Estimation of Inner Lung Motion Fields by Non-linear Registration

An Evaluation and Comparison Study

René Werner[1], Jan Ehrhardt[1], Alexander Schmidt-Richberg[1], Florian Cremers[2], Heinz Handels[1]

[1]Department of Medical Informatics,
[2]Department of Radiotherapy and Radio-Oncology,
University Medical Center Hamburg-Eppendorf
r.werner@uke.uni-hamburg.de

Abstract. Detailed analysis of breathing dynamics, as motivated by radiotherapy of lung tumors, requires accurate estimates of inner lung motion fields. We present an evaluation and comparison study of non-linear non-parametric intensity-based registration approaches to estimate these motion fields in 4D CT images. In order to cope with discontinuities in pleura and chest wall motion we restrict the registration by applying lung segmentation masks and evaluate the impact of masking on registration accuracy. Furthermore, we compare diffusive to elastic regularization and diffeomorphic to non-diffeomorphic implementations. Based on a data set of 10 patients we show that masking improves registration accuracy significantly. Moreover, neither elastic or diffusive regularization nor diffeomorphic versus non-diffeomorphic implementation influence the accuracy significantly. Thus, the method of choice depends on the application and requirements on motion field characteristics.

1 Introduction

Respiratory motion is a main problem in radiation therapy of lung cancer. Various authors emphasize the need of further analysis and quantification of breathing dynamics [1]. At present, such analysis is mostly based on 4D(=3D+t) image data. Within this field of research non-linear registration has become increasingly important, since it allows to estimate respiratory motion fields between the 3D images representing the patient's anatomy at different breathing phases. The motion fields form the basis of motion analysis and modeling issues. Thus, motion field estimates are required to be feasible and as accurate as possible. Though a wide variety of registration approaches has been proposed to estimate respiratory motion fields in 4D image sequences, there exists a substantial lack of evaluation and comparison studies for those methods [2].

Representing the few existing studies, in [2], [3], and [4] conceptually different registration approaches are compared in order to estimate inner lung motion fields (biomechanical modeling, surface models, landmark-based registration, parametric registration, non-parametric registration). On the one hand, our paper aims to complement these studies. On the other hand, we pursue a slightly different strategy: We focus on a non-linear, non-parametric, intensity-based registration scheme which we want to optimize in order to estimate inner lung motion fields. Therefore we define and evaluate different modifications of the registration scheme.

2 Materials and methods

The study is based on 4D CT data sets of 10 lung cancer patients. Spatial resolution of the CT data is between $0.78 \times 0.78 \times 1.5$ mm^3 and $0.98 \times 0.98 \times 1.5$ mm^3; image sequences consist of 10 to 14 CT images reconstructed at different breathing phases. Due to memory and computation time restrictions, the 3D data are downsampled to a spatial resolution of $1.5 \times 1.5 \times 1.5$ mm^3/voxel. For evaluation purposes we focus on the breathing phases of end-expiration (EE), mid-inspiration (MI), end-inspiration (EI), and mid-expiration (ME).

2.1 Registration approaches

Image registration can be seen as finding a transformation φ minimizing a distance between the transformed target image I_j (here: $j \in \{\text{EE, MI, ME}\}$) and a reference image I_i (here: $i = \text{EI}$) with respect to a desired smoothness of φ (represented by a regularization term). As distance measure we choose an adaptation of Thirion's demons approach, which is suitable for registration of low contrast structures like inner lung structures; for details see [5, 6]. In previous studies we used a diffusive approach for regularization, which has the advantage of an efficient implementation (time complexity of $O(n)$ [5]). Though time complexity is $O(n \log n)$, several authors propose elastic regularization in case of lung motion estimation [3]. This is due to the assumption that lungs behave like an elastic medium during respiration. Here we compare the diffusive smoothing approach (method m_1) and an elastic regularization (method m_2).

Additional requirements arise on deformation field characteristics when faced with advanced analysis and modeling issues. For instance, the generation of lung motion atlases and its use for model-based motion prediction requires the motion fields to be invertible [7]. To ensure invertibility, we adapt a diffeomorphic and a symmetric-diffeomorphic registration method [6] to our registration scheme (methods m_3 and m_4).

From a perspective of physiology, discontinuities in respiratory motion between the lung surface and the chest wall occur [4]. One approach to handle the discontinuities is to restrict force computation to the lungs by applying lung segmentation masks (here: segmented lungs at EI). The impact of masking on inner lung registration accuracy is therefore also evaluated here.

2.2 Evaluation methods

As two quality measures of the deformation fields, we determine the number of voxels with negative values of the Jacobian and analyze the symmetry properties of the fields. Voxels with negative values of the Jacobian indicate unwanted singularities of the field (deformation locally non-invertible). Analyzing symmetry means to check $\varphi_{i\to j\to i} := \varphi_{i\to j} \circ \varphi_{j\to i}$ which is ideally the identity vector field. To obtain $\varphi_{j\to i}$, the registration is performed with target and reference image being interchanged when compared to the computation of $\varphi_{i\to j}$.

Quantitative evaluation of the registration accuracy is based on 80 inner lung landmarks identified by a medical expert in each CT data set considered. To gain insights to strengths and weaknesses of the different registration methods we differentiate landmarks located in the middle of the lung (40 landmarks), near the lung borders (30 landmarks), and close to the tumor (10 landmarks). The landmark displacements between EI and the target image breathing phase (MI, EE, ME) as observed by the expert are compared to the landmark displacements obtained by applying the motion field estimates to the EI CT data and the EI landmark positions, respectively. Then, we determine the mean difference between the observed displacements and the displacements predicted by the model (mean target registration error, TRE). To check whether two registration approaches behave equivalently we apply a paired t-test [2].

2.3 Study design

Before applying the registration to the 10 patient data sets considered for this study, parameters (such as the regularization weight and step size) are optimized in order to achieve a good trade-off between a minimal number of voxels with negative Jacobian values and a small TRE. Optimization is based on a separate data set. The study itself consists of three steps where each step is a competitive study between different registration methods or adaptations of a method:

1. *masked vs. non-masked registration:* Masked and non-masked registration are compared with each other using method m_1 as registration technique and focusing on the TRE. If it cannot be shown that masking improves registration accuracy significantly, registration applied in steps 2 and 3 will be unmasked because this is the commonly used registration approach.
2. *diffusive vs. elastic regularization:* The influence of the regularization approach on registration accuracy and qualitative measures is evaluated using methods m_1 and m_2. If elastic regularization does not improve motion field estimation significantly, we will choose the diffusive approach in step 3 due to lower computational costs (Sec. 2.1).
3. *diffeomorphic vs. non-diffeomorphic registration:* The diffeomorphic registration approaches m_3 and m_4 are compared to the corresponding non-diffeomorphic registration m_1 or m_2 (depending on step 1 and 2 results).

3 Results

Registrations are performed using a bi-processor system with 3 GHz Intel Xeon dual-core processors and 16 GB RAM. Computation times for a 3D-3D registration are approximately $\frac{1}{2}$ h for m_1, $1\frac{1}{2}$ h for m_3, and 3 h for m_2 and m_4. Subsequent TRE values should be compared against the mean landmark motion of

6.82 ± 5.42 mm (EI-EE registration), 5.02 ± 3.48 mm (EI-MI), and 2.55 ± 1.97 mm (EI-ME), and the intraobserver variability of approx. 1 voxel.

3.1 Evaluation of the estimated motion fields

In Step 1 (masked vs. non-masked registration), masking of force computation turns out to improve the registration accuracy. Averaged over all landmarks, the mean TRE decreases from 2.07 ± 2.32 mm for unmasked to 1.55 ± 1.26 mm for masked EI-EE registration (EI-MI: 1.68 ± 1.20 to 1.57 ± 0.98 mm; EI-ME: 1.46 ± 0.94 to 1.45 ± 0.92 mm). This is mostly due to an increased registration accuracy for landmarks close to the lung borders (see fig. 1). The improvement can be shown to be significant (e.g., $p<0.05$ for all patients for EI-EE registration).

Step 2 (diffusive vs. elastic regularization) shows that elastic and diffusive regularization (here: masked registration) behave almost equivalently in terms of registration accuracy and motion field quality measures. For m_2, i.e., elastic regularization, the mean TRE values are 1.55 ± 1.21 mm (EI-EE), 1.51 ± 0.91 mm (EI-MI), and 1.46 ± 0.94 mm (EI-ME). TRE differences between m_1 and m_2 are significant for none of the patients (EI-EE), 4 patients (EI-MI; m_2 better in each case), and 2 patients (EI-ME; m_1 better). Mean symmetry errors are 0.88 ± 0.24 mm, 0.55 ± 0.11 mm, and 0.30 ± 0.07 mm for m_2 vs. 0.94 ± 0.33 mm, 0.62 ± 0.11 mm, and 0.34 ± 0.04 mm for m_1. For both m_1 and m_2 the number of voxels with negative Jacobian is negligible ($\ll 0.01\%$ of the lung voxels).

Step 3 (diffeomorphic vs. non-diffeomorphic registration) is based on diffusive regularization due to the preceding results. The mean TRE is 1.57 ± 1.26 mm (EI-EE), 1.58 ± 1.00 mm (EI-MI), and 1.46 ± 0.99 mm (EI-ME) for m_3, and 1.59 ± 1.28 mm, 1.57 ± 1.00 mm, and 1.46 ± 0.97 mm for m_4. Comparison of m_3 and m_1 yields that TRE differences are statistical significant for 4 patients (EI-EE; $3\times$ m_1 better than m_3, $1\times$ vice versa), 2 patients (EI-MI, $1\times$ m_1 better, $1\times$ m_3 better), and 1 patient (EI-ME, m_1 better). m_1 shows a significantly decreased TRE compared to m_4 for 4 patients (only in EI-EE registration). TRE values of m_3 are significantly lower than for m_4 for one data set (EI-ME). In short, registration accuracy is almost the same for m_1, m_3, and m_4. For the diffeomorphic implementations no negative Jacobian values are observed. In terms of the symmetry error the symmetric-diffeomorphic registration is superior to the non-diffeomorphic and the diffeomorphic implementation; the mean symmetry errors for m_4 are 0.36 ± 0.10 mm, 0.20 ± 0.04 mm, and 0.10 ± 0.02 mm. Corresponding values for m_3 are 1.18 ± 0.48 mm, 0.67 ± 0.13 mm, and 0.35 ± 0.04 mm.

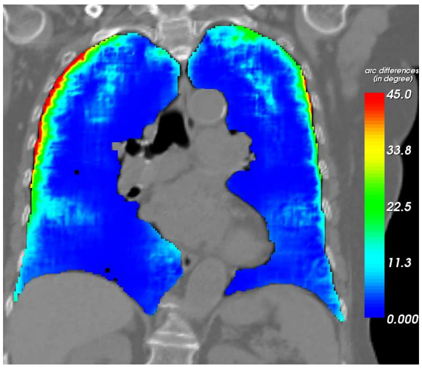
4 Discussion

In summary, neither the elastic or diffusive regularization nor diffeomorphic vs. non-diffeomorphic implementation can be shown to influence registration accuracy significantly. For the given application diffusive regularization tends to be superior to elastic regularization due to a better time complexity. Furthermore, the symmetric-diffeomorphic registration tends to be superior to the other

Fig. 1. Left: Landmark motion and TRE values for registration of I_{EI} and I_{EE}. Right: Visualization of the arc differences between EI-EE motion field estimates for patient 02 obtained by method m_1 with and without masking of force computation.

	Landmark motion [mm]	Target registration error [mm] no mask m_1	masked registration m_1	m_2	m_3^*	m_4^*
Pat. 1	6,29	2,06	1,48	1,45	1,49	1,54
Pat. 2	5,45	1,87	1,59	1,62	1,64	1,57
Pat. 3	6,19	1,70	1,55	1,61	1,57	1,57
Pat. 4	6,44	1,65	1,41	1,47	1,44	1,46
Pat. 5	4,31	1,44	1,37	1,38	1,37	1,36
Pat. 6	10,76	3,07	1,52	1,47	1,62	1,60
Pat. 7	6,40	2,85	1,99	2,00	1,91	2,01
Pat. 8	6,06	1,52	1,19	1,22	1,24	1,28
Pat. 9	7,98	2,09	1,62	1,58	1,60	1,61
Pat. 10	8,32	2,47	1,80	1,71	1,89	1,94
mean	**6,82**	**2,07**	**1,55**	**1,55**	**1,58**	**1,59**

*) diffusive regularization



methods since it minimizes the symmetry error. However, computational costs of symmetric-diffeomorphic registration are higher. Thus, if computing time is a crucial issue, non-diffeomorphic or diffeomorphic diffusive registration can be considered as better choices (depending on whether invertibility is required).

As an essential result we show that masking significantly improves registration accuracy. This demonstrates that integrating a-priori knowledge about physiological processes (here: behavior of pleura and chest wall during breathing) to registration schemes has potential to improve registration accuracy.

Acknowledgments: This work is supported by German Research Foundation (DFG, HA 2355/9-1). We thank D. Low and W. Lu from the Washington University School of Medicine, St. Louis (USA), for providing the CT data.

References

1. Li XA, et al. Point/counterpoint: Respiratory gating for radiation therapy is not ready for prime time. Med Phys. 2007;34(3):867–70.
2. Sarrut D, et al. A comparison framework for breathing motion estimation methods from 4-D imaging. IEEE Trans Med Imaging. 2007;26(12):1636–48.
3. Vik T, et al. Validation and comparison of registration methods for free-breathing 4D lung-CT. Procs SPIE. 2008;6914:2P1–10.
4. Werner R, et al. Validation and comparison of a biophysical modeling approach and non-linear registration for estimation of lung motion fields in thoracic 4D CT data. Procs SPIE. 2009.
5. Modersitzki J. Numerical Methods for Image Registration. Oxford University Press; 2003.
6. Vercauteren T, et al. Symmetric log-domain diffeomorphic registration: A demons-based approach. Procs MICCAI. 2008.
7. Ehrhardt J, et al. Generation of a mean motion model of the lung using 4D-CT image data. Procs VCBM. 2008; p. 69–76.