

Recent trends in the medical image processing

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Abstract— Segmentation is the process of dividing the image into smaller parts to extract some information from it. It is widely used in medical industry to get abnormal growth data from the medical image like MRI and CT. In this paper, we present a fast and robust practical tool for segmentation of solid tumors with minimal user interaction to assist clinicians and researchers in radio surgery planning and assessment of the response to the therapy. Particularly, a cellular automata (CA) based seeded tumor segmentation method on contrast enhanced T1 weighted magnetic resonance (MR) images, which standardizes the volume of interest (VOI) and seed selection, is proposed. Sufficient information to initialize the algorithm is gathered from the user simply by a line drawn on the maximum diameter of the tumor, in line with the clinical practice. First the seed pixels of tumor and background are fed to the algorithm. Using these seeds, the algorithm finds the strength maps for both tumor and background image. These maps are then combined to get the tumor probability map. Then the image is subjected to smoothing. Validation studies on both clinical and synthetic brain tumor datasets demonstrate 80%–90% overlap performance of the proposed algorithm with an emphasis on less sensitivity to seed initialization, robustness with respect to different and heterogeneous tumor types, and its efficiency in terms of computation time.

Keywords—tumor, CT, MRI, cellular automata, segmentation

I. INTRODUCTION

SEGMENTATION of brain tissues in gray matter, white matter, and tumor on medical images is not only of high interest in serial treatment monitoring of “disease burden” in oncologic imaging, but also gaining popularity with the advance of image guided surgical approaches. Outlining the brain tumor contour is a major step in planning spatially localized radiotherapy (e.g., Cyberknife, iMRT) which is usually done manually on contrast enhanced T1-weighted magnetic resonance images (MRI) in current clinical practice. On T1 MR images acquired after administration of a contrast agent (gadolinium), blood vessels and parts of the tumor, where the contrast can pass the blood–brain barrier are observed as hyperintense areas. There are various attempts for brain tumor segmentation in the literature which use a single modality, combine multi modalities and use priors obtained from population atlases.

Modalities which give relevant information on tumor and edema/infiltration such as Perfusion Imaging, Diffusion Imaging, or Spectroscopic Imaging provide lower resolution images compared to T1 or T2 weighted sequences, and the former are generally not preferable for geometric measurements. One of the main reasons to use multimodality images such as T2 weighted MRI is to segment edema/infiltration region which is generally not observable in T1 images. Although

the glial tumors infiltrate beyond the enhanced margin and edema/infiltration region might be of interest to fractionated radiotherapy in general, it is not possible to distinguish edema and infiltration, so usually this region is not included in primary target planning of radiosurgery, particularly in Cyberknife.

On the other hand, population atlases provide an important prior to improve segmentation by measuring the deviation from the normal brain. Deformable registration of brain images with tumor to the population atlas is an extremely challenging problem and still an active research area due to intensity variations around the tumor mainly caused by edema/infiltration, and the tumor mass effect, which also deforms the healthy tissue morphology. In some studies, affine registration has been used for this purpose, however misalignment issues arise, especially where there is a large deformation of the brain structures. Comparison to the works in the literature that use different approaches and other image types is difficult as that would require the use of the same datasets by different groups with evaluation performed by similar measures. For this reason, only the results of some studies are given, instead of a detailed comparison. Although, using manual expert segmentations as the ground truth, different performance measures such as Dice Overlap, Jaccard Index, false positive and negative volume fractions (FPVF, FNVF) were used in the literature,

(Dice) Overlap is used as a common measure for a comparison to previous methods here. With their automatic, multimodal, atlas based method, Prastawa *et al.* have reported 86.7% average overlap on a small dataset of only three patients with an average 1.5 h processing time. In more recent studies, Menze *et al.* reported 60% average overlap on 25 glioma patients and Gooya *et al.* reported 74.5% average overlap on 15 glioma patients with about 6–14 h of processing time. In contrast, Liu *et al.* reported 95.6% average overlap on only a subset of well-performing five patients over a 10 patient dataset using fuzzy clustering on only FLAIR images. It should be noted that the latter method needs intensive user interaction and correction as 8.4 min per patient on the average.

The popular trend in the area, as in the aforementioned approaches, is to be able to combine information from different sources to obtain a better segmentation. However, attempts to develop better algorithms from the image processing perspective that work on a particular MRI protocol continue in parallel not only to obtain proper information from each channel to be combined, but also due to the practical need to routinely quantify tumors in a clinical environment. Therefore, in this study, we focused on an efficient and robust segmentation of brain tumors on contrast enhanced T1 weighted MR images with minimal user interaction.

Region-based active contour models are widely used in image segmentation. In general, these region-based models have several advantages over gradient-based techniques for segmentation, including greater robustness to noise. However, classical active contours had the problem of being “only as good as their initialization,” even when using level-set surfaces in 3D. Because the tumor class does not have a strong spatial prior, many small structures, mainly blood vessels, are classified as tumor as they also enhance with contrast. Ho *et al.* used fuzzy classification of pre- and post-contrast T1 images to obtain a tumor probability map to evolve a level-set surface. Liu *et al.* have adapted the fuzzy connectedness framework for tumor segmentation by constructing a rectangular volume of interest selected through identifying the first and last slice of the tumor and specifying a set of voxels in the tumor region.

Interactive algorithms have become popular for image segmentation problem in recent years. Graph based seeded segmentation framework has been generalized such that graph-cuts (GC), random walker (RW), shortest paths, and power watersheds have been interpreted as special cases of a general seeded segmentation algorithm, which solves a minimization problem involving a graph's edge weights constrained by adjacent vertex variables or

probabilities. In , the connection between GC, RW, and shortest paths was shown to depend on different norms: (GC); (RW); (shortest paths), in the energy that is optimized. Geodesic distances between foreground and background seeds were also incorporated into other shortest path-based segmentation algorithms by .

Although it was reported that the shortest paths and RW produce relatively more seed-dependent results, it can be argued that the global minimum of an image segmentation energy is worth as good as the ability of its energy to capture underlying statistics of images, and a local minimum may produce a solution closer to the ground truth than that of a global minimum. Hence, with good prior information provided as in the case of a seeded image segmentation problem, efficiently finding good local minima becomes meaningful and worthwhile.

On the other hand, cellular automata (CA) algorithm motivated biologically from bacteria growth and competition, is based on a discrete dynamic system defined on a lattice, and iteratively propagates the system states via local transition rules. It was first used by Vezhnevets *et al.* (Grow-cut) for image segmentation, which showed the potential of the CA algorithm on generic medical image problems. However, Grow-cut was not designed for specific structures, such as tumors, which display heterogeneous content such as necrotic and enhancing tissue. Moreover, anatomic structures typically have relatively smooth boundaries, however, Grow-cut tends to produce irregular and jagged surface results, and only an *ad hoc* way of smoothing was introduced.

In this paper, we re-examine the CA algorithm to establish the connection of the CA-based segmentation to the graph-theoretic methods to show that the iterative CA framework solves the shortest path problem with a proper choice of the transition rule. Next, as our application is in the clinical radiosurgery planning, where manual segmentation of tumors are carried out on contrast enhanced T1-MR images by a radio-oncology expert, we modify the CA segmentation towards the nature of the tumor properties undergoing radiation therapy by adapting relevant transition rules. Finally, a smoothness constraint using level set active surfaces is imposed over a probability map constructed from resulting CA states. Following a brief background on seeded segmentation methods in Section II, we present our framework for brain tumor segmentation in Section III, and demonstrate its performance via validation studies on both synthetic, and radiation therapy planning expert-segmented data sets in Section IV, followed by conclusions in Section V.

II. BACKGROUND

A Seeded image segmentation

Given an undirected graph $G = (V, E)$ with vertices $v_i \in V$ and edges $e_{ij} \in E$. In image segmentation problems, vertices v_i are corresponding to image pixels, while edge weights are similarity measures between neighboring pixels based on image features (e.g., intensities). Each vertex has an attribute, which is an indicator of the probability of a label (e.g., a foreground and a background label). With the foreground F and background B seeds supplied by the user, the labeling problem is solved by

$$x^{opt} = \arg \min_x \left[\sum_{e_{ij} \in E} (w_{ij} |x_i - x_j|)^q \right] \quad \text{s.t. } x(F) = 1, \quad x(B) = 0 \quad (1)$$

In the final solution, the vertices which have the value $x_i \geq 0.5$ are labeled as foreground and $x_i < 0.5$ are labeled as background. The (1) represents the general optimization problem of labeling in graph-theoretic image segmentation. We will show that this optimization problem can be solved by a CA-based algorithm.

continuous state set on a finite machine are given

There are various attempts of using CA in image processing problems including: image enhancement (sharpening and smoothing), image filtering, edge detection, and image segmentation (Grow-cut)

Grow-cut method uses a continuous state cellular automata to interactively label images using user supplied seeds. The cells are corresponding to image pixels, and the feature vector is RGB or gray scale intensities. The state set $S(C)$ for each image pixel consists of a "strength" value θ in a continuous interval

$[0, 1]$, a label and an image feature vector C . The automata is initialized by assigning corresponding labels at seeds with a strength value between 0 and 1 where a higher value reflects a higher confidence in choosing the seed. Strengths for unlabeled cells are set to 0. A pseudo code for the Grow-cut algorithm is given below:

```

// For each cell ...
for  $\forall p \in P$ 
    // Copy previous state
     $I_p^{t+1} = I_p^t$ 
     $\theta_p^{t+1} = \theta_p^t$ 
    // Neighbors try to attack current cell for
     $\forall q \in N(p)$ 
        if  $\| \vec{C}_p - \vec{C}_q \|_2 \cdot \theta_q^t > \theta_p^t$ 
             $I_p^{t+1} = I_q^t$ 
             $\theta_p^{t+1} = g(\| \vec{C}_p - \vec{C}_q \|_2) \cdot \theta_q^t$ 
    
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where the argument is for instance, the absolute difference between the intensities of two neighboring pixels.

The surprising success of this simple algorithm, especially on medical images, motivated us to further analyze the algorithm. We showed that the result of the iterations of this algorithm converges to that of the shortest paths algorithm by modifying the similarity function used:

B cellular automata in image segmentation

A cellular automata is basically a computer algorithm that is discrete in space and time and operates on a lattice of cells

Since it was first proposed by Von Neumann and Ulam, Cellular Automata has attracted researchers from various fields in both physical and social sciences because of its simplicity, and potential in modeling complex systems.

Each individual cell is in a specific state and changes synchronously depending on the states of some neighbors as determined by a local update rule. They are parallel, local and homogeneous, since the state of any cell depends only on the states of the local neighbors at the previous time step and the update rules are same for every cell.

Formally, a cellular automaton (CA) is a triple $A = (S, N, \delta)$, where S is a nonempty set, called the state set, is the neighborhood, and $\delta: S_N \rightarrow S$ is the local transition function (rule) which is the argument of δ , indicates the states of the neighborhood cells at a given time, while S which is its value, is the state of the central cell at the next time step.

Although the usual definition for "Cellular Automata" is in favour of a finite state set (discrete and bounded), continuous state sets in which the states are real numbers are also used in CA literature under the name "Continuous CA" or "Coupled Map Lattices". A detailed discussion and some of the issues that can arise while using a

shortest paths of each pixel from the foreground seeds and the background seeds. For each pixel, the smaller distance to the foreground seeds produced the resulting segmentation.

III. METHOD

In this section, the complete segmentation framework to segment brain tumors and the necrotic regions enclosed is presented in detail. An overview of the algorithm with the pseudo-code of the implementation is given in Section III-A. Major steps of the algorithm is explained in detail in Sections III-B, III-C, III-D, and III-E followed by the datasets and methods used for performance evaluation in Section III-F.

A. Tumor-Cut Algorithm

Steps of the proposed cellular automata based tumor segmentation algorithm is shown in Fig. 1. First, (a) the user draws a line over the largest visible diameter of the tumor; (b) using this line, a VOI is selected with foreground (red)-background (blue) seeds; (c)-(d) tumor CA algorithm is run on the VOI for each two sets of seeds (for the foreground and background) to obtain strength maps for foreground (c) and background (d) at each voxel; (e) two strength maps are combined to obtain the tumor probability map P_T (6); (f) a level set surface is initialized at $I_T=0.5$ and the map P_T is used to evolve the surface which converges to the final segmentation map (g). Finally, (i) the necrotic regions of the tumor is segmented using CA based method with the chosen enhanced and necrotic seeds in (h).

In "Response Evaluation Criteria In Solid Tumors" (RE-CIST), which is a widely used procedure to evaluate the treatment response of the solid tumors, tumor progress is classified by measuring the longest in plane tumor diameter in one dimension (axial, coronal, sagittal). Our seed selection algorithm employs the same idea to follow the familiar clinical routine to which the clinicians are used to: the volume of interest (VOI), the tumor seeds and the background seeds are determined by using the line already drawn by the user to measure the longest diameter of the solid tumor. Similarly, focusing on tumor segmentation problem, the seed selection procedure starts with a single line drawn by the user along the longest visible diameter of the tumor. Afterwards, the VOI and the seeds are computed as follows: 1) The line is cropped by 15% from each end and thickened to three pixels wide to obtain tumor seeds; 2) VOI is

We note that, the original similarity function used in Grow-cut is a first order approximation to the one we utilized. In connecting shortest paths to cellular automata framework, maximizing the product of the edge weight w_{ij} was shown to be equivalent to minimizing the sum of the $-w_{ij}$'s, i.e., $\sum_{ij} -w_{ij}$, resulting in the shortest path between a seed node to any nonseed node in the graph over the negative logarithm edge weights. These weights can be interpreted similarly to the reciprocal weight w_{ij} defined in Sinop and Grady, which was shown to infer a connection between the shortest path algorithm and the general seeded segmentation optimization with L_{min} minimization.

Simultaneously and independently from our work, it has also been shown that the Grow-cut algorithm is equivalent to the Belman-Ford algorithm, which calculates the shortest paths on a weighted graph. However, there, the motivation and emphasis was on fast hardware implementation of the CA algorithms, due both increasing availability of low-cost graphical hardware (GPUs), and CA algorithm's suitability to run on parallel processors.

Shortest path idea was utilized in other works such as [10], where the Eikonal equation was solved with two different boundary conditions constructed from foreground and back-ground seeds. Image-dependent speed functions were inserted into the right handside of the Eikonal equation, whose solutions led to two distance functions:

In occasional cases of slightly concave-shaped tumors, the maximum diameter line will not be enclosed by the tumor completely. Even in these cases, the algorithm can perform the segmentation successfully if an input 1-D line is correctly drawn to fall inside the tumor region. The line enlargement parameter selected for VOI formation is determined by taking such cases into account, hence, the VOI contains the whole tumor.

C. Adapting Transition Rule to Tumor Characteristics

In the tumor segmentation application, the cells or nodes in cellular automata framework correspond to the MRI volume voxels in 3-D. A 26-cell cubic neighborhood is used in 3-D. MRI intensities are used as image features. The automata is initialized with user supplied tumor and background seeds as explained in Section III-B and iterated by the following rule:

$$I_i^{t+1} = I_i^t \text{ and } x_i^{t+1} = g(i, i^*) x_i^t, \text{ where } i^* = \arg \max_{j \in N_i} g(i, j) x_j^t \quad (3)$$

where g is a pixel similarity or transition function bounded to $[0, 1]$, which is equivalent to the edge weight function w_{ij} in the seeded segmentation framework. A typical symmetric edge weight function depending on the image features, is given by the absolute intensity difference or gradient magnitude between neighboring nodes i and j

$$g(i, j) = e^{-\beta \|I_i - I_j\|} \quad (4)$$

in the necrotic region. This sometimes causes the segmentation algorithm to get stuck at necrotic to enhancing tumor transition borders. To overcome such problems, prior knowledge that tumor voxels are brighter in post-contrast T1-MRI can be utilized. This can be achieved by modifying the transition function $g(i, j)$ by inserting a spatially-varying parameter

$$g(i, j) = \begin{cases} e^{-\beta \|I_i - I_j\|}, & \text{if } I_i > I_j \text{ and } I_j = \text{Tumor} \\ e^{-\beta \|I_i - I_j\|}, & \text{otherwise.} \end{cases} \quad (5)$$

The intuition here is based on the observation that the enhancing tumor cells are brighter than the normal tissue, and more centrally located necrotic core is darker. Therefore, by adjusting the β

selected as the bounding box of the sphere having a diameter 35% longer than the line; 3) One-voxel wide border of this VOI is used as background seeds.

Since the VOI is completely bounded by the background seeds, each path connecting inside and outside the VOI is blocked by a seed. Then, the result of labeling using only the data inside the region is equivalent to using the whole volume whereas the computation time is significantly reduced.

One obvious drawback is that the user draws the line on only a single slice of the tumor volume, hence it is not guaranteed that the depth of the tumor will also coincide with the VOI. For determining the enlargement ratio for the bounding box size, the percentage of the volume enclosed in the sphere to the total tumor volume is calculated for different enlargement ratio values, and the results are plotted in Fig. 2. For our data set, 100% coverage was achieved with 2.00 times enlargement. We used 1.35, which covers 99% of all tumors with five different initializations, which gave a reasonable trade-off between the 3-D inclusion of the whole tumor versus the computation time increases due to enlargement of the volume.

where I_i denotes the MR image intensity at node i .

In the seeded tumor segmentation application over contrast enhanced T1-weighted MRI for heterogeneous tumors, which mostly consist of a ring enhancing region around a dark necrotic core (and also irregular borders), most of the foreground seeds fall

D. Level Set Evolution on Constructed Tumor Probability Map

Smoothing is an important prior in segmentation of brain tumors from post-contrast T1 images, because of three main reasons: First, an area surrounded by tumor tissue is considered as a tumor region even the intensity characteristics are likely to be healthy. Secondly, it is possible to include misclassified necrotic regions to tumor region, which are usually surrounded by enhanced tissue. Finally, it is possible to exclude nearby vascular structures that are enhanced by administration of the contrast agent.

CONCLUSION

Here we presented a segmentation algorithm for the problem of tumor delineation which exhibit varying tissue characteristics. This algorithm needs very less user interaction. This can be widely used in clinical practices

parameter, the weight reduction (i.e., the strength loss) of a tumor state while passing through a ramp up gradient is adjusted to be lower than other cases.

Our experimental results revealed that the new tumor CA (tCA) algorithm significantly improved the results obtained, especially on glioblastomas.

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