Towards a Normative Lung Atlas: Validation of Physiologically Appropriate Temporal Reparameterization of Dynamic Lung MR Sequences

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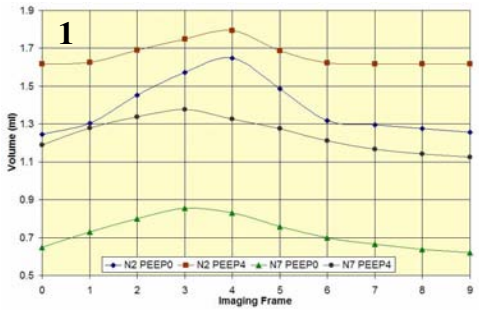
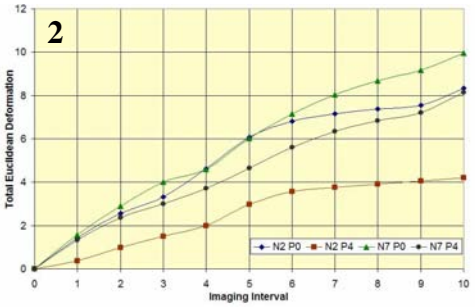
Introduction: Quantification of pulmonary deformation is useful in characterizing normal lung motion as well as the changes that occur as a result of pathological processes [4]. Magnetic resonance (MR) imaging of the lung can be used to noninvasively visualize and assess pulmonary anatomy and dynamics [3]. We have previously demonstrated and validated non-rigid image registration algorithms for computing the deformation between successive pulmonary MR images [2]. However, the problem of matching individuals with unique respiratory rates and lung capacities in both space and time is challenging. Presently, we are interested in establishing spatiotemporal correspondences between dynamic sequences from multiple individuals in order to construct a dynamic lung atlas [5]. Using an intrinsically symmetric registration algorithm (ISIR), we can interpolate at specified positions along the geodesic path between two images [1]. Our hypothesis is that we can effectively reconstruct these intermediate images using total lung deformation as our parametric basis, and thereby interpolate images in multiple individuals at the same physiologic point in their respective respiratory cycles.



Methods: We have recently established a novel method which enables mouse lungs to be imaged at specific points during respiration using cine-mode dynamic MRI in conjunction with a computer-controlled small animal ventilator (SAV). Two normal (Balb/c) mice (N2 and N7) are mechanically ventilated at a frequency of 120 breaths/min (500 ms/breath) and placed with a dorsal respiratory sensor in a 4.7 T MRI system (Biospec 47/40, Bruker BioSpin, Karlsruhe, Germany) [6]. TR is prescribed to be 1/10 of one respiration (50 ms) so that ten MR images were obtained with respiratory triggering. Other imaging parameters include TE = 1.8 ms, matrix size = 128^3, FOV = 2.56x2.56x2 cm. Imaging is performed at positive end-expiratory pressures of 0 (P0) and 4 (P4) cm H_2O in each animal to produce four datasets. Lung volumes (figure 1) are estimated via interactive, semi-automated level-set segmentation [7].



We employ the ISIR algorithm that simultaneously computes the forward and inverse registration of two images I and J [1]. Forward (I into J) and inverse (J into I) transformations $\varphi_1(t)$ and $\varphi_2(s)$, respectively, are produced. The registration determines the diffeomorphism that simulates a temporal path that can be sampled at specific intervals. Interpolants at any point along this geodesic path between the two images can be constructed via $s*(I \cdot \varphi_1(t)) + t*(J \cdot \varphi_2(s))$, where t=1-s; s=t=0.5 produces the shape and intensity average of the two anatomies. In this work, we use total lung deformation over the respiratory cycle to reparameterize each sequence and interpolate intermediate anatomies from their temporally adjacent neighbors. Deformation (D_i) along the geodesic between I and J is computed as the total magnitude (Euclidean norm) of all displacements within the lung divided by the instantaneous lung volume computed from I. These incremental deformations are summed and are plotted in figure 2. In order to validate our reparameterization scheme, we perform a leave-one-out analysis to reconstruct each image in a sequence, omitting the respiratory endpoints. Given a sequential triplet of images, A, B and C, we reconstruct image B from temporally adjacent images A and C. After registration of A to B and B to C, we determine that B is at a "distance" of $t = D_a / (D_a + D_b)$ from A to C along the geodesic path. We apply this relationship to all sequential triplets in the two image sequences, compute t for each triplet from the values in figure 2, and compare the displacement field produced from the initial pairwise registration with that from the geodesic interpolation. Errors are reported as the average distance between vector endpoints in each field as well as the average angular disparity at each location between the two resulting vector fields.

Results: In all four datasets, eight image frames are reconstructed after omitting end-inspiration and end-expiration. Figure 3 shows a sample of the original (white) and interpolated (red) displacement fields in mouse N7 in the xy-, xz- and yz-planes, respectively. Visually, there is strong correspondence between the original and interpolated fields. The average endpoint errors (in pixels) over all eight frames are: (N2 P0) 0.024±0.013, (N2 P4) 0.021±0.012, (N7 P0) 0.027±0.016, (N7 P4) 0.026±0.014. The average angular disparities (in degrees) over all eight frames are: (N2 P0) 12.3±10.5, (N2 P4) 24.9±21.0, (N7 P0) 16.6±19.3, (N7 P4) 18.2±18.4. A higher angular disparity is observed in dataset N2 P4 as compared to the other three sequences. This is likely due to numerical oscillations introduced by interpolating between virtually identical images in the expiratory phase of the sequence, thereby testing the limits of the resolution of our algorithm.

Discussion & Future Work: We are able to reparameterize dynamic lung MR image sequences according to total lung deformation using geodesic interpolation. With this approach, we can construct spatiotemporal lung atlases by temporally sampling sequences from multiple individuals at physiologically coincident points (e.g., 30% of inspiration) and computing their spatial average. In future work, we will assess the accuracy of this interpolation technique for temporally distant images, such as respiratory endpoints, and evaluate its performance on large-deformation datasets from patients and healthy volunteers. The ultimate goal of this work is to develop methods to construct a dynamic normative atlas of lung motion; the latter can be used for regional assessment of pulmonary dynamics, disease diagnosis and evaluation of therapeutic interventions.

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