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Reconstruction of 4D-CT from a Single Free-Breathing 3D-CT by Spatial-Temporal Image Registration

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Abstract

In the radiation therapy of lung cancer, a free-breathing 3D-CT image is usually acquired in the treatment day for image-guided patient setup, by registering with the free-breathing 3D-CT image acquired in the planning day. In this way, the optimal dose plan computed in the planning day can be transferred onto the treatment day for cancer radiotherapy. However, patient setup based on the simple registration of the free-breathing 3D-CT images of the planning and the treatment days may mislead the radiotherapy, since the free-breathing 3D-CT is actually the mixed-phase image, with different slices often acquired from different respiratory phases. Moreover, a 4D-CT that is generally acquired in the planning day for improvement of dose planning is often ignored for guiding patient setup in the treatment day. To overcome these limitations, we present a novel two-step method to reconstruct the 4D-CT from a single free-breathing 3D-CT of the treatment day, by utilizing the 4D-CT model built in the planning day. Specifically, in the first step, we proposed a new spatial-temporal registration algorithm to align all phase images of the 4D-CT acquired in the planning day, for building a 4D-CT model with temporal correspondences established among all respiratory phases. In the second step, we first determine the optimal phase for each slice of the free-breathing (mixed-phase) 3D-CT of the treatment day by comparing with the 4D-CT of the planning day and thus obtain a sequence of partial 3D-CT images for the treatment day, each with only the incomplete image information in certain slices; and then we reconstruct a complete 4D-CT for the treatment day by warping the 4D-CT of the planning day (with complete information) to the sequence of partial 3D-CT images of the treatment day, under the guidance of the 4D-CT model built in the planning day. We have comprehensively evaluated our 4D-CT model building algorithm on a public lung image database, achieving the best registration accuracy over all other state-of-the-art methods. Also, we have validated our proposed 4D-CT reconstruction algorithm on the simulated free-breathing data, obtaining very promising 4D-CT reconstruction results.

Keywords

4D-CT; spatial-temporal registration; radiation therapy; lung cancer

1 Introduction

A major goal of image-guided radiation therapy is to deliver the optimal radiation dose to the tumor area, while minimizing the dose to the nearby normal structures. However, patient motions, such as respiratory and muscular motion, can cause significant artifacts during 3D-CT imaging. Recently, 4D-CT imaging, with respiration phase as the fourth dimension, has been developed and becomes more and more popular since it can capture 3D-CT in each

respiration phase. Importantly, it has been shown that 4D-CT imaging helps reduce the artifacts from patient motion and thus leads to a more accurate delineation of tumor and other critical structures.

For treating lung cancer with radiation therapy, generally a 4D-CT and a free-breathing 3D-CT are acquired in the planning day. With these images, physician can manually delineate the outlines of lung, heart, tumor, and other critical structures from the free-breathing 3D-CT, or sometimes also from the inhalation and exhalation images of the 4D-CT. With these manual delineations, the optimal dose plan can be computed to maximize dose in cancer and minimize dose in nearby normal structures. In the treatment day, a free-breathing 3D-CT image is typically acquired for image-guided patient setup. Specifically, the free-breathing 3D-CT acquired in the planning day is aligned with the free-breathing 3D-CT acquired in the treatment day, i.e., through the registration of their segmented bones. Thus, the dose plan defined in the planning day can be transferred onto the treatment day for cancer radiotherapy.

However, there are two major limitations in the current lung cancer treatment pipeline. First, the 4D information available in the 4D-CT of the planning day is not well utilized for transferring of the dose plan onto the treatment day. Since the 4D-CT takes much longer scanning time and some patients have the difficulty in breath holding, only a free-breathing 3D-CT is usually acquired in the treatment day. Therefore, the dose plan in the treatment day is simply determined by registering its free-breathing 3D-CT with that in the planning day, without considering the useful information available in the 4D-CT of the planning day.

Second, it is difficult to register two free-breathing 3D-CT images, and their inaccurate registration could immediately undermine the dose plan in the treatment day. The registration challenge mainly comes from the inconsistent image information included in the two free-breathing 3D-CT images, since their corresponding slices could be acquired from the completely different respiratory phases in the planning and treatment days. Also, since the free-breathing 3D-CT is actually a mixed-phase image that never exists in the reality, it could provide misleading information to the observers. For example, as demonstrated in [1, 2], a moving spherical object could be acquired with different shapes under the free-breathing condition, depending on which phase the scanner starts to acquire the images.

In this paper, we propose a novel two-step method to overcome these two limitations by reconstructing a new 4D-CT from a single free-breathing 3D-CT for the treatment day, with the guidance from the 4D-CT model built in the planning day. Thus, the dose plan in the treatment day can be better determined based on the new reconstructed 4D-CT in the treatment day, rather than the free-breathing 3D-CT.

In the first step of our method (planning day), we develop a new spatial-temporal registration algorithm to simultaneously register all phase images of the 4D-CT acquired in the planning day, for building a 4D-CT model. Specifically, rather than equally calculating the correspondence for each image point, we propose to hierarchically select key points in each phase image and then let them drive the initial registration by robust feature matching. Also, by taking advantage of key points, we further determine their temporal correspondences across all phase images of the 4D-CT by defining a set of artificial temporal fibers to connect them along the respiratory phases. After registering all phase images, a 4D-CT model can be built to guide the reconstruction of a new 4D-CT in the treatment day for the next step.

In the second step of our method (treatment day), a new 4D-CT in the treatment day will be reconstructed from a free-breathing 3D-CT image by mapping the 4D-CT of the planning day to the treatment day. Specifically, we first determine an optimal phase for each slice of

the free-breathing (mixed-phase) 3D-CT of the treatment day by comparing with various slices in the 4D-CT of the planning day and thus obtain a sequence of partial 3D-CT images in the treatment day, with each new 3D-CT image having only the partial image information in certain slices. Then, we reconstruct a new 4D-CT for the treatment day by warping the 4D-CT of the planning day to the sequence of partial 3D-CT images of the treatment day, with the guidance from the 4D-CT model built in the planning day.

Each of the two above-described steps has been evaluated in our experiments. Specifically, our spatial-temporal registration algorithm in the first step has been tested on a dataset with ten lung 4D-CT images [3], each having a set of manually-delineated landmarks in both selected and all phase images. Our algorithm achieves the best registration accuracy, compared to the other start-of-the-art deformable registration algorithms, including diffeomorphic Demons [4] and a recently-published B-splines based 4D registration algorithm [5]. Our 4D-CT reconstruction algorithm in the second step has been evaluated on a simulated free-breathing dataset, indicating its excellent performance in reconstructing 4D-CT from a single free-breathing 3D-CT.

2 Method

The goal of our method is to reconstruct a 4D-CT $\mathbf{Q} = \{Q_s | s = 1, \dots, N\}$ with N phases for the treatment day, based on a single free-breathing 3D-CT image I taken in the treatment day, and also to build a 4D-CT model from the planning 4D-CT $\mathbf{P} = \{P_s | s = 1, \dots, N\}$ to guide the described reconstruction. Our whole method consists of two steps: (1) build a 4D-CT model by estimating deformation fields of all phase images in the planning day to a reference space R , i.e., $\mathbf{F} = \{f_s(x) | x \in \Omega_{R \rightarrow P_s}, s = 1, \dots, N\}$; and (2) reconstruct the 4D-CT $\mathbf{Q}$ for the treatment day by utilizing the 4D-CT model built in the planning day.

Fig. 1 gives an overview of our method, and also explains the difficulty in registration of the free-breathing 3D-CT images. For simplicity and easy explanation, we use an example of face expression scanning, instead of lung scanning, and also assume only two phases, smiling and angry phases, in the whole cycle of face expression, as shown in Fig. 1(a). It can be observed that the shapes of mouth and eyebrows are key to distinguish between the smiling and angry phases. Assume that a subject's face turns from smile to anger during the image acquisition, which can be used to simulate the effect of respiration in the lung imaging. Thus, the top half face (i.e., the eyes and eyebrows) can be scanned with smiling expression, while the bottom half face (i.e., the mouth) can be scanned with the angry expression. As the result, a mixed-expression face is obtained in Fig. 1(d); note that this half smiling and half angry expression may never happen in the reality. To simulate the possible shape changes during acquisition, we also simulate some local distortions around eyes (i.e., deformed from ellipse to circle) and mouth (i.e., deformed from close to open), as shown in red and blue in Fig. 1(d), respectively. It is worth noting that the direct registration of this mixed-expression face with the smile and angry phase images (in the planning day) will not provide a reasonable 4D-CT reconstruction result as shown in Fig. 1(e), since the interlaced phases in the mixed-expression image could provide misleading information.

To overcome this difficulty, we first build a 4D-CT model in the planning day by a robust spatial-temporal registration algorithm which we will explain later. As shown in Fig. 2(c), we first determine the phase for each slice of the free-breathing image by looking for the best matched slice in the corresponding phase image of the 4D-CT. In the meanwhile, the neighboring slices in the free-breathing image of the treatment day are required to be identified with similar phases. Thus, the whole free-breathing image can be de-interlaced into several 3D-CT images, denoted as $\mathbf{D} = \{D_s | s = 1, \dots, N\}$, while the image information in each D_s is not complete (see Fig. 1(c)), i.e., mouth and eyes are missing in the smile and

angry phases, respectively. After that, the spatial deformation fields $\mathbf{G} = \{g_s(x) | x \in \Omega_{P_s \rightarrow D_s}, s = 1, \dots, N\}$ between the 4D-CT in the planning day and the image sequence $\{D_s\}$ can be estimated in two ways. (1) For the slices with image content in D_s , their correspondences can be determined with P_s directly. (2) For other missing slices in D_s , their correspondences can be compensated from other phase images according to the 4D-CT model built in the planning day. For the face example, the de-interlaced results of the free-breathing image and the final reconstructed 4D-CT in the treatment day are shown in Figs. 1(c) and (b), respectively. It can be seen that the final reconstruction results are reasonable (i.e., the smiling face is still the smiling face and the angry face is still the angry face) and the local distortions around the mouth and eyebrows are well preserved in each phase.

In the following, we first present our spatial-temporal registration algorithm for building the 4D-CT model in the planning day. Then, we detail an algorithm for reconstruction of a new 4D-CT from a free-breathing image in the treatment day.

4D-CT Model in the Planning Day

Given the 4D-CT image $\mathbf{P}$ in the planning day, the 4D-CT model can be built by aligning all phase images P_s to a reference image R (i.e., the maximum inhale phase image used in this paper) by estimating the deformation fields $\{f_s\}$. Bending energy [6], denoted as $L_s(f_s)$, is used in this paper as a smoothness term for regularization of deformation field f_s , thus TPS can be used to efficiently compute the optimal f_s with minimal bending energy.

Different from other intensity-based registration methods [4, 5, 7], we propose to use the attribute vector as the morphological signature of each image point for reliable correspondence detection. Therefore, each lung CT image is first segmented into lung, bone, and body regions by [8]. Furthermore, we use the multi-scale Hessian filter [9] to delineate the tiny vessels within lung, in order to improve the registration for the vessels. After that, the attribute vector $\tilde{a}(x)$ is calculated at each location x , to include image intensity, Canny edge response, and geometric moments of structure labels (i.e., lung, bone, body, and vessel). By setting the threshold on these attributes vectors and gradually relaxing the selection criteria, a set of key points $\mathbf{X}_s = \{x_s^j | j = 1, \dots, M_s\}$ (where M_s is the overall number of key points in each P_s) can be hierarchically selected in P_s . These key points are generally locating at salient areas in the CT image, i.e., the green points in Fig. 2. Also, we can compute the attribute vectors for the reference image R and thus obtain the key points $\mathbf{Y} = \{y^i | i = 1, \dots, W\}$ in the reference space (i.e., the red points in Fig. 2).

Inspired by [10], the shape of each phase image P_s and the reference image R can be represented by its key points $\mathbf{X}_s$ and $\mathbf{Y}$. Each key point x_s^j in one phase image P_s can be considered as a random variable drawn from a Gaussian mixture model (GMM) with its centers as the deformed shape $f_s(\mathbf{Y})$ in P_s . Next, we introduce the hidden variables $m_s^{i,j} \in \{1, \dots, W\}$ (where W is the number of reference key points) to indicate the spatial assignment of a specific GMM center y^i in generating x_s^j . Therefore, the probability density function of x_s^j can be given by:

$$P(x_s^j | m_s^{i,j}, f_s(y^i)) = \mathcal{N}(x_s^j | \mu, \Sigma) \propto \exp \left\{ -\frac{\|x_s^j - f_s(y^i)\|^2}{\sigma^2} \right\} \quad (1)$$

where $\mu = f_s(y^i)$ and $\Sigma = \sigma^2 \cdot Id_{W \times W}$ denote the mean and the covariance matrix of the normal distribution $\mathcal{N}(x_s^j; \mu, \Sigma)$, respectively. $Id_{W \times W}$ denotes the $W \times W$ identity matrix. For sake of simplicity, the isotropic covariance matrix Σ is assumed here.

The appearance information of key points x_s^j and y^i are represented by their corresponding attribute vectors $\vec{a}(x_s^j)$ and $\vec{a}(y^i)$, which embed rich anatomical information from the neighborhood. Given the association $m_s^{i,j}$ between x_s^j and y^i , the attribute vector $\vec{a}(x_s^j)$ can also be regarded as the random variable generated from a GMM with its centers as the collection of attributes $\{\vec{a}(f_s(y^i))\}$. Then, given f_s , y^i , and the corresponding assignment $m_s^{i,j}$, the conditional probability of attribute vector $\vec{a}(x_s^j)$ is defined as:

$$P(\vec{a}(x_s^j) | x_s^j, m_s^{i,j}, f_s(y^i)) = \mathcal{N}(\vec{a}(x_s^j); \vec{a}(f_s(y^i)), \tau^2) \propto \exp \left\{ -\frac{\|\vec{a}(x_s^j) - \vec{a}(f_s(y^i))\|^2}{\tau^2} \right\} \quad (2)$$

where we assume elements in attribute vector are independent and have the same variance τ .

Given the assignment $m_s^{i,j}$ and f_s , the conditional probability of $(x_s^j, \vec{a}(x_s^j))$ can be formulated as:

$$P(x_s^j, \vec{a}(x_s^j) | m_s^{i,j}, f_s(y^i)) = e^{-\eta(x_s^j, f_s(y^i))}, \quad \eta(x_s^j, f_s(y^i)) = \frac{\|x_s^j - f_s(y^i)\|^2}{\sigma^2} + \frac{\|\vec{a}(x_s^j) - \vec{a}(f_s(y^i))\|^2}{\tau^2} \quad (3)$$

In our registration method, we achieve spatial-temporal correspondence in the following way: (1) The deformation field f_s is steered by the correspondences between $\mathbf{Y}$ and $\mathbf{X}_s$, and other non-key points will only follow the deformation of the nearby key points; (2) The temporal continuity constraint is performed based on the deformed position $f_s(y^i)$ in all phase images. Thus, for each y^i , its deformed position in the domain of each P_s along the respiratory phase s , denoted as $\phi_i = \{f_s(y^i) | s = 1, \dots, N\}$, can be regarded as a temporal fiber (see the blue dash curves in Fig. 2), which can be used to enforce the temporal continuity along the fiber bundle $\Phi = \{\phi_i | i = 1, W\}$. For each fiber ϕ_i , a kernel regression [11] is used to preserve its temporal continuity. Accordingly, the temporal fibers after kernel regression $\hat{\phi}_i = \{\hat{f}_s(y^i) | s = 1, \dots, N\}$ can be obtained by optimizing the following energy function L_T :

$$\operatorname{argmin}_{f_s} L_T(\hat{f}_s(y^i)) = \sum_{s'=1}^N [\hat{f}_s(y^i) - f_{s'}(y^i)]^2 \frac{1}{\sigma_s} \psi\left(\frac{s-s'}{\sigma_s}\right) \quad (4)$$

where ψ is the regression function. A Gaussian kernel with bandwidth σ_s is used in this paper.

Considering $h = (\{f_s\}, \{m_s^{i,j}\})$ as the model parameters and $v = (\{x_s^j\}, \{\vec{a}(x_s^j)\})$ as the observations, the joint probability $P(h, v)$ is given by:

$$P(h, v) = \left[\prod_{s=1}^N \prod_{j=1}^{M_s} \pi_s^{i,j} \cdot P(x_s^j, \vec{a}(x_s^j) | m_s^{i,j}, f_s(y^i)) \right] \cdot \left[\prod_{s=1}^N P(f_s) \cdot \prod_{i=1}^W P(\hat{f}_s(y^i)) \right] \quad (5)$$

where $\pi_s^{i,j} = P(m_s^{i,j} = i)$, and the probability functions of spatial transformation field $P(f_s)$ and temporal fiber bundles $P(\hat{f}_s(y^i))$ are, respectively, defined as:

$$P(f_s) = e^{-\frac{\lambda_1}{2} \|L_s(f_s)\|^2}, P(\hat{f}_s(y^i)) = e^{-\frac{\lambda_2}{2} \|L_T(\hat{f}_s(y^i))\|^2}, \quad (6)$$

where λ_1 and λ_2 are the scales used to control the smoothness of the spatial transformation field f_s^P and the temporal fiber bundles Φ respectively. Note that L_s is the bending energy [6] on spatial deformation field and L_T , defined in Eq. 4, is the residual energy after kernel regression.

To find the optimal $\{f_s\}$ and $\{m_s^{i,j}\}$ in Eq. 5, we resort to the “free energy with annealing” method in [12] to minimize the distribution distance between $p(h|v)$ and $p(h, v)$, which bounds for maximizing the likelihood of the observation $P(v)$. By omitting some constant terms and taking logarithm to Eq. 5, we obtain the free energy for our registration algorithm as:

$$E = \sum_{s=1}^N \left\{ \sum_{j=1}^{M_s} [\pi_s^{i,j} \cdot \eta(x_s^j, y^i) + r \cdot \pi_s^{i,j} \log(\pi_s^{i,j})] + \lambda_1 L_s(f_s) \right\} + \lambda_2 \sum_{i=1}^W L_T(\hat{f}_s(y^i)) \quad (7)$$

where r serves as the role of temperature in the annealing system [13] for robust correspondence detection. We will clarify it in Eq. 8.

The optimization of E in Eq. 7 is performed in the “divide-and-conquer” way. In the first step (*correspondence detection*), the probability of spatial assignment $\pi_s^{i,j}$ can be immediately computed by only minimizing E w.r.t. $\pi_s^{i,j}$:

$$\pi_s^{i,j} = \exp\left(-\frac{\eta(x_s^j, y^i)}{r}\right) / \sum_{j=1}^{M_s} \exp\left(-\frac{\eta(x_s^j, y^i)}{r}\right). \quad (8)$$

It is obvious that $\pi_s^{i,j}$ is penalized in the exponential way according to the discrepancy degree $\eta(x_s^j, y^i)$ of shape and appearance in Eq. 3. The temperature r controls the penalty from mild to aggressive as it gradually decreases with the development of registration.

Once $\pi_s^{i,j}$ has been obtained, the correspondence of each y^i w.r.t. the shape of X_s is the weighed mean location of all x_s^j s, i.e., $f_s(y^i) = \sum_{j=1}^{M_s} \pi_s^{i,j} \cdot x_s^j$, by discarding all unnecessary terms with $f_s(y^i)$ in Eq. 7. In the second step (*dense deformation interpolation*), the temporal fibers Φ can be updated according to the latest correspondences $f_s(y^i)$ in each phase. Then the dense deformation field f_s is obtained by TPS (to minimize the bending energy $L_s(f_s)$) based on the sparse correspondences $\{\hat{f}_s(y^i)\}$, which optimizes $L_T(f_s)$ in Eq. 4 after kernel smoothing on each fiber ϕ_i . By repeating these two steps, the deformation of the reference image R to all P_s can be estimated and the temporal consistency can be well preserved by implicit temporal fibers.

In the end of registration, the deformation fields $\{f_s\}$ towards the reference image are obtained, along with the implicit temporal fibers Φ , which will facilitate the reconstruction of 4D-CT in the treatment day, as detailed below.

Reconstruction of 4D-CT in the Treatment Day

The overview of reconstruction of the 4D-CT in the treatment day is summarized in Fig. 3. There are two steps, i.e., phase de-interlace and the spatial-temporal registration, involved for reconstructing the 4D-CT in the treatment day. These two steps are explained below.

To determine the phase at each slice of the free-breathing image I , all phase images $P_s (s = 1, \dots, N)$ in the planning day will roughly deform to the free-breathing image I in the treatment day, by alignment of bones since the bone will almost not move with lung. In this way, for each slice $I(z)$ (where z is from the superior to inferior of human body), we can simply determine its corresponding phase by the two criteria: (1) the image similarity between $I(z)$ and its corresponding $P_s(z)$ should as high as possible; (2) the detected phases for the neighboring slices of image I should be as similar as possible. We call this procedure as phase de-interlace. After that, several 3D volumes $D_s (s = 1, \dots, N)$ which are associated with the particular phase images P_s are obtained, although many slices in each D_s are empty. The lines in the bottom of Fig. 3, with different colors denoting for different detected phases, designate the de-interlaced results in each phase, along with the matched corresponding planning-day slices shown in the top of Fig. 3.

Here, we consider $\{P_s\}$ as the model image sequence with complete information and $\{D_s\}$ as the subject image sequence with partial information after de-interlace. As shown in the Fig. 3, the deformation field g_s from each P_s to the de-interlaced result D_s will be estimated for mapping the planning-day 4D-CT to the treatment-day space. As we will explain next that the estimation of only the deformation field g_s between P_s and D_s is not enough to obtain good registration, the temporal heuristics in the planning day is also used to compensate the missing information in D_s .

Following the spatial-temporal registration method we have proposed above, the estimation of each g_s from D_s to P_s can be performed independently by regarding D_s as the reference image R and only the underlying phase s (i.e., $N = 1$) will be considered in optimizing the energy function (Eq. 7) in registration. Similarly, the kernel regression term (the second term in Eq. 7) is also removed since N in Eq. 7 is now set to 1. Specifically, the attribute vector for each point in D_s will be calculated for feature matching. Then, the key points in D_s , i.e., $U_s = \{u_s^k | k = 1, \dots, K_s\}$, are hierarchically selected to establish the correspondences with P_s . Each key point x_s^j in P_s has the contribution in determining the correspondence for u_s^k . The contribution is computed by Eq. 8, which is the exponential function of the geometric distance between u_s^k and x_s^j as well as the difference between attribute vectors $\vec{a}(u_s^k)$ and $\vec{a}(x_s^j)$. Finally, the destination of u_s^k in P_s is the weighed mean location of all x_s^j s w.r.t. the previously calculated contributions.

Recall that only a few slices in the free-breathing image are associated with the particular D_s after de-interlacing. Therefore, no correspondence can be detected at the slice-missing areas due to the lack of key points. However, since we have roughly warp the planning-day 4D-CT to the treatment day, the detected correspondences on one D_s can be propagated to other de-interlaced images $D_{s'} (s' \neq s)$ by following the trajectory of temporal fibers established in the planning day. In this way, the motion in the slice-missing area of one D_s can be compensated from the regions in other phases where the correspondences have been identified.

Considering all the key points U_s s selected in all D_s s as the set of source points in the treatment-day space, TPS can be performed to interpolate the dense deformation field g_s one

by one. Finally, the 4D-CT in the treatment day can be reconstructed by mapping each P_s according to the estimated dense deformation field g_s .

3 Experiments

To demonstrate the performance of our proposed method, we first evaluate the registration accuracy in building 4D-CT model on DIR-lab data [3], with comparison to the state-of-the-art diffeomorphic Demons algorithm [4] and B-splines based 4D registration algorithm [5]. Then, we validate our algorithm in the reconstruction of 4D-CT for the treatment day from the simulated free-breathing 3D-CT.

Evaluation of Registration Performance on DIR-lab Dataset

There are 10 cases in DIR-lab dataset, each having a 4D-CT with six phases (from phase 1 to phase 6). For each case, 300 landmarks between the maximum inhale and the maximum exhale phases are available by repeated manual delineations, and also the correspondences of 75 landmarks for each phase are provided. Thus, we can evaluate the registration accuracy at two fixed phases and also in the entire 4D-CT. The registration accuracy is computed by the Euclidean distance between the reference landmark positions and the landmark positions propagated from the first time point to all other time points by the registration algorithm. It is worth noting that our registration is always performed on the entire 4D-CT, regardless in the evaluation of 300 landmarks in inhale and exhale phases or 75 landmarks in all 6 phases.

The registration results by Demons, B-splines based 4D registration algorithm, and our algorithm on 300 landmarks between maximum inhale and maximum exhale phases are shown in the left part of Table 1. Note that we show the results only for the first 5 cases, since the authors in [5] reported their results only for these 5 cases. It can be observed that our method achieves the lowest mean registration errors over the other two registration methods, both based on simple intensity matching. The mean and standard deviation on 75 landmark points over all six phases by the B-spline based 4D registration algorithm and our registration algorithm (which are both 4D registration methods) are shown in the right part of Table 1. In all cases, our method achieves both lower mean registration error and smaller standard deviation.

We also evaluate the temporal continuity of our spatial-temporal registration algorithm, with comparison to the Demons algorithm, since we do not have the registered landmark positions by the B-spline based 4D registration method. Two typical trajectories from the maximum inhale to the maximum exhale phases are displayed in Fig. 4(a)–(b) by using red, green, and blue curves to denote the reference landmark positions, the estimated landmark positions by Demons, and the estimated landmark positions by our algorithm, respectively. The estimated trajectories by our algorithm (blue curves) is not only closer to the reference trajectories (red curves), but also much smoother than those produced by Demons (green curves). These two reference landmarks are selected near to the diaphragm (see red crosses in Fig. 4), where the motion is generally larger during respiration.

Figs. 5(a) and (b) show the velocity magnitudes between consecutive phases for all 75 trajectories, obtained by Demons and our algorithm, respectively. The yellow curves denote the mean velocity magnitude along phases. Since we use the temporal fibers to constrain the continuity along phases, it can be observed that the velocity magnitude is much more continuous by our algorithm.

Evaluation of 4D-CT Reconstruction in the Treatment Day

To validate the performance of our reconstruction method, we simulate the free-breathing image for the treatment day as follows. We first obtain a planning-day 4D-CT as shown in Fig. 6(a), with the inhale, middle, and exhale phases displayed from left to right. We then simulate the deformation field by randomizing the parameters of B-spline control points, and apply this simulated deformation field to all phase images of the planning-day 4D-CT, for obtaining a ground-truth 4D-CT in the treatment day as shown in Fig. 6(b). Finally, we generate a free-breathing 3D-CT (Fig. 6(c)) by extracting the image slice from the corresponding phase image of the ground-truth treatment-day 4D-CT according to the phase table given for each slice in the right of Fig. 6(c). Accordingly, we can now estimate the treatment-day 4D-CT from this free-breathing 3D-CT by (1) directly registering the planning-day 4D-CT with the free-breathing 3D-CT, (2) reconstruction without temporal guidance from the planning-day 4D-CT model, and (3) reconstruction with temporal guidance from the planning-day 4D-CT model, with the respective results reported in Figs. 6(d), (f) and (h). Also, their difference images w.r.t. the ground-truth treatment-day 4D-CT images (Fig. 6(b)) are given in Figs. 6(e), (g) and (i), respectively. It is obvious that the reconstruction results have been significantly improved by utilizing the temporal model in our algorithm.

4 Conclusion

We have proposed a novel two-step method to reconstruct a new 4D-CT from a single free-breathing 3D-CT in the treatment day, for possible improvement of cancer radiotherapy which is currently using the registration of free-breathing 3D-CT images for patient setup. In our method, the 4D-CT model is first built in the planning day by robust spatial-temporal registration. Then, with the guidance of this 4D-CT model, the reconstruction of a 4D-CT in the treatment day is accomplished by warping the planning-day 4D-CT (with complete information) to the sequence of partial 3D-CT images of the treatment day (with missing image content in certain slices), obtained from the free-breathing 3D-CT after the phase de-interlace. We have extensively evaluated each step of our method with both real and simulated datasets, and obtained very promising results in building 4D-CT model and reconstructing new 4D-CT from a single free-breathing 3D-CT.

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Fig. 1.

The overview of our proposed method for estimating the 4D-CT images in the treatment day (b) from a free-breathing image in the treatment day (d), by using the 4D-CT model built in the planning day (a). The failed case of directly registering the free-breathing image to the 4D-CT is shown in (e). To avoid this potential problem, our method first de-interlaces the free-breathing image into the respective phase images (c), and then reconstructs a new 4D-CT in the treatment day (b) by warping the planning-day 4D-CT onto the de-interlaced images, with the guidance of the 4D-CT model built in the planning day.

Fig. 2.

The schematic illustration of our spatial-temporal registration on 4D-CT. The deformation fields $\{f_s\}$ are estimated based on the correspondences between key points y (red points) and X_s (green points) by robust feature matching w.r.t. their shape and appearance. Meanwhile, the temporal continuity is preserved by performing kernel regression along the temporal fiber bundles Φ (see the blue dash curves).

Fig. 3.

The scheme for reconstruction of 4D-CT in the treatment day. The de-interlaced results at each phase are designated by the lines with different colors. Note that the free-breathing 3D-CT is repeated at each phase for easy description. The reconstruction of 4D-CT in the treatment day is obtained by estimating the deformation field g_s between the de-interlaced image sequence D and the planning-day image sequence P , with the guidance of temporal heuristics obtained in the planning day.

Fig. 4. Trajectories of two landmarks (selected from 75 landmarks) are shown in (a) and (b), where red, green, and blue curves denote the reference landmark positions, the estimated landmark positions by Demons, and the estimated landmark positions by our algorithm. The locations of these two reference landmarks are also shown, by the two red crosses near to the diaphragm.

Fig. 5. The estimated velocity magnitudes from the maximum inhale to the maximum exhale, by Demons (a) and our algorithm (b), respectively. Here, the yellow curve is the mean velocity magnitude along phases.

Fig. 6.

The performance of 4D-CT reconstruction from a simulated free-breathing 3D-CT. A planning-day 4D-CT is first obtained, with its maximum inhale, middle, and maximum exhale phases shown in (a). The simulated treatment-day 4D-CT is displayed in (b), along with a simulated free-breathing 3D-CT of the treatment day shown in (c). The registration result between the planning-day 4D-CT and the free-breathing 3D-CT and its difference w.r.t. the ground-truth (b) are shown in (d)–(e), respectively. The reconstruction results without/with temporal guidance are displayed in (f) and (h), along with their corresponding differences w.r.t. the ground-truth (b) shown in (g) and (i), respectively.

The mean and standard deviation of registration error (mm) on 300 landmark points between maximum inhale and exhale phases, and on 75 landmark points in all six phases

Table 1

#	300 landmark points			75 landmark points		
	Initial	Demons	Bspline4D	Our method	Initial	Bspline4D
1	3.89(2.78)	2.91(2.34)	1.02 (0.50)	0.80(0.70)	2.18(2.54)	0.92 (0.66)
2	4.34(3.90)	4.09(3.67)	1.06 (0.56)	0.72(0.64)	3.78(3.69)	1.00 (0.62)
3	6.94(4.05)	4.21(3.98)	1.19 (0.66)	1.13(0.87)	5.05(3.81)	1.14 (0.61)
4	9.83(4.85)	4.81(4.26)	1.57 (1.20)	1.23(0.93)	6.69(4.72)	1.40 (1.02)
5	7.48(5.50)	5.15(4.85)	1.73 (1.49)	1.28(1.28)	5.22(4.61)	1.50 (1.31)