**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 3He 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 3He MRI ventilation imaging protocol. The NMR signal from intrapulmonary 3He 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 3He coils and with 3He NMR coils at the mouth that this method can be combined with 3He 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:** 3He was polarized to ~25% using a prototype spin-exchange optical pumping polarizer (Helispin, GE). Volunteers inhaled a mixture of 300 ml 3He and 700 ml N2. Coronal 3He images were obtained on a GE HDx 1.5T scanner using a Fast Gradient Echo sequence with a FOV of (38×38) cm², 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 was used to acquire ventilation images 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 3He bolus. 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 lungs, as expected in an obstructive disease such as CF and are supported by previous findings reported with SF6, LCI measurements [2]. This inhomogeneity will also lead to a range of PO2 over the lungs, leading to a higher weighting of anoxic regions in later stages of the experiment. The assumption of a constant T1 during washout from the mouth RF coil are shown in Figure 4. He washout curves show different dynamics compared to curves obtained with the SF6 method. This could be due to the very different diffusion coefficients of the two gases in air (D3He=0.86 cm²s⁻¹ [5], D216O=0.093 cm²s⁻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.

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 additional physiological information in combination with 3He ventilation imaging. As it is possible to use the same 3He bolus as used for imaging, this additional functional information comes at no extra cost or inconvenience as compared to a standard 3He MRI protocol.


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