Hyperpolarized Gas Methods in the Clinic

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Introduction
The purpose of this presentation is to explain the hardware adjustments necessary for imaging hyperpolarized gases and to describe the role of hyperpolarized gases in assessing pulmonary disease processes. Over the past few years, new techniques in MRI have emerged as an important instrument for functional ventilation imaging [1-3]. The aim of this plenary is to summarise hyperpolarized gas methods for the research and clinical arenas. Before the advent of MRI, chest radiography and CT dominated morphological lung imaging. Functional ventilation imaging was accomplished with scintigraphy. Initially, MRI was not used often for morphologic lung imaging due to technical and physical limitations. However, recent developments have considerably improved anatomical MRI, as well as advancing new techniques in functional ventilation imaging, such as hyperpolarized noble gases (He-3, Xe-129).

Methods
Hyperpolarized gas MRI using He-3 or Xe-129 is a recent approach for ventilation imaging. In contrast to the proton based techniques a dedicated gas is used as a “contrast agent”. Generally, the density of gases is too low to produce a detectable signal. This drawback can be overcome by artificially increasing the amount of spins per unit volume using an optical pumping technique. Two techniques for polarization have been established: (1) spin exchange: indirect transfer of angular momentum from a laser source to the nuclei of He-3 or Xe-129 using an alkali metal such as rubidium; (2) metastability exchange: direct transfer of angular momentum from laser light to He-3 nuclei via a radio frequency discharge. The two inert noble gases have different properties: (1) He-3 is a very rare isotope, which is a by-product from tritium decay. It is particularly suited for ventilation studies since it has no known deleterious side effects. Additionally, He-4 is widely used for decompression in deep-sea diving, special pulmonary function tests. The next step will be to define the threshold between physiological variation and pathological defects. The specific purposes of ventilation imaging, He-3 provides a number of advantages over Xe-129. The gyromagnetic ratio of He-3 is approximately three times higher than that of Xe-129, yielding a signal advantage of almost an order of magnitude. Additionally, current techniques for He-3 yield significantly higher polarisation rates than for Xe-129. The main disadvantage is the limited availability of He-3 with respect to natural abundant Xe. Most developments of hyperpolarized gas imaging have taken place on “standard” 1.5 T MR systems. A broadband amplifier and dedicated coils tuned to the Larmor frequencies of He-3 or Xe-129 are the only additional hardware requirements. Due to the greatly increased signal-to-noise ratio the technique would be ideally suited for imaging in a low field system. Straightforward gas density imaging is done in an inspiratory breath-hold after inhalation of the hyperpolarized gas using gradient-echo sequences with a low flip angle. Furthermore, dynamic imaging with high temporal resolution, measurements of the apparent diffusion coefficient (ADC) representing airspace size and connectivity as well as evaluation of T1 over time to calculate the intrapulmonary partial oxygen pressure are feasible. Kinetics of gas uptake can be assessed when using Xe which is readily absorbed through the alveolocapillary membrane.

Results
A typical gas density image series requires a breath-hold period of less than 10 seconds to obtain approximately 10 coronal images covering the whole lung. Spatial resolution is significantly better than in nuclear medicine (2.5 x 2.5 x 10 mm with 2-5 mm gap between slices). Normal ventilation is generally represented by an almost complete and homogeneous distribution of the hyperpolarized gas within the lung. Smaller ventilation defects in the dependent lung regions are regarded as physiological findings. Larger and more widespread ventilation defects are signs of disease, especially obstructive airway diseases such as asthma, chronic bronchitis and bronchiolitis. The sensitivity for the depiction of ventilation defects is higher than at scintigraphy, pulmonary function tests or CT. Thus, He-3 MRI has a potential role in the early detection of obstructive lung diseases. However, these ventilation defects are not specific for a particular disease entity. The application of complementary strategies is important to increase the sensitivity of hyperpolarized gas MRI. Dynamic imaging allows for the analysis of the distribution that is even more sensitive than breath-hold imaging for early detection of airway obstruction. Measurements of the ADC are to be used as an indicator for airspace space with increasing ADC values in emphysema or advanced fibrosis with honeycombing. The intrapulmonary oxygen concentration has a significant, linear effect on the T1-time of hyperpolarized He-3 gas. Thus, by measuring the initial T1 and its decay over time intrapulmonary oxygen concentration can be calculated on a regional basis for the first time. This is an indirect measure of regional pulmonary oxygen uptake and perfusion.

Discussion
There are several advantages to using MRI for ventilation imaging: lack of radiation, high spatial and temporal resolution, and a broad range of functional data. MRI techniques applied in patients with chronic obstructive lung disease, emphysema, cystic fibrosis, asthma, and bronchiolitis obliterans, yield a higher sensitivity in the detection of ventilation defects than ventilation scintigraphy, CT or pulmonary function tests. The next step will be to define the threshold between physiological variation and pathological defects.

References