Choose Your Own Adventure: Hyperpolarized ^{129}Xe MRI Techniques for Imaging Pediatric Lung Disease

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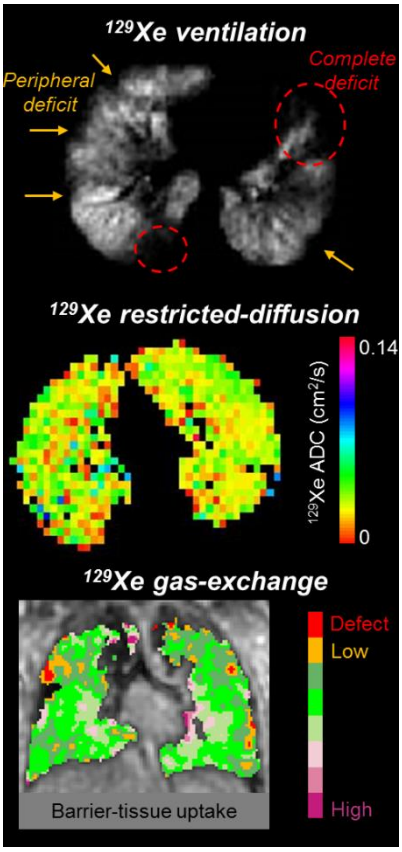
In the early 1990s, inhaled hyperpolarized ^{129}Xe has emerged as an MRI contrast agent to sidestep the challenges of conventional ^{1}H MRI of the lungs (i.e., low ^{1}H density and $T_2^*\leq 1$ ms [1]), and since then, the application of ^{129}Xe MRI in a range of adult lung diseases has been demonstrated. Recently, ^{129}Xe MRI has been increasingly applied in pediatrics, where subject compliance with clinical lung-function testing can be challenging; furthermore, clinical tests have poor sensitivity to early disease. As a result, pulmonary manifestations in pediatric patients may go undiagnosed and untreated until worsened. In this abstract, the three major techniques of hyperpolarized ^{129}Xe MRI (ventilation, restricted-diffusion, and gas-exchange) will be discussed in the context of new applications to pediatric lung disease at our institution, demonstrating how advances in clinical translation can manifest from basic magnetic-resonance science.



Ventilation: Regional lung ventilation heterogeneity can be quantified during a breath-hold of ^{129}Xe gas. Our group and others have demonstrated the exquisite sensitivity of ^{129}Xe ventilation MRI as compared to spirometry to detect early manifestations of lung in diseases including asthma [2], cystic fibrosis [3, 4], and COPD [5, 6]. At our institution, one growing area of interest is pediatric hematopoietic stem-cell transplantation (HSCT), where patients are susceptible to deadly, rejection-induced pulmonary complications. An example of a 9-year-old HSCT patient who was unable to perform reliable spirometry but could perform ^{129}Xe MRI is shown in the Figure (top); ventilation was very heterogeneous with small peripheral deficits (arrows) and larger focal regions of complete deficit (circles). The ^{129}Xe ventilation defect percentage (i.e., volume of lung < 60% mean ^{129}Xe MR signal) was 28% compared to ~6% for healthy controls, supporting ^{129}Xe ventilation MRI as a superior assessment for difficult-to-diagnose pediatric patients.

Restricted-diffusion: Inside lungs, Brownian motion of ^{129}Xe atoms is restricted by the alveolar-airspace walls. By using straightforward variants of the Stejskal-Tanner experiments (here: 5 "b-values" 0-25 s/cm^2, diffusion time Δ=3.5 ms), the apparent-diffusion coefficient (ADC) of ^{129}Xe can be measured regionally and serves as a non-invasive marker for alveolar-airspace size. ^{129}Xe ADC is sensitive to even mild airspace-enlargement (e.g., emphysema) in adults [7], and in the Figure (middle), we demonstrate how ^{129}Xe restricted-diffusion MRI can be applied to rare conditions to assess the pathophysiology. In this case, ^{129}Xe ADC was used to assess if normal alveolar development was altered by long-term chylous effusions—lymphatic fluid leaking into the thoracic cavity and compressing the lungs—in an 8-year-old boy with a rare generalized lymphatic anomaly. Despite long-term lung compression during grown, we found that the ^{129}Xe ADC was 0.029 ± 0.016 cm^2/s after the pleural effusion was treated, which was equivalent to age-matched controls, suggesting that normal alveolar growth was not impacted by ongoing effusions [8].

Gas-exchange: The primary function of the lung is to perform gas exchange with blood. Due to the unique dissolution and chemical-shift properties of inhaled ^{129}Xe gas in the pulmonary tissues and red-blood cells (peaks at 198 and 217 ppm, respectively), ^{129}Xe gas-exchange MRI can assess regional interstitial thickening or fibrosis and perfusion deficits in lung disease. Maps of ^{129}Xe ventilation, barrier-tissue uptake, and red-blood cell transfer can be generated from a single breath-hold of ^{129}Xe gas. We modified a 3D-radial sequence and 1-point Dixon technique to separate barrier-tissue and red-blood cell images [9, 10] for use in pediatric subjects. In the bottom row of the Figure, in the ^{129}Xe barrier-uptake map in a 15-year-old patient with cystic fibrosis, relatively normal and homogenous ^{129}Xe barrier-tissue uptake is shown.

Regional lung ventilation, alveolar-airspace size, and gas-exchange parameters can be quantified using hyperpolarized ^{129}Xe gas MRI, with the latter demonstrated for the first time in pediatric subjects. This unique multi-faceted breadth, in addition to high safety and non-ionizing nature of MRI, make ^{129}Xe gas a powerhouse contrast agent for describing the diverse pathophysiological spectrum of pediatric lung diseases.

References: [1] Yu*, et al.* MRM, 2011. **66**(1):248 [2] Svenningsen*, et al.* JMRI, 2013. **38**(6):1521 [3] Thomen*, et al.* JCF, 2017. **16**(2):275 [4] Kanhere*, et al.* AJRCCM, 2017. **196**(8):1073 [5] Kirby*, et al.* Radiology, 2012. **265**(2):600 [6] Kirby*, et al.* JAP, 2013. **114**(6):707 [7] Ouriadov*, et al.* MRM, 2013. **70**(6):1699 [8] Walkup*, et al.* AJRCCM, 2018. **198**(12):1573 [9] Wang*, et al.* Med Phys, 2017. **44**(6):2415 [10] Wang*, et al.* MRM, 2018.