Disease Characterization with Hyperpolarized Gases

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The lung remains one of the more challenging organs to image with MRI due to the low proton density, high susceptibility effects from many air-tissue interfaces, and motion from the heart, vessels and the lung itself. A variety of methods using proton MRI are under development to assess lung structure (e.g., UTE) and function (e.g., Fourier Decomposition). Using the hyperpolarized noble gases helium-3 or xenon-129 as inhaled contrast agents for MRI permits direct visualization of lung airspaces, and a number of strategies for evaluating the structure and function of the human lung using hyperpolarized gas MRI have been developed. Although the level of structure detail possible with lung MRI may never equal that of CT, MRI nonetheless has the potential to provide clinically useful information and be a sensitive, effort independent test of lung disease. This talk may be of interest to both clinicians and physicists with an interest in lung imaging.

By acquiring a spin density weighted image following inhalation of hyperpolarized gas, a qualitative assessment of lung ventilation is obtained. Areas of the lung with reduced ventilation contain less polarized gas and thus appear dark on the "ventilation" images. Areas of reduced ventilation, so called ventilation defects, have been observed in a number of obstructive lung diseases including asthma, COPD, and cystic fibrosis (CF). In asthma, a correlation between asthma severity and the number of ventilation defects has been observed. Further ventilation defects increase in size and number following provocation with methacholine, a bronchoconstrictor, and exercise. Ventilation defects decrease in size and number follow treatment with albuterol, a bronchodilator. An interesting finding with hyperpolarized gas MRI has been that ventilation defects tend to occur or recur in the same locations in the lung over time or following provocation. This suggests that all areas of the lung may not be equally affected by asthma with some areas being more prone to airflow obstruction than others. Without the regional information provided by hyperpolarized gas MRI, this type of information about the underlying patho-biology of asthma would be difficult to elucidate.

Ventilation defects have also been observed in patients with CF, even those with normal spirometry. CF is caused by a mutation in a gene that encodes a cell surface chloride channel, the CFTR gene. In January 2013, the first of a new class of drugs, CFTR potentiators, was approved for use in patients with CF but only for those with a specific CF gene mutation, G551D, about 5% of the CF population in the US. This drugs works not by correcting the gene expression but by, in essence, opening the chloride channel in the CFTR protein that is poorly functioning in patients with the G551D mutation. This is the first drug for CF that treats the underlying cause of the disease. In a small clinical trial of CF patients with the G551D mutation imaged before and after being treated with invacaftor, hyperpolarized helium-3 MR ventilation imaging was able to demonstrate an improvement in lung ventilation with ivacaftor treatment. This demonstrates that hyperpolarized gas MRI can be successfully used in clinical trials and has the potential to be used as an outcome measure in trials of other CFTR potentiators that are under development.

Using hyperpolarized gas and diffusion weighted MR imaging, the size and connectedness of the lung microstructure can be assessed. Studies in both animal models and human lungs with COPD have shown excellent concordance between the helium-3 apparent diffusion coefficient (ADC) and the alveolar morphology. This technique has been found to be very sensitive to smoking related changes in the lung. It may be of use in other diseases that alter the lung microstructure such as chronic lung disease of prematurity.

Other techniques such as those that assess the regional partial pressure of oxygen in the lung and the dynamics of xenon leaving the airspaces and entering the lung parenchyma and blood have been developed. However, the clinical applications for these techniques are less mature.