HHS Public Access

Author manuscript

Mol Imaging Reconstr Anal Mov Body Organs Stroke Imaging Treat (2017). Author manuscript; available in PMC 2019 December 02.

Published in final edited form as:

Mol Imaging Reconstr Anal Mov Body Organs Stroke Imaging Treat (2017). 2017 September ; 10555: 31–42. doi:10.1007/978-3-319-67564-0_4.

3D Alpha Matting Based Co-segmentation of Tumors on PET-CT Images

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Abstract

Positron emission tomography – computed tomography (PET-CT) has been widely used in modern cancer imaging. Accurate tumor delineation from PET and CT plays an important role in radiation therapy. The PET-CT co-segmentation technique, which makes use of advantages of both modalities, has achieved impressive performance for tumor delineation. In this work, we propose a novel 3D image matting based semi-automated co-segmentation method for tumor delineation on dual PET-CT scans. The “matte” values generated by 3D image matting are employed to compute the region costs for the graph based co-segmentation. Compared to previous PET-CT co-segmentation methods, our method is completely data-driven in the design of cost functions, thus using much less hyper-parameters in our segmentation model. Comparative experiments on 54 PET-CT scans of lung cancer patients demonstrated the effectiveness of our method.

Keywords

Image segmentation; Interactive segmentation; Lung tumor segmentation; Image matting; Co-segmentation

1 Introduction

Positron emission tomography – computed tomography (PET-CT) has revolutionized modern cancer imaging. Improved determination of the extent of cancer spread (staging) in patients by PET has illustrated the compelling need of acquiring this information for determining the therapeutic method to achieve improved prognoses. The integrated PET-CT, by adding precise anatomic localization to functional imaging, currently provides the most sensitive and accurate information available on tumor extent and distribution for a variety of common cancers. It increasingly plays a critically important role in tumor staging, clinical management/decision making, treatment planning, and therapy response assessment [1–3].

To make full use of the superb PET-CT imaging, accurate target delineation becomes indispensable. Current standard medical practice heavily relies on manual contouring, which is performed visually on a slice-by-slice basis by radiation oncologists for target delineation. Due to the nature of PET-CT imaging, manual contouring is cumbersome and error-prone, and suffers substantial inter- and intra-observer variability [4–7]. This may limit its use as a quantitative imaging tool or biomarker of outcome/response in large-scale clinical trial research and even for use in daily clinical care.

Substantial endeavors have been made on automated tumor definition from PET-CT scans using, for example, standardized uptake values (SUVs) based thresholding [8–11], image gradients [12,13], deformable contour models [14–16], mutual information in hybrid [17–19], random walk [20], and Gaussian mixture models for heterogeneous regions [21,22]. Recently, the co-segmentation technique for tumor delineation on both PET and CT images has been attracted great attentions [18,23–26], in which tumor contours on PET and on CT are segmented simultaneously while admitting their possible differences. As demonstrated in those previous works, the design of cost functions in the framework of graph based co-segmentation is critical to achieve good segmentation performance. Consequently, the region/unary costs were usually carefully designed based on some sophisticated image priors (e.g., Gaussian mixture models [18,23], shape prior [26], texture information [25], etc.) or clinical information from expertise [23–26], and often heavily rely on hyper-parameters selection (e.g., the number of models in Gaussian mixture models [18], the curvature parameters [26], etc.) for improved results.

In this paper, we propose a novel 3D alpha matting technique to compute the region costs for co-segmentation on PET-CT images. The “matte” values computed from the 3D matting are used to design the region costs in the co-segmentation model [23]. Compared to previous PET-CT segmentation approaches, the proposed method is completely image-derived with less image and clinical priors, and consequently with less hyper-parameters. By integrating the 3D alpha matting technique into the context-aware co-segmentation framework [23], the proposed PET-CT co-segmentation method eases the design of cost functions for segmentation, and significantly outperforms the state-of-the-art PET-CT segmentation approach [23]. Note that although 3D matting has been used as post-processing for the refinement of segmentation [27,28], no previous work has been done using it for cost function design in the segmentation framework based on graph algorithms.

2 Methodology

The proposed PET-CT tumor segmentation method is semi-automated, which mainly consists of three steps: (1) Active contour is adopted to generate larger seed regions from given initial seeds on PET and CT image pairs, respectively. (2) Based on the new seed regions, 3D image matting are conducted in both volumes to obtain the tumor object probability maps, which are further used for computing region/unary costs for the co-segmentation model [23]. (3) The co-segmentation in both PET and CT modalities is formulated as a context constrained energy minimization problem, as in Song *et al.*'s method [23], which can be solved optimally by the well-known max-flow/min-cut algorithm to

obtain the simultaneous tumor segmentation result. The flowchart is shown in Fig. 1. In the following, we will describe those three steps in detail.

2.1 Active Contour Based 3D Trimap Generation

As a standard yet important procedure in medical image processing, a preprocessing step is needed in our framework. Similar to [23,26], the PET images are first co-registered and up-sampled to have one-to-one voxel correspondence with the CT image. For each PET-CT image pair, initial foreground seeds (i.e., voxels that definitely belong to tumor object) and a background region (i.e., voxels that definitely do not belong to tumor object) are given with user interaction (for example, by drawing two spheres: the inner one indicates the tumor seeds and the region outside the outer sphere represents the background seeds). For CT image, we cut the intensity values (Hounsfield Units, HU) to the range of $[-500, 200]$ as possible tumor voxels to ignore irrelevant image details. For PET image, as suggested in literature, the raw image intensities are converted to standardized uptake values (SUV) according to de-identified patient meta-information.

Then, for each PET-CT pair, based on the given foreground seeds, the active contour technique is employed on the PET and CT images, respectively. As a consequence, we obtain an enlarged seed region on PET and CT images. However, due to the complex nature of a CT image, non-tumor voxels might also be included in the enlarged seed region, which would lead to inaccurate segmentation. To alleviate this problem, we remove some voxels by simply thresholding to keep those voxels whose HU values are in a specific range. The lower and upper bound of this range in HU are empirically set to $\max(-412, 0.1 * CT_{med})$ and $\min(CT_{max}, 1.5 * CT_{med})$. The CT_{max} and CT_{med} are maximum and median values within the initial foreground seed region on the CT image, respectively. Finally, the intersection of the enlarged foreground seed regions on both PET and CT serves as the final foreground seeds. Along with the given background seeds, a 3D trimap image is further computed to classify the image voxels into three categories of regions (i.e., the tumor region, background, and the mixed or uncertain voxel region), which will be given as inputs for the subsequent 3D alpha matting procedure.

Note that the active contour method in this step is applied to 2D slices of PET and CT images where initial foreground seed regions are given. For the purpose of illustration, some intermediate results are shown in Fig. 1.

2.2 3D Alpha Matting Based Tumor Object Probability Maps—Alpha matting is

an important tool for image and video editing, which refers to the process of extracting foreground object from an image. It usually produces a “matte” image that can be used to separate the foreground from the background in a given image. Suppose that an image I is composed of two parts: the foreground object F and the background B . The gray or color intensity of the i -th pixel is assumed to be a linear combination of the corresponding foreground (object) and background intensities: $I_i = \alpha_i \cdot F_i + (1 - \alpha_i) \cdot B_i$ where α_i , F_i and B_i are, respectively, the matte, the foreground, and the background (intensity) values of the i -th pixel. Alpha matting aims to simultaneously compute all three values for each pixel in one

image by considering a “local smoothness assumption” that both F and B are approximately constant vector over a small local neighborhood window around each pixel. Inspired by the closed-form matting [29], we extend the 2D alpha matting to 3D and propose to adopt the “matte” values to compute tumor object probability maps used for region cost computation in the subsequent co-segmentation.

Specifically, given an image with a size of $H \times W \times D$, the local smoothness assumption allows us to reformulate the “alpha” for each voxel j in the 3D image

I as $\alpha_j \approx a \cdot I_j + b$, $\forall j \in w$, where $a = \frac{1}{F_j - B_j}$, $b = -\frac{B_j}{F_j - B_j}$, w is a small neighborhood

window. The goal of 3D alpha matting is to find the alpha for each voxel, which can be modeled as the following problem:

$$J(\alpha, a, b) = \sum_{j=1}^N \left[\sum_{i=1}^{|w_j|} (\alpha_j - a_j I_i - b_j)^2 + \epsilon a_j^2 \right] = \sum_{j=1}^N \left\| \begin{bmatrix} I_1^j & 1 \\ I_2^j & 1 \\ \vdots & \vdots \\ I_{|w_j|}^j & 1 \\ \sqrt{\epsilon} & 0 \end{bmatrix} \begin{bmatrix} a_j \\ b_j \end{bmatrix} - \begin{bmatrix} \alpha_1^j \\ \alpha_2^j \\ \vdots \\ \alpha_{|w_j|}^j \\ 0 \end{bmatrix} \right\|^2, \quad (1)$$

where $|w_j|$ is the number of voxel in j -th voxel neighborhood w_j , I_k^j and α_k^j ($k = \{1, \dots, |w_j|\}$) are intensity and alpha values of k -th neighbor of j -th voxel, respectively. ϵ is a regularization constant. Using matrix notation, we have

$$J(\alpha, a, b) = \sum_{j=1}^N \left\| G_j \begin{bmatrix} a_j \\ b_j \end{bmatrix} - \bar{\alpha}_j \right\|^2. \quad (2)$$

Then, for each voxel j , we need to solve $a_j \in \mathbb{R}$, $b_j \in \mathbb{R}$ and $\bar{\alpha}_j \in \mathbb{R}^{(|w_j|+1) \times 1}$. Suppose we knew $\bar{\alpha}_j$, then we can obtain the optimal a_j and b_j as

$$\begin{bmatrix} a_j \\ b_j \end{bmatrix}^* = (G_j^T G_j)^{-1} G_j^T \bar{\alpha}_j, \quad (3)$$

then substituting this solution back into (2) and denoting

$\bar{G}_j = I_{(|w_j|+1) \times (|w_j|+1)} - G_j (G_j^T G_j)^{-1} G_j^T \in \mathbb{R}^{(|w_j|+1) \times (|w_j|+1)}$, we obtain the α -subproblem as

$$J(\alpha) = \sum_{j=1}^N \|\bar{G}_j \bar{\alpha}_j\|^2 = \sum_{j=1}^N \bar{\alpha}_j^T \bar{G}_j^T \bar{G}_j \bar{\alpha}_j, \quad (4)$$

It is easily shown that

$$\begin{aligned}\bar{G}_j^T \bar{G}_j &= I_{(|w_j|+1) \times (|w_j|+1)} - G_j(G_j^T G_j)^{-1} G_j^T, G_j^T G_j = \begin{bmatrix} \sum_{i=1}^{|w_j|} I_i^2 & \epsilon \sum_{i=1}^{|w_j|} I_i \\ \sum_{i=1}^{|w_j|} I_i & |w_j| \end{bmatrix} \text{ and } (G_j^T G_j)^{-1} \\ &= \frac{1}{|w_j| \left(\frac{\epsilon}{|w_j|} + \sigma_j^2 \right)} \begin{bmatrix} 1 & -\mu_j \\ -\mu_j & \mu_j^2 + \sigma_j^2 + \frac{\epsilon}{|w_j|} \end{bmatrix},\end{aligned}$$

where μ_j and σ_j^2 are the mean and variance of the intensities in neighborhood window w_j (typically with a size of $3 \times 3 \times 3$) around j -th voxel, and $|w_j|$ is the number of voxels in the voxel set w_j . Finally, after some simple mathematical operations, the α -subproblem is formulated as

$$\alpha = \underset{\alpha}{\operatorname{argmin}} \alpha^T L \alpha, \quad (5)$$

where $\alpha \in \mathbb{R}^{N \times 1}$ is the alpha matte vector for all $N = W \times H \times D$ voxels, and $L \in \mathbb{R}^{N \times N}$ is the matting Laplacian matrix, with (i, k) -entry being

$$\sum_{j | (i, k) \in w_j} \left(\delta_{ik} - \frac{1}{|w_j|} \right) \left(1 + \frac{1}{\left(\frac{\epsilon}{|w_j|} + \sigma_j^2 \right)} (I_i - \mu_j)(I_k - \mu_j) \right), \quad (6)$$

where δ_{ik} is the Kronecker delta. However, the above problem (5) has singular solution. Thus, by considering user-supplied constraints on alpha values as in [29], the 3D alpha matting problem is finally formulated as:

$$\alpha = \underset{\alpha}{\operatorname{argmin}} \alpha^T L \alpha + \lambda (\alpha^T - b_S^T) D_S (\alpha - b_S), \quad (7)$$

where λ is a coefficient, D_S is a diagonal matrix with an element 1 for each constrained voxel and with an element 0 for each of the remaining voxels, b_S is a vector indicating the alpha values for the constrained voxels. Since (7) is quadratic in alpha, we can obtain the final global optimum solution by solving a sparse linear system [29].

By considering the neighborhood relationships among spatially-adjacent and slice-adjacent voxels (e.g., w_j neighborhood for voxel j), the constructed matting Laplacian matrix L can better model tumor object structures, and consequently the probability generated from alpha matting would produce better segmentation results, which is validated in our experiments.

2.3 Context-Aware Co-segmentation

The context-aware graph cut based co-segmentation has been studied for tumor delineation on dual-modality PET-CT images [23]. Two sub-graphs are respectively constructed for both PET and CT images. Each sub-graph is constructed in a similar way as that in traditional graph cut based segmentation [30]. The edge weights in each sub-graph encode the region

(or unary) and boundary (or pairwise) information from the corresponding image. In co-segmentation, a key ingredient lies in the incorporation of context information between the PET and CT images, which enforces the context-aware segmentation consistency between the corresponding nodes in the two sub-graphs by adding inter-edges between two sub-graphs. The co-segmentation is finally formulated as the following energy minimization problem that can be solved by the well-known maximum flow algorithm:

$$E(l) = E_{CT}(l) + \beta E_{PET}(l) + E_{context}(l) \quad (8)$$

$$E_{CT}(l) = \sum_{v \in \mathcal{J}} D_v(l_v) + \lambda_1 \sum_{(u,v) \in \mathcal{N}_{CT}} V_{uv}(l_u, l_v) \quad (9)$$

$$E_{PET}(l) = \sum_{v' \in \mathcal{J}'} D_{v'}(l_{v'}) + \lambda_2 \sum_{(u',v') \in \mathcal{N}_{PET}} V_{u'v'}(l_{u'}, l_{v'}) \quad (10)$$

$$E_{context}(l) = \sum_{(v,v')} W_{vv'}(l_v, l_{v'}) \quad (11)$$

where $\mathcal{J}$ denotes the input CT image, $\mathcal{J}'$ denotes the input co-registered PET image, l_v and $l_{v'}$ denote the binary labels assigned to each voxel $v \in \mathcal{J}$ and $v' \in \mathcal{J}'$, respectively. $D_v(l_v)$ and $V_{u,v}(l_u, l_v)$ denote the region and the boundary costs of each node (voxel) v on CT, respectively. $D_{v'}(l_{v'})$ and $V_{u',v'}(l_{u'}, l_{v'})$ denote the region, and the boundary costs of each node (voxel) v' on the PET image, respectively. $W_{vv'}(l_v, l_{v'})$ is a context-aware cost function. β , λ_1 and λ_2 are user-defined weight coefficients. $\mathcal{N}_{CT}$ and $\mathcal{N}_{PET}$ are the neighborhood systems defined on CT and PET, respectively.

In previous co-segmentation methods, $D_v(l_v)$ is often computed based on Gaussian mixture model [23] or integration of other complex image priors (e.g., shape prior [26]), while $D_{v'}(l_{v'})$ is usually specially-designed based on clinical information (e.g., empirically-thresholded SUV values [23,26], 3D derivative costs [26], etc.). In our work, an important difference is that those region costs are generated directly from the alpha mattes computed by the 3D image matting. Take as an example the voxel v in the CT image. The region terms take the form $D_v(l_v = 1) = -\log(\alpha_v)$ and $D_v(l_v = 0) = -\log(1 - \alpha_v)$ where α_v is the alpha matte value. For the design of the boundary term and the context term, we use a similar strategy as that in [23]. For the completeness, we summarize these terms here, as follows:

$$V_{uv}(l_u, l_v) = -\log \left(1 - \exp \left(\frac{-|\nabla \mathcal{J}|^2(u, v)}{2\sigma_{CT}^2} \right) \right) \quad (12)$$

$$V_{u',v'}(l_{u'}, l_{v'}) = -\log\left(1 - \exp\left(\frac{-|\nabla \mathcal{J}|^2(u', v')}{2\sigma_{PET}^2}\right)\right) \quad (13)$$

$$W_{v,v'} = \theta(1 - |N_v - N_{v'}|) \quad (14)$$

where $|\nabla \mathcal{J}|^2(u, v)$ denotes the squared gradient magnitude on CT between u and v . σ_{CT} and σ_{PET} are Gaussian kernel parameters. N_v and $N_{v'}$ are alpha mattes between $[0,1]$ obtained from the CT and PET images, respectively. θ is a scaling parameter.

3 Experiment

3.1 Datasets

A total of 54 PET-CT scan pairs from different patients with primary non-small cell lung cancer are obtained. The image spacing varies from $0.78 \times 0.78 \times 2 \text{ mm}^3$ to $1.27 \times 1.27 \times 3.4 \text{ mm}^3$. The intra slice image size is 512×512 . The number of slices varies from 112 to 293. Manual expert tracings of the primary tumor volume is available for each scan.

The 54 scans are separated disjointly as a 10-scan training set and 44-scan testing set. The selection procedure starts by sorting all scans according to tumor volume. Then one scan out of every five scan is selected as training scan. This stratified strategy makes sure the training set is representative of the whole population in terms of tumor volume. All parameters are tuned on the training set. All reported results are from the testing set.

3.2 Experiment Settings

The same initialization procedure in [23] is employed. The user first specify two concentric spheres with the different radii to serve as object and background seeds. More specifically, all voxels inside the smaller sphere are used as object seed. All voxels outside the larger sphere are used as background seed.

The segmentation accuracy is measured by the Dice coefficient (DSC). Dice coefficient measures the volume overlap of two segmentations A and B . It is defined as $2|A \cap B| / (|A| + |B|)$, with a range of $[0,1]$. The higher the DSC is, the better volume overlap the two segmentations have.

A grid search strategy is used to select the parameters. The parameters returning highest training set DSC is used to run the co-segmentation on the test set. The values of those parameters are set, as follows: $\beta = 5$, $\lambda_1 = 5$, $\lambda_2 = 0.1$, $\sigma_{CT} = 15$, $\sigma_{PET} = 0.1$, and $\theta = 255$.

We conducted quantitative comparisons to the state-of-the-art PET-CT co-segmentation method of Song *et al.*'s [23]. For better illustration of the alphas based region costs for (co-)segmentation, two groups of experiments were conducted. In the first group, the context term was not used, and the traditional graph cut based segmentation method [30] was

applied solely on CT or PET for tumor segmentation using our proposed mattes based cost functions. In the second group of experiments, both PET and CT scans were used for our co-segmentation of tumor contours.

3.3 Results and Analysis

Table 1 reports the mean DSCs and standard deviations of the evaluated methods on the 44 test datasets. Figure 2 shows their quantitative results for each method on each case. From these results, we have the following observations. First, compared to Song's co-segmentation method, our matte based method can achieve better performance on most cases with higher DSCs (on average, 3.4% improvement) with a significant confidence (p-value of 0.005). Second, from the results of either Song's or our method, the co-segmentation can achieve better results over the traditional graph cut segmentation methods (i.e., the superiority of co-Seg. over CT-only or PET-only). Third, considering the traditional graph cut based segmentation (i.e., without context-aware information between inter-subgraphs), the segmentation results using the proposed region costs generated by 3D alpha matting outperformed those using Song *et al.*'s region costs.

Qualitatively, Fig. 3 shows the segmentation results of the compared methods on three PET-CT scans. From those figures, we can see our method is able to locate tumor boundary more accurately. Note that the ground truth was only given on CT images, we draw the contours on PET images for demonstration.

It is noted that although our method can achieve good segmentation results on most cases, it still cannot handle some hard cases. One example case for which our method achieved less accurate segmentation is shown in Fig. 4. As we can see in this figure, although our method can localize the obvious tumor boundary on CT images, it is difficult to recognize those voxels with extremely low HU values in tumor region. Possible improvements in the future lies in how to design more effective cost function for these hard cases.

Our algorithm was implemented in MATLAB on a Windows 10 workstation (3.4GHz, 32GB memory). As to the average computation time over the 44 test cases, the 3D image matting step took about 43.49s, the co-segmentation step took about 68.76s. Thus, our method took about 2min for each case, which was comparable to those reported in [23].

4 Conclusion

The novel 3D image matting can generate high-quality region cost on both PET and CT images, which can be effectively used to locate the tumor boundary. When integrated in the powerful graph cut based co-segmentation framework, it can achieve high accurate segmentation for tumor delineation. Experiments on 54 datasets demonstrated the effectiveness of the proposed method.

Acknowledgments.

This research was supported in part by the NIH Grant R21CA209874.

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Fig. 1.
The flowchart of proposed PET-CT co-segmentation framework.

Fig. 2.
Quantitative results and comparative performance evaluation based on the computed DSC values.

Fig. 3.

Segmentation results of compared methods on three PET-CT scans: No. 000577, 001255 and 001263 (from the first row to the last row). The 1st and 2nd columns: contours on CT and PET images *with* co-segmentation. The 3rd and 4th columns: contours on CT and PET images *without* co-segmentation. Red: ground truth, Green: Song's method, Blue: Our method. (Color figure online)

Fig. 4.

One example case for which our method achieved less accurate segmentation.

Table 1.

Average DSC's and standard deviations of the proposed method and Song et al.'s co-segmentation method [23].

Methods	Modalities	DSC	p-values
Song et al. [23]	CT-only	0.495 ± 0.208	
	PET-only	0.582 ± 0.134	
	PET-CT	0.768 ± 0.114	
Proposed	CT-only	0.744 ± 0.101	10^{-10}
	PET-only	0.757 ± 0.077	10^{-13}
	PET-CT	0.802 ± 0.069	0.005