Segmentation of Liver Tumor Using Efficient Global Optimal Tree Metrics Graph Cuts

Ruogu Fang[1], Ramin Zabih[2], Ashish Raj[3], and Tsuhan Chen[1]

[1] Department of Electrical and Computer Engineering, Cornell University, Ithaca, NY, USA
rf294@cornell.edu, asr2004@med.cornell.edu
[2] Department of Computer Science, Cornell University, Ithaca, NY. 14850, USA
rdz@cs.cornell.edu
[3] Department of Radiology, Cornell University, New York City, NY. 10021, USA
tsuhan@ece.cornell.edu

Abstract. We propose a novel approach that applies global optimal tree-metrics graph cuts algorithm on multi-phase contrast enhanced contrast enhanced MRI for liver tumor segmentation. To address the difficulties caused by low contrasted boundaries and high variability in liver tumor segmentation, we first extract a set of features in multi-phase contrast enhanced MRI data and use color-space mapping to reveal spatial-temporal information invisible in MRI intensity images. Then we apply efficient tree-metrics graph cut algorithm on multi-phase contrast enhanced MRI data to obtain global optimal labeling in an unsupervised framework. Finally we use tree-pruning method to reduce the number of available labels for liver tumor segmentation. Experiments on real-world clinical data show encouraging results. This approach can be applied to various medical imaging modalities and organs.

Keywords: multi-phase contrast enhanced MRI, tree-metrics graph cuts, liver tumor segmentation, color-space mapping, global optimal labeling.

1 Introduction

In the United States, liver tumor (or hepatocellular carcinoma) is one of the most common malignancies leading to an estimated one million deaths annually, and it has become the fastest growing cancer up to date [1]. Liver tumors segmentation is an important prerequisite for surgical interventions planning. The major difficulty in liver tumor segmentation is low contrasted boundaries and a large variability of shapes, sizes and locations presented by the tumor in the liver. Local intensity or intensity gradient feature based techniques are proved to be inadequate to differentiate between liver tissue and healthy structures. High performance segmentation methods should be capable to deal with the high variation in shape and gray value of the liver.

In order to alleviate this problem, multi-phase contrast enhanced MRI is used in clinical practice to characterize tumor response to contrast agent, yet most of the current methods still lack maturity in terms of quantifying tumor burden and viability. We propose to extract a set of features in multi-phase contrast enhanced MRI images,

H. Yoshida et al. (Eds.): Abdominal Imaging 2011, LNCS 7029, pp. 51–59, 2012.

and apply an efficient tree-metrics graph cuts algorithm in computer vision to segment the tumor in the liver. In this manner, we design a classifier for semi-automatic diagnosis of hepatocellular carcinoma.

The contributions and novel aspects of our proposed approach include:

1. **New Framework for Global Optimal Multi-label Segmentation in Medical Image Data.**
   This framework is based on directly clustering the available labels (intensity values or dynamic features) in medical image data, and use efficient tree-metrics graph cuts to find the global optimal labeling, while previous approaches have focused on conventional methods as active contours [2], level-sets [3], as well as machine learning [4]. The advantages of this new framework are discussed below in Section 2.2.

2. **Specific Focus on Multi-phase Contrast Enhanced MRI of Liver Tumor.**
   In contrast to the works previously [5][6], our work on tree-metrics graph cuts segmentation focuses on multi-phase contrast enhanced MRI of liver tumor, which has not been explored to the best of our knowledge.

3. **Evaluation on Real-World Clinical Data with Many Applications.**
   Our experiments employ segmentation problems of liver tumor and compared with the state-of-art work. The proposed method is also applicable to multiple image modalities, such as dynamic contrast enhanced MRI, CT perfusion.

2 Method

To find the segmentation boundary of tumor in low contrast multi-phase contrast enhanced MRI of liver tumor images, we propose a set of novel features along with the computational approaches to obtain them, and detail our framework of tree-metrics graph-cut (TM) algorithm. Finally we propose a tree-cutting approach to interpret the labeling returned by the TM algorithm for tumor segmentation in the multi-phase contrast enhanced MRI liver data.

2.1 Dynamic Feature Extraction

Here we describe the general protocol for multi-phase contrast enhanced MRI. In multi-phase contrast enhanced MRI a bolus injection of a contrast agent, usually gadolinium-DTPA (Gd) is given to the subject (patients or animals). A set of T_1-weighted MRI volumes are acquired a few seconds (pre-contrast time) before the injection and at several time points after the injection (arterial phase, portal-venous phase and delayed phase), to first obtain a baseline or pre-contrast MRI, as well as the time-varying MRI with the contrast agent. As the contrast bolus perfuses through the vasculature, the time-course of the contrast at a given voxel, indicating the MRI signal, can be characterized from the plot. The specific time points for the data collection vary for different MRI settings, and the detailed time points in our experiments are illustrated in Section 3.1.

We denote a voxel in the volume as v_i indexed by the set of voxels $i \in I$. The associated time-course curve is denoted as $y_i(t)$ where t indexes the time points in the multi-phase contrast enhanced MRI scan. The total number of voxels in the volume is $|I|$. Healthy tissue in general is less enhanced by the contrast agent than the enhancing carcinomas, but more than necrotic tissue, which basically does not enhance apparently.

The dynamic features that we extract from the time-series signals include: baseline (pre-contrast) MR signal (BL), peak enhancement (PE), and area under the enhancement curve (AUC), rise time (RT), and arrival time (AT), as depicted in Figure 1. For the coarse time-scale curves, the first three dynamic features are used, as depicted in Fig. 1(a). For more high resolution time-course curves, additional detailed dynamic features are extracted, as shown in Fig. 1(b). Our work uses both models, depending on the availability of the temporal resolution of the data.

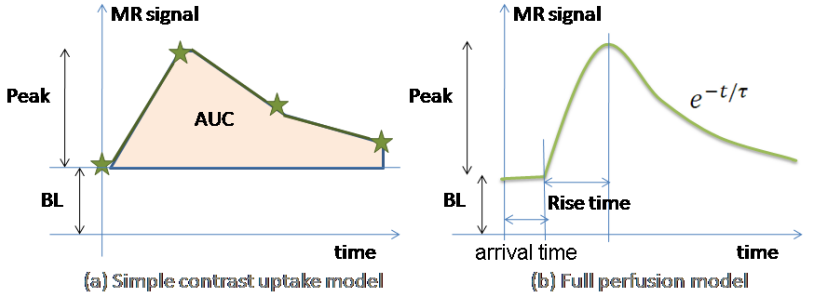

Fig. 1. Dynamic feature extracted from time-course curves of the MR signals. (a) A simple model where three features are used. (b) Full model where richer dynamic features are used.

In the multi-phase contrast enhanced images, the first three features (BL, PE and AUC) are mapped in pseudocolor onto RGB color space for better visualization. Figure 2 visualizes the baseline MR image, along with the dynamic feature-enhanced image and pseudo-color mapped image. The feature-space mapping conveys additional information unavailable in any single MRI intensity image.

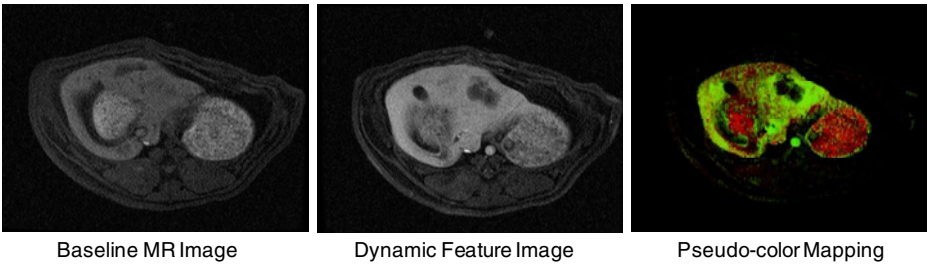

Fig. 2. Dynamic feature extraction and mapping. Left: Baseline MR image without dynamic feature extraction. Middle: MR image after using dynamic feature extraction method. Right: Pseudo-color image after feature-spacing mapping onto RGB color space.

2.2 Liver Tumor Segmentation as Metric Labeling

The liver tumor segmentation problem can be interpreted as an instance of metric labeling; specifically an instance of spatially coherent clustering, where the observations are labels and we want to assign the voxels with new label. The new labels are gray-scale intensity levels, and further tree-pruning step will generate the actual segmentation for the liver tumor in multi-phase contrast enhanced MRI. Each of the new values should be close to the observed one in the original liver tumor multi-phase contrast enhanced MRI image, and the values of nearby voxels should be similar. Spatially coherently clustering has been addressed by several papers recently [7, 8, 9, 10]. All of them rely on iterative techniques without provable error bounds. In this paper, we propose to use tree-metrics graph cuts [6] which computes a global minimum solution of an energy function, to liver tumor segmentation in smulti-phase contrast enhanced MRI. The tree-metrics graph cuts algorithm applies graph cuts [11] on a tree of labels for distance measure.

Let the dynamic features extracted from the liver multi-phase contrast enhanced MRI image be represented as an undirected weighted graph $G = (V, E)$, where vertices V correspond to voxels and E are edges between neighboring voxels. Let L be the set of labels, and let $f : V \to L$ be a labeling. Furthermore, let $d(o(v), f(v))$ be the cost for giving label $f(v)$ to object v, where $o(v)$ is the observed label and $d(a,b)$ is a distance on L. Let $d(f(u), f(v))$ be the cost for giving label $f(u)$ to object u and $f(v)$ to object v, where u and v are the neighboring voxels. The goal is to find a labeling f that minimizes the cost function

$$Q(f) = \sum_{v \in V} d(o(v), f(v)) + \sum_{(u,v) \in E} \lambda \cdot d(f(u), f(v)) \tag{1}$$

We refer to the first summation in $Q(f)$ as the "data term" and the second summation in $Q(f)$ as the "prior term" (or "smoothness term"). As our prior, we want objects connected by an edge in E to have similar labels. The weights λ decides the relative importance of the data terms and the smoothness terms. The larger the value of λ, the more smooth the output labeling. The choice of the parameter λ is detailed in the experiments in Section 3.1.

2.3 Tree-Metrics Graph Cuts

To apply the tree-metrics graph cuts (TM) algorithm [6] on multi-phase contrast enhanced MRI liver tumor segmentation, we perform a pre-processing step to create suitable inputs to the TM algorithm, and a post-processing step on the output segmentation returned by the TM algorithm to create the final segmentation.

The TM algorithm takes three things as input: a multi-phase contrast enhanced MRI liver image, a tree of labels, and a smoothness parameter $\lambda \geq 0$. We generate a tree of labels with agglomerative clustering based on the extracted dynamic features from multi-phase contrast enhanced MRI data.

Each stage of our approach – tree generation, sweep and pruning – is detailed in the sections followed.

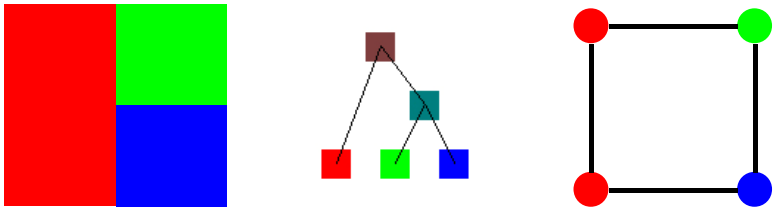

Fig. 3. An examples of tree generation. Left: A synthetic image with tree colors as input. Middle: Binary tree of labels generated from the synthetic image. Right: Graph structure of the image.

2.2.1 Tree Generation

We apply agglomerative hierarchical clustering to create a tree of labels. Closest pairs of clusters (or labels) in the feature space are repeatedly merged. We cluster all the available colors from the image based on Ward's variance criteria [12]. Fig. 3 illustrates the agglomerative clustering on a synthetic image of three colors. For multi-phase contrast enhanced MRI liver image, we perform agglomerative hierarchical clustering on the pseudo-color mapped image from dynamic features. In practice, the agglomerative hierarchical clustering is implemented in phases, and k-nearest neighbors (measured in Euclidean distance) are used as the candidate clusters and merged. Approximate nearest neighbors [13] are used when the number of clusters are very large. The stopping criterion is when the maximum variance becomes greater than two times of the minimum variance.

2.2.2 Sweep Algorithm

The tree of labels generated from the multi-phase contrast enhanced MRI pseudo-color mapped image represents the tree-metrics distance function d. Now we apply the TM algorithm to the multi-phase contrast enhanced MRI liver image, with the tree of labels and a smoothness parameter $\lambda \geq 0$. The TM algorithm will minimize the cost function for a distance d and labeling f:

$$Q(f) = \sum_{v \in V} d(o(v), f(v)) + \lambda \sum_{(u,v) \in E} d(f(u), f(v)) \tag{2}$$

We use graph cuts [11] to optimize the objective function $Q(f)$ in Equation (2), and use tree-metric distance to measure the cost in both the data term and the smoothness term. Compared with conventional graph cuts where the distance function is the Euclidean distance, the upmost advantages of using tree-metrics graph cuts are the global optimality and the efficiency. The TM algorithm computes the globally optimal labeling f for the cost function Q(f) in Equation (2) in O(log(k)(g(n)+k)) time for n voxels and k labels, where g(n) is the running time of the min-cut algorithm on graph with n nodes.

2.2.3 Tree Cutting

The labeling returned by TM algorithm is usually more than the required number of segments in the multi-phase contrast enhanced MRI liver image. Therefore we need to interpret the labels returned from the TM algorithm to find the exact tumor boundary in the liver. To reduce the number of labels, we "cut" the binary tree of labels at depth

d; for each node at depth d (where the root node is depth 0), their child subtrees now map to the same label as their ancestor node at depth d). By cutting the tree at depth d, we are left with N labels, where $N = \sum_{n=0}^{d} 2^n$. Finally, we use an interactive interface to ask radiologist to pick the segment (or label) of the tumor in the liver.

3 Experimental Results

Significant experimental work has been completed towards a new framework for liver tumor segmentation using tree-metrics graph-cuts in multi-phase contrast enhanced MRI.

3.1 Liver Tumor Segmentation in Rabbit HCC Model

Our method was developed and tested on data from a pre-existing study at John Hopkins University involving hepatocellular carcinoma (HCC) grown in a rabbit model. It has been shown that rabbit model demonstrates a physiology similarity to that of humans. The multi-phase contrast enhanced MRI exams were obtained using a standard T1-weighted MR acquisition sequence, with the following timed phases: pre-contrast phase (0s), arterial phase (20s), portal-venous phase (60) and delayed phase (120s). Tumor size was determined through pathologic dissection in all animals. Dissections were performed by pathologists under guidelines and techniques that ensure accurate and reproducible measurement of tumor size. This pathology data served as the gold standard. A novel liver-specific Gadolinium-based contrast agent Gadoxetate Disodium (Eovist®) was intravenously injected. In our experiment, 11 rabbit liver multi-phase contrast enhanced MRI volumetric data were used.

In the energy minimization problem in Equation 2, the smoothness parameter λ decides the level of smoothness in the output segmentation. We experimented with different λs for the rabbit HCC 4-phase multi-phase contrast enhanced MRI data and found that the proper range of λ is between 2 to 10, depending on the specific dataset. In our experiment, we fixed λ to be 5 for all the 11 rabbit multi-phase contrast enhanced MRI volumetric data.

Fig. 4 shows one frame of the segmentation results on 3D volumetric multi-phase contrast enhanced MRI liver tumor data. Using feature-space mapping and tree-metrics graph cuts, the segmentation results on rabbit liver tumor is promising. We have designed an interactive interface for radiologists to actively choose the tumor region by clicking on the segment and the algorithm eases the task of liver tumor segmentation by performing an initial segmentation of the tumor and other tissue types.

We also compared our tumor segmentation results with a recent work on liver tumor segmentation [14]. In their work, Raj et.al. also applies the dynamic feature mapping method to improve the contrast between the tumor and the other tissue types. However, after the dynamic feature extraction, they use K-means to cluster the voxels and segment out the tumor. K-means algorithm takes $O(n^{dk+1} \log n)$ for running time, where n is the number of entities to be clustered, k is the number of clusters and d is the distance measure, compared to $O(\log(k)(g(n)+k))$ of our method. Moreover K-means clustering does not give the globally optimal labeling. A comparison of the liver tumor segmentation result using our method and [14] is shown in Fig. 5.

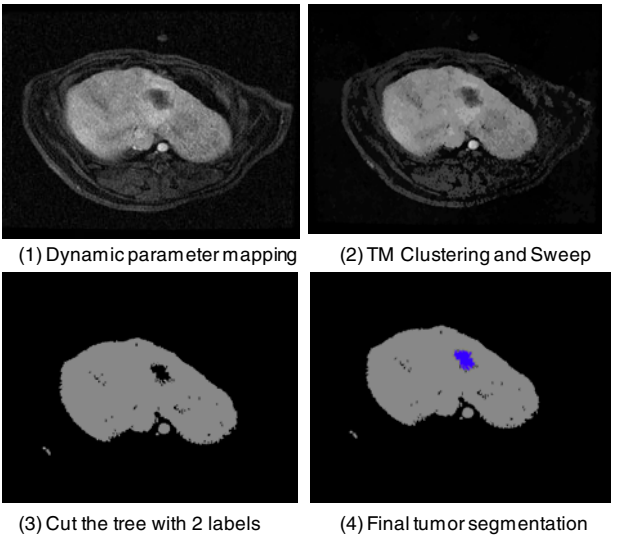

Fig. 4. Experiment results of rabbit liver tumor segmentation using tree-metrics graph cuts. The parameters are λ=5, d = 2.

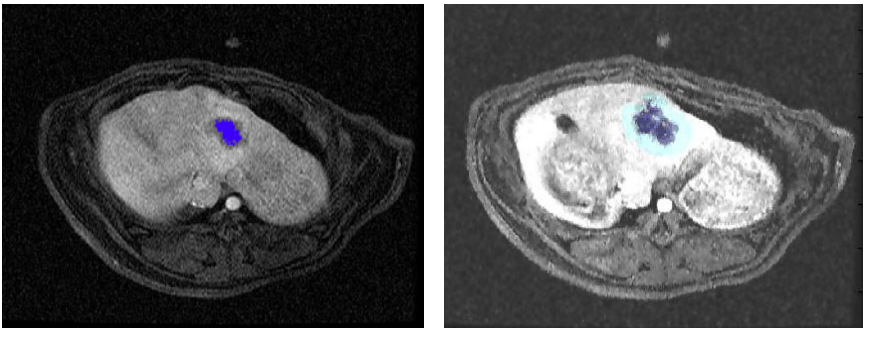

Fig. 5. Comparison of our algorithm (left) with [14] (right) on rabbit liver. The dark blue region in the right image is the final tumor segmentation using methods in [14].

Quantitative evaluation of our method is conducted by correlating the liver tumor size using our method (DPM+TM) with the gold standard, and compare with the segmentation results of [14] (DPM+K-means) on the same dataset. We use our proposed method to segment the liver tumor on 11 rabbit liver multi-phase contrast enhanced MRI 3D volumetric data and Fig. 6 shows the regression between our method and the gold standard, compared with that of [14] on the same dataset. The figure demonstrates that our method correlates with the dissections of pathologists with higher accuracy, while the volume size of the segmented tumor using [14] deviates from the gold standard at higher variation.

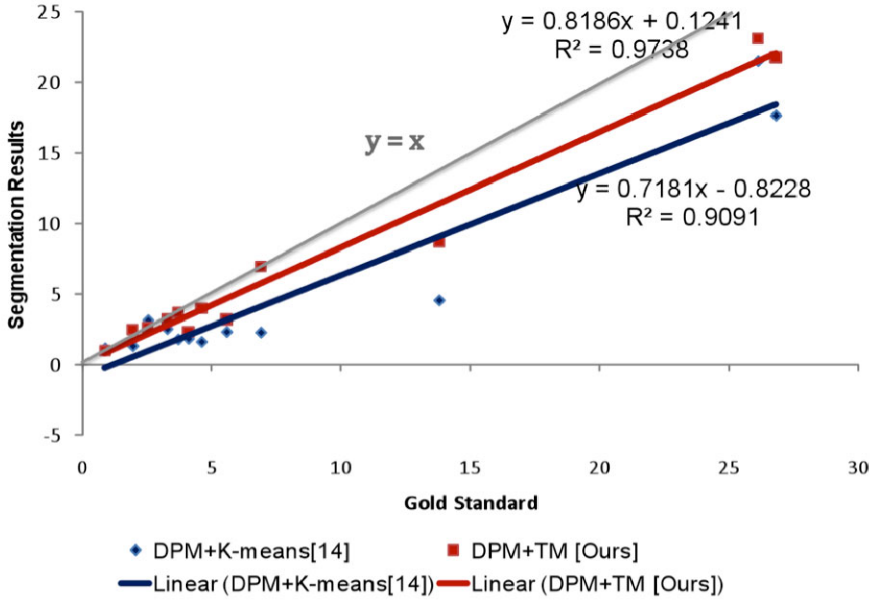

Fig. 6. Comparison of our method with [14] on the regression plot with gold standard

4 Conclusion

In this paper, we present a novel approach to apply dynamic feature mapping and tree-metrics graph cuts with tree pruning to the liver tumor segmentation in dynamic enhanced abdominal MRI data and compare our results with the state-of-art method. Our approach, which is efficient in computation and globally optimized in the tree-metrics labeling, performs better than the conventional existing approaches in terms of qualitative visualization, quantitative tumor size measure, and avoids iterated method which is computational intense.

There are several interesting directions for future work on this problem. To learn the proper structure of the tree, for instance, the optimal degree of the tree and the clustering criterion, will improve the segmentation result for arbitrary number of segments in the output. To find the accurate segmentation of the liver tumor from the initial segmentation of TM algorithm, an active learning approach can be adopted to determine the optimal smoothing parameter in the sweep stage and pruning depth in the cutting stage.

References

1. Fong, T.L., Schoenfield, L.J.: Hepatocellular Carcinoma (Liver Cancer), `http://www.medicinenet.com`
2. Lu, R., Marziliano, P., Thng, C.H.: Liver Tumor Volume Estimation by Semi-Automatic Segmentation Method. In: Proceedings of the 2005 IEEE Engineering in Medicine and Biology 27th Annual Conference, pp. 3297–3299 (2005)

3. Popa, T., Ibanez, L., Levy, E., White, A., Bruno, J., Cleary, K.: Tumor Volume Measurement and Volume Measurement Comparison Plug-Ins for Volview Using Itk. In: Proceedings of the SPIE: The International Society for Optical Engineering, vol. 6141, pp. 395–402 (2006)
4. Li, Y., Hara, S., Shimura, K.: A Machine Learning Approach for Locating Boundaries of Liver Tumors in CT Images. In: Proceedings of the 18th International Conference on Pattern Recognition, pp. 400–403 (2006)
5. Fang, R., Chen, Y.H., Zabih, R., Chen, T.: Tree-Metrics Graph Cuts For Brain MRI Segmentation With Tree Cutting. In: IEEE Western New York Image Processing Workshop. IEEE Press (2010)
6. Felzenszwalb, P., Pap, G., Tardos, E., Zabih, R.: Globally Optimal Pixel Labeling Algorithms for Tree Metrics. In: IEEE Conference on Computer Vision and Pattern Recognition. IEEE Press (2010)
7. Zabih, R., Kolmogorov, V.: Spatially coherent clustering using graph cuts. In: CVPR, pages II: 437–444 (2004)
8. Figueiredo, M., Cheng, D., Murino, V.: Clustering under prior knowledge with application to image segmentation. In: NIPS (2007)
9. Ishikawa, H., Geiger, D.: Segmentation by grouping junctions. In: CVPR, pp. 125–131 (1998)
10. Sfikas, G., Nikou, C., Galatsanos, N.: Edge preserving spatially varying mixtures for image segmentation. In: CVPR, pp. 1–7 (2008)
11. Boykov, Y., Veksler, O., Zabih, R.: Fast approximate energy minimization via graph cuts. PAMI 23(11), 1222–1239 (2001)
12. Ward Jr., J.: Hierarchical grouping to optimize an objective function. Journal of the American Statistical Association 58(301), 236–244 (1963)
13. Arya, S., Mount, D., Netanyahu, N., Silverman, R., Wu, A.S.: An optimal algorithm for approximate nearest neighbor searching fixed dimensions. JACM 45(6), 891–923 (1998)
14. Raj, A., Juluru, K.: Visualization and segmentation of liver tumors using dynamic contrast MRI. In: Conf. Proc. IEEE Eng. Med. Biol. Soc., pp. 6985–6989 (2009)