Characterizing Surface-to-Volume Ratio Using Hyperpolarized Xenon-129 Exchange Dynamics in a Rabbit Model

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Introduction:

The surface-to-volume ratio (S/V) of the lungs is an important physiologic parameter that, to our knowledge, cannot be accurately measured in-vivo. Magnetic resonance spectroscopy (MRS) of hyperpolarized xenon-129 (HP Xe-129) can measure Xe-129 gas exchange between the lung parenchyma and alveolar volume. This technique can characterize certain aspects of the lung structure and detect changes in lung-tissue density [1]. S/V information can be extracted from the dynamic exchange rate of HP Xe-129 during short exchange times since in the short-time regime the increase in the dissolved-phase signal is proportional to S/V. Quantification of S/V in porous materials using this approach has been performed in a previous study [2]. In this study we investigated whether this technique can characterize the S/V in a rabbit model of lung emphysema by using a single-shot multiple-time-delay MRS sequence to measure Xe-129 gas exchange.

Materials and Methods:

8 New Zealand rabbits were used in the study. Lung emphysema was induced in 5 rabbits by elastase injection, producing alveolar destruction and subsequent S/V changes; 3 rabbits were used as a control group and were injected with saline. Prior to imaging, each rabbit was anesthetized with a mixture of Xylazine/Ketamine and intubated with an endotracheal tube, and then ventilated with 50cc of enriched (85% Xe-129) xenon gas polarized at 8-12% (Model 9600, MITI, Durham, NC). All MRS experiments were performed on a 1.5 Tesla whole-body MR scanner (Magnetom Sonata, Siemens, Malvern, PA) using an RF coil tuned to the Xe-129 resonant frequency. A MRS sequence capable of probing multiple exchange times in a single 7-second breath-hold was applied to measure the depolarization of the Xe-129 gas-phase signal in the lungs. Variable flip angles were used so that the sequence made optimal use of the available magnetization, thereby maximizing the signal-to-noise ratio at each delay time. Delay times were arranged in a way such that the most important data points were acquired first to minimize the overall error. This multiple-time-delay technique was validated against the standard single-time-delay technique. For each rabbit, the depolarization of the Xe-129 gas-phase signal was measured at 8 delay times (1, 3, 5, 7.5, 10, 15, 20 and 40 ms) and the resulting experimental data was fitted to equation (21) in Ref. [1]. The fitted depolarization curve was then plotted as a function of the square root of the delay time. The slope corresponding to the initial linear range of the fitted depolarization curve was also determined. Results from the control group were compared with those from the emphysema group. Rabbits were euthanized following the MRS experiments, and histology/morphometry of lung tissue samples from each rabbit was performed in order to determine the alveolar mean chord length (MCL). Pulmonary S/V of each rabbit was then calculated by the standard formula S/V=4/MCL in stereology [3]. Slopes calculated from the MR Xe-129 exchange studies were then plotted as a function of the S/V to determine the correlation.

Results:

In Figure 1, representative data from a single rabbit shows excellent agreement between depolarization values measured with the multiple-time-delay technique and those measured with the single-time-delay technique. Figure 2 demonstrates that the fitted depolarization curve increases linearly as a function of the square root of the delay time up to a delay time of about 12ms for both the control and emphysema groups. Overall, the emphysema group showed a lower depolarization slope (0.732±0.1062) than that for the control group (0.907±0.0448), indicating a slower gas exchange process in the emphysematous lung than that in the normal lung, presumably due to the lung-tissue destruction. The average S/V value of the control group (44.806±5.4933 mm^{-1}) matches well with the results from the literature [4], and the emphysema group showed a decreased average S/V value (36.412±6.3580 mm^{-1}). The depolarization slope correlated well (r=0.9551) with the S/V from morphology, as shown in Figure 3.

Discussion:

These experiments suggest that MRS measurements of HP Xe-129 gas inter-phase exchange might be sensitive to the changes in S/V caused by induced-emphysema in a rabbit model, and thus may be useful for characterizing pulmonary structure and detecting early changes from tissue destruction in diseases such as COPD.

References:

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Acknowledgements:

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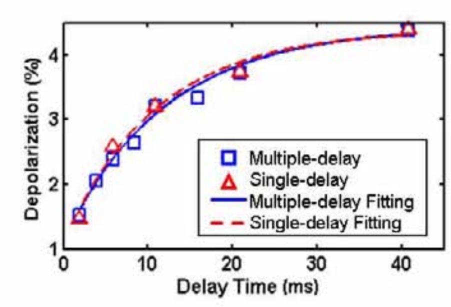

Figure 1. Depolarization curves measured using multiple-time-delay and single-time-delay. All experiments were performed in a single rabbit on the same day.

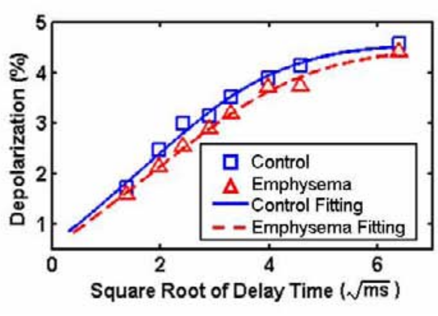

Figure 2. Representative depolarization curves as a function of the square root of delay time from a control rabbit and an emphysematous rabbit.

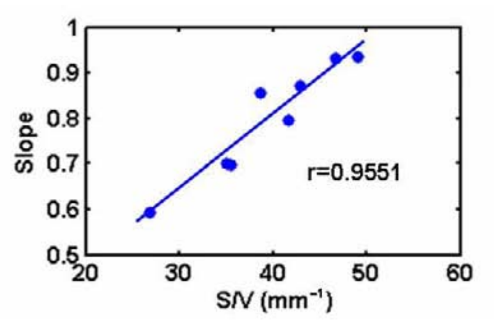

Figure 3. Correlation between the slope of the depolarization curve and the S/V values from the histology studies.