Detecting Emphysematous Lung in a Rabbit Model using XTC MRI

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Introduction: Apparent diffusion coefficient (ADC) measurements performed with hyperpolarized Helium-3 (HHe-3) MRI have been very successful in detecting the breakdown of the alveolar lung structure as it occurs during the formation of emphysema (1). Similar studies using hyperpolarized Xenon-129 (HXe-129) have also shown promise but suffer from a large signal-to-noise penalty compared to HHe-3, which, at least in the current sequence implementation, results in a substantially reduced sensitivity (2). Xenon polarization transfer contrast (XTC) MRI (3,4) is a promising technique that exploits the gas exchange of HXe-129 between the alveolar gas phase and the lung-parenchyma dissolved phase to obtain information about lung function and certain parameters characterizing pulmonary physiology. In this work we evaluated whether XTC MRI is sufficiently sensitive for the detection of elastase-induced emphysema in rabbit lungs.

Methods: Experiments were performed on a 1.5-T commercial whole-body imager (Sonata, Siemens Medical Solutions, Malvern, PA) using a custom-made transmit-receive birdcage RF coil (IGC Medical Advances, Milwaukee, WI). The two imaging segments of the XTC acquisition were asymmetric FLASH sequences (75% of *k*-space sampled) with excitation flip angles of 3.6° and 10.1°. The following sequence parameters were used: non-selective excitation with a 160μs Gaussian RF pulse; matrix size 64×64; TR/TE 7.9/3.8 ms; FOV 170-210 mm; receiver bandwidth 260 Hz/pixel. The two FLASH image acquisitions were separated by a series of 22 contrast-generating 180°/-180° RF pulse pairs with an inter-pulse delay of 40ms applied at the dissolved-phase resonance frequency of 202 ppm for the XTC experiment or at -202ppm for the control experiment. Six New Zealand rabbits (4.5–6.0 kg) received a single endotracheal instillation above the carina with a high-pressure microsprayer (PennCentury, Philadelphia, PA), guided by fluoroscopy. Three were instilled with 30 units of porcine elastase diluted with saline and three were instilled with saline only (control group). All animals were anesthetized with a mixture of Xylazine/Ketamine and intubated before being imaged. The animals were ventilated with 50cc of isotopically enriched (85% ^{129}Xe) xenon gas, polarized to approximately 10-15% via spin exchange with an optically pumped rubidium vapor (Model IGI 9600Xe Xenon Polarizer, MITI, Durham, NC). The polarizer had been optimized to increase the achievable polarization levels. Our findings were compared to those obtained with HHe-3 and HXe-129 ADC measurements. The protocol was approved by our Institutional Animal Care and Use Committee.

Results: Figure 1 depicts the changes in XTC MRI depolarization maps (Figs. 1C, F) and, for reference, the HHe-3 (Figs. 1A, D) and HXe-129 (Figs. 1B, E) ADC maps, between baseline (Figs. 1A-C) and 8 weeks after (Figs. 1D-F) elastase administration for the rabbit with the largest detected pathology. For the three rabbits that had been treated with elastase the median gas phase depolarization dropped by 7.3%, 14.3% and 29.6%, while the average HHe-3 (HXe-129) ADC values increased 0% (0%), 16.7% (6.9%) and 15.8% (9.1%), respectively, in the same animals. Surprisingly, the control animals that had been administered saline also showed a decrease in depolarization accompanied by fluctuations in ADC values, although these were more localized and transient.

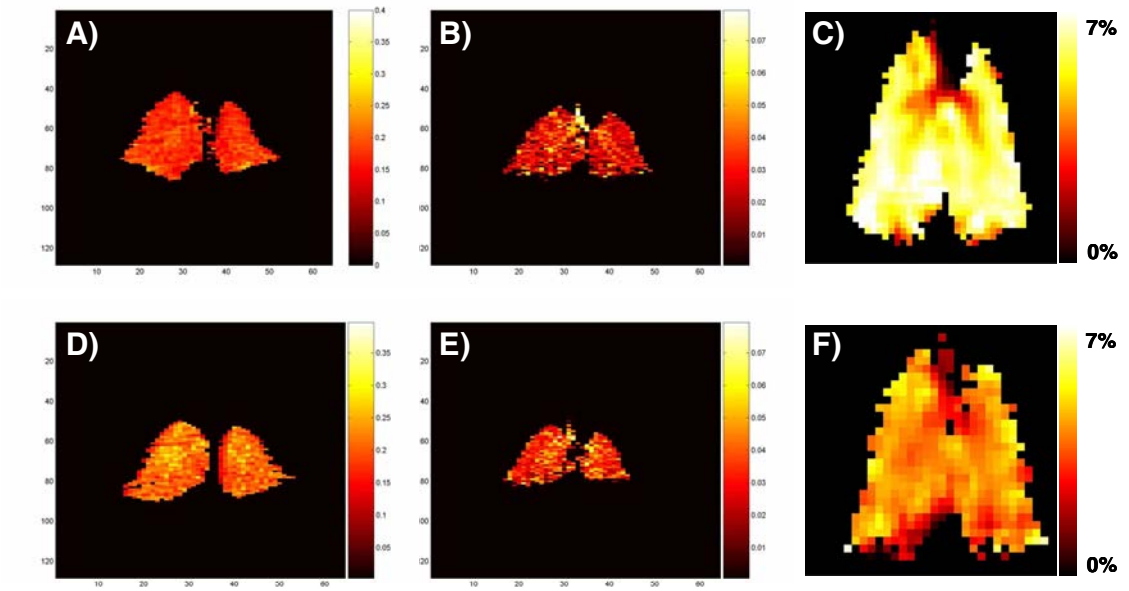

Figure 1: ADC and XTC MRI findings at baseline (top row) and 8 weeks after elastase administration (bottom row). A, D) HHe-3 ADC maps. B, E) HXe-129 ADC maps. C, F) XTC MRI-based gas-phase depolarization maps proportional to the lung tissue volume involved in gas exchange.

All maps reflect a large-scale breakdown of the alveolar wall structures 8 weeks after elastase administration. The highest relative changes were observed in the XTC MRI experiments (~30%) followed by the HHe-3 ADC (~16%) and HXe-129 ADC (~9%) studies.

Conclusion: By choosing a sufficiently long delay time (~40ms) between the contrast-generating RF inversion pulse pairs, the depolarization maps obtained from XTC MRI data sets become highly correlated with the volume of lung tissue compartments involved in gas exchange (4). Consequently, in this configuration, these maps should provide information similar to the tissue density measured by CT although with a functional component because only those tissue compartments immediately involved in gas exchange are detected. The sensitivity to emphysema appears to be at least competitive with HHe-3 ADC and somewhat superior to HXe-129 ADC measurements in their current implementation (2). The observed fluctuations in the control animals are still unexplained and might be due to inflammatory responses.

References

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