Methods

Four 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 mm². 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 the 3He 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 anatomatic atlas of the lung lobes.

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 deformorphisms. 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 deformations. 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 ADC, ADC calculation at and subtraction between timepoints are performed over the semantically 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 be 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 mm²/sec at baseline and was virtually unchanged at 21.7 +/- 3.7 mm²/sec six months later (average change = 0.2 +/- 1.0 mm²/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 mm²/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.

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