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Segmentation of Intima-Media Thickness in Intravascular Ultrasound (IVUS) Images for Detection of Atherosclerosis

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***Abstract*— Cardiovascular diseases (CVD's) are the leading cause of deaths in most of the developed nations. In many cases the adverse CVDs are related to coronary artery disease: a condition caused due to the accumulation of fatty lesions called plaques on the vessels that nourish the heart with blood. Early detection of plaque deposition aids in better treatment procedures. In recent decades the Intravascular Ultrasound (IVUS) imaging modality has captured considerable attention in the diagnosis of CVD's. IVUS is a catheter based imaging technique that provide the cross sectional view of the blood vessels in real time and reveal more information about the plaque deposition. Generally coronary artery consists of three distinct regions: Media, Intima and Luminal region. Intima-Media Thickness (IMT) is perceived as a significant indicator in the risk evaluation process, tracking the amount of atherosclerosis development. The segmentation of IMT of the Common Carotid Artery (CCA) poses varied challenges such as removal of speckle noise, echo shadows, artifacts and contrast enhancement. In this paper, the segmentation techniques such as Multi-Level set based technique, Otsu's segmentation, Active Contour method and Watershed segmentation are compared. From the performance analysis it has been observed that the Multi-Level Set based technique performs better than the other aforementioned techniques.**

Keywords: *Cardiovascular Disease, Intra-Vascular Ultra Sound Imaging, Intima-Media Thickness, Common Carotid Artery.*

INTRODUCTION

Heart and blood vessel diseases include numerous problems, which are related to a process called atherosclerosis. Atherosclerosis is a condition due to accumulation of a substance called plaque deposits in the walls of the arteries. This accumulated substance narrows the arteries making it harder for blood flow. If a clot forms, it can block the blood flow completely, which can cause a heart attack or stroke. When there is complete block in the wall, the part of the heart muscle supplied by artery begins to die. Whereas in case of ischemic stroke, a blood vessel that feeds the brain gets blocked due to a clot. When the blood supply to a part of the brain is cut off, some brain cells will begin to die. This can result in the loss of body functionality controlled by that part of the brain, such as walking or talking.

Adipose tissues are anatomically distributed along the different parts of the human body. Their distribution depends upon the various factors such as sex, age, diet, hormonal levels and medication of the individuals. Body fat tissue is traditionally distributed into two main compartments with different metabolic characteristics: Subcutaneous Adipose Tissue (SAT) and Visceral Adipose Tissue (VAT). While both of these tissue types are important, particular attention has been directed to visceral adiposity owing to its association with various medical pathologies.

The visceral fats are highly inflamed in obese patients. Also, a patient with metabolic syndrome gets highly affected. Additionally, they are capable of secreting large quantities of pro-inflammatory cytokines and free fatty acids. There is a direct involvement of these regional adipose tissue deposits in the development of atherosclerosis and related events need to be reviewed extensively [1].

The diagnosis and treatment of the disease require visualizing the blood vessel and the level of plaque deposition. IVUS imaging modality has captured considerable attention in the diagnosis of CVD's. IVUS is a catheter based imaging technique that carries a catheter holding a guided transducer at the tip. Very high frequency sound waves called ultrasound are emitted by the transducer. These ultrasounds wave bounces off the various tissue structures of the heart vessel and the backscattered waves are converted into images. The information regarding the degree of vessel obstruction and the amount of plaque deposited is obtained through the segmentation of Intima- Media region of the IVUS image. This information is important to determine how to treat the disease. In general manual analysis using visual interpretation of IVUS images is difficult because each components of plaque shows complicated patterns. Also if the deposition is not recognized properly, it will lead to misdiagnosis of the disease. Hence, an automatic segmentation technique needs to be developed for identification of the level of plaques for proper treatment. There are several factors which reduce the accuracy of segmentation and ultimately cause difficulty in interpretation of the disease level.

The remaining sections of this work are structured as follows: Section II examines some of the existing work related to research area. Section III provides a comprehensive explanation of the segmentation techniques used in the analysis. Section IV presents the performance results of the segmentation methods implemented. Finally, the paper ends with the conclusion and future work in Section V.

EXISTING WORK

In [3] the modern developments in the imaging of the coronary arteries are surveyed. This paper describes the benefits of intravascular imaging used in the visualizing of percutaneous coronary and atherosclerosis imaging used for the indication of the developing plaque deposition. The composition of tissue images is also essential for analyzing the lesion occurrence. Also the modern inventions which are used for the unstable atherosclerotic plaque imaging is discussed.

Four kinds of classification algorithms such as Support Vector Machine with Linear Kernel, Support Vector Machine with Radial Basis Function Kernel, AdaBoost and Random Forest to effectively integrate the features from the ultrasound images are used [4]. They iteratively estimated and calculated the probability maps for pixel-wise classification. The plaque segmentation is identified from the generated probability maps.

In [5], the authors studied about the atherosclerotic disease in the peripheral arteries, which provides the better idea about the elusive multifaceted disease. A comparison of various imaging modalities available for visualizing the process of atherosclerosis, confirming and expanding "in vivo" mechanism is studied. There are many restrictions that hamper the translatability of the presently existing imaging modalities even in the level of peripheral arteries. How the ultrasound imaging contributed to detect atherosclerosis through earlier and prior prediction of plaques is discussed in [6]. Evaluation of the biomechanical consequences of atherosclerosis in the vessel walls is done. The molecular imaging technique is used to express the disease-relevant molecules present in the vessel walls. The main drawback with the molecular imaging is its inability to distinguish attached microbubbles from those of freely circulating.

A deep learning framework, which have the capability to discriminate the different plaque constituents such as lipid core, fibrous cap and calcified tissue area is analyzed [7]. A convolutional neural network has been proposed which repeatedly extracted the information from the images essential for the various kind of plaque constituent's identification. Fast edge detection method based on random forest classifier for the efficient measurement of Intima Media Thickness for analyzing the development of atherosclerosis in the artery wall is discussed [8].

Computer aided methods for diagnosing Myocardial Infraction, Carotid Atherosclerosis and Coronary Artery Diseases (CAD) using thoracic and Intravascular Ultrasound (IVUS) Images are investigated [9]. For the CAD, the IVUS have been found used frequently than the thoracic US. A study using subjects without cardiac, cerebral or peripheral vascular symptoms and normal carotid ultrasound to determine the vascular risk factors is made [10]. The research revealed the presence of plaques in subclavian arteries for detection of subclinical atherosclerosis.

The prevalence of Nano Obstructive Carotid Atherosclerosis (NOCA) in the adults with Cryptogenic Stroke (CS) is investigated [11]. Plaque thickness, length and volume is estimated to identify the symptomatic NOCA. A comparison of the Magnetic Resonance Imaging (MRI) with B mode Ultrasound technique in detecting carotid artery plaques is done and evaluated the extent of atherosclerosis [12]. The estimated plaque height using ultrasound and MRI showed the similarity estimation when the height is greater than 2.5 mm. Small structured plaques are detected well in ultrasound then the MRI.

Investigation of the endothelium-targeted panel Microbubbles (MB) ultrasound contrast agents is done [13]. The behavior of a minor peptide ligands is used especially for analyzing the high-risk atherosclerotic plaque. These molecular targets have been presented on the surface of the plague deposited wall. This work concluded that the ultrasound contrast agents which are bearing tiny peptide ligands showed the possible plague deposition areas. This was aimed over the molecules of the endothelial cell adhesion for the inflammatory cells for imaging the innovative atherosclerotic disease. An innovative method of fusing the intravascular ultrasound and optical coherence tomography is proposed [14]. The information acquired by incorporation of the two kind of imaging techniques improved the quality of the images. The proposed technology gives additional data about the plague deposition to support better diagnosis. In [15], the authors deliberated the PAI principles and the current PAI growths which was used to develop the imaging of the cardiovascular. This work also discussed the possible areas for the research. The lipid content of atherosclerotic plaques in the PAI was utilized for the purpose of the plaque rupture correlation and also the morphology.

METHODOLOGY

The study of existing research work mainly focuses on the efficient way to segment the plaque deposited region for deciding the type of treatment to be given at the right time. The flow of the proposed work is depicted in Fig.1. In the proposed method the data set is taken from [17]. The data set consists of 100 B mode IVUS images. The first step is preprocessing of IVUS Image for noise removal and image enhancement for sharpening the edges. Further, morphological operation is performed for Intima-Media region detection. Following the detection, segmentation of ROI is done using techniques such as Multi-Level set based technique, Otsu's segmentation, Active Contour method and Watershed segmentation.

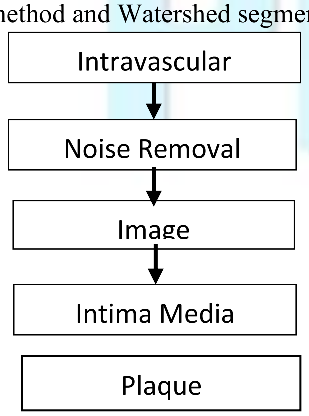

Fig.1. Flow diagram of Plaque Segmentation in IVUS Image

Preprocessing

Pre-processing is an essential step in image processing. Input images is taken from the database and preprocessed to enhance its quality by removing the noise. The input IVUS image is shown in Fig.2. Total Variance Regularization is used to remove the speckle noise. This method is based on the principle that images with excessive and spurious details have high total variance. Thus by reducing the total variance of the image, the unwanted details are removed with edge preservation. The mathematical equation of Total Variance Regularization is given as:

$$T(u) = F(b \mid Au) + \lambda \, \|\Delta u\| \qquad (1)$$

Where F is the data fidelity term, which depends on the noise model

λ is the regularization parameter

The multiplicative model is represented as:

$$b = (Au).\,\zeta \qquad (2)$$

A is the observation operator, u is the noise free data and ζ is the noise

Assuming that u and ζ are independent random variables with the probability density function f_u and f_z, then for

$$b = u.\zeta,\ u>0$$
$$fz(b/u).\ 1/u = f(b/u) \qquad (3)$$

The filtered image is shown in Fig.3.

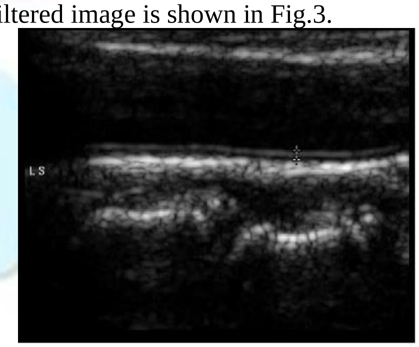

Fig.2.Input Image

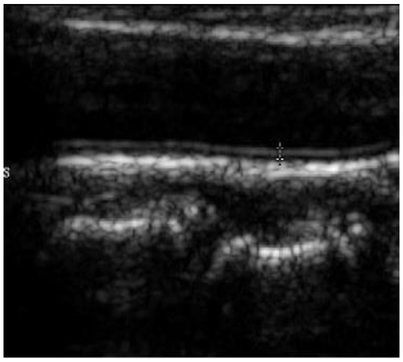

Fig. 3. Filtered Image

Further, image enhancement technique is applied to sharpen the pixel intensity of the input image. In this method Contrast Limited Adaptive Histogram Equalization (CLAHE) is used to the increase the contrast. CLAHE belongs to special type of Adaptive Histogram Equalization (AHE) technique which operates on the small region of the image called tiles. The general AHE technique amplifies the contrast of the image in near-constant regions. This tends to cause the noise also to be amplified. CLAHE is a variant Adaptive Histogram Equalization method which limits the contrast by clipping the histogram at a predefined value before performing the Cumulative Distribution Function (CDF). The enhanced image is shown in Fig.4.

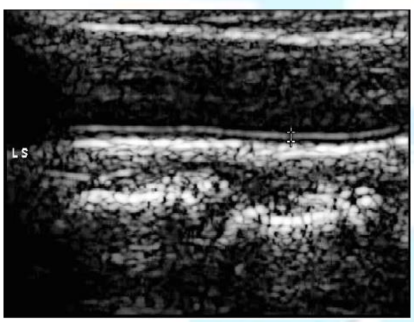

Fig.4. Enhanced Image

Intima-Media Detection

The detection of Intima – Media (IM) layers in the IVUS image is of prime importance in identifying the quantity of plaque deposition. Though the IMT measurement does not directly helps in visualizing the coronary arteries, it assists in indicating the presence of coronary atherosclerosis. The variation in its thickness helps in predicting the deposition level of plaques. In this work Morphological Operation is performed in determining the IM borders. Morphology is a broad set of image processing operations implemented to process the images based on shapes. The borders of the Intima- Media region are identified using the morphological operation. The output image identifying the IM region is shown in Fig.5.

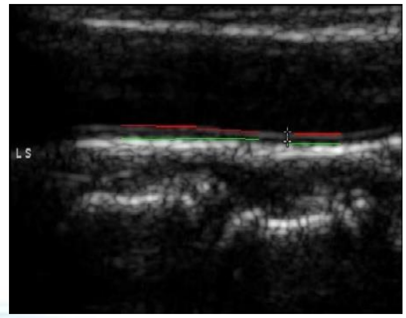

Fig.5. Intima – Media Detected Image

Segmentation

Image segmentation is the process of partitioning a digital image into multiple segments. The goal of segmentation is to simplify and/or change the representation of an image into something that is more meaningful and easier to analyze.

At first the Region of Interest (ROI) is extracted from the enhanced image. It is shown in Fig.6.

Fig.6. ROI Extraction

Once the thick region is detected, the plaque quantity is estimated using an Intima-Media Thickness (IMT) measurement algorithm. Segmentation techniques such as Multi-Level set based technique, Otsu's segmentation, Active Contour method and Watershed segmentation are implemented to identify the plaque deposition in the coronary artery.

Multi – Level Set Based Segmentation: The multi-level set algorithm descried below is implemented for extracting the plaque region [18]. To estimate the plaque, the ROI extracted image is taken as input image I with a mask region M_K. The Multi-level set algorithm is detailed below.

Step 1: Initialize the φ, outer region L_{out} and inner region L_{in}
Step 2: Update the position for all elements which are presented in the φ,
$for\ i = 1\ to\ incr_{step}$ // $incr_{step}$ – incremental speed steps
$for\ p = 1 : size(I)$ // each pixel I in L_{out}

If $M_k == 1$
Switch the $I(p)$ from L_{out} region to L_{in} region.

B-spline function based curvature Updation

$$I(p_1) = \begin{cases} 1 & if\ p_i < p < p_{i+1} \\ 0 & otherwise \end{cases}$$

$$I(p_i) = \frac{p-p_i}{p_{i+k-1}-p_i} I(p_{i-1}) + \frac{p_{i+k}-p}{p_{i+k}-p_{i+1}} I(p_{i-1})$$

Remove the L_{out} at $I(p)$

$for\ i = 1\ to\ incr_{step}$ // $incr_{step}$ – incremental speed steps
$for\ p = 1 : size(I)$ //each pixel I in L_{out}
If $(\varphi(p) < 0)$
Switch the $I(p)$ from L_{out} region to L_{in} region.

B-spline function based curvature Updation

$$I(p_1) = \begin{cases} 1 & if\ p_i < p < p_{i+1} \\ 0 & otherwise \end{cases}$$

$$I(p_i) = \frac{p-p_i}{p_{i+k-1}-p_i} I(p_{i-1}) + \frac{p_{i+k}-p}{p_{i+k}-p_{i+1}} I(p_{i-1})$$

Remove the L_{out} at $I(p)$

$for\ i = 1\ to\ incr_{step}$ // $incr_{step}$ – incremental speed steps
$for\ p = 1 : size(I)$ // each pixel I in L_{out}

If $(\varphi(p) > 0)$
Switch the $I(p)$ from L_{in} region to L_{out} region.

B-spline function based curvature Updation

$$I(p_1) = \begin{cases} 1 & if\ p_i < p < p_{i+1} \\ 0 & otherwise \end{cases}$$

$$I(p_i) = \frac{p-p_i}{p_{i+k-1}-p_i} I(p_{i-1}) + \frac{p_{i+k}-p}{p_{i+k}-p_{i+1}} I(p_{i-1})$$

Remove the L_{in} at $I(p)$

Step 3: Final segmented result, S = I(p)

In this work B-spline function is implemented for random curve updation. When performing the numerical analysis, B-spline function is less dependent on the degree, smoothness and domain partition. Also, any spline function of the given degree can be expressed as a linear combination of B-splines of that degree. Since the heart vessels are curve shaped, the accuracy of the segmentation is increased by a high margin. The Fig.7 shows the segmented output.

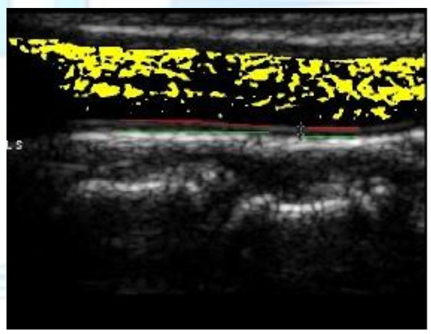

Fig.7. Segmented Image

Otsu's Segmentation: The Otsu's segmentation technique used in several image processing applications employs histogram based image thresholding technique to segment the ROI. The algorithm assumes that the image consists of bimodal histogram (foreground and background pixel) and evaluates the optimum threshold value by partitioning the image into two classes. This partitioning technique reduces the inter class variance of the image. The optimum threshold value evaluated will minimizes the inter class variance of the image. The variance equation after thresholding is determined using weighted sum of variances of two classes. It is given as

$$\sigma_w^2(t) = \omega_0\ (t).\sigma_0^2(t) + \omega_1(t).\sigma_1^2(t) \qquad (4)$$

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where $\omega_0(t)$ and $\omega_1(t)$ are the probabilities of two classes separated by threshold t.

$\sigma_0^{\,2}(t)$ and $\sigma_1^{\,2}(t)$ are the variances of two classes [16].

The Otsu's segmented output is shown in Fig.8.


Fig.8. Otsu's Segmented Output

Active Contour Segmentation: It is used for delineating the object boundaries from a noisy 2D input image. This technique is also called as snakes model, widely used in applications such as object tracking, shape recognition, segmentation, edge detection and stereo matching. Snakes model generally matches the deformable curve to the image boundaries by means of energy minimization. The energy formulation of the snake model is given as the sum of its internal energy and external energy. The equation is given as

$$E_*^{snake} = \int_0^1 E_{snake}\,(v(s))ds =$$

$$\int_0^1 E_{internal}\,(v(s)) + E_{external}\,(v(s))\,ds$$

$E_{internal}$ is the internal elastic energy which is used to control the deformation made to snake

$E_{external}$ is the external energy that controls the fitting of contour to the image. It is the combination of the forces due to the image E_{image} and the constrain force exerted on the image $E_{con.}$

The segmented plaque region using is shown Fig.9.

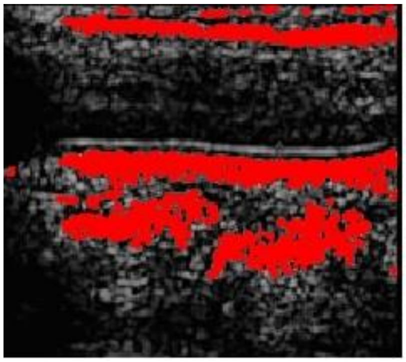
Fig. 9. Active Contour Segmented Region

Watershed Segmentation: Geologically a watershed is a dividing technique that separates the adjacent basins. In watershed segmentation algorithm the image is considered as a topographic map, with the brightness of each point representing its height and identifies the lines that run along the tops of ridges. The aim of the watershed technique in image processing is to segment two regions that are close to each other specifically when their edges touch each other. There are two approaches used in implementing the watershed transformation:

i. The watershed marker is chosen from the local minima of the gradient of the image. In some applications this method produces over segmentation of image.
ii. Marker positions are either explicitly defined by the user or determined automatically with morphological operators.

In this analysis the second approach of watershed technique is implemented to segment the IVUS image. The result is shown in Fig.10

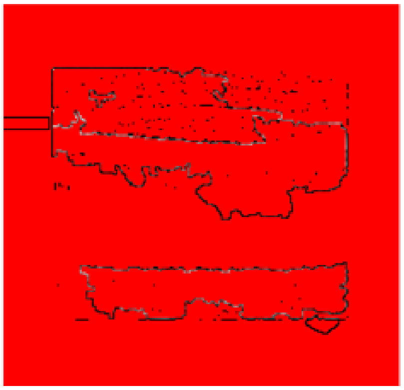
Fig. 10. Watershed segmented Region

RESULTS AND DISCUSSIONS

The segmentation methods considered in this study are implemented in MATLAB environment using an Intel Core i3 processor @ 3.40 GHz. The performance metrics used for the analysis are Jaccard index, DICE, Kappa, Rand Index (RI), Variation of Information (VOI) and Global Consistency Error (GCE).

Calculation of Overlap based Metrics

DICE coefficient is commonly used metric in validating the image volume segmentation. DICE is a measure of reproducibility as a statistical validation of manual annotation. The pairwise overlap of the repeated segmented region is calculated using DICE [16].

$$DICE = \frac{2\left|s_g^1 \cap s_t^t\right|}{\left|s_g^1\right| + \left|s_t^1\right|} \qquad (5)$$

Jaccard Index(JAC) between two sets is defined as the intersection between test segmented region to ground truth [16].

$$JAC = \frac{DICE}{2-DICE} \qquad (6)$$

Global Consistency Error (GCE) is an error measurement between two segmentations [16]. Let R (S, x) be defined as set of all voxels residing in the segmented region. Then the error between two segments S_1 and S_2 at the voxel x is given as

$$E(S_1, S_2, x) = \frac{\left|R(S_1,, x)/R\,(S_2, x)\right|}{\left|R(S_1,, x)\right|} \qquad (7)$$

Calculation of pair counting based metrics

1) Rand Index (RI) is the measure of similarity between clusters [16]. It is one of the important properties that is not based on the labels and thus can be used to evaluate the clusters as well as the classifications.

2) Information theoretic based metrics: Variation of Information (VOI) measures the amount of information lost or gained when changing from one variable to other. It is defined using Entropy and Mutual Information between two segments. The VOI is given as

$$VOI\ (S_g, S_t) = H(S_g) + H(S_t) - 2MI\ (S_g, S_t) \qquad (8)$$

Probabilistic Metrics: Cohen Kappa Coefficient (KAP) measures the agreement between two samples [16]. KAP is given as

$$KAP = \frac{P_a - P_c}{1 - P_c} \qquad (9)$$

The table 1.1 shows the comparison of performance metrics for the segmentation methods considered in this work.

Table 1.1 Comparison of Performance Metrics

Metrics	Multi -Level	Otsu's	Active Contour	Watershed
JAC	0.2474	0.1716	0.1208	0.3117
DICE	0.3966	0.2929	0.2156	0.2323
KAP	0.3608	0.1750	-0.0271	-0.0070
RI	0.8152	0.6767	0.7081	0.7400
GCE	0.0537	0.2270	0.1569	0.0680
VOI	0.6027	0.1478	0.1841	0.1740

The plot of the metrics is shown in the Fig.11.

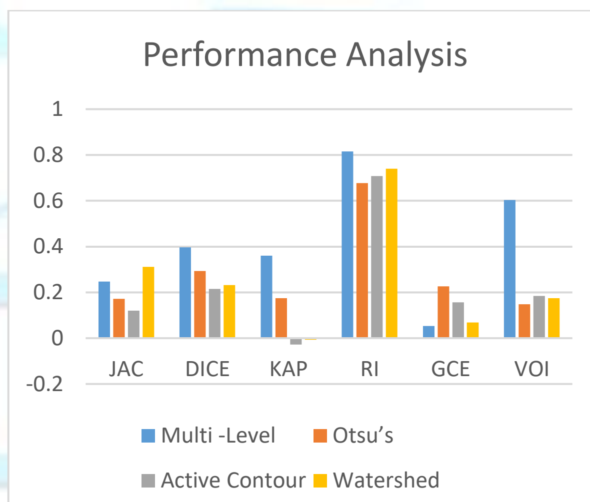

Fig.11. Performance Analysis

The performance analysis indicates that the Multi-Level Set Based segmentation algorithm outperforms the other existing methods by a huge margin thereby indicating its superiority over other methods like Otsu's, Active Contour and Watershed.

CONCLUSION

The paper focuses on detecting the plaque deposition in the coronary arteries for treating cardiovascular diseases. IVUS images of coronary artery for the detection of plaque deposition is considered for the analysis. At first, preprocessing is performed for denoising and enhancing the overall contrast of the image. Then morphological operation is performed to detect the thickness of intima-media region. Further, segmentation is performed for ROI extraction and detection of plaque region using Multi – Level set algorithm. Other existing segmentation technique included in the analysis are Otsu's, Active Contour and Watershed methods. Performance analysis is performed to identify the efficiency of the segmentation algorithms implemented in the work. Performance metrics such as Jaccard index (JAC), DICE, Kappa, Rand Index (RI), Variation of Information (VOI) and Global Consistency Error (GCE) is calculated. Based on the experimental results, it can be concluded that Multi – Level Set Based Segmentation technique outperforms the other existing methods in a huge margin.

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