Measurement of Regional Ventilation in Large Animals by Hyperpolarized 3He MRI: One Step Closer to Human Studies

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INTRODUCTION: Pulmonary ventilation is an important marker in lung physiology because of its sensitivity to obstructive and restrictive lung diseases. Conventional techniques for measuring regional ventilation are based on delivery/clearance rates of radioactive gases or xenon-contrast detected by x-ray CT. These techniques, however, expose subjects to radiation and preclude the frequent screening necessary for monitoring progression of disease or response to therapy. Hyperpolarized (HP) ^{3}He MRI has emerged as a novel technique with unique capabilities in visualizing ventilated airspaces noninvasively.

Earlier techniques developed to measure lung ventilation using this technology were limited to use in rodents, since they utilize many HP ^{3}He breaths (typically 30~50) and consequently require a relatively long acquisition time and an impractical amount of ^{3}He. A method recently developed in our group [1] for measuring regional lung ventilation can be implemented much faster, requires substantially fewer ^{3}He breaths, and was shown to be in good agreement with older methods in rodents. We have now successfully implemented this technique in large animals and the results suggest a practical extension to human studies.

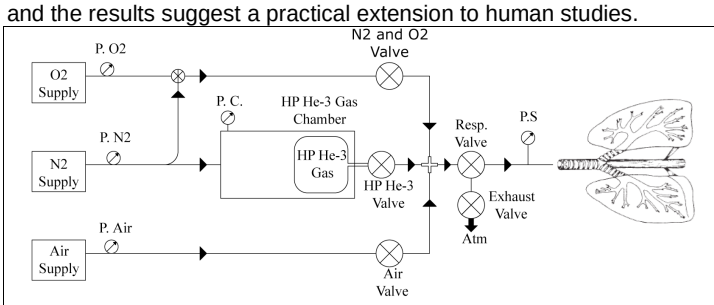

Figure 1. (↑) Functional diagram of our custom-design animal ventilator capable of mixing up to 3 different gases with an accuracy of 100 μL per breath.

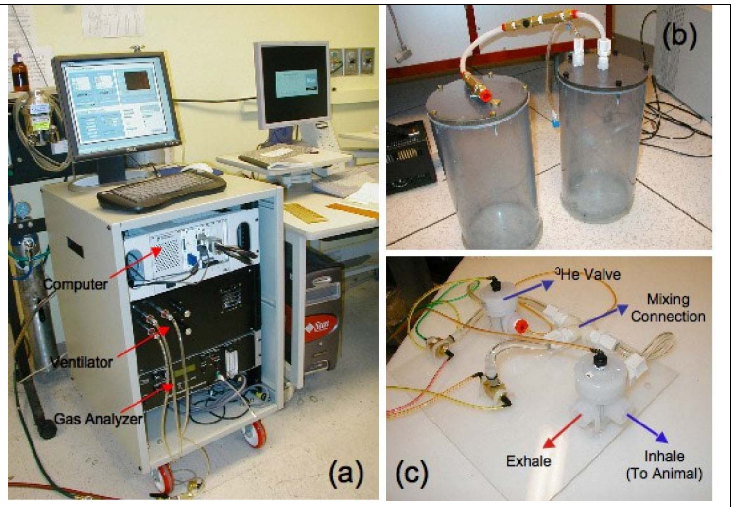

Figure 2. (→) (a) Control hardware and electronics for the programmable ventilator; **(b)** the helium dispensing gas chambers capable of delivering up to 1L of ^{3}He per breath; **(c)** close-up of the respiration unit gas handling valves for imaging pig lungs. A separate valve setup will be used for any smaller species with smaller dead-space.

METHODS: A versatile MR-compatible programmable ventilator capable of mixing up to three different gases (e.g. ^{3}He, O_2, N_2 and air) at different ratios (Figure 1), designed and prototyped in our group was used to carry out the studies. The ventilator gas-handling unit (Figure 2) is composed entirely of pneumatic and nonmagnetic delivery valves, which therefore may be placed on or near the imaging coil as close as possible to the animal. This ventilator is capable of delivering the gas in a wide range of volumes and rates, suitable for species ranging form mice (TV≈0.3mL @ 120BPM) to pigs (TV≈250mL @ 20BPM). Regional ventilation was measured using the hybrid breathing-imaging sequence described earlier [1] (Figure 3) in Yorkshire pigs (Figure 4) and New Zealand rabbits (not shown). For the shown dataset, a male 25-kg Yorkshire pig was ventilated with a TV=250mL @ 15 BPM and I:E=1:2. A single-slice gradient echo pulse sequence was used to acquire the images with the following parameters: FOV=24×24cm^2, α=5°, MS=64×64, ST=20mm, T_R/T_E=11.6/3.4ms. A measurement of flip-angle using repeated images at the same lung inflation (not shown) was used to correct the fractional ventilation for RF-induced signal loss at each breath. An additional correction taking into account diffusion of non-imaged gas into the slice of interest, was judged negligible and was not pursued.

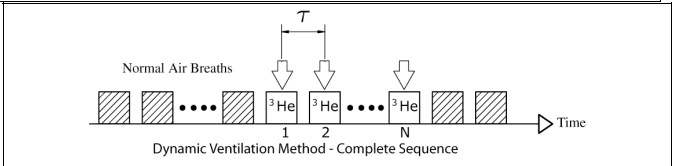

Figure 3. Hybrid breathing/imaging sequence to measure regional fractional ventilation.

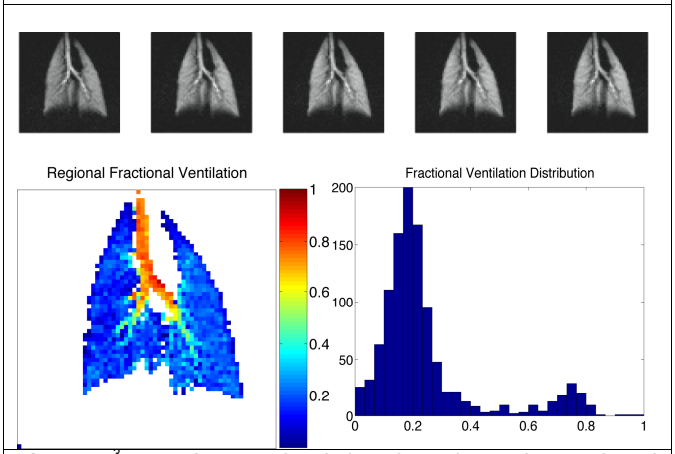

Figure 4. ^{3}He MR images of a pig lung for an increasing number of hyperpolarized ^{3}He breaths (TOP); The regional distribution of fractional ventilation (*r*) in the lung of a healthy pig (BOTTOM).

RESULTS AND DISCUSSION: Regional fractional ventilation was successfully measured in large species (Yorkshire pigs and New Zealand rabbits) to assure feasibility of these measurements before human studies are attempted. The fractional ventilation in the lung parenchyma is measured at around 0.2 (i.e. 20% of the gas in those regions is replaced with one breath). As expected, a near-unity value is seen in the trachea and major bronchi. The similarity between porcine and human respiratory physiology suggests that implementation in human studies will be similarly successful. In the latter case, no mechanical ventilation will be necessary. Instead peak respiratory pressure will be monitored real-time and a gas delivery device will control the gas flow and mixture into the human lung and trigger the scanner in synchronization with breathing pattern.

REFERENCE: [1] Emami K, *et al.* A Novel Approach to Measure Regional Lung Ventilation Using Hyperpolarized 3He MRI – Potential in Clinical Studies; ISMRM 16th Scientific Meeting, Berlin, Germany: May 2007.