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Biomechanical Deformable Image Registration of Longitudinal Lung CT Images Using Vessel Information

Guillaume Cazoulat, Dawn Owen, Martha M Matuszak, James M Balter, and Kristy K Brock

Department of Radiation Oncology, University of Michigan, Ann Arbor, MI 48109, USA

Abstract

Spatial correlation of lung tissue across longitudinal images, as the patient responds to treatment, is a critical step in adaptive radiotherapy. The goal of this work is to expand a biomechanical model-based deformable registration algorithm (Morfeus) to achieve accurate registration in the presence of significant anatomical changes. Six lung cancer patients previously treated with conventionally fractionated radiotherapy were retrospectively evaluated. Exhale CT scans were obtained at treatment planning and following three weeks of treatment. For each patient, the planning CT was registered to the follow-up CT using Morfeus, a biomechanical model-based deformable registration algorithm. To model the complex response of the lung, an extension to Morfeus has been developed: An initial deformation was estimated with Morfeus consisting of boundary conditions on the chest wall and incorporating a sliding interface with the lungs. It was hypothesized that the addition of boundary conditions based on vessel tree matching would provide a robust reduction of the residual registration error. To achieve this, the vessel trees were segmented on the two images by thresholding a vesselness image based on the Hessian matrix's eigenvalues. For each point on the reference vessel tree centerline, the displacement vector was estimated by applying a variant of the Demons registration algorithm between the planning CT and the deformed follow-up CT. An expert independently identified corresponding landmarks well distributed in the lung to compute Target Registration Errors (TRE). The TRE was: 5.8 ± 2.9 , 3.4 ± 2.3 and 1.6 ± 1.3 mm after rigid registration, Morfeus and Morfeus with boundary conditions on the vessel tree, respectively. In conclusion, the addition of boundary conditions on the vessels significantly improved the accuracy in modeling the response of the lung and tumor over the course of radiotherapy. Minimizing and modeling these geometrical uncertainties will enable future plan adaptation strategies.

1. Introduction

Adaptation of lung cancer radiation therapy (RT) on anatomical or biological responses has significant clinical potential (Guckenberger et al. 2011; Grootjans et al. 2015). These responses can correspond to anatomical variations, changes in metabolic activity, or change in pulmonary function. The images used to map metabolic and physiologic images are often positron emission tomography (PET) or single photon emission computed tomography (SPECT) scans, nominally from systems that acquire CT image volumes for attenuation correction and anatomic mapping of tracer distributions. In all cases, analysis of temporal

response relies on the capability to establish a spatial correlation between the lung tissues on the planning CT and on the follow-up CT. Because of anatomical variations occurring during the treatment, and differences in the breathing state from one image to another, deformable image registration (DIR) has been considered an important tool to provide accurate longitudinal mapping of the lung tissues.

A large number of DIR algorithms have been proposed for the alignment of lung CT images. In particular, significant research has focused on the registration of different phases of the breathing cycle from four dimensional CT images (4DCT) or full inhale/exhale breath-hold CT image volumes. In the context of radiotherapy, estimated respiratory motion maps have been applied to evaluate or improve treatment delivery strategies (Guerrero, G. Zhang, et al. 2005; Boldea et al. 2008) or to estimate local ventilation distributions (Guerrero, Sanders, et al. 2006; Ue et al. 2007; Reinhardt et al. 2008; Ding et al. 2010; Kipritidis et al. 2015). A very limited number of studies involved the registration of CT images potentially showing RT response. Previous studies evaluated the use of DIR for automatic contour propagation between the planning 4DCT and midtreatment 4DCT or 4D-Cone Beam CT (Hardcastle et al. 2013; Balik et al. 2013). Robertson *et al* proposed a block matching registration approach to automatically propagate the tumor from the planning CT to another scan acquired four to seven weeks after the start of treatment (Robertson et al. 2014). The capability of these methods to provide accurate anatomical point to point correspondences has, however, not been evaluated. While respiratory motion states can partially confound longitudinal image alignment for response assessment and adaptation, the main difficulties come here from anatomical variations. Tumor shrinkage is indeed known to occur for a large proportion of patients (Woodford et al. 2007; Zwienen et al. 2008; Feng et al. 2009; Kataria et al. 2014). Other typical anatomical variations that make DIR challenging include changes in atelectasis and dissolving/increasing pleural effusion (Zwienen et al. 2008).

In the current study, the registration of longitudinal CT images from patients treated with conventionally fractionated radiotherapy is investigated. The performance of Morfeus, a biomechanical model-based deformable registration algorithm (KK Brock et al. 2005) which models the lungs and body as finite-elements (FE) and applies boundary conditions on the chest wall, is evaluated. Al-mayah *et al* previously evaluated this approach when registering inhale to exhale phases of CT and demonstrated that the registration accuracy was significantly improved when including a sliding interface between the lungs and chest wall (A Al-Mayah et al. 2008). The accuracy in aligning internal lung tissues however relies on the correlation between their displacements and those estimated by mechanically propagating the deformations of the lung surface. This correlation may be limited when registering longitudinal images. A previous study investigated the use, of Morfeus as an initiation step, followed by an intensity-based alignment to refine the displacement field (Samavati et al. 2015). This approach was effective in registering inhale to exhale phases in 4DCT images where the intensity was consistent between images. However, in the context of this study, the varying content of the lung and the complexity of the associated deformations will affect the robustness of the intensity-based registration algorithm when applied to the entire image. Specifically, this method is likely to fail to estimate the deformations when the tumor response is characterized by erosion, i.e. when the tumor is responding but the underlying anatomy is remaining fixed. More control on the deformation

in this area could be achieved by preserving the biomechanical transformation model and adding boundary conditions on consistent neighboring tissues.

In order to improve the accuracy and robustness of Morfeus, the approach proposed in this paper consists of adding boundary conditions on the vessel tree. Vessels are easily identifiable as bright tubular structures. Many methods for the segmentation of the vessel tree in CT images have been proposed but the number of studies extracting those features and using them to improve DIR is limited. Cao *et al*/proposed to add a vesselness similarity term in the global similarity function between the two images (Cao et al. 2012). This method assumes a vesselness preservation between the two images which may not be valid in the case of anatomical changes. Other studies also proposed to combine intensity information and correspondences between automatically detected bifurcations in the vessel tree (B. Li et al. 2008; Loeckx et al. 2010). Hilsmann also proposed to establish correspondences between bifurcation points, with the full deformation computed using thin-plate spline interpolation (Hilsmann et al. 2007). The biomechanical model proposed in this paper aims to provide a more robust and physically plausible estimation of the deformation in the whole lung.

2. Materials and methods

2.1. Patient data

Under an institutional review board-approved protocol, six patients treated with conventionally fractionated radiotherapy were retrospectively evaluated. All subjects had 4DCT scans at planning as well as following three weeks of treatment.

The exhale phases of the 4DCT scans were selected for image registration. The spatial resolution of all images was $1.27 \times 1.27 \times 3$ mm.

In order to quantify the influence of the anatomical variations on the registration accuracy, the performance of the method was also evaluated by registering images presenting a difference in lung inflation. To this end, the proposed DIR method was applied to the publicly available POPI dataset provided by the Léon Bérard Cancer Center & CREATIS lab, Lyon, France. This dataset contains one 4DCT for six patients with 100 reference landmarks placed in the inhale and exhale frames (Vandemeulebroucke, Simon Rit, et al. 2011). For those images, the spatial resolution was $0.97 \times 0.97 \times 2$ mm.

2.2. Registration framework

The workflow of the proposed extension of Morfeus can be divided in four main steps as depicted in Figure 1. In the first step which corresponds to standard Morfeus, a finite-element model (FEM) of the lungs and body was generated from the delineations of the reference CT. Three additional steps were added to minimize the residual mismatch of the internal structures. In step 2, the vessel trees were segmented on the two images. In step 3, correspondences between the vessel trees were established. Finally, in step 4, each estimated correspondence was used as an additional boundary condition in a second numerical simulation. All steps of this workflow are detailed in the following parts.

2.2.1. Step 1: Finite element modeling - First numerical simulation—When using a contact surface in the biomechanical model, boundary conditions need to be applied to the chest wall in a way that the lung surface will be pushed. As a consequence, the CT image considered as the reference image $\mathcal{R}$ was automatically identified as the one presenting the most inflated lung. The other image was denoted the moving image $\mathcal{M}$. For both the reference CT and moving CT, triangular surface meshes of the lungs and body were created. The meshes corresponding to the organs of the reference image were then transformed into volumetric tetrahedral meshes using a finite element preprocessor (Hypermesh, Altair Engineering) with an average element volume of 0.05 and 0.14 cm³ for the lungs and body, respectively. Based on a previous study (Adil Al-Mayah, Moseley, Velec, and Kristy Brock 2011), the organs were assigned a linear elastic behavior with a Poisson's ratio of 0.4 and a Young's Modulus of 60 and 78 kPa for the lung and body, respectively. In order to allow a sliding motion of the lung relatively to the chest wall, the contact interface mentioned above was added to the model considering a zero friction coefficient which simulates the pleural lubricating fluid (A Al-Mayah et al. 2008). A surface projection algorithm previously described in (KK Brock et al. 2005) was applied between the lung triangular surfaces of the reference CT and moving CT.

Displacements of the surface nodes computed by this algorithm were assigned as boundary conditions to the chest cavities in the RADIOSS finite-element solver (Altair Engineering) in order to compute the displacements of the nodes in the reference volumetric mesh. Figure 2 provides an example of constructed FEM (a) and the boundary conditions applied on the chest wall (b). The sparse displacement field computed by RADIOSS $\mathcal{S}$ was then resampled into a dense displacement field $\mathcal{D}_{Morphous}$ on the grid of the reference image. For each voxel at the 3D coordinates $\mathbf{x}$ in the reference image space, the encompassing tetrahedron t was identified. $\mathcal{D}_{Morphous}(\mathbf{x})$ is then given by:

$$\mathcal{D}_{Morphous}(\mathbf{x}) = \lambda_1 \mathcal{S}(v_1) + \lambda_2 \mathcal{S}(v_2) + \lambda_3 \mathcal{S}(v_3) + \lambda_4 \mathcal{S}(v_4) \quad (1)$$

where λ_1, λ_4 are the barycentric coordinates of t and v_1, v_2, v_3 and v_4 the coordinates of its vertices.

Finally, the moving image $\mathcal{M}$ was transformed into $\mathcal{M}'$ on the reference image grid:

$$\mathcal{M}'(\mathbf{x}) = \mathcal{M}(\mathbf{x} + \mathcal{D}_{Morphous}(\mathbf{x})) \quad (2)$$

At this stage of the workflow, the lung surfaces in $\mathcal{R}$ and $\mathcal{M}'$ were in principle already aligned. In the following parts, we describe a way to register the vessel tree in order to reduce the possible residual mismatch of the internal lung tissues.

2.2.2. Step 2: Vessel tree segmentation—In order to detect the vessels in the lung, a vessel enhancement method was first applied to the image. The method is based on the analysis of the eigenvalues of the Hessian matrix $\mathcal{H}$ of the image I given by:

$$\mathcal{H}(\mathbf{x}) = \begin{bmatrix} \frac{\partial^2 I(\mathbf{x})}{\partial^2 x} & \frac{\partial^2 I(\mathbf{x})}{\partial x \partial y} & \frac{\partial^2 I(\mathbf{x})}{\partial x \partial z} \\ \frac{\partial^2 I(\mathbf{x})}{\partial y \partial x} & \frac{\partial^2 I(\mathbf{x})}{\partial^2 y} & \frac{\partial^2 I(\mathbf{x})}{\partial y \partial z} \\ \frac{\partial^2 I(\mathbf{x})}{\partial z \partial x} & \frac{\partial^2 I(\mathbf{x})}{\partial z \partial y} & \frac{\partial^2 I(\mathbf{x})}{\partial^2 z} \end{bmatrix} \quad (3)$$

At each voxel location, a combination of the three eigenvalues λ_1, λ_2 and λ_3 ($\lambda_1 \geq \lambda_2 \geq \lambda_3$) of $\mathcal{H}$, interpreted at the principal curvatures, allows for the determination of the likelihood of the voxel to belong to a sheet, blob or tubular structure (Koller et al. 1995; Lorenz et al. 1997; Sato, Nakajima, Shiraga, et al. 1998; Frangi et al. 1998; Q. Li et al. 2003). Depending on the sign of the eigenvalues, either bright or dark structures can be detected. In this study, vessels were considered as bright tubular structures in a dark environment. Typically, the image I is convolved with a Gaussian kernel G_σ where the variance σ is scaled as a function of the size of the structures to enhance.

The function used in this study to enhance the vessels was proposed in (Sato, Nakajima, Atsumi, et al. 1997). Briefly, let I be an image representing an ideal vessel oriented toward the z direction and presenting a Gaussian intensity profile of variance σ_v at each cross-sectional plane:

$$I(x, y, z) = \exp\left(-\frac{x^2 + y^2}{2\sigma_v^2}\right) \quad (4)$$

In this case, for each point of the central region of the central cross-section, $\lambda_1 = 0$ and $\lambda_2 = \lambda_3 \ll 0$. Based on this model, Sato *et al* proposed as a measure of similarity to a vessel the function L proportional to λ_2 and which decreases as λ_1 deviates from 0:

$$L(\lambda_1, \lambda_2) = \begin{cases} \lambda_2 \cdot \exp\left(-\frac{\lambda_1^2}{2(\alpha_1 \lambda_2)^2}\right) & \lambda_1 \leq 0, \lambda_2 \neq 0 \\ \lambda_2 \cdot \exp\left(-\frac{\lambda_1^2}{2(\alpha_2 \lambda_2)^2}\right) & \lambda_1 > 0, \lambda_2 \neq 0 \\ 0 & \lambda_2 = 0 \end{cases} \quad (5)$$

The sign of λ_1 was taken into account in equation 5 in order to be more robust to signal losses which would create fragmented vessel lines. Indeed, where there was a discontinuity in the vessel line due to a signal loss, the intensity profile along the line became concave and so λ_1 positive. By taking $\alpha_1 < \alpha_2$, the vesselness measure decreases less rapidly as λ_1 deviates from 0 in the positive direction, making it more robust to fragmented vessel lines. α_1 and α_2 were fixed to 0.5 and 2, respectively.

In the workflow, the images were first resampled on the z axis with a tri-linear interpolation to obtain isotropic-sized voxels and then convolved with a Gaussian kernel G_σ with $\sigma = 1\text{mm}$. In order to measure the vesselness of voxels corresponding to internal lung tissues only, a mask of the lung of interest was created from the delineations by applying a morphological dilatation followed by an erosion with ball-shaped structuring elements of

radii 10 and 15mm, respectively. The vesselness images $L_{\mathcal{R}}$ and $L_{\mathcal{M}}$ corresponding to the reference image $\mathcal{R}$ and the moving image $\mathcal{M}$ were then computed following (5).

We assumed that the volume of the vessel tree in the two images was roughly the same. Segmentations of the trees were then obtained by thresholding the vesselness images at a fixed percentage of the number of voxels in the image histograms. Additionally, to remove noise, a connectivity filter was applied in order to preserve structures composed by at least 200 voxels ($\sim 400\text{mm}^3$). $B_{\mathcal{R}}$ and $B_{\mathcal{M}}$ denote the resulting binary images in which each voxel belonging to the vessel tree and background were attributed the values 1 and 0, respectively.

2.2.3. Step 3: Correspondences selection—To estimate displacements of the reference vessel tree in $B_{\mathcal{R}}$, a displacement field $\mathcal{D}_{\text{Demos}}$ that minimizes the sum of squared intensity differences was estimated by applying a variant of the Demons registration algorithm (Wang et al. 2005) between the reference image $\mathcal{R}$ and the previously deformed image $\mathcal{M}'$. The displacement field aligning the vessel trees represented in $B_{\mathcal{R}}$ and $B_{\mathcal{M}}$ is then given by:

$$\mathcal{D}(\mathbf{x}) = \mathcal{D}_{\text{Morpheus}}(\mathbf{x}) + \mathcal{D}_{\text{Demos}}(\mathbf{x}). \quad (6)$$

The centerline of the vessel tree in the image $B_{\mathcal{R}}$ was extracted using the skeletonization algorithm proposed by Lee *et al* (Lee et al. 1994). $P = \{\mathbf{p}_1 \dots \mathbf{p}_N\}$ denotes the set of locations where a voxel belongs to the extracted centerline and $C = \{\mathbf{c}_1 \dots \mathbf{c}_N\}$ the set of correspondences $\mathbf{c}_i = (\mathbf{p}_i, \mathbf{p}_i + \mathcal{D}(\mathbf{p}_i))$.

As a condition for a correspondence $\mathbf{c}$ to be considered reliable and preserved in a final set C' , the estimated displacement vector has to point to a vessel point in the other image $B_{\mathcal{M}}$:

$$C' = \{\mathbf{c}_i \in C | B_{\mathcal{M}}(\mathbf{p}_i + \mathcal{D}(\mathbf{p}_i)) = 1\}. \quad (7)$$

2.2.4. Step 4: Second numerical simulation—The set of correspondences C' was used as additional boundary conditions on the vessel tree. Al-Mayah *et al* (Adil Al-Mayah, Moseley, Velec, Hunter, et al. 2010) previously demonstrated that incorporating the vessel tree in the FEM model with its own material properties had little effect on the global deformation. For this reason, the lung was considered in this study as a homogeneous organ and the additional conditions were placed on the closest node in the tetrahedral mesh of the lung. The final displacement field was computed similarly as described in section 2 and applied to the moving image $\mathcal{M}$ for visual inspection.

2.3. Accuracy evaluation

For the six patients, an observer independently identified corresponding landmarks in the planning and follow-up images, well distributed in the lung containing the tumor. The observer was asked to spend extra effort in placing points in the region around the tumor but only when there was high confidence in matching actual anatomical landmarks. The

landmarks were selected a second time by the same observer on the follow-up image in order to quantify intraobserver variability. In order to evaluate the performance of the registration specifically in the tumor area, landmarks located at a maximal distance of 15mm from the tumor boundaries were identified. Target Registration Error (TRE) was calculated as the difference between manually measured landmark positions and those determined after applying the proposed Morfeus extension, and compared to the initial TRE between measured positions and those determined using rigid registration and Morfeus without the additional boundary conditions.

3. Results

3.1. Patient population

Table 1. summarizes patient-specific information that potentially influenced the registration performance such as tumor volume change, lung volume change or other observations. Due to those factors, the number of identified anatomical landmarks also differed from one case to another. For patient 4, the tumor seemed to be elastically attached to the surrounding vasculature as it shrank. For Patients 2 and 6 the tumor was more likely eroding. For Patient 5, the tumor appeared to behave both ways.

3.2. Vessel boundary conditions

Figure 3 shows an example of a computed vesselness image (b) compared to the initial image (a). Most of the non-tubular structures are suppressed, especially the large tumor in the posterior part of the lung. The volume rendering of the vesselness image displayed in (c) highlights that a segmentation of the vasculature can then be easily obtained.

Experiments showed that for all cases, thresholding of the vesselness image at 95% of the vesselness measures resulted in a segmentation of the vessel, which, although potentially missing some part of the tree, likely only included voxels belonging to vessels. Figure 4 displays the result of the segmentation for the reference and the moving image, the extracted centerline of the reference image and the correspondences selected by the method described in section 2.2.3. Using this method, equation 7 rejected an average of 47% of the correspondences estimated by the Demons algorithm. The number of additional boundary conditions specified on the vessel tree was on average 995 ± 419 . As explained in section 2.2.4, each vessel tree correspondence was moved to the nearest nodes in the tetrahedral mesh. The mean distance between the vessel tree and the applied boundary conditions, which depends on the resolution of the tetrahedral mesh, was 2.9 ± 1.1 mm. However, due to the smoothness of the deformation field, the final vessel tree displacements differed by only 0.4 ± 0.3 mm from what was initially estimated.

3.3. Registration accuracy

Figure 5 displays the TRE measured following either a simple rigid registration, Morfeus considering boundary conditions on the chest wall only (Morfeus-std), or Morfeus with the additional boundary conditions on the vessel tree (Morfeus-vbc). For all patients the TRE measured after Morfeus-vbc was significantly lower than after Morfeus-std ($p < 0.001$). The images of Patient 5 appeared more challenging to register than for the other patients because

of a complex tumor regression scheme combining erosion and elastic shrinkage. Table 2. provides the group mean TRE in the tumor area and rest of the lung. As expected, registration errors in the tumor area were larger than for the rest of the lung. Yet, with a TRE of $2.3 \pm 1.9\text{mm}$, Morfeus-vbc significantly improved the alignment of this area compared to Morfeus-std. An overall mean accuracy of $1.6 \pm 1.3\text{mm}$ was achieved with Morfeus-vbc.

The intraobserver variability in picking the reference landmarks, which is a limit to the achievable accuracy, was equal to $0.5 \pm 0.3\text{mm}$ in the tumor area and $0.4 \pm 0.2\text{mm}$ in the rest of the lung.

Figure 6 displays an overlay of the reference image and the registered image for Patient 2 using, rigid registration (a), Morfeus-std (b) or Morfeus-vbc (c). It shows that the residual misalignment of the vessels after Morfeus-std is considerably reduced with Morfeus-vbc. Intensity differences still appear in the tumor area defined by the red contour. Those differences should however not be interpreted as resulting from a poor alignment since in this case the tumor tissues are more likely regressing than being displaced.

Table 3. shows the TRE measured when applying Morfeus to the POPI dataset. In this case, the anatomical variations are limited to the breathing motion and the definition of boundary conditions on the lung surface alone with Morfeus-std significantly improved the registration accuracy compared to the rigid registration ($p < 0.01$). This accuracy was again significantly improved when using Morfeus-vbc to reach a mean TRE of 1.1 ± 1.0 ($p < 0.01$).

4. Discussion and conclusion

A biomechanical registration method has been proposed and adapted to the alignment of longitudinal CT images during lung cancer radiotherapy.

In our dataset of longitudinal images, the exhale phases of the 4DCT were chosen for the registration. While more details may be observed as the lung is distended on the inhale phases, imaging of the exhale state is generally more reproducible. This reproducibility produces images with more consistent lung content information which is helpful for image registration.

The first step of the method is an initialization of the transform that allows the algorithm to take into account the sliding motion of the lung relative to the chest wall. It has been shown in previous studies that, allowing this discontinuity in the displacement field on the pleural contact surface improved the alignment of internal lung tissues (A Al-Mayah et al. 2008; Werner et al. 2009; Vandemeulebroucke, Bernard, et al. 2012; Schmidt-Richberg et al. 2012; Risser et al. 2013). This first initialization step appeared crucial for some patients for which a notable difference in the lung volume was observed. In the second step, a variant of the popular Demons registration algorithm was employed to reduce the residual mismatch of the internal tissues. The use of a conventional intensity-based registration algorithm could lead to unpredictable results due to the complexity of the anatomical deformation. However, we are confident in the ability of such algorithm to refine the alignment of the vessels which are generally consistent in shape and volume. The approach then consisted of reducing the dense displacement field estimated with the Demons algorithm to a subset of local vessel

correspondences which were used as additional boundary conditions in a final biomechanical simulation.

Segmentations of the vessel trees were approximate, as not all of the tree was included. This segmentation was however sufficient to delimit a region in which the intensity-based registration was considered reliable to refine the deformation. For all of the patient cases, the field of selected vessel correspondences appeared dense enough to significantly improve the registration accuracy compared to the previous Morfeus method. The absence of identifiable anatomical landmarks in the rest of the lung, for example inside the tumor, makes evaluation difficult in those areas. The biomechanical model in this study has the advantage of providing a physically plausible deformation where reliable information is missing. Future work to improve registration accuracy should address the characterization of the tumor regression. A few studies (S. Rit et al. 2010; Sonke et al. 2010; Hugo et al. 2013) have illustrated different tumor shrinkage schemes. Two main classes of tumor were identified as being, either elastically attached to or invading the surrounding tissues. The dataset used in this study included these two kinds of tumors regression. For one case (Patient 5), in which a combination of both types of tumor regression was observed, the proposed approach lead to substantially less accurate alignment of the tumor area than for the five other cases, as evident by the outlier points in Figure 5. Adapting the registration strategy according to an appropriate tumor response classification might improve the accuracy in this critical area.

In this paper, an evaluation of longitudinal CT DIR during lung RT is reported. The average accuracy achieved with the proposed method was 1.6mm. An average TRE of 1.1mm was obtained with the POPI dataset which is close to the best previously published results (Weistrand et al. 2015). The difference in accuracy with our data suggests that anatomical variations introduced more challenge for the registration, though it can also be partially explained by the larger slice thickness. The goal of this study being to provide a method that will serve to map dose or functional images in a context of adaptive radiotherapy, the reported accuracy has to be relativized to the resolution of those images. The dose grid voxels for the included cases had a size of 2mm and PET/SPECT generally presents an even lower resolution. The use of the proposed registration method thus appears interesting in future studies investigating lung treatment response.

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Figure 1.
Workflow of the proposed deformable registration method.

Figure 2.

(a) Example of Finite-Element Model consisting of the body and lungs separated by a contact surface; (b) Representation of the computed boundary conditions on the chest wall by red arrows.

Figure 3.

(a) CT intensities in an axial slice of the defined lung mask ; (b) Same slice of the vesselness image; (c) Volume rendering of the vesselness image.

Figure 4.

Left: surfaces of the segmented vessel tree; Top right: centerline extracted from reference vessel tree; Bottom right: correspondences selected as additional boundary conditions in the biomechanical model.

Figure 5. Boxplot of the Target Registration Error (TRE) for all patients and all considered registration approaches.

Figure 6. Overlay of the follow-up image for patient 2 with the planning image: (a) after rigid registration; (b) after Morfeus std; (c) after Morfeus vbc.

Table 1

Patient-specifics information.

Patient	Tumor volume Plan-Follow-up (cm ³)(vol%)		Lung volume change (cm ³)(vol%)		Observations	Landmarks (tumor / normal lung)
P1	52-46	(−12%)	65	(+4%)	-	3/46
P2	54-33	(−38%)	221	(+13%)	Tumor erosion	7/59
P3	57-44	(−16%)	88	(−6%)	Emphysema Tumor elastic	8/67
P4	431-319	(−26%)	60	(−6%)	shrinkage; Pleural effusion Tumor	7/88
P5	205-128	(−39%)	238	(+16%)	erosion/elastic shrinkage	5/52
P6	189-103	(−46%)	32	(−3%)	Tumor erosion	19/28

Table 2

Group mean Target Registration Errors (TRE).

Registration	TRE group mean (mm)		
	Tumor area	Rest of the lung	Overall
Rigid	5.8±2.9	5.8±2.6	5.8±2.9
Morfeus	5.4±3.3	3.3±2.1	3.4±2.3
Morfeus_vbc	2.2±1.9	1.5±1.1	1.6±1.3

Table 3

TRE for the POPI dataset.

Patient	TRE (mm)		
	Rigid	Morfeus std	Morfeus_vbc
POPI1	5.9±2.7	2.0±1.0	0.9±0.4
POPI2	14.0±7.2	3.3±1.6	1.3±1.1
POPI3	7.7±5.1	2.1±1.0	1.0±0.6
POPI4	7.3±4.9	2.8±2.2	1.3±1.7
POPI5	7.1±5.1	2.6±1.6	1.2±0.9
POPI6	6.7±3.7	1.9±0.9	1.0±0.6
Mean	8.1±5.6	2.4±1.5	1.1±1.0