Locally Constrained Active Contour: A Region-Based Level Set for Ovarian Cancer Metastasis Segmentation

Jianfei Liu\(^a\), Jianhua Yao\(^a\), Shijun Wang\(^a\), Marius George Linguraru\(^b\), Ronald M. Summers\(^a\)

\(^a\)Radiology and Imaging Sciences, National Institutes of Health Clinical Center, Bethesda, MD USA 20892-1182;
\(^b\)Sheikh Zayed Institute for Pediatric Surgical Innovation, Children’s National Medical Center, Washington, DC, USA 20010

ABSTRACT

Accurate segmentation of ovarian cancer metastases is clinically useful to evaluate tumor growth and determine follow-up treatment. We present a region-based level set algorithm with localization constraints to segment ovarian cancer metastases. Our approach is established on a representative region-based level set, Chan-Vese model, in which an active contour is driven by region competition. To reduce over-segmentation, we constrain the level set propagation within a narrow image band by embedding a dynamic localization function. The metastasis intensity prior is also estimated from image regions within the level set initialization. The localization function and intensity prior force the level set to stop at the desired metastasis boundaries. Our approach was validated on 19 ovarian cancer metastases with radiologist-labeled ground-truth on contrast-enhanced CT scans from 15 patients. The comparison between our algorithm and geodesic active contour indicated that the volume overlap was 75±10\% vs. 56±6\%, the Dice coefficient was 83±8\% vs. 63±8\%, and the average surface distance was 2.2±0.6mm vs. 4.4±0.9mm. Experimental results demonstrated that our algorithm outperformed traditional level set algorithms.

Keywords: Ovarian Cancer Metastasis, Tumor Segmentation, Region-based Level Set, Localization

1. INTRODUCTION

Clinical studies reveal that volume measurement provides the best indication of tumor response to treatment\(^1\). Accurate volume measurement demands reliable and automatic tumor segmentation. This is especially important for ovarian cancer metastases because 75\% of women with ovarian cancer already have metastases\(^2\). Due to its ability, unlike most other cancers, to spread throughout the peritoneum, ovarian cancer metastasis segmentation poses significant challenges. Many metastases are adjacent to the abdominal wall musculature, which has similar intensity to metastases (Fig. 1a). Thus, the boundaries between metastases and muscle are indistinct. Moreover, the metastases have a wide range of shapes, e.g., elongated and spherical.

Figure 1: Comparison of ovarian cancer metastasis segmentation results on the example image (a).

The level set algorithm\(^3\) has become popular for tumor segmentation\(^4,5,16\) because it can explicitly integrate image information into a PDE-framework and easily handle topology changes. It is generally classified into two categories: edge-based and region-based. The edge-based methods extract objects by localizing image edges. Fig. 1(b) shows the...
metastasis segmentation by using a geodesic active contour, an edge-based approach. One observes that the bottom part of the metastasis is missing because of image heterogeneity and the elongated tumor shape.

Instead of using local image gradients, region-based methods compute global image statistics and perform region competition to drive level sets. The under-segmentation issue in Fig. 1b can thus be resolved by using global image region information. The Chan-Vese model is a typical region-based level set formulation, in which a level set decomposes an image into foreground and background regions, identified by their mean intensity values. In their formulation, the level set stops at the object boundary that maximizes the mean intensity difference. However, the image is easily over-segmented as shown in Fig. 1c. One solution is to identify tumor regions by embedding multiple active contours to partition the image into several object regions, the so-called multi-phase/object level set. However, determining the number of objects prior to image segmentation still remains an open question. In addition, we are only interested in extracting tumors, and place less emphasis on segmenting other objects in the human body. Alternative approaches are to embed shape priors into the level set framework to constrain the level set propagation. Finding a common shape representation is extremely challenging because metastases are highly variable.

In this paper we propose a region-based level set with localization constraints to extract ovarian cancer metastases. The key contribution is the embedding of dynamic localization function and intensity prior information without object determination or shape learning. Level set is constrained by a localization function to propagate in a local way and avoid over-segmentation. On the other hand, our method can still preserve the advantages of the region-based level set, such as insensitivity to weak edges and elongated shapes. Fig. 1d shows our improved segmentation of one example metastasis. The validation on contrast-enhanced CT images from 15 patients also confirmed that our method could accurately extract metastases.

2. METHODOLOGY

In this section, we begin by introducing the Chan-Vese model and develop a region-based level set with localization constraints. We then give the implementation details based on the additive operator splitting (AOS) scheme.

2.1 Level Set Formulation

Given an image \( I : \Omega \rightarrow R \), metastasis segmentation aims to separate tumor regions \( \Omega_t \) and non-tumor regions \( \Omega_i \) via a level set function \( \phi \). Chan and Vese first designed a region-based level set method to partition image regions, described mathematically as

\[
E(\phi) = \int_{\Omega} \left( \lambda_t H(\phi)(I(x) - c_t)^2 + \lambda_i (1 - H(\phi))(I(x) - c_i)^2 + vH(\phi) \right) dx + \int_{\Omega} \mu \delta(\phi) |\nabla \phi| dx \quad (1)
\]

where \( \mu, v, \lambda_t, \) and \( \lambda_i \) are constant values to balance different terms in Eq. 1. \( c_t \) and \( c_i \) are the mean intensities of tumor and non-tumor regions. \( H \) is the Heaviside function, and \( \delta \) is the one-dimensional Dirac function,

\[
H(\phi) = \begin{cases} 
1 & \text{if } \phi \geq 0 \\
0 & \text{if } \phi < 0 
\end{cases}, \quad \delta(\phi) = \frac{d}{d\phi} H(\phi) \quad (2)
\]

Minimizing Eq. 1 forces the level set to propagate towards the boundaries that separate tumor and non-tumor regions with maximum mean value difference. The Chan-Vese method is also called a piecewise constant model since it uses the mean values \( c_t \) and \( c_i \) to represent objects and background. However, as demonstrated in Fig. 1c, the level set computed from Eq. 1 often over-segments because \( c_t \) and \( c_i \) are estimated from the entire image domain. Lankton only allows the level set to propagate within a fixed image region, so as to address over-segmentation. We follow this idea but develop a dynamic localization function to relax initialization requirements. Our function is dependent on the locations of the zero level set, and is given by

\[
B(x) = \begin{cases} 
1 & \text{if } |\phi(x)| \leq r \\
0 & \text{otherwise} 
\end{cases} \quad (3)
\]

where \( r \) is the width of active image regions in which the level set is permitted to propagate.
The task of tumor segmentation is often done in conjunction with tumor detection\textsuperscript{15}. The detection algorithm can predict the approximate tumor locations and provide an initial level set inside the tumor. Thus, tumor intensity prior information is directly computed from the image regions within the initial level set curve in our framework. Embedding the dynamic localization function and tumor intensity prior into Eq. 1 yields

\[
E(q) = \int_{\Omega} B(x) \left( \lambda_1 H(q)(I(x) - c_1)^2 + \lambda_2 (1 - H(q))(I(x) - c_2)^2 + \nu H(q) \right) dx \\
+ \int_{\Omega} \alpha B(x) H(q)(c_1 - c_m)^2 dx + \int_{\Omega} \mu \delta(q) \left| \nabla q \right| dx
\]  

Eq. 4 allows for an energy minimization by means of the gradient descent derived from the Euler-Lagrange equation.

\[
\partial_t q = \delta(q) B(x) \left( \lambda_2 (I(x) - c_2)^2 - \lambda_1 (I(x) - c_1)^2 - \alpha (c_1 - c_m)^2 - \nu \right) + \mu \delta(q) \text{div} \left( \frac{\nabla q}{\left| \nabla q \right|} \right)
\]  

Here, $c_m$ is the mean value prior of the metastasis, and $\alpha$ is the weight of this data term.

The mean values $c_1$ and $c_2$ in Eq. 5 are computed as

\[
c_1 = \frac{\int_{\Omega} B(x) \lambda_1(I(x)H(q) + \alpha c_m) dx}{\int_{\Omega} B(x)(\lambda_1 H(q) + \alpha) dx}, \quad c_2 = \frac{\int_{\Omega} B(x)(1 - H(q))I(x) dx}{\int_{\Omega} B(x)(1 - H(q)) dx}
\]

Level set propagation constrained by the localization function is similar to the narrow band method\textsuperscript{1}. However, we are focusing on local region competition through constraining mean value comparison within an image band, instead of reducing computational cost. The level set is designed to dynamically propagate in a local way. Therefore, image over-segmentation is efficiently controlled.

### 2.2 Implementation

We use the additive operator splitting (AOS) scheme developed by Weickert et al.\textsuperscript{10} to perform the numerical computation. The essential idea behind AOS is to decompose the multi-dimensional computation into efficient one-dimensional calculations with large time steps to propagate the level set. The final solution is the combination of all one-dimensional results.

To fit the AOS scheme, Eq. 5 is first converted into a mean-curvature evolution framework. This conversion can be deemed reliable as Zhao et al.\textsuperscript{11} proved that $\delta(q)$ and $\nabla q$ are interchangeable.

\[
\partial_t q = \delta(q) B(x) \left( \lambda_2 (I - c_2)^2 - \lambda_1 (I - c_1)^2 - \alpha (c_1 - c_m)^2 - \nu \right) + \mu \text{div} \left( \frac{\nabla q}{\left| \nabla q \right|} \right)
\]

Following the same derivation as Weickert and Kühne\textsuperscript{12}, the AOS scheme of Eq. 7 becomes

\[
q^{n+1} = \frac{1}{M} \sum_{i=1}^{N} (1 - \tau A_i(q^{n+1}))^{-1} \left( q^n + \frac{\delta(q) B(x)}{\mu} \left( \lambda_2 (I - c_2)^2 - \lambda_1 (I - c_1)^2 - \alpha (c_1 - c_m)^2 - \nu \right) \right)
\]

where $M$ is the number of image dimensions, and $\tau$ is the time step. $\mathbf{I}$ is the identity matrix and $\mathbf{A}_i$ is the matrix describing the interaction in the $l$ direction. Assuming that $i$ and $j$ represent two pixels, $\mathbf{A}_i$ is defined as

\[
a_{ij}^l = \begin{cases} 
\frac{\left| \nabla q \right|_{i}}{\left| \nabla q \right|_{i} + \left| \nabla q \right|_{j}} & j \in N_l(i) \\
\frac{M}{\sum_{k \in N_l(i)} \left| \nabla q \right|_{k} + \left| \nabla q \right|_{j}} & j = i \\
0 & \text{else}
\end{cases}
\]
where $N(i)$ denotes $i$’s neighborhood along the $l$ direction. Finally, Eq. 8 can be efficiently computed by using the Thomas algorithm\textsuperscript{18}, which yields our metastasis segmentation in Fig. 1d.

3. EXPERIMENTAL RESULTS

Our segmentation algorithm was evaluated on abdominal contrast-enhanced CT images from 15 patients. The slice thickness ranges from 2mm to 5mm. Retrospective analyses of these images were approved by our Institutional Review Board. Our algorithm segmented all 19 metastases attached to the liver or spleen from the selected CT images. Their mean (±st. dev.) size was 30.2±12.1mm.

![Fig. 2: Metastasis segmentation. Each row corresponds to a patient. The first column illustrates the initial level set (spheres in 3D) represented by green circles in the current image plane, where the sphere center is determined by our automated detection algorithm\textsuperscript{15} and the radius in Eq. 3 is fixed to 4 pixels in all experiments. The second and third columns show the corresponding metastasis segmentation in red from geodesic active contour (GAC) and our algorithm. The fourth column gives the 3D visualization of the segmented metastases (red), as well as liver (green) and spleen (blue). The liver and spleen were segmented automatically using the method by Linguraru et al.\textsuperscript{17}.](image-url)

The left image in the first row of Fig. 2 shows a patient image with an elongated metastasis. Geodesic active contour (GAC) under-segments the metastasis in the second image because the level set is controlled by the mean curvature evolution and GAC is incapable of processing the elongated shape. In contrast, our algorithm can successfully extract the entire metastasis regions in the third image. The fourth image gives the 3D visualization of the segmented metastasis in red. The CT image in the second row of Fig. 2 is low resolution, with a slice thickness of 5mm. The metastasis also has weak boundaries, with muscles in the left side of the image. Consequently, GAC produces over-segmentation in this case, while our algorithm accurately identifies the entire metastasis. In the third row, the metastasis size is smaller than the previous two examples. Meanwhile, its intensity values are higher because of metallic streak artifact. GAC causes over-segmentation in the vertical direction while under-segmentation along other directions. Our algorithm is robust to small metastases and finds the actual metastasis boundaries. The last row in Fig. 2 illustrates the segmentation results on
a patient with three metastases. Two of them are attached to the liver, and the remaining one to the spleen. In this case, the results from GAC and our algorithm are comparable. However, the segmentation of the metastasis in the bottom image depicts that our algorithm generates less under-segmentation than GAC.

An experienced radiologist manually labeled the 19 metastases in our datasets, which were used as the ground-truth against our automatic segmentation results and GAC results. Six metrics used in our earlier work were chosen to quantitatively evaluate the segmentation accuracy. These are 1) volumetric overlap (VO); 2) relative absolute volume difference (VD); 3) Dice coefficient (DC); 4) average symmetric absolute surface distance (ASD), the distance between boundary voxels from the segmented metastases to the reference, and vice versa; 5) symmetric root mean square surface distance (SSD); 6) maximum symmetric absolute surface distance (MSD). Table 1 gives detailed quantitative validation on 19 metastasis segmentation results by comparing our method to the geodesic active contour (GAC).

Table 1. Comparison between our segmentation algorithm and GAC on 19 metastases.

<table>
<thead>
<tr>
<th>Method</th>
<th>VO (%)</th>
<th>VD (%)</th>
<th>DC (%)</th>
<th>ASD (mm)</th>
<th>SSD (mm)</th>
<th>MSD (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>GAC</td>
<td>56±6</td>
<td>28±16</td>
<td>63±8.0</td>
<td>4.4±0.9</td>
<td>5.9±1.0</td>
<td>20±6.1</td>
</tr>
<tr>
<td>Ours</td>
<td>75±10</td>
<td>17±9.6</td>
<td>83±8.4</td>
<td>2.2±0.6</td>
<td>2.9±0.6</td>
<td>10±2.1</td>
</tr>
</tbody>
</table>

4. SUMMARY

In this paper, we described a region-based level set algorithm with localization constraints to segment ovarian cancer metastases. Metastasis segmentation manifests significant challenges. They frequently spread to the peritoneum and many organs including the liver and spleen. Metastases are also adjacent to the abdominal wall musculature, which has similar intensity to the metastases. Moreover, metastases present a wide range of shapes. These difficulties hinder the research progress on this topic. To the best of our knowledge, the algorithm described in this paper is the first solution to this problem.

Our algorithm combines advantages of edge-based and region-based level set approaches. Similar to region-based method, it is insensitive to weak boundaries and elongated shapes. However, our method differs from techniques that estimate region statistics from the entire image domain. The level set in our method is driven by local region statistics computed within a dynamic narrow band to resemble edge-based algorithms. Therefore, tumor over-segmentation is efficiently controlled. The beneficial properties of our algorithm are achieved by embedding the localization function and the tumor intensity prior into the level set evolution. Our algorithm was validated on 19 metastases from 15 patients in both low and high resolution CT images. The validation results showed that our method outperformed geodesic active contour. The Dice coefficient of metastasis segmentation was improved from 63% to 83%, while the average surface distance error was reduced from 4.4mm to 2.2mm. The method is fully automatic and, in combination with our previous work, supports both the detection and segmentation of ovarian metastases in the abdomen.

ACKNOWLEDGEMENTS

This work was supported by the Intramural Research Program of the National Institutes of Health, Clinical Center.

REFERENCES