Segmentation of Lung Tumor in Multimodality PET-CT Image using a New Modified Variational Level Set Method

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***Abstract*— Medical image segmentation is a vital process in medical diagnosis and evaluation of tumor response to therapy. Current segmentation methods works only on single modality image like Positron Emission Tomography (PET) has low resolution and gives only functional information; Computed Tomography (CT) has low contrast and provides structural information. This paper focus on segmentation of multimodality PET-CT image. In recent days PET-CT is advanced multimodal imaging equipment, which gives both functional and anatomical information in a single image. This multimodal image is very essential in detection of cancer, such as rectal cancer, lung cancer, head and neck cancer so on. The manual delineation of gross tumor volume (GTV) is done by radiologist on CT with the help PET image is inaccurate hence this paper presents a method to segment and identify the other information about size, shape and location of the tumor. Basic deformation models for image segmentation such as snakes, gradient vector flow, active contour and level sets have some limitations that is convergence rate is slow hence these methods are not more suitable for multimodal image segmentation. Modified Variational level set method is introduced in this paper to increase the convergence rate and computational efficiency. Both qualitative and quantitave results shows that efficiency of the algorithm compared to existing methods. This method is robust in delineation of tumor in therapy treatment.**

***IndexTerms*— CT, Deformation model, GTV, Level set, PET.**

I. Introduction

Now days the death rate of cancer patients is increasing. This rate can be decrease by early detection of cancer and proper treatment. After therapy it is important for physicians to know the tumor response so that they can decide to continue the current treatment or not. Usually evaluation of tumor response to particular therapy is done by visually or by measuring anatomical changes using CT images. In many malignancies PET images can also be used, which gives metabolic changes and it has some advantages over anatomical images. Evaluation of metabolic changes is also done by visually and semi quantitatively measuring the changes in tumor standard uptake value (SUV) in PET image according to the PET response criteria in Solid Tumors (PERCIST). SUV is calculated as:

$$SUV = \frac{Q}{\frac{Q_{inj}}{W}} \qquad (1)$$

Where Q is the radiotracer concentration, Q_{inj} is injected activity and W is body weight. Furthermore, early and accurate tumor response evaluation is difficult using clinical trials. CT images gives anatomical information, it provides high spatial resolution but poor in contrast. In CT of lung cancer patient lung tumor may be present adjacent to structure of chestwall or diaphragm which has same contrast or intensity as compare to lung tumor. Hence it is difficult to distinguish tumor from normal tissues using normal segmentation algorithm. Distinguish between lung tumor and normal tissues can be done in PET images, due to lack of spatial resolution segmentation of lung tumor is limited and not accurate. To overcome form the limitations of single modality images such as CT and PET images, PET/CT scanner provides an image which provides both anatomical and function information with high spatial resolution and good contrast.

In recent years many computer aided analysis methods of PET/CT images for the evaluation of tumor response to therapy are proposed by many researches. Volumetric information are provided by computerized approaches and segmentation of tumor is much needed to verify the effectiveness of different cancer therapies and to know the size (gross tumor volume), shape and delineation of tumor. So many methods are proposed for the segmentation of lung tumor on PET/CT images. Images provided by different modalities has different features hence development of robust segmentation algorithm is difficult for multimodality images. This paper proposes a new modified variational method for tumor segmentation in PET/CT image.

II. RELATED WORK

Inherently, PET-CT images are more advantageous compared to single modality images such as CT alone, PET alone and MRI. In figure.1 PET image shows the presence of lesions but location of lesion cannot be seen, in CT image lesions are not visible but in PET-CT image locations of lesions can be clearly seen. PET-CT image has both anatomical information and functional information hence localization of lesions is easy. Automatic detection of tumor volume in PET-CT image is a challenging task due to presence of image artifacts and patient movement during acquisition. Many researchers proposed several algorithms for single modality images[2], with some modifications same algorithms can be used for multimodality images. Yu et al[1] used a region based texture analysis method for detection of cancer in Head-Neck PET-CT images but the limitation was it does not preserves the spatial connectivity. To overcome this limitation, El Naqa et al [3] proposed active contours for the segmentation PET-CT images with some weighting factors. Bagci et al [4] proposed a graph-based random walk image segmentation to identify the appropriate weighting factors for a disease site. A graph based morkov model and adaptive growing algorithms are developed by Song et al [5,6] and Tan et al [7]. najman et al.[8] and Li and Xiao[9]have proposed Adaptive smoothing is an iteractive filtering preprocessing technique that creates a gradient image that smoothes homogeneous region yet preserves and enhances boundaries. By using this adaptive gradient image , rather than a standard gradient image the smoothing effect reduces the number of minima and therefore the over-segmenation. However, over-segmentation remains for the images with weak edges, especially for MR images. Although statistical and fuzzy technique are designed to reduce over-segmentation produced by watershed [10,11] but problem remains for some specific applications. Xin and Y an [12] have proposed the combination of Mumford-shah model and watershed algorithm to solve the computational complexity of [13]. This method uses a Tap Hat transform for identifying noise in images. This method can be well adapted to the topological structure and achieves good result. However, the narrow capture range of the initial contour snake has limited applications. Gauch [14] has proposed the morphological multiscale gradient watershed hierarchies. This method uses scale spaces for the images to be segmentation and then watershed algorithm Is applied . it is suitable for colour segmentation also. However, due to background noise spurious edges produced which cause over-segregation and degrade the output of the watershed transform.

III. MATERIALS AND METHODS

Variational Level Set Method: The main advantage of this method is that it is a region based model, to control the evaluation it uses the statistical features present inside or outside the contour, soothe growth of contour will not distruct due to the local noise or edge and re-initialization is not required. Variational level sets can detect exterior and interior boundaries simultaneously, because the level sets are very less sensitive to the location initial contour. Chan-vese model (15 is one of the most region based model utilizing a variational level set formulation and Mumford-Shah segmentation technique has been used in this model [16]. The initial contour may be starts from anywhere in the image, this model can detect all contours automatically. Piecewise-constant is a set of constants which approximates the statistical information of an image with in a subset. Moment of deformable contours of piecewise-constant active contour model is towards minimizing energy function instead of searching edges. The difference of the actual image intensity at each pixel and piecewise-constant is measured by the energy function. The level set evaluation equation given by chan-vese [15] model is formulated by minimizing the following energy equation

$$E_{Chan-Vese} = \lambda_1 \int_{inside(c)} \left| I(x) - C_1 \right|^2 dx + \lambda_2 \int_{outside} \left| I(x) - C_2 \right|^2 dx, x \in \Omega \quad (2)$$

Average intensities of inside and outside contours are denoted by two constants C_1 and C_2 respectively. With the level set method, assume

$$\begin{cases} C = \{x \in \Omega : \phi(x) = 0\} \\ inside(C) = \{x \in \Omega : \phi(x) > 0\} \\ outside(C) = \{x \in \Omega : \phi(x) < 0\} \end{cases} \quad (3)$$

by minimizing equation (2) solve C_1 and C_2 , then

$$C_1(\phi) = \frac{\int_\Omega I(x).H(\phi)dx}{\int_\Omega H(\phi)dx} \quad (4)$$

$$C_2(\phi) = \frac{\int_\Omega I(x).(1-H(\phi))dx}{\int_\Omega (1-H(\phi))dx} \quad (5)$$

By incorporating the length and area energy terms into equation (2) and minimizing them ,the corresponding variational level set formulation as follows:

$$\frac{\partial \phi}{\partial t} = \delta(\phi)\left[\mu \nabla \left(\frac{\nabla(\phi)}{|\nabla(\phi)|} \right) - v - \lambda_1 (I - C_1)^2 + \lambda_2 (I - C_2)^2 \right] \quad (6)$$

Where μ≥0, v≥0, λ_1 >0, λ_2>0 are fixed parameters, the smoothness of zero level set is controlled by μ, v increases the propagation speed, λ_1 and λ_2 control the image data driven force inside and outside and outside the contour respectively. ∇ is the gradient operator. H(ϕ) is the Heaviside function and δ (ϕ) is the Dirac function. The regularized values are selected as follows

$$H(Z)=\frac{1}{2}\left(1+\frac{2}{\pi}arc\tan\left(\frac{Z}{\varepsilon}\right)\right) \qquad (7)$$

$$\delta(Z)=\left\{\frac{1}{\pi}.\frac{\varepsilon}{\varepsilon^2+z^2},Z\in R\right. \qquad (8)$$

This method does not use the gradient of the image instead it uses the region based information of the image. This method is robust to detect the objects in presence of noise and weak edges. But minimizers are not unique hence this method is not suitable for segmenting tumor in PET/CT images. uses region based information provided by the image rather than gradient of the image . it is most robust in the presence of noise and weak edges and it can detect objects both with and without gradient, discontinuous boundaries or with holes. However, due to lack of uniqueness among minimizes, this method not suitable for uniform throughout the image.

To overcome this drawback an alternative energy functional is proposed in [17]. Internal and external energy term is considered in this variational energy function method. This function uses the gradient of the image that minimizes the overall energy function. When the iteration rate is high this method achieves high convergence rate but this increases the computational complexity. The internal energy is give as,

$$p(\phi)=\int_\Omega\frac{1}{2}(|\nabla(\phi)|-1)^2dxdy \qquad (9)$$

The energy minimization functional of the variational level set is given as

$$E_{VLS}(\phi)=\mu p_{\text{int}ernal}(\phi)+w_{external}(\phi) \qquad (10)$$

Where $w_{externel}$ (ϕ) is the external energy given as

$$w_{external}(\phi)=\lambda L_g(\phi)+vA_g(\phi) \qquad (11)$$

Where $L_g(\phi)$ and $A_g(\phi)$ are the length and area terms respectively.

$$L_g(\phi)=\int_\Omega g\delta(\phi)|\nabla(\phi)|dxdy \qquad (12)$$

$$A_g(\phi)=\int_\Omega gH(-\phi)dxdy \qquad (13)$$

Where, δ(ϕ) and H(ϕ) are the univariate Dirac and Heaviside functions respectively. By calculus of variations, the Gateaux derivative [68] or first variation of the energy functional of the variational level set is given as,

$$\frac{\partial E}{\partial t}=-\mu\left[\Delta\phi-div\left(\frac{\nabla(\phi)}{|\nabla(\phi)|}\right)\right]-\lambda\delta(\phi)div\left(g\frac{\nabla(\phi)}{|\nabla(\phi)|}\right)-vg\delta(\phi) \quad (14)$$

Where, λ and v are constans, g is the edge indicator function. This gradient is the evolution equation for the variational level set.

Disadvantages of variational Level set method

- The gradient flow entails the tunning several parameters to achieve the convergence, resulting computational complixity.
- Leaking or bleeding of the boundaries, especially in multispectral brain images
- It is unable to step the contours at weak edges and images with intensity in homogeneity.

Before moving into the proposed variational level set method, several general conclusions can be drawn based on the earlier discussion of various deformable models.

The traditional snakes provide an accurate location of the edges only if the initial contour is given sufficiently near the edges. further, they are prone to local minimum, failing to detect the exterior and interior boundaries and also the capture range depends on the initial position of the contour.

Gradient vector flow methods are insensitivity to initialization and ability to move into concave boundary regions. The technique uses spatial diffusion of the gradient of an edge map of the image. The disadvantages of this method are that, the strong edges as well as weak edges create a similar flow due to the diffusion of the flow information and generation of GVP is iterative and computationally intensive. Geometric active contour models further enhanced the idea of snakes by developing a curve evolution flow which can better accommodate the object geometry and the changing topology as the curve evolves. These methods have the disadvantage that they are sensitive to noise and performance is poor for images with weak edged and they cannot converge to concave regions.

These methods utilize statistical information inside and outside the contour to control the evolution. They are less sensitive to noise and have better performance for images with concave boundaries. Further re-initialization problems completely eliminated. However, tuning of several parameters in the evolution equation results the high computational complexity and also poor proximity of the contour towards the object boundary

There are a variety of different properties of the problem that can be exploited For example, in case of variation l level sets based on mumford-shah models proposed by chan-vesa [15] boundaries are automatically detected no matter where the initial contour starts and can efficiently detect interior and exterior boundaries simultaneously . however, this method relies on the homogeneity of the localized spatial features instead of the image gradient.

Similarly, in case of [17], the internal energy and external energy functions are incorporated in the evolution equation in such way that the penalizing effect of the internal energy term overcome the re-initialization problem and the external energy is introduced as a function that depends on images data. This external energy consists of length and area functions; in the external energy consists of length and area functions; the area function in the external energy is responsible to speed up the curve evolution. But the convergence of the contour towards the object boundary is poor when the tissues are overlapped.

To overcome this limitation of existing variational level sets, a modified variational level set is proposed. This method incorporates many of the ideas presented in the previous works, but further modifies the algorithm in order to improve the proximity of the contour towards the object boundary.

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IV. PROPOSED METHOD

This section proposes a modified variational level set method. This general frame work can be applied on the noisy image with blurred and weak edges with intensity in homogeneity.

The gradient information of the image is used as stopping criteria for curve evolution in the existing level set techniques and provides the force to the zero level set from a target boundary.

Be that as it may, if there should arise an occurrence of picture with power in homogeneity, the gradient based term can never completely stop the set development notwithstanding for perfect edges, making spillage regularly unavoidable. In this technique a novel edge work for level set development by presenting another speed term, is proposed. This speed term improves the compelling separation of the pulling in drive and furthermore gives powerful edge estimation. Further, the spillage issue is kept away from adequately as a rule and furthermore catch go is enhanced contrasted with customary level set techniques.

Speed function:

In segmentation, the moving contours and object boundaries are lines. The interaction between contours and object boundaries in the proposed model is defined based on the interaction between line defects or dislocation in solids [68, 95] the energy associated with these lines in the image plane can be defined in the 2-D space. In the level set method a curve is evolved to get the object boundaries and these two dimensional curves in a plane are represented by the zero level set function ϕ. Evolution of the contour is determined by the evolution of the level set function. This evolution speed depends on the interface between the moving contour and object boundary. Hence, selection of proper speed term leads to achieve good convergence towards the object boundary. Where to incorporate the speed term in the evolution equation of the level set, let ϕ be the level set function and q be the speed term for interaction between moving contour and object boundary during the contour evolution. Then the evolution is given as

$$\frac{\partial \phi}{\partial t} = q(x, y)\left|\nabla(\phi)\right| \quad (15)$$

Where, q(x, y) symbolize a speed of the contour extended to the whole image plane. To define the speed term q, both the moving curve and objects are placed in the image plane.

Based on [18], the energy related with the moving curve and the object boundaries is defined as follows:Let γ(s) be the parametric curve in the 2-D space, then the energy associated with γ (s) is given by

$$E(\gamma) = \min \int \frac{1}{2}(s_1^2 + s_2^2)dxdy \qquad (16)$$

$$\nabla .s = \delta(\gamma)\tau \qquad (17)$$

Where $(s_1^2 + s_2^2$), is function of 2-D space and τ is the unit tangent vector of $\gamma(s)$, $\delta(\gamma)$ is the delta function of the curve γ (s). The function s can be solved by using [18] analytically, which is given as;

$$s(x, y) = -\int_{C(s)} \frac{l.n}{r^3} dxdy \quad (18)$$

Where l is the vector between point (x, y) of p and a point $(x(s), y\ (s))$ on $C(s)$, $r = |l|$ denotes the Euclidian distance between these two points and n represents the normal direction. Then the value of the l is the distance between the two points.

$$l = \sqrt{(x - x(s))^2 + (y - y(s))^2} \qquad (19)$$

Dirac delta function is used in image segmentation for the regularization of images and is given by

$$\delta_\zeta(s)=\begin{cases}0, & |s|>\zeta \\ \frac{1}{2\zeta}\left(1+\cos\left(\frac{\pi s}{\zeta}\right)\right) & |s|\le\zeta\end{cases} \qquad (20)$$

The regularization of the moving curves, Heaviside functions are used and is given by

$$H(\phi)=\begin{cases}0, & |\phi|\le-\rho \\ \frac{1}{2}\left(1+\frac{1}{\pi}\sin\left(\frac{\pi\phi}{2\rho}\right)+1\right) & -\rho<|\phi|\le\varepsilon \\ 1 & |\phi|\ge\rho\end{cases} \qquad (21)$$

Interaction energy is calculated using two curves. The interaction energy is strongly attractive when they are in opposite direction that means is minimum among all possible relative directions and is repulsive when they are in same direction that means energy is maximum among all possible relative directions. Now the incorporation of speed function for image segmentation problem defined above is as follows.

Let an image be (x, y) located in the Z=0 plane. The speed is set to depend on the intensity values in the images by replacing the normal direction n in (18) by image gradient ∇I. however; the image based speed function is singular on the contour C(s). the singularities can then be smeared out by replacing n with the gradient of the smoothed image $\nabla(G_\sigma * I)$, where G_σ is Gaussian smoothing filter with standard deviation σ. By replacing s(x, y) as p(x, y) in (18) then the image based speed term q is given as

$$q(x,y)=q=-\int_{C(s)}\frac{l.n}{r^3}dxdy \qquad (22)$$

$$q=-\int_{\Omega}\frac{l.\nabla(G_\sigma * I)}{r^3}dxdy \qquad (23)$$

Where Ω denotes the image domain and (x, y) ∈ Ω. Another important property is that, the sign of the speed depends on the object boundary and the direction of the contour, so that the contour is not necessarily to be placed entirely inside or near the object boundary. In equation (23) the photo noise also impacts the moving curve, resulting in spurious contours. The velocity generated with the aid of the noise is exceptionally small in comparison with that through the object boundary. This noise can be eliminated via adding the interplay within the moving contour. The speed term q is now defined as

$$q=-\int_{\Omega}\frac{l.\nabla(G_\sigma * I+wH(\phi))}{r^3}dxdy \qquad (24)$$

where, w is the adjustable weight , H(ϕ) is the Heaviside function defined in (24) and p is constant. Now the value of the speed term is calculated using FFT transform for the fast evolution of the contour and incorporated in the energy minimization equation of the Variational level set.

$$\frac{\partial E_{Mvls}}{\partial t}=-\mu\left[\Delta\phi-div\left(\frac{\nabla(\phi)}{|\nabla(\phi)|}\right)\right]-\lambda\delta(\phi)div\left(g\frac{\nabla(\phi)}{|\nabla(\phi)|}\right)-q.g\delta(\phi) \qquad (25)$$

This Gautex derivative [40] or the first variation of the energy function results a new energy minimization function for the proposed deformable model.

Proposed algorithm:

The basic procedure and steps involved in the proposed algorithm are summarized as follows.

1. Preprocess the image using noise filters.
2. Calculate the value of the edge indicator function g as $g_I(x,y)=\frac{1}{1+|\nabla G_\sigma * I|^2}$ (26)
3. Compute $G_\sigma(x, y)$*I (x, y) to smooth the image by Gaussian and scale the parameter in Gaussian kernel by specifying the value of σ .
4. Set the coefficient of Dirac delta function $\delta_\varepsilon(s)$ using equation (20), which is used in regularization of images.
5. Set the coefficient of Heaviside function H(ϕ) using the equation (21), for regularization of the moving curve.
6. Select the time step τ_1 suitably for the stable interaction. The selection of the time step is in such way that, the time step τ_1 and the coefficient μ must satisfy the condition τ_1 μ<$\frac{1}{4}$, normally τ_1 ≤10.0.
7. Calculate the coefficient of the internal energy penalizing term, coefficient of the weighted length term & coefficient of the weighted area term. Set these parameter parameters accordingly.
8. Initialize the level set function ϕ (x, y) by using the following condition

$$\phi_0(x,y)=\begin{cases}-c_0 & (x,y)\in u_0-\partial u_0 \\ 0 & (x,y)\in\partial u_0 \\ c_0 & u-u_0\end{cases} \qquad (27)$$

Where, ϕ_0 is the initial level set function, u_0 be a subset in the image domain u and ∂u_0 points on the boundaries of u_0 here $-c_0$ corresponds to outside the boundary 0 for on The boundary and c_0 for inside the boundary.

9. Regularize the level set function by computing the curvature function k for the smooth evolution of the contour.
10. Compute the spatial derivative by applying the central difference and update the level set function until the contour converges to the desired object boundary.

The justification for various steps of the proposed algorithm is as follows

Read the input image and remove the noise using noise filters as mentioned in steps 1 & 2. Compute the value of edge indicator function which highlights in features in the image so that minimization procedure guided by external forces will push or pull the contour towards the edge feature in the image. This is done in steps 3 & 4. Regularization of the image and Heaviside edges in the image and noise and noise in the contour are reduced. This is carried out in steps 5. Choosing the proper value of time step is very important for the stable evolving of the contour. This is performed in step 6. Area and length coefficients of the contour are adjusted in step 7. Initial level set function is initialized based on the region of interest by applying proper boundary conditions as given in step 8. The curvature value for the smooth evolution of the contour is calculated using step 9. Spatial partial derivatives are approximated by using the central difference scheme as mentioned and finally the level set function is updated to evolve the contour to converge the desired object boundary in step 10.

Advantages of the proposed method

In contrast to the deformable models and other medical image segmentation techniques, the proposed method has the following advantages.

- This method can extract interior boundaries of the object by setting the initial contour anywhere.
- This model can handle images with weak edges and image with intensity in homogeneity.
- The gradient indicator function embedded with speed term can stop the level set evolution even for ideal edges, without leakage of the contour & it is robust to noise.
- It can selectively extract the desired object boundary by setting the initial contour surrounding the boundaries.

The evolution direction can be controlled so that segmentation efficiency can be improved.

V. EXPERIMENTAL RESULTS

This section presents a set of experiments to validate performance of the proposed frame work. The real image data set contains the PET/CT images, imaged on a PET/CT which gives both functional and anatomical information. The test dataset consists of tumors of different shapes, locations, sizes, intensity and enhancement as shown in figure.1. The database consists of several anonymous patient's lung tumor as well as the standard segmentation (an experienced radiologist manually segmented the tumors) results called ground truth of tumors from these scans. The evolution of the segmentation results are performed through a quantitative comparison with the results of a ground truth. In this experiment, four performance measures are used to evaluate the results.

$$\textit{Dice}\ \text{Similarity Coefficent}=\frac{2(A\cap B)}{A+B} \quad (28)$$

Where, A and B are sets of segmented pixels from algorithm method and ground truth respectively. For the similarity index, above 0.7 is considered as good segmentation results. Further, the segmentation results are evaluated by using another three performance measures namely.

$$Sensitivity=\frac{TP}{TP+FN} \quad (29)$$

$$Specificity=\frac{TN}{FP+FN} \quad (30)$$

$$Accuracy=\frac{TP+TN}{(TP+TN+FP+FN)} \quad (31)$$

Where ,TP,TN,FP,FN, stand for the number of pixels being labeled as true positive, true negative, false positive and false negative respectively.

The proposed algorithm is implemented in MATLAB 8.3 on a 2GHz Intel Pentium Iv PC. The performance of the proposed algorithm is compared with the existing deformable model a such as snake, GAC, GVF, LEVEL SET, Variational level set. Segmentation results of deformable models and proposed method is shown in figure.1 and Table.1

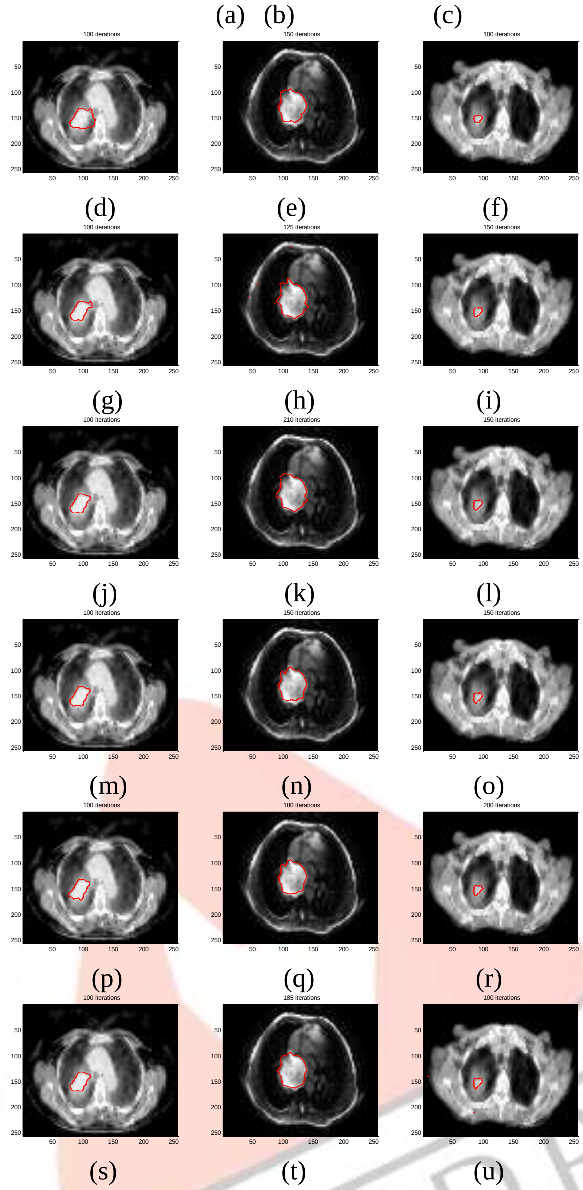

Figure.1. Final segmentation results:(a)-(c) original images, (d)-(f) Snake model, (g)-(i) GAC model, (j)-(l) GVF model, (m)-(o) Level set method, (p)-(r) Variational Level set method, (s)-(u) Proposed method

Table.1 Performance measures of deformable models with proposed method

Performance Measure	**Snakes**	**GAC**	**GVF**	**Level sets**	**Variational Level sets**	**Proposed Method**
Computation Time in secs	**1.73**	**1.54**	**1.78**	**16.34**	**13.23**	**10.09**
Segmentation Accuracy(%)	**64.92**	**67.07**	**71.1**	**77.03**	**78.15**	**88.08**
Similarity index	**0.603**	**0.685**	**0.719**	**0.737**	**0.818**	**0.895**
Sensitivity (%)	**67.01**	**73.61**	**76.1**	**79.1**	**82.3**	**87.62**
Specifivity (%)	**67.8**	**75.7**	**76.6**	**81.8**	**84.2**	**86.6**

VI. CONCLUSIONS

PET/CT scanner provides an image which gives both functional and anatomical information and this lead to better delineation of lung tumor. This paper proposes a new modified variational level set algorithm for the segmentation lung tumor in PET/CT image. The analysis started with traditional snake, GVF, GAC, level set, variational level set, they all implemented and performance measures. All deformable models are implemented and tested on PET/CT images and comparisons with the various deformable models are demonstrated. The proposed method is efficient in converge of the contour towards the object boundary and also robust in the presence of various types of noises. For lung tumors which locate near other tissues with similar intensities in PET and CT images, such as when they extend into the chest wall or the mediastinum, this method was able to achieve more effective tumor segmentation. In future work, we will further test the reliability of this method with more clinical data.

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