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Deformable Registration of the Inflated and Deflated Lung for Cone-Beam CT-Guided Thoracic Surgery

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Abstract

Intraoperative cone-beam CT (CBCT) could offer an important advance to thoracic surgeons in directly localizing subpalpable nodules during surgery. An image-guidance system is under development using mobile C-arm CBCT to directly localize tumors in the OR, potentially reducing the cost and logistical burden of conventional preoperative localization and facilitating safer surgery by visualizing critical structures surrounding the surgical target (e.g., pulmonary artery, airways, etc.). To utilize the wealth of preoperative image/planning data and to guide targeting under conditions in which the tumor may not be directly visualized, a deformable registration approach has been developed that geometrically resolves images of the inflated (i.e., inhale or exhale) and deflated states of the lung. This novel technique employs a coarse model-driven approach using lung surface and bronchial airways for fast registration, followed by an image-driven registration using a variant of the Demons algorithm to improve target localization to within ~ 1 mm. Two approaches to model-driven registration are presented and compared – the first involving point correspondences on the surface of the deflated and inflated lung and the second a mesh evolution approach. Intensity variations (i.e., higher image intensity in the deflated lung) due to expulsion of air from the lungs are accounted for using an a priori lung density modification, and its improvement on the performance of the intensity-driven Demons algorithm is demonstrated. Preliminary results of the combined model-driven and intensity-driven registration process demonstrate accuracy consistent with requirements in minimally invasive thoracic surgery in both target localization and critical structure avoidance.

1. Introduction and Purpose

With more than 200,000 new cases in the USA each year, lung cancer remains the most prominent cancer of both genders.¹ An increasing trend in the rate of tumor findings, either

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through incidental findings or low-dose CT screening^{2,3} of at-risk patients, has resulted in an increased frequency of small, early-stage lung cancers presenting for treatment. Surgical resection – either by open lobectomy or by lesser, more conservative resection – remains the preferred method of curative treatment for these early-stage lung cancers. A move to less invasive surgery over the last decade demonstrates equivalent outcomes to open lobectomy, improved morbidity, faster recovery, and better preservation of normal lung function.⁴ However, minimally invasive approaches can limit a surgeon's ability to palpate the lung and localize small tumors, relying on a finger placed through ~1-2 cm intercostal ports into the pleural space, thus confounding identification of lesions even a short distance from the pleura. A variety of adjunctive techniques have been used – the most common involving preoperative CT with placement of a wire/coil or dye to mark the nodule.^{5,6} Such preoperative localization is logistically cumbersome and costly, requiring coordination of two invasive procedures within a fairly short time to prevent marker migration. The approach increases the cost, risk and complexity of care. We propose a registration method based on cone-beam CT (CBCT) images acquired intraoperatively from a mobile C-arm to directly localize tumors in the OR. In addition to potentially obviating the cost and logistical burden of preoperative localization, intraoperative CBCT could facilitate safer surgery by visualizing also the critical structures surrounding the surgical target (e.g., pulmonary artery, airways, etc.).

The last decade saw significant advances in deformable image registration, with most work in thoracic contexts aimed at geometrically resolving the inhale, exhale, and intermediate states of the lung during respiration. Adapting such techniques to the deflated lung (Fig. 1) is new territory. Sadeghi et al. used an extrapolation technique to estimate the deformation field computed from the inhale-exhale states in 4D CT extrapolated to the deflated state.⁷ The approach showed sub-mm accuracy in specimens where lung motion continued along the same trajectory (sup-inf) as natural respiration – limited largely to needle procedures (brachytherapy) in which the lung is drawn under negative pressure, but without pleural breach and deflation as in video-assisted thoracic surgery (VATS). The anatomical deformations in VATS are distinct from 4D CT or fine needle procedures, as illustrated in Fig. 1, where the deflated lung is seen to collapse medially upon breach of the pleura. The proposed research combines two promising deformation techniques: first, a robust model-driven method matching the lung surface and airway bronchial trees between inflated and deflated states to achieve lung nodule localization within the target wedge (~10 mm required localization accuracy); then, an intensity-corrected variant of the demons algorithm^{8,9} refining registration to ~1-2 mm precision to localize both the tumor and surrounding critical anatomy. The combined approach thus promises to yield accuracies respective of minimally invasive thoracic surgery requirements.

This manuscript presents methods and results in three sections. First, the basic registration required to bring preoperative CT to the intraoperative context is described: registering the inflated lung to intraoperative CBCT acquired prior to pleural breach. A novel deformable registration method is then presented which deforms the inflated lung CBCT to the deflated lung CBCT using both anatomical models and image intensity information. The method was applied to CBCT images of a cadaveric porcine specimen acquired using a mobile C-arm.¹⁰ At each step of the algorithm, the geometric accuracy of the registration process is presented

in terms of two metrics: target registration error (TRE, estimating the error in localizing distinct anatomical points in the lung) and normalized cross-correlation (NCC, defining a similarity measure between the warped CBCT image (i.e., deformed image of the inflated lung) and the (fixed) deflated lung CBCT).

2. Preoperative Registration of the Inflated Lung: CT-to-CBCT

Immediately prior to pleural breach and lung deflation, a CBCT image of the inflated lung is acquired as a basis for registering preoperative data to the operating scene. This initial scan is acquired with the target lung matching the lung state captured in the preoperative diagnostic scan. Following a rough rigid alignment using high-intensity bony structures (e.g., the spine), the registration is achieved using an “iterative intensity match” (IIM) variant of the Demons algorithm.⁹ IIM Demons was previously applied to head and neck surgery cases, where it was shown to be robust against image intensity differences between the preoperative CT and intraoperative CBCT and demonstrated sub-voxel accuracy in registration. This initial step provides visualization of preoperative planning data in intraoperative (inflated lung) CBCT and forms the starting point (moving image) for registration of intraoperative CBCT data. It similarly registers all planning data defined in the preoperative CT (e.g., segmentation of the tumor and surrounding critical anatomy) to the inflated lung CBCT.

3. Intraoperative Registration of the Inflated and Deflated Lung: Part 1: A Model-Driven Approach

An overview of the general algorithm, which is composed of two major stages, is presented in Fig. 2. The first stage is a model-driven approach utilizing structures segmented from the intraoperative CBCT image to coarsely initialize the second stage, which refines the registration using an image-driven approach (Demons variant). The initial (model-driven) stage is anticipated to provide registration within ~10 mm accuracy, suitable for gross localization of the target wedge, and the second (image-driven) stage is anticipated to register within ~1-2 mm accuracy, suitable for localization of the tumor and adjacent critical anatomy. The entire process is intended to operate within the time constraints of intraoperative workflow, although initial implementation focused on algorithmic steps and potential accuracy (rather than optimization of computational speed).

The aim of the model-driven registration is to use anatomy that is readily identifiable (i.e., more easily segmented by automatic or semi-automatic methods) and pertinent to the surgical task and to extrapolate the sparse motion resulting from their alignment to the rest of the image. For this particular step, segmentation of lung surfaces and bronchial airway trees were used. A semi-automatic method was chosen to perform the segmentation, employing manually placed “seeds” and an edge-constrained active contours algorithm. Initial results showed that segmentation of the lung surface was straightforward for the lateral aspects (inflated or deflated) and more challenging for the medial aspects (mediastinum). Segmentation of the airway performed well by virtue of good intraoperative image quality in mobile C-arm CBCT¹¹ and airway patency out to 3-4 generations of the bronchial tree. The resulting segmentations were subsequently processed to reduce noise by

choosing the largest connected component, filling holes in the segmentations, and smoothing the edges.

3.1 Point Correspondence Based on Lung Surface Normals

Identifying correspondences between two objects traditionally involves finding and matching features; however, when the objects of interest are highly deformable structures like the lung, identifying reliable features can be challenging. The inflated lung, in both the inhaled and exhaled states, contains a number of such features - e.g., airway and vessel bifurcations. However, many of these features are lost as the lung collapses upon deflation during surgery, and it is difficult to define a sufficiently rich set of point correspondences throughout the entire lung.

As a first order approximation, a simple method employing point correspondences defined on the lung surface was investigated. This highly oversimplified approach assumed lung motion between the inflated and deflated states along surface normals of the deflated lung (i.e., outward pointing normal vectors computed on the deflated surface segmentation). Based on this approximation, triangular meshes of the inflated and deflated lungs were generated using a marching cubes algorithm and decimated to contain ~ 1000 triangles. The surface normal vectors computed for the deflated surface were then projected outward to intersect the triangles of the inflated surface, and the point of intersection on the inflated surface was defined as the point correspondence. The total population of these displacements was median-filtered to reject outliers, specifically large erroneous displacements which otherwise produce adverse effects on the interpolated displacement field. For the TRE results (Fig. 3), 60 bronchial airway bifurcations were defined as target points by repeated localization in CBCT by a single observer. As shown in Fig. 3, the method based on surface control points alone improved TRE from ~ 6 -10 mm (unregistered) to ~ 5 -6 mm, with further improvement to ~ 4 -5 mm using additional corresponding points defined in the airways (below). A corresponding increase in NCC is also evident. Examination of images registered by this method showed moderately good alignment of features in the bulk of the lung but was subject to significant error at extrema - e.g., the lower lobes, diaphragm interface, and costophrenic angle.

3.2 Lung Surface Mesh Morphing with Affine Bounding Box Initialization

Although the first-order approximation described above provided a coarse, fast initialization of the surface boundaries, the assumptions made about the nature of lung deflation make the approach susceptible to gross errors in segmentation, particularly at inferior and medial surfaces. Most importantly, the motion assumption only holds for convex surfaces, which is not the case for the inferior aspect of the lung. The method also assumed that the direction of motion along the normal is toward the exterior mesh, which was observed to be not always true. Such cases resulting from the simple assumptions thus motivated the development of an improved method.

The improved method first makes use of bounding boxes to affinely initialize the two surfaces. Since the basis images were already rigidly aligned, the affine transform that aligns the corners of the bounding boxes reduces to a simple scaling operation (i.e., no shearing).

For the lung, such initialization serves to approximate matching of extreme points that would otherwise involve computationally complex operations to identify and match features such as the apex of the lung or the diaphragm edge.

Following affine initialization, the mesh representing the inflated lung is morphed on to the deflated surface using an iterative mesh evolution approach.¹² For each motion step t , each vertex v of the triangular mesh S is displaced along its current normal at a magnitude proportional to its distance to the closest point u on the target mesh (Eq. 1):

$$\vec{\mathcal{F}} = \frac{\partial S}{\partial t} = - (u - v(t)) \cdot \mathbf{N}(v(t)) < \alpha \cdot \bar{e}(v(t)) \quad (1)$$

This displacement is bounded by a user-defined upper limit α and the local average edge length at v . The small step size achieved by a lower bound ensures smoother convergence at the cost of an increased number of iterations. Additional steps were also taken to address the problem of how to maintain the manifold properties of the surface while it undergoes strong deformations that may cause topological changes. The solution by Zaharescu et al.¹³ was used to detect and resolve self-intersecting triangles through adaptive remeshing, as well as optimizing vertex valences and applying a Laplacian smoothing to the mesh at each iteration.

3.3 Identifying and Matching Bronchial Airway Junctions

While lung surfaces carry information on the bulk motion of the lung boundary, the airways provide insight into the motion of the inner structures. Their registration is similar to the surface approach, but the problem of identifying correspondence is better justified by the unique tree structure of the airways. Well-defined coordinates for points within the airways are defined as “junctions” of bronchial branches. Midline extraction using the method of Lee et al.,¹⁴ followed by automatic labeling based on voxel-neighborhood, was used to automatically determine the junction locations. Correspondence between airway junctions was then formed by first identifying a source node (e.g., carina) via permutative matching of neighboring graph edge lengths (branch sections). The resulting directed graph is then traversed in a breadth-first fashion¹⁵ to find corresponding junctions (40 junctions mapped in Fig. 5) by matching the edge length from the current node to the last identified correspondence. The method thus aims to provide robustness against missing pieces of the graph, potentially due to differences in volume extent and/or failure to detect branches in the deflated lung.

The model-driven registration using both surfaces and airways yields a sparse set of points that describes the deflation of the lung. To identify the motion of points in between, the point correspondences obtained separately for the surface (mesh evolution) and airways (directed graph) were interpolated on to the image voxel-grid. An inverse distance-weighted interpolator was employed as a variant of Shephard's method.¹⁶

3.4 Results: Model-Driven Registration

The model-driven registration methods described above were applied to registration of the inflated and deflated lung of a cadaveric porcine specimen undergoing simulated VATS guided by C-arm CBCT. Both the inflated and deflated lung volumes were first extracted using the same segmentation that drives the surface registration. The results below are presented in a qualitative fashion using CBCT slice overlays in addition to quantitative metrics describing the evolution (improvement) in TRE and NCC in each step of the algorithm.

When compared with the point correspondence based on lung surface normals (Fig. 3), the bounding box initialized mesh morphing method (Fig. 6) performed considerably better and achieved a significantly higher NCC (95.5%) and lower TRE (1 ± 0.6 mm). The final results for the model-driven registration are consistent with the basic requirement for coarse localization of the nodule within the target wedge.

4. Intraoperative Registration of the Inflated and Deflated Lung Part 2: An Image-Driven Approach

4.1 Multi-Scale Demons Registration

The model-driven registration provides a good initialization for higher-precision registration of both the target and surrounding critical anatomy. Image-driven techniques, which use all of the image features and gradients (not just a sparse set of points) to drive a registration that is robust against local minima and spurious deformation are a good candidate solution. The Demons algorithm employed here involves a multi-resolution, intensity-driven approach in which a morphological pyramid improves speed and avoids local minima. A “smart” convergence criterion at each level of the pyramid has also been shown to minimize the number of iterations.⁸ Variants of the Demons method have been applied to soft-tissue and piecewise rigid anatomical deformation scenarios ranging from the head and neck to pelvis in surgery and radiation therapy. The basic form of the Demons algorithm is adaptable to a variety of data types, is reasonably fast, and has demonstrated accuracy at the level of the voxel size, provided good rigid initial registration. Among the challenges addressed below is the fact that the Demons method depends on the image intensities in the moving and fixed images (assumed equal) and therefore requires modification to account for the change in lung density between the inflated and deflated states.

4.2 Intensity Matching Using A Priori Lung Density Modification

The standard Demons algorithm is known to perform poorly in registering images that differ in image intensity. Although intensity variations may occur even in non-deforming anatomy, simply due to CT calibration, acquisition artifacts, scatter, and other sources, for the deflated lung the dominant factor is presented by the change in lung density between the inflated and deflated state. Due to the partial volume effect, the mean intensity of inflated lung parenchyma is ~ -700 HU, which represents volume-averaging on a tiny scale (i.e., over the volume of each voxel) of soft-tissue and air components (0 and -1000 HU, respectively). Reduction in air volume as the lung deflates increases the bulk density, giving an increase in voxel intensity – for example, ~ -100 HU for the deflated lung parenchyma with ~ 10 -20%

air retention. Two approaches can help overcome this limitation: an “iterative intensity match (IIM)” shown to provide robust Demons registration over broad variations in image intensity;⁹ and an a priori lung density modification (APLDM).¹⁷ The latter was chosen in our application, since it addresses the problem explicitly in the lung context. APLDM uses an input breathing axis and lung region boundaries to linearly correlate a deflated lung slice z_{def} to an inflated slice z_{inf} .

$$I'_{\text{inf}}(x) = I_{\text{inf}}(x) + \bar{I}(z_{\text{inf}}) - \bar{I}(z_{\text{def}}) \quad (2)$$

where I_{inf} at voxel x is corrected by offsetting the difference of the mean intensities at corresponding slices containing voxel x . This process was fully automated using the previous model-driven step, which provides the bounding slices from segmentations, and the breathing axis that is inferred from the resulting interpolated displacement field (i.e., the axis with the largest mean displacement). As illustrated in the histograms of Fig. 8, the APLDM method is shown to match intensities between equivalent slices in the inflated (~ 700 HU) and deflated lung (~ 100 HU) due to air expulsion in the latter.

4.3 Results: Image-Driven Registration

Following initialization provided by the model-driven registration (i.e., surface mesh evolution and airway point correspondences), the image-driven step shows significantly improved alignment of the surface boundary, as well as air-tissue interfaces throughout the lung as illustrated in Fig. 9. TRE measurements show improved precision to within 1 mm, and although the difference to the model-driven method is not dramatic (0.78 ± 0.44) – since the target fiducials are close to airway junctions – both the qualitative images and the NCC (96.8%) capture the improvement in areas not covered by the segmented models. In short, the model-driven half of Fig. 2 provides bulk registration at the scale of ~ 10 mm, and the image-driven half “cleans up” the details at the $\sim \text{mm}$ level.

5. Discussion and Conclusion

A novel technique for deformable registration of the inflated to deflated lung has been presented. The algorithm develops and integrates two distinct registration methods – the first employing lung surface and bronchial airway models for fast initialization of the registration process to within ~ 3 mm, and the second employing a variant of the Demons algorithm applied to intensity-corrected images for registration accuracy within ~ 1 mm. The geometric performance was quantified in terms of TRE and NCC and qualitatively validated throughout the lung volume by visualization of slice overlays. The model-driven step aims to provide target localization within the target wedge (to be resected) even under conditions in which the tumor may not be directly visualized in CBCT. The image-driven registration then yields high-precision localization of the target as well as registration of adjacent critical anatomy and landmarks identified in preoperative planning. Future work is underway to improve the proposed approach, including more advanced methods for the initial lung segmentation, such as deformable models, the random walker algorithm, and graph cuts. Methods will be specifically tested to improve segmentation at the medial surface of the lung collapsed against the mediastinum. Alternative methods for vector field interpolation

will be investigated, allowing increased robustness to noise and erroneous correspondence, and weighting the importance of vectors at airway tree junctions versus those on the surface. Vector spline methods will be implemented using fast numerical methods that avoid large matrix inversions, permitting the displacement vectors that arise from the most salient image features to more strongly drive the deformation and be more robust to errant vectors in noisy data. Finally the algorithm will be implemented in an in-house image guidance system¹⁸ to facilitate the workflow analysis of advanced navigation techniques.

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Figure 1. (left) Image-guided video-assisted thoracic surgery (VATS) setup using a CBCT-capable C-arm. (right) Axial CBCT slices of a porcine specimen, depicting the volume and intensity differences between an (a) inflated and (b) deflated lung. Changes in lung intensity and structural shifts are visible in the deflated lung after post-pleural breach.

Figure 2.

Deformable registration of the inflated and deflated lung. The two-stage method involves: 1) model-driven registration using surface and airway structures to achieve coarse registration; and 2) image-driven registration using an intensity-invariant Demons registration. Different approaches discussed in the manuscript are presented as bullet points for each step.

Figure 3. TRE (left axis, blue box plot) and NCC (right axis, red dashed line) results using the simple lung surface point correspondence method.

Figure 4.
Triangular mesh of the lung surface with normal vectors depicted in yellow.

Figure 5.
Surface rendering of the airways with marked junctions and their displacement.

Figure 6.

(left) CBCT slice overlays of the deflated lung (cyan) and deformed inflated lung (magenta) qualitatively depicting the co-registration of features throughout the lung volume. (right) Analysis of registration performance in terms of TRE (geometric accuracy in the alignment of specific anatomical target points) and NCC (image similarity). Analysis of each metric at each step of the algorithm demonstrates the evolution in performance (monotonic reduction in error) as the algorithm progresses.

Figure 7.

TRE and NCC results using model-driven initialization followed by image-based (Demons) registration. The Demons steps are seen to under-perform in this case due to a lack of image intensity matching, resolved in Fig. 8 using the APLDM method.

Figure 8.
Intensity histograms of the deflated and deformably registered inflated lungs.

Figure 9. (left) CBCT slice overlays of the deflated lung (cyan) and deformed inflated lung (magenta). The overlay demonstrates the improved quality of the combined model-driven and image-driven approach. (right) Quantitative analysis of TRE and NCC shows the evolution in registration performance across each step of the process outlined in Fig. 2. The improved performance of the Demons steps compared to Fig. 7 is the result of the APLDM intensity correction.