Automatic Respiratory Gas Delivery Device for Noninvasive Administration of Hyperpolarized Gaseous Contrast Agents to Consciously Breathing Subjects

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INTRODUCTION: Hyperpolarized (HP) gas MRI has enabled pulmonary researchers to investigate various facets of lung function and structure regionally and non-invasively. Diffusion-weighted HP gas MRI allows for assessing lung microstructure, whereas ventilation scans give a qualitative picture of respiratory gas distribution and gross defects, both with a single-breath HP gas bolus. More sophisticated methodologies have been recently developed for oxygen-weighted and quantitative ventilation imaging. These techniques however pose certain requirements on the delivery pattern and mixture content of the gaseous contrast agents. Oxygen-weighted imaging requires real-time mixing of a HP gas agent and oxygen at a prescribed ratio immediately before inhalation. Fractional ventilation imaging additionally demands delivery of multiple identical breaths to a voluntarily breathing subject while blending the HP gas buffer with oxygen in each breath to reach a normoxic mixture (reminiscent to multi-breath imaging protocols in mechanically ventilated animals). This work describes the design and utility of a simple semi-automated passive-reactive HP gas mixing and delivery device to address this unmet need in human HP gas MRI protocols.

METHODS: The main design objectives were accuracy in mixing and delivery of the contrast and buffer gases (both in timing and concentration), as well as safety and comfort of the subject. The intention was to eliminate the need for supervision in such a way that the device would respond to subject's voluntary respiratory effort, deliver a predefined volume of gas mixture and synchronize imaging on the MRI scanner without operator intervention. **Figure 1** shows a schematic diagram of the gas administration device, and pictures of the actual prototype successfully tested with HP ^{3}He in a 1.5-T Siemens Sonata MRI scanner are shown in **Figure 2**. The main idea is to use custom-made MRI-compatible differential pressure pneumotachometers (from off-the-shelf components) that independently report the flow rate of each gas component and trigger the pneumatic valves and the MRI scanner when the target volume is reached. The subject then commits a voluntary breath-hold during which images are acquired, exhales freely, and the sequence is repeated as desired. Flow calibration is performed using the effective molecular weight of the gas mixture in each bag, and also experimentally by withdrawing a known quantity of gas from the bags and comparing the volume to the time integral of the flow sums. Finally the calibration coefficients are tested and fine-tuned with the subject inhaling the total volume of the desired gas mixture (with ^{3}He replaced by ^{4}He) before committing the MRI. The system allows for real-time fine-tuning of flow ratios by optionally placing the reservoir bags in chambers filled with an inert gas where their internal pressure is continuously adjusted (within 0–10 cmH_2O) to compensate for the nonlinear behavior of shrinking bags, different line resistance, etc.

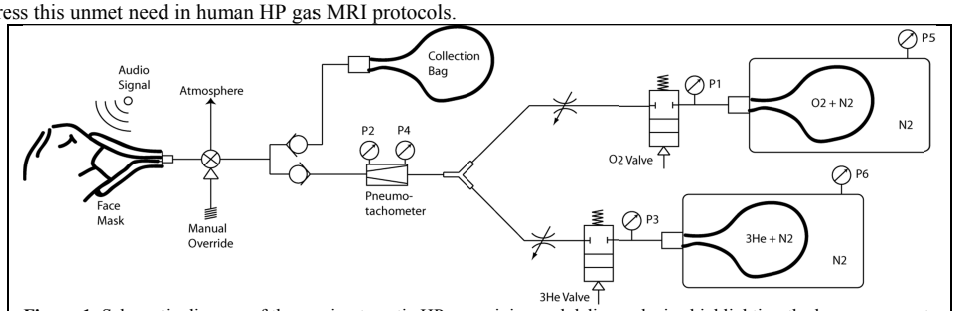

Figure 1. Schematic diagram of the semi-automatic HP gas mixing and delivery device highlighting the key components of the system. This setup allows for real-time mixing of two gas sources, commonly a HP gas species (e.g. ^{3}He or ^{129}Xe mixed in N_2 buffer) and O_2, at a prescribed ratio and tidal volume over a series of breaths, while synchronizing image acquisition with MRI scanner.

RESULTS & DISCUSSION: The P1–P4 and P3–P4 pressure differences were used to estimate the real-time flow of the two channels respectively. The P4–P2 pressure difference was used to sense the presence of flow and to threshold the baseline noise. **Figure 3** shows a representative real-time readout of flow from both channels and the computed inhaled volume over two respiratory cycles. Representative coronal lung images of a healthy volunteer (25-yrs old male) are shown in **Figure 4**, acquired during 5 back-to-back breaths (V_T=700mL, I:E~3:4, ~8 BPM) from two separate bags (^{3}He-N_2 and O_2-N_2, 2.1 L each, for a total of ^{3}He:N_2:O_2≈25:55:20, V_T=700mL, I:E~3:4, ~10 BPM). The device can be used either with a mouthpiece or a facemask and allows the subject to maintain a respiratory pattern very similar to normal breathing, with only the addition of a short breath-hold (approximately one second for a set of images covering the entire lung, especially when combined with image acceleration). The volume delivery repeatability was experimentally evaluated at better then ±50 mL per breath (5–7% for an adult breath size). The performance is fairly sensitive to the gas mixture composition. In order to avoid the need to recalibrate the system before every single experiment, it is beneficial to maintain a similar gas ratio in different bags (e.g. O_2 in bag 1, and ^{3}He:N_2=1:1 in bag 2) for different studies. Otherwise an initial calibration coefficient can be assumed based on the molecular weight of the gas species, and then fine-tuned by patient inhaling a few single breaths of the desired gas mixture at the prescribed tidal volume. The system in its proposed layout monitors the inspiration flow only, given the focus on inspiratory ventilation imaging. Its utility however can be easily extended to monitor expiratory flow by installing an additional pneumotachometer on the exhale path. This functionality may be of value when it is required to reach a target expiratory volume before commencing the MRI. It should be however noted that this arrangement exposes several more components of the system to expired gas and therefore necessitated disposing of them for each study.

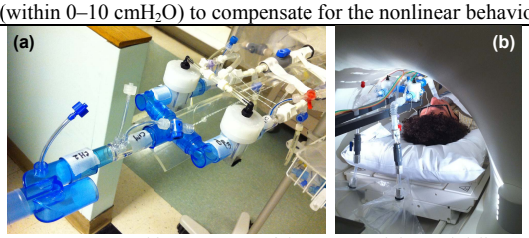

Figure 2. (a) Working prototype of the HP gas mixing and delivery device shown in Figure 1; **(b)** Positioning of the device inside the MRI scanner for delivery of HP gases to subject.

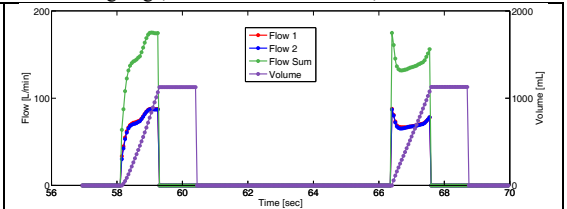

Figure 3. Representative recordings of real-time flow and volume measurements. Flow rates in the two channels or very close and overlay on top of each other.

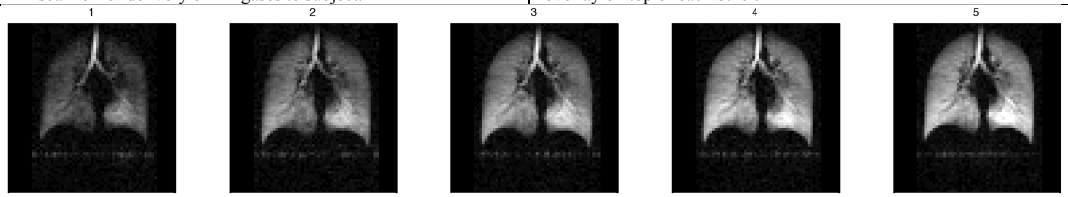

Figure 4. Ventilation images acquired in a healthy volunteer over five successive breaths of ^{3}He:N_2:O_2 at a tidal volume of 700 mL.

CONCLUSION: In addition to enabling specific HP gas MRI measurements that require a stringent delivery pattern and gas concentration, the presented HP gas delivery device can assist in improving measurement repeatability and standardizing HP gas MRI protocols across different sites and on multiple days, and eliminate the problems associated with manual delivery of HP gas to voluntarily breathing subjects. As described in a recent study of oxygen-weighted MRI study in humans [1], one of the factors contributing to measurement accuracy and repeatability was a robust and simultaneous delivery of ^{3}He:N_2 and O_2 mixtures to the subjects. In addition, multi-breath MRI protocols (e.g. fractional ventilation imaging [2]), which up to now have been only possible in mechanically ventilated animals, can be implemented in conscious human subjects. Feasibility of this imaging protocol in humans is reported for the first time by authors in another abstract submitted to this conference.

REFERNCES: [1] Hamedani H, *et al.* Magn Reson Med. 2011; [2] Emami K, *el al.* Magn Reson Med. 2010.