

Quantification and temporal study of physiologic lung changes in animal models of lung disease using 2D and 3D-CSI with Xe-129

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Introduction: Previous implementations of 2D-CSI of the lung with hyperpolarized xenon-129 (Xe-129) have been demonstrated (1). Here, we report the preliminary evaluation of this optimized technique using a rabbit model of lung fibrosis and another of emphysema. We also report the acquisition of multiple contiguous slices with a 3D-CSI version that covers the entire lung in ~15s. From the CSI data, we directly calculate images reflecting the amount of Xe-129 in the airspaces, and dissolved in the lung tissue, blood, and other compartments, thus obtaining detailed spatial information regarding how Xe-129 is distributed in those different compartments and providing regional information about lung physiology.

Methods: Three New Zealand White rabbits underwent hyperpolarized Xe-129 2D or 3D-CSI one four different days: one before and 2,4 and 7 weeks after the endotracheal instillation of beomycin which induces lung fibrosis, one before and 3 days after the endotracheal instillation of porcine elastase which initially induces lung inflammation but later induces emphysema, and one control animal with no intervention. Animals were anesthetized with a mixture of Ketamine/Xylazine (50/5mg/Kg) and intubated. All scans were done in a 1.5 Tesla clinical system (Avanto, Siemens Medical Solutions) using a transmitter/receiver birdcage RF coil (IGC Medical Advances, Milwaukee, WI) tuned to the Xe-129 frequency. Isotopically enriched (~87%) Xe-129 was polarized to ~35% using a commercial prototype polarizer (Xemed LLC, NH). For each 2D or 3D acquisition, a single 40-cc volume was administered to the animal, and respiration was suspended for the acquisition (~15s). For the 2D-projection CSI acquisition, a matrix of 26x26 voxels, interpolated to 32x32 voxels, was positioned over the lungs, with a FOV of 90x90 mm², corresponding to an in-plane resolution of 2.8x2.8mm² and TR/TE = 27/2.3ms. For the 3D-CSI acquisition, a matrix of 16x16x8 voxels, interpolated to 32x32x16 was used, with a FOV of 110x110x110 mm³. For each excitation an RF pulse with duration 1280 μs and bandwidth 3125 Hz was applied at the frequency of the dissolved-phase Xe-129. This frequency is approximately 200 ppm from that for Xe-129 gas in the airspaces. The protocol was approved by our Institutional Animal Care and Use Committee.

2D-CSI (Fig. B) and 3D-CSI (Fig. C, D, E) map production and post-processing was performed using the 3DiCSI (Qi Zhao, Columbia University, NY) and MATLAB (MathWorks, Natick, MA) software packages. The free-induction decay (FID) corresponding to each voxel was filtered with a Gaussian, zero filled to 2048 points, Fourier transformed and corrected for frequency shifts. Subsequently, each separate peak in the spectrum was fitted with a Gaussian curve and the areas under the peaks were determined. CSI maps based on the integrals of the multiple-dissolved peaks and gas peak were calculated separately for each animal. The minimum and maximum intensity was standardized for studies compared directly. The mean and standard deviation was determined for the map area.

Results: High-resolution 2D-CSI maps of the animal in the lung fibrosis group showed the presence of a third dissolved-phase peak at about 185ppm from the alveolar gas peak, and adjacent to the dissolved-phase tissue peak (Fig. A). The CSI map for this particular peak (Fig. B) shows that it is mostly localized in the heart and in the intermediate lobe, positioned in some animal species, like in the rabbit, between both lungs (Fig. B). This Xe-129 dissolved-phase peak is not well resolved in normal rabbits and it was not seen in our control animal. The appearance of high signal in the heart and aorta in the tissue-peak image may reflect Xe-129 in the plasma, or may be signal contamination from the adjacent, large blood peak. Further analysis will be directed at clarifying this issue. Quantification of the CSI maps for the animal in the fibrosis model group show an almost two fold increase in the normalized tissue and blood peaks (tissue/gas and blood/gas) following the instillation of bleomycin. The mean±std for the tissue/gas ratios at baseline, 2, 4 and 7 weeks post bleomycin were 1.6±0.38, 1.6±0.41, 2.3±0.39 and 2.6±0.39, respectively. For the blood/gas ratio the values were essentially identical, and at the same time points were: 1.5±0.39, 1.6±0.43, 2.4±0.39 and 2.7±0.40, respectively. For the rabbit in the elastase group, the ratios at 3-days post induction were even higher, especially the blood/gas ratio, likely due to an acute inflammatory response from the elastase instillation. The ratios at baseline and 3-days post elastase were 1.5±0.32 and 3.9±0.30 for the tissue/gas; 1.7±1.4 and 7.1±3.5 for the blood/gas. 3D-CSI maps (Fig. C, D, E) were used correlatively and compared with the respective 2D-CSI maps. Due to their lower resolution at this time and the presence of some truncation artifacts, no significant additional findings were observed.

Conclusions: Maps from 2D-CSI acquisitions for each of the resolved peaks show that blood and tissue maps appear identically spatially distributed at 1.5T, perhaps due to signal contamination from their very close spectral proximity at this magnetic field strength. 2D and 3D-CSI acquisitions at magnetic fields higher than 1.5T will have a larger separation of the peaks from each lung compartment and will thus likely provide more detailed anatomical and physiological information. The single breath-hold 3D-CSI maps presented here are a promising development of this technique.

References: [1] Mata J et al. ISMRM, Honolulu, 2009.

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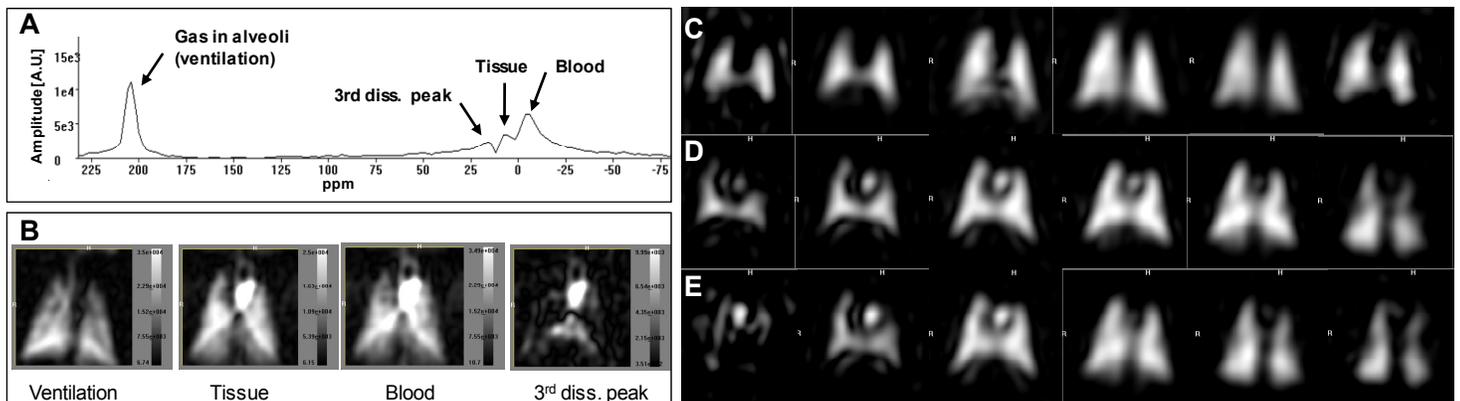


Figure – A: Full spectrum, from a single voxel, obtained during a 2D-CSI acquisition of the rabbit in the fibrosis model group, at 7 weeks post. B: 2D-CSI maps for each of the peaks indicated in figure A. Figures C, D and E: contiguous maps obtained during a single breath-hold 3D-CSI acquisition of the control animal. Figure C (top row) shows the gas-peak (ventilation) images, D (middle row) the tissue peak images, and E (bottom row) the images from the blood peak.