Method for Correction of Breathing-Dependent Signal Changes in Dynamic Lung Oxygen-Enhanced MRI – Improved Sensitivity in Smokers

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INTRODUCTION

Oxygen enhanced MRI (OE-MRI) has been used to assess lung function by measuring the enhancement ratio between breathing air and 100% oxygen, and also by measuring the time to plateau of the increased signal effect, i.e. the oxygen wash-in rate. Lung MRI is hampered by intrinsically low proton density, the large susceptibility differences caused by the air-tissue interfaces of the alveoli and airways, and respiratory and cardiac motion. As OE-MRI is sensitive to varying diaphragm position [1], breath-holding is often used [2], which however has the potential to distort the lung function information one seeks to measure, and is not well tolerated by all subjects. Respiratory triggering also allows diaphragm position to be controlled, but is not ideal for dynamic acquisitions where an uneven breathing pattern may reduce temporal resolution. Post-processing alternatives may involve retrospective gating [1], which is also impractical for maintaining temporal resolution in dynamic studies. Another approach is to use registration to warp the lung shape to a reference position (e.g. [3]). In this work we demonstrate that post-registration residual breathing-dependent signal variation is comparable in magnitude to the oxygen induced enhancement, even when the registration process is effective. We subsequently present a method to correct these variations empirically, hence allowing more accurate estimation of OE-MRI parameters. As obstructive lung disease is thought to lengthen the wash-in time for oxygen, and as smoking is the leading cause of chronic obstructive pulmonary disease (COPD) [4], we have demonstrated the benefits of this technique in increasing the sensitivity of the OE-MRI parameters in a group of smokers.

METHODS

Smokers: A group of 10 smokers were recruited (5 males, 5 females, ages 29-57) with no previous diagnosis of COPD, or any other lung disease, for whom pack years (PY) were recorded (i.e. number of years in which 20 cigarettes a day were smoked).

Imaging: Scanning was carried out on a 1.5 T-Philips Intera system. A Hudson mask (Henleys Medical Supplies Ltd., Welwyn Garden City, UK) was used to administer medical air (21% oxygen) and 100% oxygen gas at a flow rate of 15 l/min. A single coronal slice positioned in the posterior mediastinum was used for dynamic observation of oxygen wash-in. Subjects were breathing freely throughout acquisition, without use of respiratory or cardiac triggering. For fast and direct T_1 mapping a snapshot FLASH (T1-Turbo Field Echo, T_1TFE) implementation of the TOMROP imaging technique [5] with radiofrequency (RF) spoiling and non-selective inversion pulse was used; TE = 1.0 ms, TR = 2.2ms, $\alpha = 5°$, slice thickness =15 mm, image matrix = 128 × 256, reconstructed to 256 × 256, FOV = 445 × 445 mm^2. Each T_1 measurement involved 25 repeat post-inversion acquisitions, the first at an inversion time (TI) of 74 ms, with successive at intervals of 143 ms, giving a total acquisition time of approximately 3.5 s. A gap of approximately 2.5 s was allowed for inversion recovery before the next inversion, i.e. an effective temporal resolution of 6 s. T_1 values were calculated using the methods presented in [5,6]. Imaging began while the subject was breathing air and 30 repeat acquisitions (3 min) were made before the gas supply was switched to 100% oxygen. Wash-in was observed for 60 acquisitions (6 min) followed by a further 3 min of acquisitions to observe the oxygen plateau.

Post processing: Signal images were registered to the maximum expiration position prior to T_1 mapping [3]. As T_1TFE is an intrinsically low signal to noise method, a Gaussian filter (3 x 3 pixels, 0.75 FWHM) was applied to the registered images. It was noted that the T_1 dynamic sequences were affected by large amplitude noise which varied according to where the acquisition fell within the breathing cycle. A marker for the breathing pattern position was obtained from the area within the lung outlines output from the registration algorithm. To investigate the dependency of the signal on the breathing pattern, separately for each of the 25 TI times (using the 30 air-breathing T_1TFE acquisition sets and the last 30 oxygen-breathing sets) the average lung area signals were plotted against breathing pattern position (figure 1). It was found that the highest signal magnitudes were measured during end expiration and the lowest during end inspiration, with values varying approximately linearly in between. This finding is consistent with the knowledge of the tissue density changes over the cycle, along with the effect of air-tissue interfaces on field inhomogeneity and its potential to reduce signal by decreasing T_2*. It is also possible that blood flow or varying gas composition within the lungs throughout the breathing cycle contribute to these fluctuations. The registration method [3] originally incorporated a step to rescale each pixel according to the magnitude of the linear stretch, to account for varying lung density over the cycle. As this correction was found inadequate to compensate for the fluctuations demonstrated here, an empirical correction was implemented by carrying out linear fitting on the data as plotted in figure 1. Slope and intercept values were calculated for each TI time (example values displayed in the equations in figure 1) and used to rescale the signal intensities of the whole dynamic set to a reference breathing position, and this was carried out individually for each pixel. The end expiration position was chosen as the reference, being the most reproducible and hence the most stable across the cycle, and giving the highest signal values. Maps of the right lung exponential wash-in times (t_c) were generated from the R_1 values ($1/T_1$) using dynamic T_1 data from both the uncorrected and corrected data sets, and the median values were compared between smokers with low pack years (PY) (range 1.6-9, mean = 5.2PY) and high PY (range 21-40, mean = 28.2PY).

Figure 1

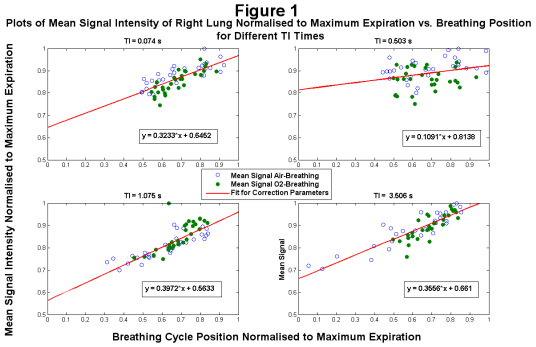


Figure 2

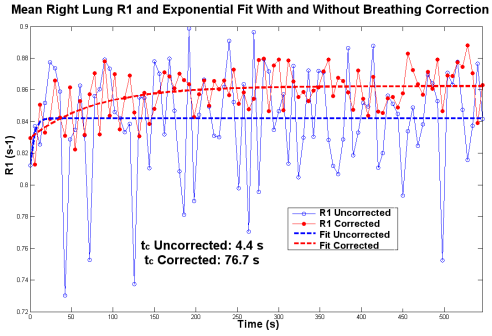
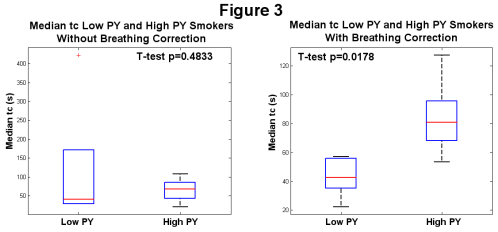


Figure 3



RESULTS

Figure 2 plots the R_1 wash-in curve obtained from the average over the uncorrected right lung (blue with open circles), compared with the curve obtained after pixel-wise correction (red with filled circles). The noise has been roughly halved by the correction and the corrected t_c value is a more realistic 76.7 s, as opposed to 4.4 s. Figure 3 shows the t_c times obtained for the low and high PY groups with and without correction, with the p-values of a 2-tailed t-test. After correction the groups have a significantly different t_c, with longer times for higher PY, as consistent with [4]. The uncorrected wash-in times are not significantly different between the groups.

DISCUSSION AND CONCLUSION

We have presented a corrective procedure for lung OE-MRI that normalises for volumetric, and perhaps also physiological changes, over the breathing cycle, hence improving the sensitivity of OE-MRI parameters. Furthermore the method can compensate for inadequacies of the simplistic linear stretch model and errors incurred during registration of the lung outline. **REFERENCES**: 1. Arnold J, et al, *J Magn Reson Imaging*, 26, 637-645, 2007; 2. Jakob P et al, *Magn. Reson. Med.*, 51, 1009-1016, 2004; 3. Naish J et al, *Magn Reson Med*, 54, 464-469, 2005; 4. Ohno Y, Proc. ISMRM 2006 p.33; 5. Deichman R et al, *J Magn Reson* 96, 608-612, 1992; 6. Deichmann R, *Magn Reson Med*, 54, 20-27, 2005. **Acknowledgements**: DMMcG and JN are supported by AstraZeneca