Quantitation of Pulmonary Structure via Registration and Normalization of Serial ^{3}He MR Images

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Introduction A method for in vivo characterization of changes in lung structure would potentially be helpful in disease diagnosis, monitoring tissue response to therapy in clinical and experimental studies of lung injury, and in short clinical trials facilitating development of drugs for treatment. MR imaging of the lungs following inhalation of approximately 1 L hyperpolarized helium (Helispin™, GE) has been shown to provide reproducible measures of lung structure reported as the mean apparent diffusion coefficient (ADC) of the helium [1]. Mean ADC, however, does not capture any of the spatial information available in the images. To enable anatomically detailed, quantitative characterization of pulmonary ADC values in serial studies of different subject groups, this study examined the hypothesis that MR Helispin™ images acquired of an individual at different timepoints may be spatially aligned, and that individual measurements may be anatomically normalized with respect to a reference coordinate system established by a CT-based lung atlas. The intra-individual registration would account for differences in lung configuration during serial imaging, and thus enable changes in ADC to be calculated via direct voxelwise subtraction of the ADC values measured at different times for each subject. The ability to warp MR Helispin™ images into alignment with a reference atlas would in turn allow this ADC information to be compared across different subjects. The change in ADC values over time in the different subject groups can then be determined by comparing 1) regional ADC differences using anatomic structures defined over the lung atlas, and 2) voxelwise ADC differences within a standardized atlas space.

Methods Eleven healthy control subjects were imaged at two timepoints 6 months apart. The scans were acquired during a breathhold after the subject had inhaled approximately 1 L of hyperpolarized gas mixture from functional residual capacity, with the following parameters: 10 coronal slices, 15 mm thick, in-plane pixel size of 3.7 x 3.7 mm^2. Note that each scan consists of diffusion-weighted acquisitions at two different b values as required for calculating ADC. The atlas used in this study was manually constructed from an end-inspiratory HRCT dataset acquired in a patient with no known lung disease. Images were reconstructed using a high spatial frequency algorithm to obtain contiguous sections with matrix 512 x 512, 0.63 mm in-plane resolution and 1.25 mm slice thickness. The lung atlas consists of a lobar segmentation of the lungs. There are two lobes in the left lung (upper and lower—LUL and LLL, respectively) and three lobes in the right lung (upper, middle and lower—RUL, RML and RLL, respectively). Both lungs were first semi-automatically segmented from whole-chest HRCT data using SNAP software [2]. The trachea was omitted from the segmentation because it is only faintly visible in some of the ^{3}He data. The lobes were then manually segmented slice-by-slice in the lung-only image volumes. The pulmonary fissures—natural anatomical divisions between lung lobes—are visible as higher-intensity curves on the sections, and can be traced to construct an anatomic atlas of the lung lobes.

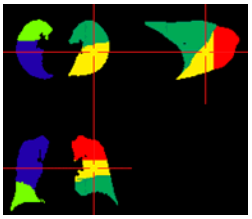

Figure 1. Tri-planar view of the HRCT-based atlas used in this work. The cursor is positioned in the right middle lobe. The atlas is shown in its repositioned form so that it matches the global position of the lungs in the ^{3}He data. The pulmonary lobes are shaded as follows: LUL (blue), LLL (light green), RUL (red), RML (yellow), RLL (dark green).

For each subject, the b0 image at time 2 was aligned with the b0 image at time 1, which in turn was registered with the HRCT image of the atlas. Intra-subject registration was performed by optimizing the intensity difference between images over the transformation space of elastic diffeomorphisms. The lung shape (rather than raw intensity) was used to guide the b0 alignment by first segmenting the lung in the images using manual thresholding. In contrast, the b0-CT registration was obtained by optimizing a cross-correlation metric over the intensity images and the general family of large deformation diffeomorphisms. In each case, the registration solution preserves topology by construction (and, consequently, the mean ADC value of the warped Helispin™ images) and was estimated using the Lagrangian push forward (LPF) method [3] with a rigid-affine initialization [4]. The b value images needed to compute the voxelwise ADC map at time 2 are all warped into the lung configuration A at time 1 using the registration transformation estimated from the relevant b0 images. ADC calculation at and subtraction between timepoints are performed over the segmented HRCT volume that constitute the atlas (which has been warped into alignment with A), thus excluding the trachea from consideration. Regional quantitation of ADC values and their differences over time was performed by summing over the voxels for each of the lobes identified in the individualized atlas—the total in each region is the basis for inter-group lobar comparisons. For voxelwise comparison of these quantities, the subject-specific ADC related information is mapped, using the b0-CT registration transformation, into the anatomical space established by the lung image from which the atlas is derived. Group statistics can then compiled by examining the normalized ADC data for all the subjects at every voxel location within the atlas.

Results Figure 1 shows the lung atlas. The alignment of the b0 image for one subject is shown in Figure 2. The warping of the b0 image into the atlas had no effect on the mean ADC value because mean ADC was constrained to be preserved in the warping algorithm. Before warping the mean ADC value for the 11 healthy control subjects was 21.5 +/- 4.1 mm^2/sec at baseline and was virtually unchanged at 21.7 +/- 3.7 mm^2/sec six months later (average change = 0.2 +/- 1.0 mm^2/sec). The warped images at baseline and 6 months later were compared to calculate the average change in ADC for all of the voxels in the warped image for each subject. The mean change in ADC for each subject ranged from -1.5 to +2.2 mm^2/sec with an average value of 0.8 +/- 1.2 which was not significantly different from zero or the value determined from the pre-warped images.

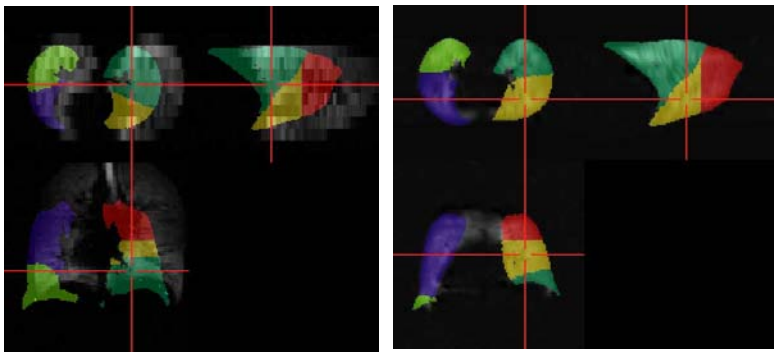

Figure 2. The b0 image before (left) and after (right) mapping into the labeled atlas space with our topology preserving large deformation registration algorithm, the LPF method.

Discussion & Future Work In this work, we demonstrate that registration can be performed both to align longitudinal data acquired of an individual using MR Helispin™ imaging and to anatomically normalize Helispin™ data from different individuals to a CT-based lung atlas. The former capability enables maps of longitudinal changes in ADC value to be obtained in an automatic, reproducible and objective way. The latter spatial normalization to a labeled atlas allows comparison of corresponding voxels (and regions) in different subject groups and thereby captures the spatial information that is not available when comparisons are made between ADC histograms. Furthermore, the warping maintains the mean ADC (by design) and yields a value for the change in ADC over 6 months in a study of healthy control subjects that is not significantly different from zero. Further validation of the developed registration methodology is required to precisely characterize the accuracy of its performance. Nevertheless, preliminary results indicate that this technique may be valuable for detecting the small regional changes in lung structure that one would expect to find in patients with emphysema.

References [1] S. Diaz et al. *Proc. Eur. Resp. Society Meeting*, 1546, 2004. [2] P. Yushkevich et al. *Insight Journal*, 1, 2005. [3] Avants et al. *Med. Image Anal.*, in press. [4] P. Burstein et al. *Proc. MICCAI*, 2005.