Rapid Measurement of Oxygen Extraction Fraction (OEF) Maps using a Combined Multiple Gradient and Spin Echo Bolus Contrast Sequence

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Introduction: In the last few years, we have developed an MRI method that allows high-resolution quantitative measurements of the level of blood oxygenation (SO2) in the brain [1]. The technique is based on the specific extraction of the oxygenation information from baseline T2* measurements using a mathematical model and independent measurements of T2, B0, and the cerebral blood volume (CBV). The results obtained in healthy rat brain have shown good correlation with systemic blood gas analysis in various conditions of oxygenation. We have also obtained variations of MR_SO2 in different models of cerebral tumors, brain ischemia, and traumatic brain injuries [2]. However, the method employs a steady-state approach (involving the use of USPIO contrast agent) [3] for the determination of CBV that is only applicable in rodents. The objective of the present study was to translate the method into a clinical environment suitable for human studies. We propose a rapid acquisition scheme that consists of monitoring a bolus of a gadolinium based contrast agent with an EPI spin and gradient echo (SAGE) sequence [4]. SAGE Baseline scans were used for T2*/T2 estimates whereas perfusion-weighted imaging (PWI) was used to derive CBV maps. MR_SO2 was measured in 4 healthy subjects and one stroke patient.

Material and Methods: Magnetic resonance imaging was performed at 3T using a GE Discovery MR750 whole-body scanner (GE Healthcare, Waukesha, WI) and an 8-channel head array. The study was approved by the IRB and all subjects signed written informed consent. Five subjects were scanned using the following protocol: MR acquisitions with 5-echo SAGE-EPI sequence with echo times $TE_{1\text{-}5}$ = 16.6, 34.0, 61.8, 79.2, (gradient echoes) and 97.0 (spin echo) ms. Fifteen 5 mm thick slices with in-plane resolution of 84x84 voxels were acquired with FOV = 24 cm. A 90° spectral-spatial RF excitation pulse was followed by a 180° spin echo refocusing pulse. Both pulses were developed using SLR design with the goal of a good match between RF pulses to limit the signal drop associated with non-matched slice profiles [5]. PWI was based on the subsequent acquisition of 60 EPI volumes with TR = 1800 ms. A single-dose bolus (0.1 mmol/kg body weight) of a Gadolinium-based contrast agent was administered with a power-injector after the onset of the dynamic image acquisition sequence (typical bolus injection delay of 15-18 seconds). Hemodynamic maps (CBF, CBV, MTT, and Tmax) were created with the RAPID software toolbox [6] using automatic AIF detection and circular SVD [7]. The first 10 acquisitions of the SAGE sequence (without presence of contrast agent inside the brain vasculature) were averaged and used to compute baseline relaxation maps. T2* and $T2^*_B$ (T2* acquired after the 180 degree pulse during the regrowth of the signal) were obtained pixel-wise using a non-linear exponential fit of the first 2 gradient echoes (TE=1216.6-34.0-30 ms) and the 3 last echoes (TE=61.8-79.2-97.0 ms) respectively. T2 was computed as $2/(1/T2^*+1/T2^*_B)$ and T2' as $2/(1/T2^*-1/T2^*_B)$ [8]. MR_SO2 maps were derived according to our quantitative BOLD approach using $(1\text{-MR\_SO2})=(R2^*\text{-}R2)/(CF\cdot CBV\cdot\gamma\cdot\Delta\chi\cdot Hct\cdot B0)$. Where Hct=0.42·0.85 is the microvascular hematocrit fraction and $\Delta\chi=0.264\cdot10^{-6}$ is the difference between the magnetic susceptibilities of fully oxygenated and fully deoxygenated haemoglobin. CF is a correction factor for CBV values. In this study, for simplicity, this factor was kept constant and set to 2. MR_Oxygen extraction fraction (OEF) maps were derived as 1-MR_SO2. Regions of interest were manually drawn over the entire brain. Voxels with T2>150ms were excluded from the analysis to remove the effect of CSF. MR_SO2 values inferior to 0 or superior to 100% were considered as out of the range of validity and were also excluded.

Results

Fig 1: Parametric maps obtained with the protocol in the brain of: A) healthy subject; and B) stroke patient.

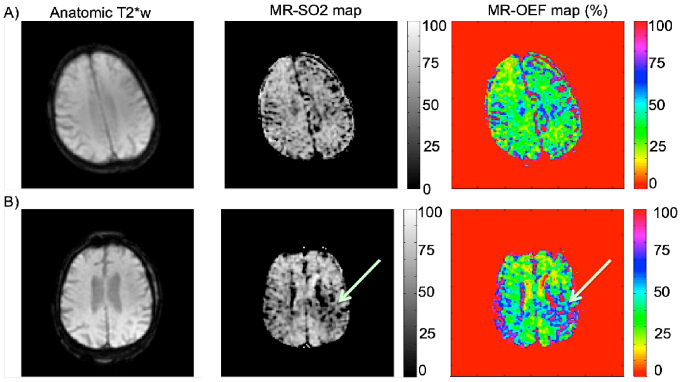

Fig 2: Quantitative values obtained in the brain of all subjects.

Subject	T2* (ms)	T2 (ms)	CBV (mL/100g)	MR-SO2 (%)
#1	55±12	71±22	3.5±1.6	62±22
#2	57±13	76±27	3.6±1.8	63±21
#3	54±11	68±20	3.8±2.0	65±21
#4	55±12	73±25	4.0±2.0	63±20
#5 Contra	53±11	75±25	3.5±1.2	60±17
#5 Lesion	51±09	78±28	3.5±1.1	44±18

Parametric maps from two subjects are presented in Figure 1. Blood oxygenation saturation and OEF maps are relatively homogeneous over the entire brain in the healthy subject (A). It can however be seen that low SO2 values (high OEF) are present in the affected region of the stroke patient (B) (green arrows). The MR_SO2 values averaged over the entire healthy brain (Fig 2) are consistent with previously reported oxygenation values (MR_SO2=63±2%). A T2* of 55±2 ms and a T2 of 72±3 ms are also consistent with the literature. An averaged CBV of 3.7±0.2 % was found in the 4 healthy subjects.

Conclusion: This study suggests that MR_SO2 maps can be obtained in human brain with a quantitative BOLD approach. This approach does not require additional time compared to standard PWI experiments and is a side-product from a conventional SAGE PWI study. The values obtained in healthy brains agree with results from previous studies using MR or NIRS [1]. A higher-order shim procedure to remove background B0 inhomogeneities, an adaptative CF derived from combined ASL/PWI experiments [9], and possibly a longer pre-bolus baseline acquisition could potentially further improve the quality of the data. More acquisitions in patients will help to understand the meaning and utility of such parameters.

References: [1] T Christen et al, NMR in Biomed, 2010. [2] T Christen et al, ISMRM09, #1353. [3] I Troprès et al, Magn Reson Med, 2001. [4] Newbould et al., Proc ISMRM07, #1451. [5] Schmiedeskamp et al., Proc ISMRM10, #2962. [6] Straka et al., JMRI 2010. [7] Wu et al., MRM 2003. [8] Ma and Wehrli, J Magn Reson B, 1996. [9] G Zaharchuk et al, MRM, 2010.

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