

A Chance-Constrained Programming Level Set method for longitudinal segmentation of lung tumors in CT

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Abstract—This paper presents a novel stochastic level set method for the longitudinal tracking of lung tumors in computed tomography (CT). The proposed model addresses the limitations of registration based and segmentation based methods for longitudinal tumor tracking. It combines the advantages of each approach using a new probabilistic framework, namely Chance-Constrained Programming (CCP). Lung tumors can shrink or grow over time, which can be reflected in large changes of shape, appearance and volume in CT images. Traditional level set methods with a priori knowledge about shape are not suitable since the tumors are undergoing random and large changes in shape. Our CCP level set model allows to introduce a flexible prior to track structures with a highly variable shape by permitting a constraint violation of the prior up to a specified probability level. The chance constraints are computed from two given points by the user or from segmented tumors from a reference image. The reference image can be one of the images studied or an external template. We present a numerical scheme to approximate the solution of the proposed model and apply it to track lung tumors in CT. Finally, we compare our approach with a Bayesian level set. The CCP level set model gives the best results: it is more coherent with the manual segmentation.

I. INTRODUCTION

In this work we aim to estimate longitudinal tumor volumes to compute accurately the change in tumor volume. Among the large number of methods for estimating tumor change or tumor tracking, the following three approaches are most popular: (1) Analyzing the difference of images: this approach consists in analyzing the registration error between two images. One image is considered as the reference image and the second one is registered toward this reference. The difference between the registered image and the reference image allows detecting tumor changes [7], [5]; (2) Analyzing the deformation field: as in the previous approach the registration of the images to a common reference is required. However, in this approach instead of working with the registration, the deformation field is analyzed to define tumor changes [12], [10]; (3) Sequential segmentation: this is the standard method to detect tumor change. The segmentation of the tumors is followed by a comparison of the segmented data to evaluate the tumor changes over time [6], [9]. The two first approaches have the limitations inherent to registration methods. Indeed, spatial normalization of images in the

presence of pathologies is still a very challenging problem. The registration algorithms are often based on the assumption of topological equivalence between the fixed and the mobile images. The presence of tumors in one image and not in the second one violates this assumption. Furthermore, the use of non-rigid registration can deform the tumor so much that the changes in the tumor cannot be detected in the difference map of images. The third approach is hampered by the difficulty to extract accurate target volumes. The estimation of tumor volume is still a very challenging problem.

While there are many studies of longitudinal tumor or lesion tracking in brain diseases such as Multiple Sclerosis (MS), there are few studies related to lung tumors. The lack of longitudinal tracking studies of lung tumors is due to the complexity of the deformation that the lung is undergoing during respiration, and the difference between the physical properties of the tumors and the lung tissue. Furthermore, the significant change of the tumor shape and appearance during long periods makes longitudinal tracking of lung tumors more challenging. In longitudinal tracking of lung tumors much effort has been dedicated to the development of techniques for segmentation, a follow up of the segmented data through time is then performed to detect tumor changes.

In this paper we introduce a method for the longitudinal tracking of tumors that combines the advantages of registration based and segmentation based approaches. Indeed the registration error is integrated in a temporal segmentation process using a new probabilistic framework. We propose a stochastic active model to incorporate prior knowledge about the evolution of the tumors from the previous CT images to constrain the tracking process in the current image. The model does not require an initialization at each time point, only information given by the user from a reference image is needed. The information given by the user can be a segmentation of the tumor in the reference image or only two points, one point given inside the tumor and the second point on the tumor surface. This input is used as key points to construct a probabilistic function to constrain the evolution of level sets inside the image. One important aspect of our stochastic active contour is that it is flexible to allow the level sets to fit the boundary of the target tumor.

The first level set method with prior knowledge about shape was introduced by Leventon et al. [8]. Recent improvements of this approach were proposed in [2]. These methods are more adapted to segment structures with small changes in shape. However, the tumor shape does not at all respect this property: the same tumor can have different shapes between two longitudinal acquisitions. Tumors can

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shrink or grow over time, which can be reflected in CT-images in large changes of shape, appearance and volume. All these approaches use a Bayesian framework to constrain the evolution of the level sets. Our approach introduces a new active contour using a different probabilistic framework, namely chance constraints [3]. Chance constraints programming (CCP) permits constraint violation up to a specified limit and ensures explicitly that the constraints will hold even with high a probability. In contrast, the Bayesian models do not ensure this latter characteristic of CCP models. They take into account information obtained through sampling and then formulate a decision problem. More generally, optimization under CCP is the unique probabilistic framework that ensures that constraints will hold with a high probability. The proposed CCP level set method allows to incorporate a flexible prior using local and global confidence maps to weigh the evolution of the level set. The local confidence map corresponds to a voxel-wise registration error between the reference image and the target. The reference image is used to measure the evolution of the tumor in the studied images compared to this reference, it can be one of the images studied or an external template. The second confidence map corresponds to a α -quantile that regulates globally the evolution of the level set in the image. The whole process of our method is summarized into the following three steps: (1) estimate the position and shape of the tumors in the reference image; (2) construct probabilistic constraints from the position estimated at the first step; (3) extract the tumors at each time point using the constraint defined in the second step. In Section II, we will give more details about each step and how to use it for longitudinal tracking in CT images. In Section III we apply our approach on CT data.

II. STOCHASTIC LONGITUDINAL SEGMENTATION

A. Chance-constrained level set method

While the level set method introduces regularization to smooth the deformation and to deal with noise, it does not introduce a bias towards the target structure. Bayesian models were proposed in the literature to incorporate prior knowledge about the target structure to constrain the evolution of the level set [8]. These models are adapted to segment an object with well defined shape. However the tumor shape is undergoing large changes over long time periods and it is difficult to define a model that describes the evolution of tumors over time from image information. This makes the definition of an accurate prior for tumor tracking a very challenging problem that has led us to introduce chance constraints. Our approach consists in minimizing the Chan and Vese functional \mathcal{V} , see [1], [11], in the probabilistic admissible space: $\mathcal{A}_{1-\alpha} = \{\phi : P(x, \phi) > 1 - \alpha, \text{ for almost all } x \in \Omega\}$, where P is a probabilistic constraint that introduces a priori information about the target from a given prior defined by the user from the reference image. For high values of the probabilistic constraint the prior introduced by this function constrains the tracking process strongly whereas for small values the constraint is very weak. The α -quantile ($0 < \alpha < 1$) regulates the

influence of these probabilistic constraints in the tracking process. In Section III, we will see that α can be chosen in a large range for tumor tracking in CT. In the next section we will present the methods used to construct the probabilistic constraints and how to apply it to tumor tracking. This model is flexible and adapted to follow tumors. The level set evolution is monitored by the local and global confidence maps that we have defined in the previous section.

We formulate our optimization approach using the penalization method, which is well adapted to stochastic optimization. The basic idea of the penalization method is to transform the constrained optimization problem into an unconstrained optimization problem:

$$E(\phi, c_1, c_2) = \mathcal{V}(\phi, c_1, c_2) + \rho \int_{\Omega} \max(0, 1 - \alpha - P(x, \phi))^2 \delta_{\epsilon}(\phi) dx, \quad (1)$$

where $\rho > 0$ is a penalty parameter¹; the factor term δ_{ϵ} allows us to restrict the shape prior within the region of interest. As usual, we use an Euler-Lagrange formulation to solve this optimization problem, for details see [11].

B. Design of the probabilistic constraints

In this section we describe the method used to construct the probabilistic constraints that guide the evolution of our stochastic active contour. The method consists of the two following steps: (1) construct a deterministic prior; (2) construct the probabilistic constraints. In the first step we extract prior from the reference image. This prior can be a segmentation of the tumors from this reference image. The segmentation of each tumor corresponds to a surface which approximates the boundary of this tumor. The segmentation can be replaced by two points given by the user for each tumor, the first point is required to be inside the tumor and the second point on the tumor surface. These two points allow us to approximate the tumor boundary with a closed surface centered at the point chosen inside the tumor and with a radius defined by the second point. At the end of this first step we construct a set of surfaces, where each surface approximates the boundary of one tumor in the reference image.

The aim of the second step is to build from these surfaces probability maps that we use to constrain the evolution of the level. We propose to use chance constraints [3], these constraints being defined from a set of random constraints. Each surface allows us to construct a component g_p of the random constraint such that the level set function ϕ satisfies:

$$g_p(x, \phi, \Lambda) \leq c_p, p = 1, \dots, n_t \quad (2)$$

where n_t is the number of tumors detected in the reference image and $c_p, p = 1, \dots, n_t$ are real constants; Λ is a random vector, with a multi-variate normal distribution, describing the uncertainty about the localization and the shape of the tumor boundary in the current image. We can picture each component of the random constraint as a surface that oscillates around the boundary of one tumor in the reference

¹Note that if $\phi \in \mathcal{A}_{1-\alpha}$, the penalty is null whereas for $\phi \notin \mathcal{A}_{1-\alpha}$ a second term is added to the functional \mathcal{V} to introduce a penalty for violating the constraint $\phi \in \mathcal{A}_{1-\alpha}$.

image. The oscillations are monitored by the random vector Λ , the dimension of Λ corresponds to the number of tumors in the reference image and the covariance matrix is estimated from the registration errors of the reference image and each target image. The registration error is computed before the evolution of the levels and is used as confidence map in the stochastic term. Locally, the level set follows the target image in regions with a high voxel-wise registration error while it follows the prior in regions with low voxel-wise registration errors. We give here an example of the random constraints that we will use in our experiments. We consider the case of only one tumor ($n_t = 1$) and $c_p = 0$; for this tumor we generate from the user input a surface \mathcal{S} that approximates the tumor boundary in the reference image. Let ϕ be defined as the signed distance associated with the surface \mathcal{S} . We consider the following random constraint:

$$g(x, \phi, \Lambda) = e(x) \Lambda + (\phi(x) - \tilde{\phi}(x))^2 \leq 0. \quad (3)$$

where e is the registration error and Λ is a random variable with a Gaussian distribution with the variance σ^2 . Consequently the random variable $\Upsilon = e\Lambda$ has a Gaussian distribution with the variance $(e\sigma)^2$ and with the normal distribution p_Υ .

The global confidence map corresponds to a α -quantile such that:

$$P(x, \phi) = \mathbb{P}\left(g_p(x, \phi, \Lambda) \leq c_p, p = 1, \dots, n_t\right) > 1 - \alpha. \quad (4)$$

The α -quantile is used to monitor the evolution of the level set according to the random constraints (2): the model allows the active contour to evolve towards regions that violate the constraint for a small amount of realizations when no alternative solution is found. For a large α the level set follows the data while for small α the level set follows the prior. The α -quantile is given by the user to introduce his knowledge about the evolution of tumors in the studied images. This parameter can be also estimated from the registration error: when the registration error is small we can introduce a strong prior from the reference image to constrain the tracking process. Moreover, we will show in Section III that the parameter α can be chosen in a large range. For the constraint (3), the estimation of the probabilistic constraint and its gradient are computed analytically, for details see [11]. Fig. 1 shows examples of the probabilistic constraints. However, in the case of more than one tumor or when several random constraints are needed, the probabilistic constraint can be intractable analytically. The authors in [3] present a Monte Carlo method adapted to this situation.

C. Chance-Constrained Programming vs Bayesian model

In the previous section we introduced a new probabilistic framework to constrain the level set evolution, namely the chance-constrained level set method. In this section we compare this approach with the traditional approach of introducing shape priors in the level set formulation: the Bayesian model. In the formulation (3), we introduce as a probabilistic constraint that the similarity between ϕ and $\tilde{\phi}$ is superior to a given quantile. In the Bayesian formulation the prior is

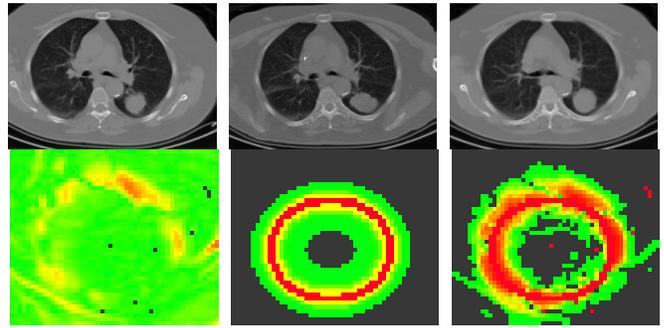


Fig. 1. Confidence map, only one slice is shown but the method is applied in 3D. First row, left: image acquired in 2007 (mobile image); center: image acquired in 2008; right: registered image using rigid transformation. Second row, the left panel shows the registration error (ROI on the tumor); the center panel shows the probabilistic constraint computed without registration error; the right panel shows the confidence map computed using the registration error. The red color corresponds to high values, the yellow to medium values, and green to low values.

introduced through sampling and then a decision problem is formulated. The model is formulated as a minimization problem of a global energy composed of two terms. The first term corresponds to a deformation energy for a standard region based level set method and the second term introduces the shape prior:

$$E_b(\phi, c_1, c_2) = \mathcal{V}(\phi, c_1, c_2) + \frac{\gamma}{2\sigma^2} \int_{\Omega} (\phi - \tilde{\phi})^2 \delta_{\epsilon}(\phi) dx,$$

where γ is a weight parameter on the prior. We will see in the result section how this parameter affects the segmentation results in the Bayesian and CCP level set methods. Details about the estimation of the minimizer are given in [11].

III. RESULTS

The data are composed of two CT data sets from two patients and each data set is composed of at least two images acquired at different time points: for patient 1, data were acquired on 02/2007 and 03/2008 and for patient 2 on 06/11/2007, 05/14/2008, and 07/24/2008. The patients held their breath at full inspiration during the acquisition. The resolution of the data is $1.172 \times 1.172 \times 5$ mm and we take into account the anisotropy of voxel dimensions in the level set propagation by using a weighted distance [4].

To construct the random constraints (3) for the CCP model (1), we have used a rigid registration method since non-rigid registration deforms the tumor so much that changes in the tumor are not well detected in the difference image. Fig. 2-center shows a comparison between the manual segmentation and the results obtained with our CCP level set method using different values of α , the best results were obtained with $0.6 < \alpha < 0.85$. This shows also that the quantile α can be chosen for CT longitudinal segmentation in a large range. For α smaller than 0.6 the probabilistic constraint constrains strongly the segmentation process and as we can see in Fig. 2 the results are very close to the level set prior, whereas for α superior to 0.8 the constraint is very weak, therefore the propagation leaks outside the region of interest (localization of the tumor). The manual segmentation

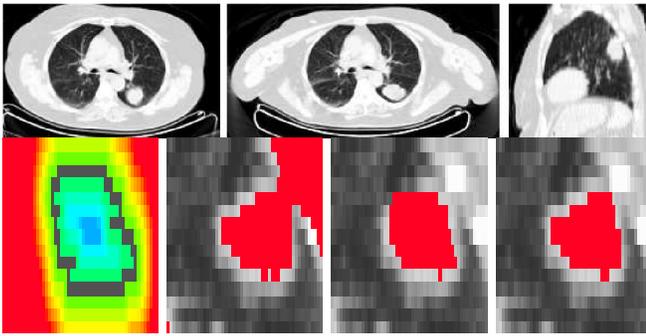


Fig. 2. 3D longitudinal segmentation of tumors with our CCP level set method. First row, left: CT image acquired in 2007 (axial view); center and right panels show axial and sagittal views, respectively, of the CT image acquired in 2008. Second row, right panel: the signed distance from the initial contour (the prior ϕ), the level zero of this distance corresponds to the black contour; the second panel shows the results obtained with $\alpha = 1$ (no prior); the third panel corresponds to $\alpha = 0.47$ (very strong prior); the right panel corresponds to $\alpha = 0.7$ (medium prior).

Patient	Dice similarity		Sensitivity		Specificity	
	CCP	BAY	CCP	BAY	CCP	BAY
1	0.898	0.851	0.815	0.774	1.000	0.945
2	0.875	0.826	0.784	0.705	0.991	0.996

TABLE I

COMPARISON OF THE CCP AND THE BAYESIAN MODEL

of tumors is performed by a medical expert by hand drawing on every 2D slice and is subjective. Therefore, the manual segmentation is not an “absolute” ground truth. In Table I, we compare the results obtained with our CCP level set method and the Bayesian model using the CT data for the two patients. We evaluate the effect of the weight on the prior for each approach: γ for the Bayesian model and α for the CCP model (see Fig. 3). The CCP model gives the best results in terms of Dice measure. Furthermore, the Bayesian model suddenly leaks outside the tumor when a weak or medium weight on the prior is used. This can be explained by the fact that the prior in the CCP model is introduced as an explicit constraint which allows us to constrain the segmentation more efficiently. However, for the two patients considered in this study, a strong prior leads to an underestimation of the area of the tumor for both models.

IV. DISCUSSION AND CONCLUSION

We present a novel approach for the longitudinal tracking of tumor in CT images. Our approach combines the registration and segmentation to derive a model that benefits from the advantages of each approach. We introduce chance constraints to incorporate priors for the shape and localization of the tumors. The prior is computed from the registration error and the user input. Our results illustrate the efficiency and the flexibility of our approach: the method is adapted to large changes in tumor shape and the user can introduce priors easily from different sources. The prior is used to build chance constraints to constrain the evolution of the level set in the CT images. The CCP makes it possible to introduce an explicit constraint and permits the violation of the constraints up to a specified level. However, the

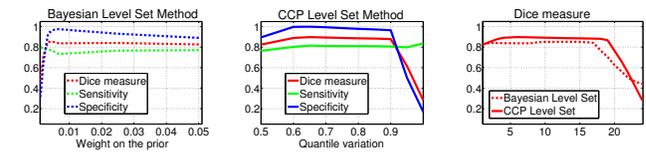


Fig. 3. CCP level set method versus Bayesian level set model. The left and panel show the effect of the variation on the prior parameters for CCP (parameter: quantile α) and Bayesian (parameter: weight on the prior γ) level set methods on the evaluation measures: Dice similarity, Sensitivity, and Specificity; the right panel shows the variation of the Dice measure for the CCP and Bayesian level set methods versus the number of experiments for different values of γ and α .

constraints can be hold even at a high probability. On the one hand, the deterministic approach is too rigid to allow constraint violations. Therefore a solution that satisfies the constraint everywhere except for a very small set of image points will be rejected even when this solution gives the best minimizer except for this insignificant set of points. On the other hand the Bayesian models which introduce priors through sampling and then formulate a decision problem do not ensure that the constraint holds at a high probability. This makes chance-constrained programming a powerful and unique tool for optimization problems under uncertainty. CCP is therefore very suitable for medical image analysis where uncertainties and risk are omnipresent.

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