Simultaneous ΔR1 and ΔR2* Quantification in 5s to Monitor Blood and Tissue Oxygenation with Dynamic (C)O_2 Enhanced MRI

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Introduction

The monitoring of respiratory challenges with (C)O_2-enhanced MRI is gaining increasing interest for the assessment of tumor oxygenation, vasoreactivity, vessel maturity and function, all being important parameters that decide about optimal treatment strategies [1,2]. In these experiments, a patient's blood CO_2 or O_2 level is modulated either by inhalation of (C)O_2-enriched air or by breathholds, and the tissue response is recorded using BOLD sequences. Changes in tissue oxygenation are measured indirectly via changes in blood oxygen saturation, affecting R2*. Subsequent or additional R1 quantification was shown to directly represent changes in the amount of dissolved oxygen in tissue and plasma [3,4]. This increases the specificity of the experiment but necessitates additional (C)O_2-enhanced scans or impedes dynamic sampling of the response. However, dynamic sampling of the response is necessary to deal with the variable response kinetic of a pathology with unkown vasoreactivity. In this work, we therefore present an approach to simultaneous and dynamic ΔR1/ΔR2* estimation that combines the beneficial features of currently used sequences for dynamic R1 quantification in Gd-enhanced-MRI (DCE) and dynamic R2*-quantification in (C)O_2-enhanced MRI.

Methods

The approach exploits the R1 weighting of the steady-state magnetization M0, acquired with a dynamic spoiled gradient-echo sequence, which was extended by a multi-echo readout for dynamic R2* quantification (3D, TR=74ms, 7 echoes, α=25°, 1.8x1.8x3mm^3, SENSE 1.5 RL, t_D=4.8s). Baseline and dynamic values were derived from the average of the first 3 dynamics ($R2^*_0$ and $M0_0$) and all consecutive multi-gradient echo signals ($R2^*_t$ and $M0_t$), respectively, using a non-linear least squares fit to Eq. 1. The change of M0 was translated into dynamic $R1_t$ measures by the logarithm of Eq. 2. The baseline $R1_0$ and $B1_0$ values were obtained with a combined IR-TSE sequence [5] (MS, TSE-factor = 40, 1.8x1.8x5mm^3, TR_{IR}/TR_{SE}=3s/1.3s) and an actual flip angle imaging sequence (AFI, 3D, α=50°, 3.6x3.6x3mm^3) with interleaved TRs at 17ms and 77ms, respectively. Imaging was performed at 1.5T on a clinical whole body scanner (Philips Achieva, The Netherlands) with an 8 channel head coil. The accuracy of the approach was evaluated in a phantom (Test Object 5, Eurospin II Test System, Diagnostic Sonar LTD), in which R1 and R2* changes were mimicked by stepwise exchanging 4 samples of known R1 and R2 values (R2 and R2* are assumed to be of same value in a homogeneous phantom), Fig 1a. To evaluate robustness and sensitivity of the approach, ΔR1 and ΔR2* response curves and maps of significant changes in a healthy brain ($p < 0.2$) during a breathhold (33s after expiration) were obtained from statistical tests as described in [6], Fig 1b. All data were registered using rigid-body motion correction.

$$S_t = M0_t \cdot \exp(-TE \cdot R2^*_t) \quad \textbf{Eq. 1}$$

$$E1_t = \frac{1 - m + E1_0(m - \cos[\alpha \cdot B1_0])}{1 - m\cos\alpha + E1_0\cos[\alpha \cdot B1_0] \cdot (m-1)},\ E1_t = \exp(-TR \cdot R1_t),\ m = M0_t / M0_0 \quad \textbf{Eq. 2}$$

Results

Figure 1. Phantom (a) and Breathhold (b) exams.

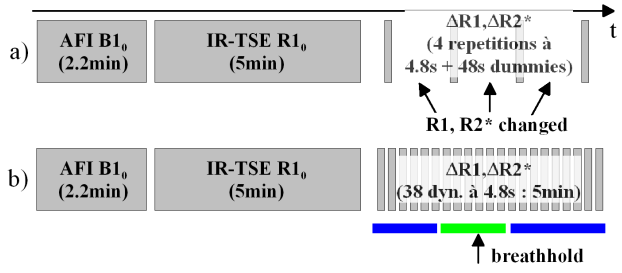


Figure 2. ΔR1 and ΔR2* accuracy (Phantom experiment, Fig 1a)

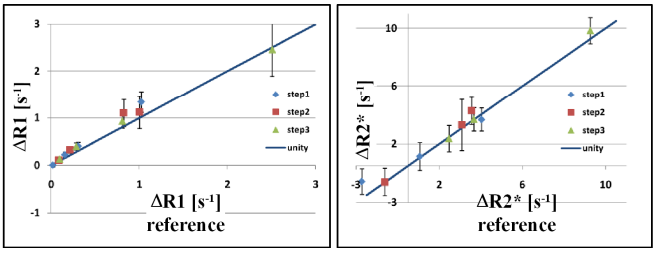
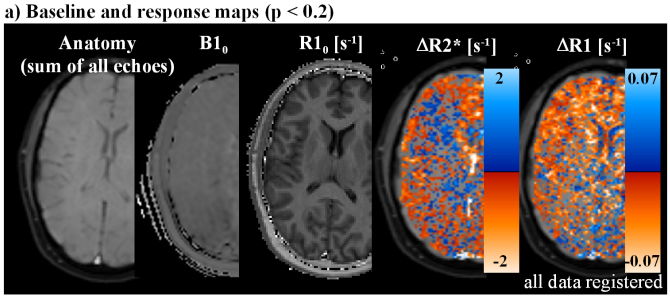
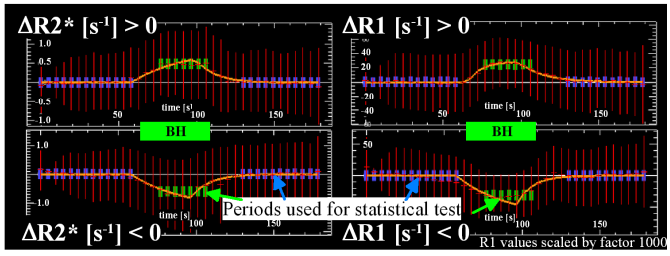


Figure 3. Breathhold experiment, Fig 1b.
a) Baseline and response maps ($p < 0.2$)



b) Global response curves of significant positive and negative changes



In the phantom experiment, the average ΔR1 and ΔR2* error was 0.11s^{-1} and 0.26s^{-1}, respectively (Fig. 2). Simulations (not shown) revealed that the ΔR1 errors mainly arose from systematic $R1_0$ overestimation (%), delivered by the IR-TSE sequence. Replacing the $R1_0$ measurement with the values given by the phantom manufacturer, the ΔR1 error was reduced down to -0.06s^{-1}. The breathhold ΔR2* response map revealed regional differences of positive (white matter, WM) and negative changes (gray matter, GM, consistent to [7]), whereas the ΔR1 pattern did hardly distinguish between GM and WM, but between CSF and GM/WM. The kinetics of the average response curves of all significantly changed voxels were nicely compassed by the <5s temporal resolution of the dynamic scan.

Discussion/Conclusion

Previous studies of dynamic R2* changes in response to Carbogen or CO_2/air inhalation have already revealed significant differences between tumors and normal tissue regarding the strength and kinetic of the response, although interpretation becomes difficult in the absence of a significant BOLD response [7]. This work presents an approach to simultaneous ΔR2* and ΔR1 quantification, which employs 3D spoiled gradient-echo sequences (with preceding baseline B1 and R1 quantification) as they are typically used for DCE-MRI, extended by a multi-gradient-echo readout for R2* quantification and dedicated postprocessing. The technique delivered accurate ΔR1 and ΔR2* values that could be further improved by optimizing baseline $R1_0$ quantification. The approach was further shown to be sensitive and fast enough to even cope with the rapid and subtle hemodynamic changes induced by a breathhold at 1.5T. It thus enables dynamic and simultaneous monitoring of both tissue and blood oxygenation and can therefore be expected to increase the specificity of classical BOLD response measurements during respiratory challenges. Alternatively, 2D sequences and the utilization of higher flip angles would further increase the inflow-sensitivity of R1 [8], yielding supplementary feedback about vasoreactivity.

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