3He NMR washout monitoring combined with 3He ventilation MRI: initial experience in healthy volunteers and cystic fibrosis.

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Introduction: Inert gas washout techniques have been used in lung physiology for a long time [1], and recently utilized diagnostic markers such as the lung clearance index (LCI) have been shown to be more sensitive to peripheral lung disease than conventional measures [2]. However, these indices only provide global information of lung function. Hyperpolarized ^{3}He MRI on the other hand is a regional lung imaging technique, providing information on lung ventilation and function. This work demonstrates combination of the global physiological measurement of inert gas washout with a spatially resolved ^{3}He MRI ventilation imaging protocol. The NMR signal from intrapulmonary ^{3}He is used to monitor gas washout from the lungs, to investigate pulmonary function in a manner comparable to inert gas washout techniques. We show using whole body ^{3}He coils and with ^{3}He NMR coils at the mouth that this method can be combined with ^{3}He ventilation imaging in a single exam, using the same bolus of hyperpolarized gas. Washout monitoring is demonstrated in healthy volunteers and in one patient with cystic fibrosis (CF).

Materials and Methods: ^{3}He was polarized to ~25% using a prototype spin-exchange optical pumping polarizer (Helispin, GE). Volunteers inhaled a mixture of 300 ml ^{3}He and 700 ml N_2. Coronal ^{3}He images were obtained on a GE HDx 1.5T scanner using a Fast Gradient Echo sequence with a FOV of (38×38) cm^2, 10 mm slice thickness, 128×128 pixels, a flip angle of 7° at TE=1.1 ms and TR=3.6 ms. After the imaging sequence a spoiled pulse-acquire sequence with a TR of 200-300 ms and a flip angle of 1° was started, and the volunteer was asked to exhale by relaxed tidal breathing. The global signal from the ^{3}He chest coil was recorded for a total time of 60 s. Washout monitoring alone was tested in 4 healthy volunteers; it was combined with ^{3}He imaging three times in a healthy volunteer, and once in a CF patient (f, 9yrs). In another experiment the washout was monitored in healthy volunteers using a pulse-acquire sequence with a second RF coil (solenoid) wound round a mouthpiece to mimic the LCI method, and compared to SF_6 gas washout monitored by a photoacoustic gas analyzer [2]. All experiments had approval by the local Ethics committee.

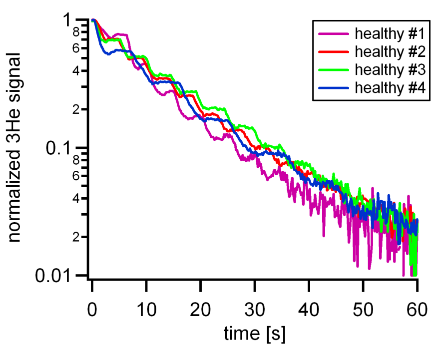

Figure 1: ^{3}He signal intensity during tidal washout in healthy volunteers, corrected for RF depolarization and T_1 decay.

Washout curves were obtained from the intensities of real absorption spectra, and corrected for RF depolarization and T_1 decay. RF depolarization can be modeled according to $S_n=S_{n-1}\cdot\cos(\alpha)$, where n is the phase encode view number, α the flip angle and S_n the signal intensity after the nth RF pulse. For healthy volunteers the T_1 relaxation time was obtained by fitting an exponential to the plateau at the inhalation phase of the washout curves after RF correction, assuming that T_1 decay was the only source of signal loss during this phase, and re-inhalation of ^{3}He could be neglected. This method could not be applied in the CF patient because of apparent partial re-inhalation of expired ^{3}He, preventing doubtless identification of the inhalation plateau.

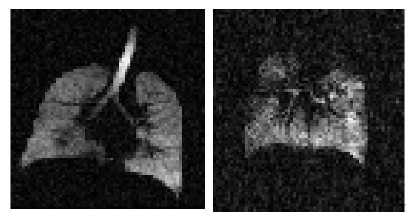

Figure 2: Ventilation images obtained before washout from a healthy volunteer (left) and a CF patient (right).

In this case we estimated T_1=25 s, corresponding to an intrapulmonary pO_2 of 104 mbar, in the range reported previously for patients with impaired lung function [3]. All washout curves were normalized to the initial signal intensity after breath-hold.

Results and Discussion: Figure 1 depicts ^{3}He washout curves obtained from healthy volunteers (m, 29-38 yrs). The ^{3}He signal decreases mono-exponentially until it reaches the detection threshold of about 4% of the initial signal. This is consistent with a model of constant mass exchange fraction, and the lung can essentially be regarded as a homogeneous reservoir with uniform airway recruitment. Figure 2 shows exemplary ventilation images taken immediately before washout from a healthy volunteer (m, 36 yrs) and a CF patient (f, 9 yrs, FEV1 90.1% predicted). The washout curves in figure 3 were taken immediately after imaging, using the same ^{3}He bolus.

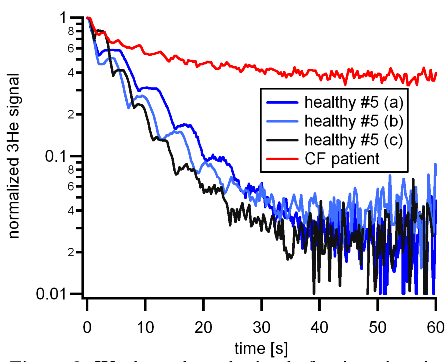

Figure 3: Washout data obtained after imaging, in a healthy volunteer and a CF patient.

The experiment was repeated three times in a healthy volunteer, and carried out once for the CF patient. The difference between healthy volunteers and the CF patient is apparent in both the ventilation images and the washout curves. The former show the heterogeneous ventilation typically found in patients with CF [4], compared to homogeneous gas distribution in healthy subjects. In the washout curves the corrected signal from the healthy volunteer decreases to less than 4% of its initial value within 30 s, while in the CF patient it does not fall below 40% within one minute. The red curve also shows a deviation from mono-exponential washout behavior in the CF lung when compared to healthy volunteers. These two observations could be indicative of inhomogeneous gas exchange within the lung, as expected in an obstructive disease such as CF and are supported by previous findings reported with SF_6 LCI measurements [2]. This inhomogeneity will also lead to a range of pO_2 over the lungs, leading to a higher weighting of anoxic regions in later stages of the experiment. The assumption of a constant T_1 can only be an approximation in this case.

Washout curves obtained with the mouth RF coil are shown in Figure 4. ^{3}He curves show different dynamics compared to curves obtained with the SF_6 method. This could be due to the very different diffusion coefficients of the two gases in air (D_{3He}'=0.86 cm^{2}s^{-1}[5], D_{SF6}'=0.093 cm^{2}s^{-1}[6]), and the different posture in which the experiments were conducted (supine vs upright). A more detailed comparison between the two methods is planned for the future.

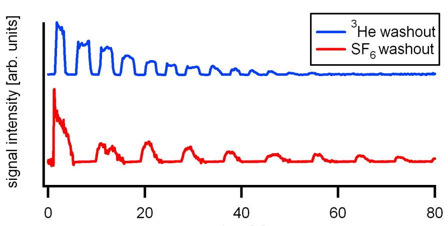

Figure 4: Washout data monitored at the mouth by ^{3}He NMR (top) and by SF_6 gas analysis (bottom)

In this study, all subjects were asked to exhale freely during washout monitoring. However, washout dynamics are certainly effort dependent, and the difference between patient and healthy volunteer observed here will at least partially result from the difference in age and lung volumes in addition to the effects of obstructive airway disease. Thus, the patient data presented here has to be regarded as preliminary. In order to obtain more quantitative results, measuring the flow of expired gas and prevention of re-inhalation will be necessary. Nevertheless, the method proposed here to monitor ^{3}He washout analogously to global inert gas washout techniques has the potential to yield useful additional physiological information in combination with ^{3}He ventilation imaging. As it is possible to use the same ^{3}He bolus as used for imaging, this additional functional information comes at no extra cost or inconvenience as compared to a standard ^{3}He MRI protocol.

References: [1] Larsson *et al.*, J. Appl. Physiol. 65, 2030-2039 (1988); [2] Horsley *et al.*, Thorax 63, 135-140 (2008); [3] Gast *et al.*, Eur. Radiol. 18, 530-537 (2008); [4] Koumellis *et al.*, J. Magn. Reson. Imaging 22,420-426 (2005); [5] Fain *et al.*, JMRI 25, 910-923 (2007); [6] Rudolph *et al.*, J. Atmos. Chem. 23, 253-273 (1996).

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