## Block paradigm optimization for dynamic oxygen-enhanced MRI of the lung

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**Introduction:** In oxygen-enhanced MRI ( $O_2$ -MRI) of the lung, the inhalation of pure oxygen ( $O_2$ ) reduces the longitudinal relaxation time,  $T_1$ , of blood, which can be detected by  $T_1$ -weighted MRI [1–8]. Frequently, a block paradigm is used for  $O_2$ -MRI consisting of a series of  $T_1$ -weighted scans acquired during alternating blocks with inhalation of room air and  $O_2$ . This block design results in a signal-time course for each pixel that contains information about the lung function. By fitting a model function to the acquired time course, several parameters such as the relative or absolute signal increase as well as the  $O_2$  wash-in and wash-out time constants (describing the signal dynamics) can be obtained [3,5,7,8].

A number of different block paradigms with different numbers of blocks and different durations of each block have been used in previous studies. The purpose of the present study was to compare differently designed block paradigms of constant total duration in order to find the optimal paradigm design for pixelwise parameter fitting in terms of maximized precisions and accuracies of all estimated parameters.

**Methods:** First, respiratory-gated  $O_2$ -MRI measurements in 11 healthy volunteers (acquired with a T1-weighted inversion-recovery HASTE sequence; acquisition paradigm: 80 acquisitions:  $20 \times air$ ,  $20 \times O_2$ ,  $20 \times air$ ,  $20 \times O_2$ ) were pixelwise evaluated as described in [8] in order to obtain typical statistical distributions (median value, 16th...84th percentile) of all parameters relevant for the subsequent simulations: absolute signal enhancements, wash-in and wash-out time constants, as well as the respiratory frequency and the signal-to-noise ratio (SNR) of the signal intensity in a single pixel. The latter was obtained both by evaluating the temporal standard deviation over the 20 initial baseline scans and by evaluating the normalized sum of squares ( $\chi^2$ ) of the differences between the fitted model function and the acquired data.

Then, respiratory-gated  $O_2$ -MRI measurements were simulated with different block paradigms as illustrated in Fig. 1. Both, the number of initial baseline scans and the number of scans in the subsequent blocks (of alternating  $O_2$  and air inhalation) were varied over a wide range (number of baseline scans: 1...75; number of scans/block: 2...64). The total number of scans was set to 80 in all simulations. Each simulated paradigm was evaluated for  $N=10\,000$  samples representing typical lung tissue. To obtain a realistic parameter distribution, random samples were generated with parameters distributed (based on an asymmetric log-normal distribution) as in the evaluated volunteer measurements (with respect to median and 16th...84th percentile).

For each simulation, the mean systematic and stochastic relative deviation of each fitted parameter (i.e. of signal enhancement, wash-in and wash-out times) were determined and displayed as color-coded maps. From each map, we generated a mask of those 30 % of all results with the lowest deviations and added these masks to obtain "quality maps" indicating parameter combinations with joint minimal total deviations of all three fitted parameters.

**Results:** The respiratory frequencies in the 11 evaluated volunteer measurements had a mean value (standard deviation) of 7.7 (1.6) min<sup>-1</sup>. The pixel signal showed a median baseline intensity of 72 arbitrary units (a.u.) and a median temporal standard deviation of 3.8 a.u. over the baseline scans and, in good agreement, of 4.0 a.u. over the fitted time course. The absolute signal enhancement had a median of 11.5 a.u. (16th...84th percentile: 6.0 a.u...22.8 a.u.), the wash-in time of 29.4 s (6.9 s...79.4 s) and the wash-out time of 25.1 s (5.4 s...64.8 s).

Results of the simulations based on these values are shown in Fig. 2: All maps show the different numbers of baseline scans on the vertical axis and the different numbers of scans per block on the horizontal axis (as indicated in detail in the bottom map). Combining all results into a single quality map, the optimal paradigm design can be established to consist of about 7 to 20 baseline scans and of about 40 to 56 scans per block (indicated as elliptic blue region in the bottom map).

**Conclusions:** Our results indicate that both the determination of the  $O_2$ -induced signal enhancement and of the  $O_2$  wash-in time constant improve considerably with longer block durations (more scans/block), while the estimation of the  $O_2$  wash-out time constant is less sensitive to shorter block durations. Thus, the optimal paradigm designs for dynamic  $O_2$ -MRI are based on the acquisition of only three blocks of different durations (i.e. with different numbers of respiratory-triggered scans). In summary, we recommend a block design consisting of 15 baseline scans, followed by 45  $O_2$  scans, and concluded by a final block of 20 room air scans, similar as the bottom example in Fig. 1.

**References:** [1] Edelman RR et al. Nat Med 1996;2: 1236–9 [2] Mai VM et al. J Magn Reson Imaging 2002;16:37–41 [3] Arnold JFT et al. MAGMA 2004;16:246–53 [4] Dietrich O et al. Magn Reson Med 2005; 53: 1317–25 [5] Naish JH et al. Magn Reson Med. 2005; 54: 464–9 [6] Molinari F et al. Invest Radiol 2006; 41: 476–85 [7] Ohno Y et al. AJR Am J Roentgenol 2008;190:W93-9 [8] Dietrich O et al. Invest Radiol. 2010; 45: 165–73

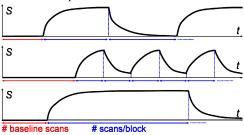


Fig. 1: Examples of different paradigm designs; the number of initial baseline scans (red; during administration of room air) and the block duration (blue) for alternating administration of  $\mathbf{O}_2$  and room air were varied while the total number of acquisitions was kept constant.

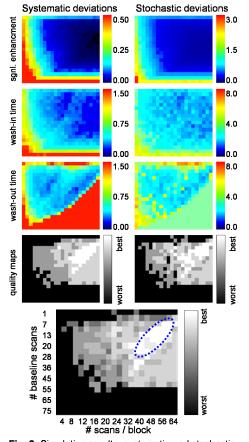


Fig. 2: Simulation results: systematic and stochastic deviations for all evaluated paradigms (for axes scaling see bottom map). Quality maps show areas in white where the deviations of all 3 fitted parameters were minimal. The quality map at the bottom combines the result for the systematic and stochastic deviations.