## Three-dimensional oxygen-enhanced human lung MRI using ultra-fast balanced Steady-State Free Precession

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Target audience. Physicist and physicians interested in lung imaging methods.

**Purpose.** Oxygen-enhanced (OE) MRI has been proposed for the assessment of the regional lung function  $^1$ , exploiting the weak paramagnetic properties of oxygen in blood resulting in shortened  $T_1$  and  $T_2$ \* relaxation times in the lung tissue when breathing air with an increased concentration of oxygen. The main limitation of contemporary OE functional MRI methods arises from the combination of a weak contrast effect with a low signal-to-noise imaging method. Ultra-fast balanced steady-state free precession (ufSSFP) imaging, however, was shown to provide increased signal in the lung parenchyma. Here, we explore three-dimensional (3D) OE lung MRI with ufSSFP in healthy volunteers taking into account a possible bias in OE contrast images due to volume-dependent signal intensity modulations.

## Methods.

*MR data acquisition:* All measurements were performed on a whole body 1.5 T MR-scanner (Siemens MAGNETOM Avanto) using a 12-channel thorax and a 24-channel spine coil. Three healthy volunteers were scanned using 3D ufSSFP with the following parameters: TE/TR = 0.47/1.19 ms, flip angle  $\alpha$  = 15°, RF pulse length = 80 µs, 1563 Hz/pixel bandwidth, field-of-view =  $400 \times 400 \times 250$  mm<sup>3</sup>, two averages, isotropic resolution = 3.1 mm<sup>3</sup>, reconstruction matrix =

 $128^2 \times 80$ , parallel imaging GRAPPA factor 2, total acquisition time = 17 s. The scans were performed in end-expiratory breath-hold for improved reproducibility of the total lung volume. For each volunteer, ten scans were acquired while breathing room air (RA) and, after a 5 min  $O_2$  wash-in phase, ten scans while breathing  $O_2$ . Oxygen was delivered at a flow rate of 25 L/min using a face mask with a 1.5 L reservoir bag.

Image postprocessing and analysis: First, to be blinded, the 3D ufSSFP datasets were randomized. Second, the datasets were median filtered<sup>4</sup> (filter size  $5\times5\times5$  voxels) to reduce signal noise and vasculature overlaying the pulmonary tissue. In each dataset, both lungs were segmented separately using the 3D-marching implemented in the Medical Imaging Interaction Toolkit<sup>5</sup>. The segmentations were visually verified slice-by-slice for consistency in between datasets from different acquisitions. Subsequently, mean signal intensity (SI) was analyzed along all segmented volumes to take into account a possible bias in the  $O_2$  contrast images due to volume-related signal intensity modulation in the lung tissue. Consequently, the mean relative contrast enhancement from  $O_2$  was determined for each volunteer as the signal (SI) difference between a linear regression analysis of the RA and  $O_2$  data with respect to the common mean lung volume.

Finally, 3D image registration was performed on unfiltered datasets, and OE contrast images – taking into account volume-related effects – were calculated for both unregistered and registered images. Registration of  $O_2$  datasets to a single RA dataset was performed with an MRF-based trilinear deformable registration<sup>6</sup>.

Results. Exemplary native ufSSFP and median filtered images are shown in Figure 1. Due to the very short TR provided by ufSSFP, no banding is visible in the lung tissue. The signal intensity in the lung parenchyma measured in a healthy volunteer as a function of the lung volume for both RA and  $O_2$  datasets is presented in Figure 2. A linear regression analysis (dashed lines in Fig. 2) yields a mean oxygen contrast enhancements of 6.1% for a mean lung volume of 1.8L. Similar results were observed for the other two volunteers, i.e. 5.5% and 3.8% for respectively 3.1L and 2.6L lung volumes, in good agreement with literature values.

Illustrative 3D OE contrast images for unregistered and registered datasets are shown in Figs. 3a and 3b, respectively. Misalignment artifacts manifesting as hyperintense structures at the diaphragm and chest wall, which are no longer visible in the registered images. The mean calculated signal enhancements evaluated for the coronal slices were, 12.7% (unregistered), and 16.8% (registered). Finally, Figs. 3c and 3d show OE contrast images corrected for volume related signal intensity changes, yielding 5.6% (unregistered), and 9.2% (registered).

**Discussion and Conclusion.** In this work, we have demonstrated the feasibility of 3D oxygen-enhanced ufSSFP lung MRI, providing full chest coverage in 17 s with an isotropic resolution of about 3 mm<sup>3</sup> using simple breath-hold acquisitions. This represents a considerable scan time reduction as compared to contemporary 2D multi-slice HASTE methods. Image post-processing not only involved segmentation and volume registration for motion compensation between separate breath-hold acquisitions, but also volume-related signal intensity corrections. Residual registration deficits, however, still persist indicating the need for improved registration algorithms. Moreover, our results indicate that volume-related signal variations are typically on the same order as the overall expected oxygen-related contrast enhancement, and can thus not be neglected. Future studies will focus on the potential of oxygen-enhanced 3D ufSSFP imaging for subjects with lung diseases.

**References:** [1] Edelman R et al., Nat Med 1996;2(11):1236-9; [2] Kruger S et al., NMR Biomed 2014;doi:10.1002/nbm.3158; [3] Bieri O, Magn Reson Med 2013;70:657-663; [4] Bieri O, ISMRM 2014;2300; [5] Maleike D et al., CMP Biomed 2009; 96: 72–83; [6] Heinrich H et al., IEEE Transactions 2013;1239-1248.

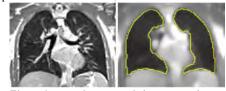


Figure 1. Exemplary coronal chest image obtained using 3D ufSSFP pulse sequence at 1.5T (left). Post-processed image from the corresponding slice location after 3D median filtering and segmentation (right).

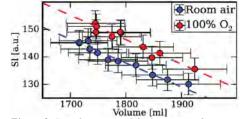


Figure 2. Signal intensity of the lung parenchyma in the 3D ufSSFP images measured at different expiratory volumes after breathing room air and 100% O<sub>2</sub>. The dashed lines show the linear relationship between lung volume and SI.

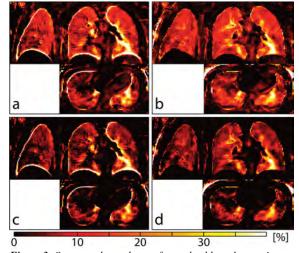


Figure 3. Oxygen-enhanced maps from a healthy volunteer in sagittal, coronal and axial reformats generated using unregistered (a,c), and registered (b,d) datasets. The maps in the lower row take into account the volume-dependent signal intensity of the lungs.