Hyperpolarized ^{3}He Magnetic Resonance Image Registration Tools for Longitudinal and Multi-Modality Studies

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Motivation:
Despite decades of research focussed on novel methods for the specific contouring of radiation doses for lung cancer treatment, radiation-induced lung injury (RILI) still occurs in over 1/3 of thoracic radiation treatment cases and more importantly, lung cancer survival has not improved over the last 30 years. Predictive schemes for risk of RILI that could be used to amplify and alter radiation treatment strategies and accelerate the physics research critically required to do so have not resulted in therapy improvements. Our goal is to develop pulmonary image guidance methods and image-based prediction schemes as a solution to this important problem. Towards this goal, we are developing novel hyperpolarized ^{3}He magnetic resonance imaging measurements of regional lung function and structure with high spatial and temporal resolution. An important step towards realizing the potential of ^{3}He MRI as an image guidance tool for lung cancer treatment, image registration techniques must be developed. In lung cancer patients, registration of ^{3}He MRI scans from the same patient at different time points can be used to enable detection of regional changes in lung function over time, while registration of ^{3}He scans to x-ray computed tomography (CT) provide a way to determine underlying inflammation and emphysema.

Methods:
Image Acquisition: Magnetic resonance imaging was performed on a whole body 3.0 Tesla Excite 12.0 MRI system with broadband imaging capability. For hyperpolarized ^{3}He diffusion-weighted imaging, multi-slice coronal images were obtained using a fast gradient-echo method with centric k-space sampling. For ventilation or T1-unweighted imaging, multi-slice coronal images were obtained using a fast gradient-echo method with centric k-space sampling. All imaging was acquired during a 10-14 second breath hold of hyperpolarized ^{3}He, provided by a turn-key, spin-exchange polarizer system. Doses (5 mL/kg) were administered in 1 L plastic bags diluted with ultrahigh purity, medical grade nitrogen. Image acquisition began once inspiration of the bag was complete.
Registration: Registration accuracy and variability was evaluated from a dataset previously acquired consisting of subjects who were scanned longitudinally at our center. Time between baseline (BL) and follow up (FU) visits was determined by study protocol, and varied based on disease. We determined the *Fiducial Localization Error (FLE,* Figure 1) by repeating the localization of the fiducials 5 times in each image. From this the FLE intra-observer reproducibility was determined. After optimizing landmark identification, we registered pairs of breath-hold matched ^{3}He MR images acquired from the same subject longitudinally and determine the *Fiducial Registration Error* (*FRE*).

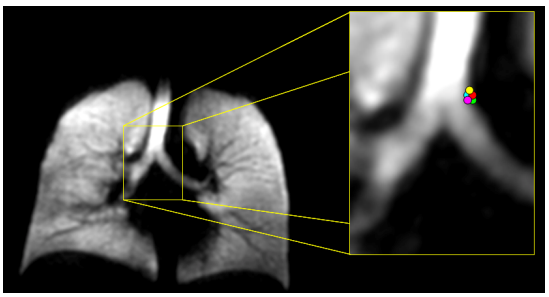

Figure 1. Fiducial localization error

Registration accuracy and variability was evaluated from a dataset previously acquired consisting of COPD and RILI patients who were scanned with both MRI and CT within approximately 1 month. An additional 5 pairs of ^{3}He MRI – CT images were registered to determine the *FRE*.

Results
Five fiducial markers were used for registration of ^{3}He – ^{3}He MR images, including the carina for every subject, and four other points. The mean FLE across all five point was 1.20 ± 0.51mm [range=0.47-2.26mm], with no statistically significant differences for FLE between subjects. Intra-observer reproducibility (as determined by the intra class correlation coefficient) for fiducial marker localization was ICC=0.99, $p<0.001$. FRE was 7.28 ± 4.27mm for healthy elderly volunteers with 25 ± 1 months between scans, and 6.12 ± 2.19 mm for subjects with radiation-induced lung injury (22 ± 0.8 weeks BL-FU).

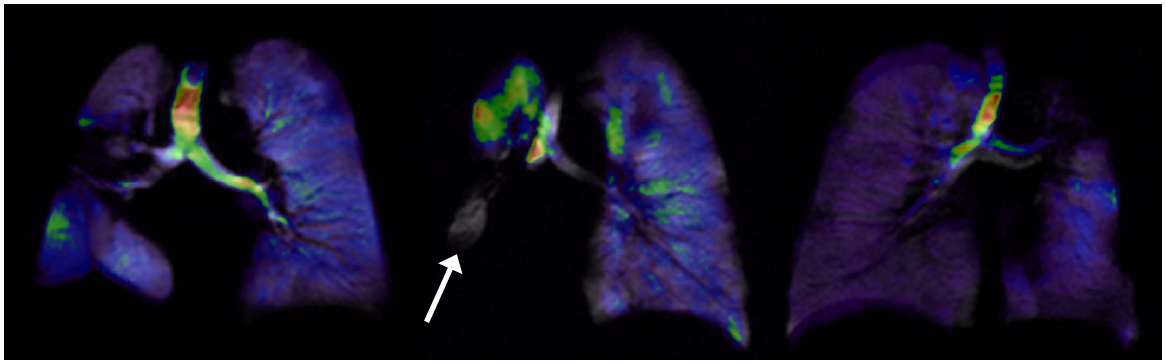

Figure 2. Registration of longitudinally acquired 3He MRI in 3 subjects with RILI. Baseline gray-scale image shown with followup image (colour) registered. Arrow points to main differences.

Conclusions
We show that by using a set of fiducial markers, registration of ^{3}He MRI across time points can be performed with a high level of precision, which will be crucial in future longitudinal clinical studies. The precise registration of ^{3}He MR images acquired longitudinally will allow for a more robust analysis of regional differences in ventilation over time, which will greatly improve the utilization of ventilation information contained in these high resolution images. The application of this technique for multi-modality registration (^{3}He MRI to CT datasets) is critical for the direct comparison of these two modalities, and will aid in ascertaining the cause of ^{3}He MRI ventilation changes.