the heart from the surrounding structures. From long time the CT has been used to quantify the deposition of epicardial fat [9].

D. Lumen quantification

Lumen narrowing or stenosis is caused due to the buildup of plaque in the arteries, which results in narrowing of the blood vessel. There are many tests available for detection of coronary artery disease (CAD). Quantitative coronary angiography (QCA) is the gold standard imaging technique for diagnosing CAD and quantifying the degree of stenosis. Next to quantification of the stenotic region, it also allows to assess the type of plaque (calcified, soft). Stenosis degree is measured using the QCA scan. The degree of stenosis can also be quantified on a CTA scan.

Computed tomography coronary angiography (CTA) is increasingly used to perform the same task and has the advantages of imaging in 3D. Additional information such as the plaque composition can also be derived from the CTA scan. The presence of contrast material within the coronary arteries makes it easier to visualize and quantify the lumen morphology[12].

E. Caronary stenosis

It is a condition in which a coronary artery becomes tapered and backed up with materials like fat or cholesterol. Cholesterol in the bloodstream can build up, causing coronary stenosis. Hence coronary stenosis is one of the important biomarkers of CAD [13].

F. Caronary plaque

Coronary artery disease develops when the coronary arteries become damaged or diseased. Cholesterol containing deposits (plaque) in the arteries and inflammation creates coronary artery disease[14].

Coronary computed tomography angiography (CCTA) is an emerging modality for comprehensive non-invasive assessment of coronary artery disease (CAD). CCTA was traditionally used for anatomical assessment of coronary plaque[15].

III. Literature review of various techniques for diagnosis of cardiovascular diseases

Atta Elalfi et al [21] proposed artificial neural networks in medical images for diagnosis of heart valve diseases. This method is implemented using image processing techniques by extracting texture features from medical echocardiography images, combining intensity histogram features and Gray Level Co-occurrence Matrix (GLCM) features, then developing an artificial neural network for automatic classification based on back-propagation algorithm to classify heart valve diseases more accurately.

Olivier et al [22] proposed an automatic model-based approach to segmentation of cardiac CT images. Fully automatic segmentation is performed using generalized Hough transform (GHT) technique which is used to localize the heart in the 3-D image. After heart detection, three successive steps combining parametric and deformable adaptations to extract the cardiac anatomy are applied.

Tsai et al [23] presented a comparison of three different methods i.e., neural network with backpropagation learning, neural network with genetic-algorithm-based learning, and genetic-algorithm-based (GA-based) fuzzy logic approach for automated discrimination of myocardial heart disease. Four statistical features, namely angular second moment, contrast, correlation and entropy were extracted from each image.

Du-Yih Tsai et al [24] proposed fuzzy-reasoning-based computer-aided diagnosis for automated discrimination of myocardial heart disease from ultrasonic images. This fuzzy classification approach uses the GA-based training for optimization of membership functions. Gaussian-distributed membership functions(GDMFs) .

Yousifet al [25] proposed a method on improvement of nuclear cardiology images for Ischemic patients using image processing techniques. This method estimates noise statistics in nuclear cardiology images.

Lathaet al [26] proposed a new approach based on coactiveneuro-fuzzy inference system (CANFIS) for prediction of heart disease. The CANFIS model is combined with the neural network adaptive capabilities and the fuzzy logic qualitative approach which is then integrated with genetic algorithm to diagnose the presence of the disease.

Du-Yih Tsai et al [27] proposed a genetic-algorithm (GA) based fuzzy-logic approach for computer-aided diagnosis scheme in medical imaging. The method is applied to discriminate myocardial heart disease from echocardiographic images and to detect and classify clustered micro calcifications from mammograms.

Manikandanet al [28] proposed a novel approach on segmentation and classification of carotid artery ultrasound images using active contours. This method measures the intima-media thickness of the carotid artery ultrasound image. s is a non-invasive and sensitive technique for identifying and quantifying the presence of plaque in the carotid artery.

Vikaset al [29] presented a review on cardiac MR imaging perfusion using image processing technique. Cardiac magnetic resonance imaging perfusion (cardiac MRI perfusion, CMRI perfusion), also known as stress CMR perfusion is a clinical magnetic resonance imaging test performed on patients with known or suspected coronary artery disease to determine if there are perfusion defects in the myocardium of the left ventricle that are caused by narrowing of one or more of the coronary arteries. Two major components of image processing techniques such as registration and segmentation are discussed.

Dongwooet al [30] presented a review on heart chambers and whole heart segmentation techniques. There are four types of methods categorized to segment the heart chamber and whole heart. They are 1) the boundary driven techniques, 2) the region-driven techniques, 3) the graph-cuts techniques, and 4) the model-fitting techniques. Various techniques for cardiac image analysis are depicted in Table I.

IV. CARDIAC IMAGE SEGMENTATION USING TRADITIONAL TECHNIQUES

There are typically three stages in cardiac image disease diagnosis, which are a) feature extraction b) segmentation and c) classification. Among these stages segmentation plays a vital role. In this section performance of various segmentation techniques based on K-means [16], FCM [16] and Otsu thresholding [17] are compared using cardiac CTA images. Five cardiac images are used for the experiments in this study. The cardiac image modality of the used images is CT(Computed Tomography) image. The file format of the image is DICOM(Digital Imaging and Communications in Medicine). Table II shows the five cardiac images used in this study.

The performance of cardiac image segmentation can be computed based on the validity of the pixels using the quality measures. Some of the quality measures used in this study for comparison is PSNR (Peak Signal to Noise Ratio), MSE (Mean Square Error), and Structural Similarity Index (SSIM).

The Peak Signal to Noise Ratio (PSNR) is the performance measure widely used to measure the quality of images [18]. The higher PSNR indicates the higher quality of images. The PSNR depends on Mean Squared Error (MSE). MSE represents the mean squared error between the original image and segmented image. The lower the value of MSE is the lower the error.MSE is calculated using

$$MSE = \sum_{m,n}[I_1(m,n) - I_2(m,n)]^2 \quad (1)$$

where M, N are the number of rows and columns in the input images. I1 is the original image and I2 is the segmented image. After calculating MSE value, the PSNR value is calculated using the following equation

$$PSNR = 10 log_{10}\left[\frac{R^2}{MSE}\right] \quad (2)$$

where R is the maximum fluctuation in the input image data type.

The SSIM index can be viewed as a quality measure of one of the images being compared provided the Structural SIMilarity (SSIM) index is a method for measuring the similarity between two images [20].

$$SSIM(f,g) = l(f,g)c(f,g)s(f,g) \quad (3)$$

Where

$$l(f,g) = \frac{2\mu_f\mu_g + C_1}{\mu^2 f + \mu^2 g + C_1} l(f,g) = \frac{2\mu_f\mu_g + C_1}{\mu^2 f + \mu^2 g + C_1},$$

$$c(f,g) = \frac{2\sigma_f\sigma_g + C_2}{\sigma^2 f + \sigma^2 g + C_2} c(f,g) = \frac{2\sigma_f\sigma_g + C_2}{\sigma^2 f + \sigma^2 g + C_2},$$

$$s(f,g) = \frac{\sigma_{fg} + C_3}{\sigma_f\sigma_g + C_3} s(f,g) = \frac{\sigma_{fg} + C_3}{\sigma_f\sigma_g + C_3}$$

The first term $l l$ is the luminance comparison function which measures the closeness of the two images, meanluminance (μf and $\mu g \mu f$ and μg). This factor is maximal and equal to 1 only if $\mu f = \mu g \mu f = \mu g$. The second term is the contrast comparison function which measures the closeness of the contrast of the two images. Here the contrast is measured by the standard deviation σf and $\sigma g \sigma f$ and σg. This term is maximal and equal to 1 only if $\sigma f = \sigma g$ $\sigma f = \sigma g$. The third term is the structure comparison function which measures the correlation coefficient between the two images f and g f and g. Here $\sigma fg \sigma fg$ is the covariance between f f and gg.

Hence the positive values of the SSIM index are in [0,1]. A value of 0 means no correlation between images, and 1 means that $f = gf = g$. The positive constants $C\,1, C2$ $C\,1, C2$ and $C3C3$ are used to avoid a null denominator. Table III shows the performance measure of the cardiac image segmentation using K-Means, FCM and Otsu thresholding using the quality measure MSE, PSNR, SSIM.

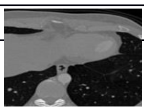
TABLE I

VARIOUS TECHNIQUES AVAILABLE IN THE LITERATURE FOR DIAGNOSIS OF CVDs

Cardiac Imaging modality	**Techniques**	**Features**
ECG image [21]	Gaussian filter, Gabor filter-Preprocessing, Intensity histogram,GLCM feature-Feature Extraction, BPN-Classification	Provides good classification efficiency.
CT [22]	GHT used to localize heart in 3D image	Provides fast quantitative image analysis for clinical diagnostics.
ECG [23]	NN with BP learning, NN with GA-based learning, and GA-based fuzzy logic approach	GA based fuzzy logic approach is superior to other two methods in terms of classification.
US [24]	GA-based training for fuzzy classification approach.GDMF membership function used.	Provides better performance.
SPECT [25]	Gaussian Scale Mixture model,Block Processing Large Images technique	Estimates noise statistics in nuclear cardiology images.
ECG [27]	GDMFs are optimized by a genetic-algorithm learning process.Compared with three methods, BP–NN, GA–NN, and fuzzy approaches.	GA based fuzzy method is superior to the other method.
US [28]	Kaunn filter-Preprocessing, Active contour-feature extraction, SVM-classification	Fully automatic, Achieves lower absoloute error.
MRI [29]	A review on segmentation and registration techniques	Segmentation classified as model independent based and model based for cardiac images.
All Cardiac images [26] [30]	CANFIS, NN, Fuzzy logic, GA. Boundary-driven, Region-driven, Graph cut, Model fitting methods	Provides better training performances and classification accuracy. Evaluates cardiac anatomy and function.

TABLE III

CARDIAC IMAGES USED IN THIS STUDY

	**Image 2**

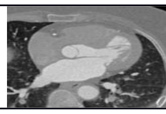
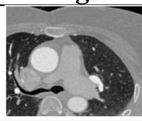
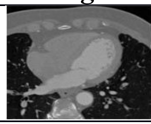
	
Image 3	**Image 4**
	

TABLE IIII

PERFORMANCE MEASURE OF THE CARDIAC IMAGE SEGMENTATION BASED ON TRADITIONAL METHODS

Image	**Segmentation Method**	**MSE**	**PSNR**	**SSIM**
Image 1	K Means	2.6415	27.3506	0.7294
	FCM	0.5420	74.9068	0.9274
	Otsu	0.4691	75.5347	0.9267
Image 2	K Means	3.0074	24.0229	0.7013
	FCM	0.6604	74.0490	0.913
	Otsu	0.4638	75.5834	0.9405
Image 3	K Means	2.9452	24.5304	0.7058
	FCM	0.6428	74.1663	0.9151
	Otsu	0.4665	75.5583	0.9402
Image 4	K Means	2.7393	26.3746	0.7199
	FCM	0.5741	74.6577	0.9226
	Otsu	0.4667	75.5568	0.9402
Image 5	K Means	2.4063	30.0248	0.7526
	FCM	0.4645	75.5774	0.9404
	Otsu	0.4645	75.5774	0.9402

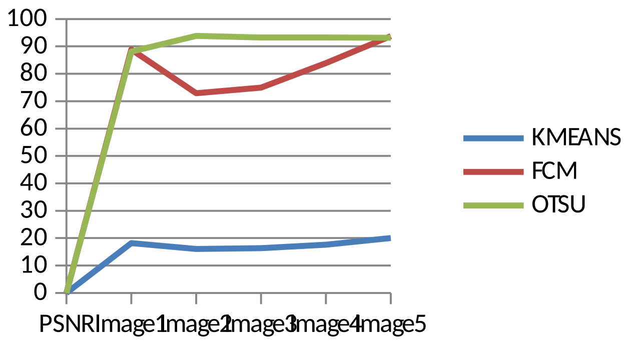


Fig .1 Comparison of segmentation methods based on K-Means, FCM, Otsu technique using PSNR.

Fig 1 gives the comparison of segmentation techniques using PSNR plotted as a graph.

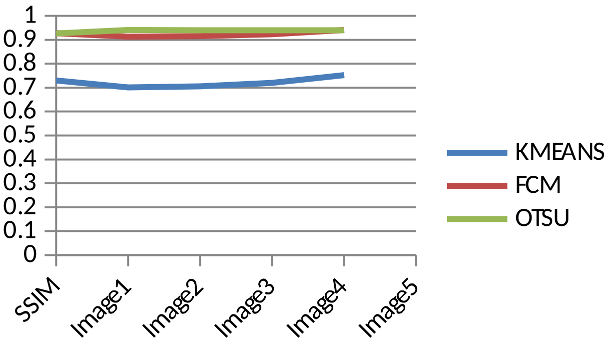


Fig .2 Comparison of segmentation methods based on K-Means, FCM, Otsu technique using SSIM.

Fig 2 gives the comparison of segmentation techniques using SSIM plotted as a graph.

The results show that the cardiac image segmentation results obtained using Otsu thresholding technique are better compared with the results obtained using K-Means and FCM.

V. CONCLUSIONS

Cardiac image processing is an emerging research field in the area of image processing and analysis. Cardiac biomarkers are detectable biological sources that are associated with heart function, damage or failure. This review gave a brief description of various biomarkers which is used to detect the presence and severity of an acute heart condition as soon as possible so that appropriate treatment can be initiated. It also presented a brief review of various research works carried out in the field of CAD for CVD. Finally the cardiac images are segmented using three classical techniques viz., K-means, FCM and Otsu thresholding and the results are presented. For the images considered for the study, Otsu thresholding produces very impressive results that are better compared with the results obtained using K-Means and FCM.

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