Automatic Landmark Detection and Non-linear Landmark- and Surface-based Registration of Lung CT Images

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Abstract. Registration of the lungs in thoracic CT images is required in many fields of application in medical imaging, for example for motion estimation or analysis of pathology progression.
In this paper, we present a feature-based registration approach for lung CT images based on lung surfaces and automatically detected inner-lung landmark pairs. In a first step, an affine pre-registration of surface models generated from lung segmentation masks is performed. Following, an automatic algorithm is used for the landmark identification and landmark transfer between fixed and moving image. The result of this landmark detection and the result of a non-linear diffusion-based surface registration are used to generate the final deformation field by thin-plate-splines interpolation.
The approach is evaluated based on 20 CT scans provided for the EMPIRE10 study for pulmonary image registration. In this study, the approach reached a final placement of 21 out of 34 participating algorithms. The evaluation shows a very good alignment of lung boundaries in contrast to a disappointing matching of inner lung structures, although landmark pairs were detected correctly with the automatic algorithm.

Keywords: landmark detection, thin-plate-splines, surface registration

1 Introduction

This paper describes a feature-based approach for the registration of lung CT images. The idea of our approach is to exploit the criteria used in the EMPIRE10 challenge for the evaluation of registration methods. Since the participants were not provided with all data used for evaluation, this was only partly possible. The evaluation criteria for pulmonary image registration in the EMPIRE10 study are (see ref. [10]):

(1) alignment of the lung boundaries,
(2) alignment of the major fissures,
(3) correspondence of annotated point pairs, and
(4) analysis of singularities in the deformation field.

The data of the EMPIRE10 study consists of 20 pairs of chest CT scans, each pair taken from a single subject. In addition to the CT data, binary lung masks are provided for each scan. The lung masks can be used to optimize the registration according to criterion (1). The segmentation of the the major fissures in chest CT images is a difficult problem. Although few automatic methods were published, we have not implemented and tested one of these methods due to reasons of time. Therefore criterion (2) cannot be taken into account in our registration approach. The annotated point pairs used for evaluation were not provided for the participants. However, in earlier studies we implemented an automatic landmark detection and landmark transfer method for 4D CT images [14]. This method is used to detect corresponding point pairs in the fixed and moving image of the 20 pairs of chest CT scans, and our registration method optimizes criterion (3) according to these automatically detected point pairs. The deformation field is computed based on thin-plate-splines under the constraints derived from criterion (1) and (3). In this way, singularities in the deformation field [criterion (4)] are avoided as long as surface and point correspondences are consistent.

2 Methods

The goal of our registration approach is to calculate a transformation $\boldsymbol{\varphi} : \Omega_F \rightarrow \Omega_M$ that matches a fixed image $I_F(\boldsymbol{x}) : \Omega_F \rightarrow \mathbb{R}$ and a moving image $I_M(\boldsymbol{x}) : \Omega_M \rightarrow \mathbb{R}$ according to criteria (1)-(4) (see sec. 1). Ω_F and Ω_M denotes the domain of fixed and moving image, respectively, and $\boldsymbol{\varphi}(\boldsymbol{x})$ denotes the coordinate in the moving image I_M corresponding to the coordinate $\boldsymbol{x}$ in the fixed image I_F.

The registration method presented in this paper consists of five steps. In the first step of our registration approach, surface models $\boldsymbol{S}_F$ and $\boldsymbol{S}_M$ of the lung are generated from the lung segmentation masks. These surface models are generated by the Marching Cubes algorithm, followed by a triangle decimation and a surface smoothing in order to obtain smooth surfaces with appropriate surface normals and to reduce the computational complexity in the following steps. Second, the surface models $\boldsymbol{S}_F$ and $\boldsymbol{S}_M$ are coarsely aligned by an affine pre-registration using the Iterative-Closest-Point (ICP) algorithm [2]. The resulting affine transformation $\boldsymbol{\varphi}_{aff}$ is used to initialize the third step: an automatic template matching approach to detect corresponding inner-lung landmarks in the chest CT scans I_F and I_M. In the fourth step, a symmetric non-linear surface registration enables the precise alignment of the lung boundaries. The results of the surface registration and the automatically detected corresponding inner-lung landmarks are used to generate the final transformation $\boldsymbol{\varphi}$ based on thin-plate-splines (TPS) in the last step.

Standard implementations provided by the Visualization Toolkit [13] are used for the surface generation and affine pre-registration, hence, in this paper we focus on the description of the automatic detection of corresponding landmark pairs and our approach for symmetric non-linear surface registration.

2.1 Automatic detection of corresponding landmark pairs in the lungs

The algorithm for the automatic detection of corresponding inner-lung landmarks follows to a large extent the approach described in [8, 9] and is detailed in algorithm 1 (see also [14]). It consists of two steps: identification of appropriate landmark candidates in the fixed image I_F and robust transfer of the candidates to the moving image I_M.

Landmark identification: Landmarks should be characteristic anatomical points of the lung, like prominent bifurcations of the vessels or the bronchial tree. To identify such points, so-called distinctiveness values [8, 9] are computed for all voxels within the eroded lung segmentation mask M'_F. The computation of the distinctiveness values consists of two terms: First, the dissimilarity of intensity values in a local neighborhood of the voxel considered and the intensity values around the neighboring voxels is determined. This dissimilarity term is then weighted by a feature-based term. In [9], the weighting term is based on the magnitude of the intensity gradients. As bifurcations of the bronchial tree or vessels feature specific curvature characteristics, we propose in this paper to use a curvature based differential operator instead, the Förstner operator [7]. Additionally, landmark candidates were supposed to be approximately well distributed throughout the lungs. Analogously to [9], this was achieved by postulating a minimum Euclidean distance between landmark candidates.

Landmark transfer: Landmark candidates of the fixed image are transfered to the moving image by template matching (here: restricted to translations only). We performed two runs: first, a template matching based on the intensity values (Hounsfield Units, HU), followed by a second run using the answer of the applied curvature based operator. The template was centered at the position of the landmark candidate in the fixed image. The search space was a subregion of the moving image. It was centered at the original landmark candidate position in the fixed image space, but transformed by φ_{aff}. Its size was chosen based on a-priori knowledge about breathing motion amplitudes. For both runs, the correlation coefficient was maximized to establish an optimal matching.

For robustness purposes of following registration steps, landmark candidates are discarded if the correlation value of the first template matching run is below a correlation threshold $r_{\mathrm{HU,min}}$ or the transfered landmark positions differ by more than a prescribed distance $d_{\max}$ for the two runs.

2.2 Non-linear registration of lung surfaces

The surface-based non-linear registration algorithm presented in this paper is related to the Geometry-Constrained-Diffusion algorithm presented in [1]. The Geometry-Constrained-Diffusion of the displacement field $\boldsymbol{u} : \mathbb{R}^3 \to \mathbb{R}^3$ mapping

Algorithm 1 Detection of corresponding landmark pairs

Input:
CT images $I_F : \Omega_F \to \mathbb{R}$, $I_M : \Omega_M \to \mathbb{R}$,
eroded lung segmentation mask $M'_F : \Omega_F \to \{0, 1\}$,
number N_l of landmarks candidates.
Output:
Lists $\mathbb{L}_F = (\boldsymbol{x}_1, \ldots, \boldsymbol{x}_{n_l})$ and $\mathbb{L}_M = (\boldsymbol{y}_1, \ldots, \boldsymbol{y}_{n_l})$ with $\boldsymbol{x}_i \in \Omega_F, \boldsymbol{y}_i \in \Omega_M, n_l \leq N_l$ of corresponding landmarks in I_F and I_M.

1: Let $\boldsymbol{x}, \boldsymbol{x}' \in \Omega_F$ be the lung voxels in I_F, i.e. all voxels with $M'_F = 1$.
Then, compute for each $\boldsymbol{x}$ the associated *distinctiveness* $D(\boldsymbol{x})$:

$$D(\boldsymbol{x}) := \frac{[\det \underline{C}(\boldsymbol{x}) / \operatorname{trace} \underline{C}(\boldsymbol{x})]}{\max_{\boldsymbol{x}'} [\det \underline{C}(\boldsymbol{x}') / \operatorname{trace} \underline{C}(\boldsymbol{x}')]} \sum_{\boldsymbol{x}'' \in \mathbf{Q} \subset \mathbf{S}^2_{\mathbf{r}}(\mathbf{x})} \frac{\operatorname{MSD}(B_{r'}(\boldsymbol{x}), B_{r'}(\boldsymbol{x}''))}{|Q|}$$

where $[\det \underline{C}(\boldsymbol{x}) / \operatorname{trace} \underline{C}(\boldsymbol{x})]$ denotes the Förstner-Operator [7] and

$\underline{C} := \overline{\nabla I_F (\nabla I_F)^T}$ with ∇I_F the image gradient of I_F,
$S^2_r(\boldsymbol{x})$: 2-sphere of radius r, centered at $\boldsymbol{x}$,
$B_{r'}(\boldsymbol{x})$: 3-ball of radius r', centered at $\boldsymbol{x}$.

Let $\left(\boldsymbol{x}_1, ..., \boldsymbol{x}_{|B_{r'}(\boldsymbol{x}) \cap \Omega_F|}\right)$ and $\left(\boldsymbol{x}'_1, ..., \boldsymbol{x}'_{|B_{r'}(\boldsymbol{y}) \cap \Omega_F|}\right)$ be correspondingly sampled sequences of the voxels in $B_{r'}(\boldsymbol{x})$ and $B_{r'}(\boldsymbol{x}')$. Then, MSD is defined as

$$\operatorname{MSD}\left(B_{r'}(\boldsymbol{x}), B_{r'}(\boldsymbol{x}')\right) := \frac{1}{|B_{r'}(\boldsymbol{x}) \cap \Omega_F|} \sum_{i=1}^{|B_{r'}(\boldsymbol{x}) \cap \Omega_F|} \left(I_F(\boldsymbol{x}_i) - I_F(\boldsymbol{x}'_i)\right)^2.$$

2: Sort points $\boldsymbol{x}$ with $|\nabla I_F(\boldsymbol{x})| \geq \theta_{\nabla I_F}$ in descending order acc. to $D(\boldsymbol{x})$ into list $\mathbb{P}_F$.
3: If size of $\mathbb{P}_F$ is $< N_l$, decrease gradient threshold $\theta_{\nabla I_F}$.
4: If size of $\mathbb{P}_F$ is $< N_l$ and $\theta_{\nabla I_F} > 0$, go to line 2.

5: **for all** points $\boldsymbol{x}$ in list $\mathbb{P}_F$ **do**
6: Move $\boldsymbol{x}$ to $\mathbb{L}_F$ if its Euclidian distance to all points in $\mathbb{L}_F$ is $> \theta_{\text{dist}}$.
7: If size of $\mathbb{L}_F$ is N_l, then continue with line 9.
8: **end for**
9: If size of $\mathbb{L}_F$ is $< N_l$, decrease the minimum distance θ_{dist}.
10: If size of $\mathbb{L}_F$ is $< N_l$ and $\theta_{\text{dist}} > 0$, go to line 5.

11: **for all** elements $\boldsymbol{x}_i$ in $\mathbb{L}_F$ **do**
12: Extract a $\mathrm{m_x} \times \mathrm{m_y} \times \mathrm{m_z}$ subimage $T(\boldsymbol{x}_i)$ of I_F (the template to be matched), centered at $\boldsymbol{x}_i$, and search the voxel $\boldsymbol{y}_i \in \Omega_M$ such that the $\mathrm{m_x} \times \mathrm{m_y} \times \mathrm{m_z}$ subimage $T'(\boldsymbol{y}_i)$ of I_M maximizes the correlation r_{HU} of the intensity values of T and T'.
13: Analogously do a *template matching* for the Förstner images of I_F and I_M.
14: **if** the correlation r_{HU} is smaller than a prescribed minimum correlation $r_{\text{HU,min}}$ **or** the returned voxels $\boldsymbol{y}_i$ of the template matching processes (lines 12 and 13) differ by more than a prescribed Euclidean distance $d_{\max}$ **then**
15: Remove $\boldsymbol{x}_i$ from list $\mathbb{L}_F$.
16: **else**
17: Append voxel $\boldsymbol{y}_i$ to list $\mathbb{L}_M$.
18: **end if**
19: **end for**

the surface $\boldsymbol{s}_1 : \mathbb{R}^2 \to \mathbb{R}^3$ to the surface $\boldsymbol{s}_2 : \mathbb{R}^2 \to \mathbb{R}^3$ is given by [1]:

$$\partial_t \boldsymbol{u} = \begin{cases} \Delta \boldsymbol{u} - \boldsymbol{n}_2 \dfrac{\boldsymbol{n}_2 \cdot \Delta \boldsymbol{u}}{\|\boldsymbol{n}_2\|^2} & \text{if } \boldsymbol{x} \in \boldsymbol{s}_1 \quad (1a) \\ \Delta \boldsymbol{u} & \text{if } \boldsymbol{x} \notin \boldsymbol{s}_1, \quad (1b) \end{cases}$$

where $\boldsymbol{n}_2$ is the surface normal of $\boldsymbol{s}_2$ at position $\boldsymbol{x} + \boldsymbol{u}(\boldsymbol{x})$. The term $\boldsymbol{x} - \boldsymbol{n}\frac{\boldsymbol{n}\cdot\boldsymbol{x}}{\|\boldsymbol{n}\|^2}$ in eq. (1a) represents a projection of a vector $\boldsymbol{x}$ to the tangent plane with normal $\boldsymbol{n}$. Thus, only the tangential part of the diffusion along the surface is kept and the points $\boldsymbol{x} + \boldsymbol{u}(\boldsymbol{x})$ for $\boldsymbol{x} \in \boldsymbol{s}_1$ are allowed to travel only along the surface $\boldsymbol{s}_2$. After a sufficient initialization of $\boldsymbol{u}$, Andresen and Nielsen propose an iterative three-step algorithm to solve eq. 1: (1) Convolve the displacement field $\boldsymbol{u}$ with a Gaussian kernel, (2) For all points on the deformed surface $\boldsymbol{s}_1$: find the corresponding point on the target surface $\boldsymbol{s}_2$, and (3) For all points on the deformed surface $\boldsymbol{s}_1$: change the displacements $\boldsymbol{u}$ according to the match. The resulting transformation $\boldsymbol{\varphi}(\boldsymbol{x}) = \boldsymbol{x} + \boldsymbol{u}(\boldsymbol{x})$ is given for $\partial_t \boldsymbol{u} = 0$.

In this paper we propose an alternative implementation of a diffusive surface registration to address two issues: reduction of the computational complexity and symmetry according to the ordering of source and target images. In contrast to the implementation in [1, 6] the displacement field $\boldsymbol{u}$ is not computed on an image grid. Instead, we compute displacement vectors for the surface points only. Given two point sets $\mathbb{S}_F = \left\{\boldsymbol{x}_1, \ldots, \boldsymbol{x}_{N_F} | \boldsymbol{x}_i \in \mathbb{R}^3\right\}$ and $\mathbb{S}_M = \left\{\boldsymbol{y}_1, \ldots, \boldsymbol{y}_{N_M} | \boldsymbol{y}_j \in \mathbb{R}^3\right\}$, we search for the set of displacement vectors $\mathbb{U} = \left\{\boldsymbol{u}_1, \ldots, \boldsymbol{u}_{N_F} | \boldsymbol{u}_i \in \mathbb{R}^3\right\}$ to match $\mathbb{S}_F$ onto $\mathbb{S}_M$ and $\mathbb{W} = \left\{\boldsymbol{w}_1, \ldots, \boldsymbol{w}_{N_M} | \boldsymbol{w}_j \in \mathbb{R}^3\right\}$ to match $\mathbb{S}_M$ onto $\mathbb{S}_F$. The registration method is summarized in algorithm 2.

Two essential steps of the algorithm are now explained in greater detail: the determination of the closest points and the Gaussian smoothing of the displacement vectors. The differential characteristics of the surfaces contain important information about the correspondence of surface points. Therefore, as proposed in [6], surface normals and local curvature characteristics are used for closest point determination: For a point $\boldsymbol{x}$ on surface $\boldsymbol{S}_F$ find the corresponding point $\boldsymbol{y}$ on surface $\boldsymbol{S}_M$, which minimizes:

$$D(\boldsymbol{x}, \boldsymbol{y}) = \alpha\|\boldsymbol{x} - \boldsymbol{y}\|^2 + \beta\|\boldsymbol{n}(\boldsymbol{x}) - \boldsymbol{n}(\boldsymbol{y})\|^2 + \gamma(\kappa_\epsilon(\boldsymbol{x}) - \kappa_\epsilon(\boldsymbol{y}))^2. \tag{2}$$

$\boldsymbol{n}(\boldsymbol{x})$ denotes the surface normal and $\kappa_\epsilon(\boldsymbol{x})$ denotes a curvature value of point $\boldsymbol{x}$. The normal vectors $\boldsymbol{n}$ of the triangulated surface models are calculated as proposed in [13]. To determine the surface curvature, a moment-based curvature measure of discrete surfaces κ_ϵ is used [5]. First, the barycentre $\boldsymbol{B}_\epsilon(\boldsymbol{x})$ of a small neighborhood of the surface point $\boldsymbol{x}$ is determined. Then the distance

$$\kappa_\epsilon(\boldsymbol{x}) = \frac{1}{\epsilon}\left(\boldsymbol{n}(\boldsymbol{x}) \cdot (\boldsymbol{B}_\epsilon(\boldsymbol{x}) - \boldsymbol{x})\right) \tag{3}$$

between $\boldsymbol{B}_\epsilon(\boldsymbol{x})$ and the tangential plane through the point $\boldsymbol{x}$ with surface normal $\boldsymbol{n}(\boldsymbol{x})$ is computed. The size of the regarded neighborhood is given by the built-in scale parameter ϵ. The curvature measure κ_ϵ allows to distinguish smooth regions

Algorithm 2 Diffusion-based surface registration

Initialize $\forall \boldsymbol{u}_i \in \mathbb{U}$ with the displacements of the affine pre-registration $\boldsymbol{\varphi}_{aff}$ and $\forall \boldsymbol{w}_i \in \mathbb{W}$ with the inverse affine transformation $\boldsymbol{\varphi}_{aff}^{-1}$, set $k = 0$
repeat
  Deform the point sets: $\mathbb{S}_F^k = \left\{ \boldsymbol{x}_i^k = \boldsymbol{x}_i + \boldsymbol{u}_i | i = 1, \ldots, N_F \right\}$ and
  $\mathbb{S}_M^k = \left\{ \boldsymbol{y}_j^k = \boldsymbol{y}_j + \boldsymbol{w}_j | j = 1, \ldots, N_M \right\}$
  for all $\boldsymbol{x}_i^k \in \mathbb{S}_F^k$ **do**
    Find the closest point $\boldsymbol{y}_j$ on $\mathbb{S}_M$, which minimizes $D(\boldsymbol{x}_i^k, \boldsymbol{y}_j)$
    Set $\boldsymbol{u}_i = \boldsymbol{y}_j - \boldsymbol{x}_i$ and $\boldsymbol{w}_j = \boldsymbol{x}_i - \boldsymbol{y}_j$, where $\boldsymbol{x}_i$ is the point position on $\mathbb{S}_F$
  end for
  for all $\boldsymbol{y}_j^k \in \mathbb{S}_M^k$ not processed in the last step **do**
    Find the closest point $\boldsymbol{x}_i$ on $\mathbb{S}_F$, which minimizes $D(\boldsymbol{y}_j^k, \boldsymbol{x}_i)$
    $\boldsymbol{w}_j = \boldsymbol{x}_i - \boldsymbol{y}_j$, where $\boldsymbol{y}_j$ is the point position on $\mathbb{S}_M$
  end for
  $\forall \boldsymbol{u}_i \in \mathbb{U}$: compute the Gaussian weighted average of all displacement vectors in the neighborhood of $\boldsymbol{x}_i$
  $\forall \boldsymbol{w}_j \in \mathbb{W}$: compute the Gaussian weighted average of all displacement vectors in the neighborhood of $\boldsymbol{y}_j$
  Swap $\mathbb{S}_F$ and $\mathbb{S}_M$ as well as $\mathbb{U}$ and $\mathbb{W}$
  Let $k \leftarrow k + 1$
until a stop criterion is fulfilled, i.e. the algorithm converges

($\kappa_\epsilon \approx 0$) from convex surface regions ($\kappa_\epsilon < 0$) and from concave surface regions ($\kappa_\epsilon > 0$). The presented method is an extension of the curvature classification via local zero order moments as suggested in [4]. *Kd–trees* are used to perform an efficient closest point search.

To smooth the computed displacement, for each of the displacement vectors in $\mathbb{U}$ ($\mathbb{W}$ respectively), we determine the set of displacement vectors in the neighborhood of its surface location $\boldsymbol{x}$: $\mathbb{N}(\mathbb{U}, \boldsymbol{x}) = \{\boldsymbol{u}_j \in \mathbb{U} \mid \|\boldsymbol{x}_j - \boldsymbol{x}\| \leq 3\sigma, \boldsymbol{x}_j \in \mathbb{S}_F\}$. Following, a Gaussian weighted average is constructed and divided by the sum of the weights:

$$\bar{\boldsymbol{u}}_i = \frac{1}{\sum_j w_j} \sum_{\boldsymbol{u}_j \in \mathbb{N}(\mathbb{U}, \boldsymbol{x}_i)} w_j \boldsymbol{u}_j, \tag{4}$$

where $w_j = e^{\left(-\frac{\|\boldsymbol{x}_j - \boldsymbol{x}_i\|^2}{2\sigma^2}\right)}$ is the Gaussian weighted distance between $\boldsymbol{u}_i$ and $\boldsymbol{u}_j$.

The standard deviation of the Gaussian σ, the weights of the distance measure α, β, γ, and the scale parameter ϵ are the only parameters in the numerical implementation. The point sets $\mathbb{S}_F$ and $\mathbb{S}_M$ are given by the triangle vertexes of the surfaces $\boldsymbol{S}_F$ and $\boldsymbol{S}_M$.

2.3 Deformation field generation

Given the set of corresponding landmark pairs $\mathbb{L}_F$ and $\mathbb{L}_M$ computed in section 2.1 and the surface correspondences computed in section 2.2, we want to construct a dense transformation $\boldsymbol{\varphi} : \Omega_F \rightarrow \Omega_M$ that matches I_F and I_M.

We chose to use thin-plate-splines [3] to generate $\boldsymbol{\varphi}$. Thin-plate-splines ensure a smooth, interpolating transformation by minimizing the bending energy subject to a given set of corresponding point pairs. To extract corresponding point pairs from the matched surfaces, we select sampling points on the fixed surface $\boldsymbol{S}_F$ in such a way that all selected points have a minimum distance of radius R. The displacement $\mathbb{U}$ computed in section 2.2 is used to select the corresponding point on $\boldsymbol{S}_M$. The computation time to calculate the TPS transformation is proportional to the number of given point pairs. To minimize the number of sampling points and generating an adequate matching of the surfaces simultaneously, we include the curvature characteristics for the selection of sampling points. Surface areas with high curvature feature prominent surface details as ridges or edges. Therefore, surface points with high curvature are selected first to ensure the matching of these prominent surface details: we select points with $\kappa_\epsilon(\boldsymbol{x}) > t_\kappa$ first and lower the threshold iteratively until a dense surface sampling is reached.

From the corresponding surface point pairs and the inner–lung landmark pairs we compute the parameters of the TPS transformation $\boldsymbol{\varphi}^{TPS}$ as shown in [3]. Following, we generate a dense displacement field by computing $\boldsymbol{u}(\boldsymbol{x}) = \boldsymbol{\varphi}^{TPS}(\boldsymbol{x}) - \boldsymbol{x}$ for each voxel position in the fixed image.

2.4 Parameter selection

For all registered image pairs the same set of parameters was used. Most parameters were determined empirically based on test runs. Test runs were not limited to the EMPIRE10 data sets, and so registration of other thoracic CT images should lead to similar registration quality using the parameter values described.

Surface generation and affine pre-registration: The parameters for surface decimation are selected in such a way that the number of surface vertexes was reduced to approximately 50%. The resulting lung surfaces have between 60.000 and 600.000 vertex points depending on the image resolution. A Laplacian surface smoothing was applied (relaxation factor 0.5 and 15 iterations). The affine ICP registration of the generated surfaces is stopped either after a maximal number of iterations ($k^{max} = 50$) or if the mean point distance is below a threshold ($t = 0.01$).

Landmark identification: $N_l = 150$ landmark candidates with a minimum pairwise distance of initially $\theta_{\text{dist}} = 50$ voxel (decremented by 5 for each loop run) were identified in I_F. The search space for landmark candidates was restricted by the eroded lung mask where a spherical erosion kernel of 8 voxel radius was applied. For computation of the distinctiveness values, sphere and ball radius were $r = 8$ and $r' = 5$ voxel with 45 points well distributed on the sphere [11]. The initial gradient magnitude threshold $\theta_{\nabla I_F}$ was 300 (loop decrement: 10).

Landmark transfer: For this study, a template size of $\mathrm{m_x} \times \mathrm{m_y} \times \mathrm{m_z} = 15 \times 15 \times 15$ voxel and a search space of size $3 \times 3 \times 5cm$ were used. The minimum correlation threshold which indicated a reliable transfer was $r_{\mathrm{HU,min}} = 0.9$ and the maximum distance of the transferred candidate positions as obtained by the two template matching runs was $d_{\max} = 1$ voxel.

Non-linear surface registration and deformation field generation: The parameters of the non-linear surface registration are optimized with respect to the computation times and the registration quality. Registration quality was measured with respect to the alignment of the lung boundaries and the number of singularities in the displacement field. To speed up the determination of point correspondences and to avoid the re-calculation of surface normals and curvatures, we set $\alpha = 1$, $\beta = 0$, and $\gamma = 0$ in eq. (2). We use $\sigma = 5mm$ as a compromise between the computation times and the number of singularities in the generated TPS deformation. The registration stops either after a maximal number of iterations ($k^{max} = 100$) or if the mean point distance is below a threshold ($t = 10e^{-5}$). The surface curvature κ_ϵ is computed with $\epsilon = 5mm$. The minimum distance radius for surface point selection is set to $R = 10mm$. The radius is successively decreased if less than 800 points were selected.

For the test data sets between 800 and 1000 corresponding surface point pairs and between 100 and 150 landmark pairs were selected to generate the TPS deformation.

3 Results

The results of our approach are summarized in table 1. In the EMPIRE10 study, the approach reached a final placement of 21 out of 34 participating algorithms. This suggests that other approaches are more suitable for lung CT registration.

With regard to the alignment of the lung boundaries only, our feature-based registration approach reached a placement of 4. This demonstrates the high accuracy of our surface-based registration algorithm. However, the algorithm does not guarantee diffeomorphic transformations and thus singularities occur in 6 out of 20 computed deformation fields. Regarding the correspondence of annotated point pairs only, the algorithms reached a placement of 28. A visual inspection showed that algorithm 1 detected the landmark pairs correctly. Thus, the high registration error is due to the different landmark sets used for TPS interpolation and evaluation.

Computation time strongly depends on the image size, the number of landmarks to detect, the number of lung surface points, the number of selected point pairs for TPS calculation, and the number of iterations performed with regard to the stop criterion. A standard PC with Quad-Core Intel Xeon E5504 CPU (2.0 GHz) and 24 GB memory was used to perform the registration. The automatic detection of approx. 150 corresponding landmark pairs takes between 10 and 30 minutes. Surface generation and affine pre-registration takes less than 2 minutes for all data sets. The following non-linear surface registration needs between 8 minutes and 70 minutes, whereof approximately half of the computation time is needed for TPS interpolation and deformation field generation.

	Lung Boundaries		Fissures		Landmarks		Singularities	
Scan Pair	**Score**	**Rank**	**Score**	**Rank**	**Score**	**Rank**	**Score**	**Rank**
01	0.00	5.00	0.96	20.00	3.92	19.00	0.01	26.00
02	0.00	11.00	0.00	31.00	1.04	31.00	0.01	30.00
03	0.00	5.50	0.00	26.00	1.10	31.00	0.00	12.00
04	0.00	5.00	0.00	16.50	2.02	21.00	0.00	14.00
05	0.00	27.00	0.00	16.00	0.66	29.00	0.00	13.50
06	0.00	16.00	0.02	33.00	0.79	32.00	0.00	14.00
07	0.02	13.00	1.46	19.00	3.95	20.00	0.00	22.00
08	0.00	9.00	0.59	23.00	1.58	23.00	0.00	12.50
09	0.00	18.00	0.00	16.00	1.02	28.00	0.00	13.00
10	0.00	3.00	0.00	15.00	3.58	22.00	0.00	13.50
11	0.00	8.00	0.47	22.00	1.85	19.00	0.00	24.00
12	0.00	21.00	1.67	33.00	2.38	32.00	0.00	32.00
13	0.00	6.00	0.26	29.00	1.36	29.00	0.00	13.00
14	0.00	6.00	3.07	13.00	4.57	18.00	0.00	23.00
15	0.00	8.00	0.00	20.00	1.07	30.00	0.00	12.50
16	0.00	3.50	0.44	27.00	1.47	21.00	0.00	13.50
17	0.00	6.50	0.04	12.00	1.47	30.00	0.00	14.00
18	0.00	9.00	3.50	18.00	3.28	19.00	0.00	10.50
19	0.00	14.00	0.00	29.00	1.05	30.00	0.00	14.50
20	0.00	7.00	4.10	19.00	3.52	20.00	0.00	10.50
Avg	0.00	10.07	0.83	21.87	2.08	25.20	0.00	16.90
Average Ranking Overall								18.51
Final Placement								21

Table 1. Results for each scan pair, per category and overall. Rankings and final placement are from a total of 34 competing algorithms.

4 Discussion

In this paper, we presented a feature based registration approach for lung CT images. Section 2.1 proposes an automatic algorithm for landmark identification and landmark transfer between fixed and moving image. The result of this landmark detection and the result of the non-linear surface registration presented in section 2.2 are used to generate the final deformation field by TPS interpolation.

The evaluation of the EMPIRE10 study shows a very good alignment of lung boundaries for our approach in contrast to a disappointing matching of inner lung structures. Although landmark pairs were detected correctly with algorithm 1, the final deformation showed a high landmark registration error in the EMPIRE10 evaluation. We conclude from this that TPS interpolation based on a set of sparse landmarks is not suitable to represent the complete inner-lung motion. Here, intensity based registration approaches are more suitable, and a combination of surface and intensity registration is presented in [12].

A serious issue of the approach is the computation time. In the current implementation the algorithm does not fulfill the requirements of the clinical practice. However, the current implementation is in an experimental state with numerous possibilities for optimization. For example, a multi-resolution scheme will be added to improve robustness and speed of the surface registration.

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