Airway Disease: Hyperpolarized Gas MRI

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Introduction: Magnetic resonance imaging using signal from hyperpolarized noble gases [1], is proving to be an important technique for imaging airway disease. Pulmonary disease results in considerable morbidity and mortality, and techniques that yield high contrast images of the lungs are crucial to its diagnosis and staging. Many of the available imaging modalities, however, lack sensitivity and disease specificity. MRI is non-invasive, and can produce slice selective and 3-D images, but conventional proton MRI is ineffective for lung imaging, both because the gas space is water-free, and because protons have an inconveniently short T1 in lung tissue. After inhalation of a hyperpolarized noble gas, however, the airways and alveolar gas spaces can be imaged with high SNR by MRI. Imaging lung perfusion and lung parenchyma should also be possible. This talk will focus on the development of practical and clinical applications of hyperpolarized gas MRI, review the results to date, and discuss future directions of this technique.

The special promise of hyperpolarized gas MRI: The two non-radioactive noble-gas isotopes with spin-1/2 nuclei, 3He and 129Xe, are MR-detectable, but the low concentrations achievable in living subjects makes conventional MR approaches futile. The technique of hyperpolarization by laser optical-pumping of rubidium, followed by spin-exchange hyperpolarization of the 129Xe and 3He nuclei [2], can result in non-equilibrium polarizations about 105 times greater than the thermal equilibrium polarization obtainable with typical imaging magnets. Hyperpolarized 3He and 129Xe MRI offer a new range of exploitable responses and contrast, and promise time and space resolutions equal to that obtainable with conventional proton MRI. Moreover, in hyperpolarized gas MRI, the polarization of 129Xe or 3He is largely independent of the applied magnetic field (B0), which allows the use of less expensive low-field magnets for imaging.

3He or 129Xe, that is the question: 3He has a gyromagnetic ratio (γ) 2.7 times greater than that of 129Xe which yields a similar improvement in the SNR. In specially prepared containers, the T1 of 3He is several days, which can be arranged for 129Xe only in a liquid-helium cooled cryostat. Clearly, 3He is the preferred signal source for imaging the gas space of the lung, but its low blood and tissue solubility precludes its use in investigations of the blood vasculature and distal tissues. 129Xe (as are all inhalation anesthetics) is lipophilic, and it dissolves readily in blood and diverse tissues. This implies that hyperpolarized 129Xe investigations can be extended to lung perfusion and lung parenchyma studies.

Two methods of noble gas hyperpolarization: The spin-exchange technique involves optical pumping of rubidium vapor and transfer of the polarization to xenon or helium atoms through spin exchange collisions [2]. Metastability-exchange, practical only for helium, is a direct optical method that uses use metastable states of helium atoms and transfers the polarization through metastability exchange collisions, at a low pressure [3]. The hyperpolarized 3He is then compressed to densities required for imaging.

Animal Studies: The first hyperpolarized gas images were reported by researchers at Stony Brook and Princeton, who demonstrated 129Xe imaging of a mouse lung [1]. Researchers from Duke have used a projection imaging technique, gated to the respiratory cycle, to obtain high resolution 3He images of the guinea pig lung, clearly revealing the global lung, the trachea, major bronchi, and airways [4]. Airway branching can be traced to the fourth generation and cartilaginous ring structures are evident in the conducting airways. Hyperpolarization images of gas distribution in the lungs have been obtained during different phases of the breathing cycle [5]. Pulmonary airway obstruction in an animal model has also been imaged using 3He to detect intraluminal, localized obstructions [6]. In addition, the line shape of 3He spectra reflects the local microstructure in the lung; changes in microstructure may be indicative of lung pathologies [7].

Hyperpolarized 129Xe images of the lung gas space, and tissue resonances have been reported from the thorax of mice by researchers at the Brigham and Women's Hospital [8] and Stony Brook, respectively [9]. 129Xe resonances have been identified in blood plasma, in red blood cells, and in lung parenchyma [8].

The wash-in and accumulation of xenon in the rat pulmonary tissues has been explored using the signal from hyperpolarized 129Xe. The long hyperpolarized 129Xe lifetimes (T1) of 12-50 s in the tissues and the spectral resolution achieved promises acquisition of differential images of lung airways, vasculature, and parenchymal tissues, and points to the possibility of acquiring both ventilation and perfusion images in a single imaging session [8]. In mice, susceptibility-induced chemical shift variations of the xenon tissue-phase thorax spectra have been observed to correlate with the pulmonary ventilation cycle [9]; this pattern might prove to be sensitive to airway disease.

Human Studies: Thick-section coronal FLASH images were acquired at Duke from healthy volunteers who had inhaled approximately 0.75 liters of 12% polarized 3He [10]. A timed sequence of images show regional ventilation differences, with the apices of the lungs showing the lowest signal intensity due to its poor ventilation. Researchers at the University and Medical Centers of Mainz and Heidelberg, Germany [11, 12] have obtained 3He images showing anatomical details of the lung cavity and the low cost laser, the trachea, and the lungs of healthy volunteers using 3He polarized to 35-45% by metastable optical pumping.

The first hyperpolarized 129Xe images of the human lungs have been obtained at the University of Virginia using a FLASH sequence, from healthy volunteers who had inhaled 300-500 mL of enriched (70%) 129Xe gas that was polarized to 2% by spin-exchange [13]. Cross-sectional images of the lung gas spaces were obtained, with a voxel volume of about 1 cm3. Three dissolved-phase resonances were detected from the chest, which displayed a striking resemblance to those reported in the previous study of the rat thorax [8].

Clinical Studies: In the first clinical study, performed at Mainz Medical Center, a 3-D FLASH sequence was used to image eight healthy, nonsmoking volunteers and ten patients breathing 600 mL of 35-45% polarized 129Xe gas [14, 15]. Six patients were suffering from chronic obstructive pulmonary disease (COPD); two presented with bronchogenic carcinoma and two presented with pneumonia. Findings were compared with clinical data, pulmonary function tests (PFT), chest X-ray, CT, and ventilation scintigraphy. 129Xe lung imaging scans were conducted during a 22-42 s breath-hold period, which was well tolerated by most subjects. A homogeneously high signal intensity throughout the air spaces was observed in volunteers with normal ventilation. In smokers with COPD, however, severe localized and diffuse inhomogeneities in signal intensity were detected. Scans from patients with bronchogenic carcinoma, bilhar lymphadenopathy, or a unilaterally destroyed lung produced images with large signal intensity defects. Patients with pneumonia or bronchiectasis showed wedge-shaped defects in the lung images. Lesions presented as ventilation defects in the images that were larger than the lesions themselves; i.e. areas of low signal intensity extended beyond the lesion. In smokers with known COPD, the marked signal intensity inhomogeneities are an indication of the severe abnormalities in pulmonary ventilation [14].

Conclusions: The first clinical studies indicate that hyperpolarized gas MRI is effective for imaging airway disease. Continued technical improvements, e.g., the production of larger volumes of gas at higher polarization, optimized pulse sequences, and specialized RF coils, should enable 129Xe imaging of lung perfusion and lung parenchyma and provide improved detection of pulmonary disease.

References: