Measuring Brain Oxygenation in Humans using a Quantitative BOLD Approach

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Introduction: In the last few years, we have developed a new magnetic resonance imaging (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. Instead of the steady state approach, we used a recent approach combining ASL and bolus perfusion-weighted imaging (PWI) measurements to obtain accurate quantitative CBV measurements [4] in human brain. MR_SO2 was measured in 5 healthy volunteers.

Material and methods: Imaging was performed at 3T using a GE Signa 750 whole-body scanner (GE Healthcare Systems, Milwaukee, WI) and an 8-channel head coil. Five subjects were scanned using the following protocol:
- **T2* maps** were acquired using a 3D multiecho gradient echo sequence (TR=75ms, 10echoes, TE=10 to 55ms, FOV=22*22, ST=1mm, 256*256, 24slices). Each of the thin slices (1mm) were averaged to form a 5mm slice thickness. Nonlinear exponential fitting of the signal evolution was using to obtain T2* with reduced effect of B0 inhomogeneities.
- **T2 maps** were acquired using a 2D multiecho spin echo sequence (TR=1000ms, 8echoes, TE=10 to 55ms, FOV=22*22, ST=5mm, 256*256, 4slices). Nonlinear exponential fitting of the signal evolution was using to obtain T2.
- ASL CBF maps (6 min) were acquired using pseudocontinuous labeling (label time/post label delay 1.5/2.0 s) and background-suppressed 3D fast spin-echo readout with a resolution of 3 x 3 x 4 mm [5].
- Bolus PWI (2 min) was performed using a single-shot EPI gradient echo PWI method (TR/TE = 1800/40 ms, flip angle 60°, 0.1 mmol Gd) [6]. Hemodynamic maps (CBF, CBV, MTT, and Tmax) were created using automatic AIF detection and circular SVD [7].

Corrected CBV maps were obtained using the recently described CAD method [4]. Briefly, a correction factor (CF) is derived by comparing ASL_CBF and PWI_CBF maps in regions with low Tmax values. This CF is then used to scale the PWI CBV map.
MR_SO2 maps were derived according to our quantitative BOLD approach using (1-MR_SO2)=(R2*-R2)/(CBV.γ.Δχ.Hct.B0). Where Hct=0.42*0.85 is the microvascular hematocrit fraction and $\Delta\chi=0.264*10^{-6}$ is the difference between the magnetic susceptibilities of fully oxygenated and deoxygenated hemoglobin.
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 one subject.

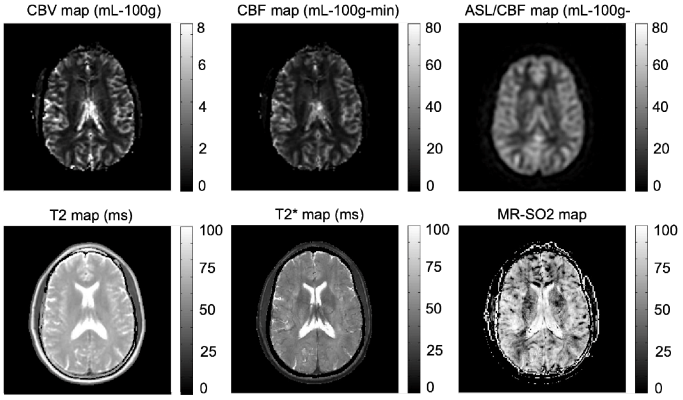

Fig 2: Quantitative values obtained in the brain of all subjects.

Subject	T2*(ms)	T2(ms)	CBV(%)	SO2(%)	CF_{CAD}
#1	53±10	68±9	4.6±3.2	63±21	4.6
#2	53±11	69±9	3.6±2.8	58±25	2.0
#3	51±8	69±7	4.4±3.1	64±20	2.1
#4	54±8	70±7	4.5±3.6	62±20	3.0
#5	56±10	70±7	3.3±2.0	58±25	3.3

Parametric maps from one subject are presented as Figure 1. One can notice the high quality of the T2 and T2* maps. Blood oxygenation in human brain is believed to be homogeneous over the brain. However, the MR-SO2 map shows contrast between white and gray matter. Values in deep gray matter also appear to be low. These observations have also been noticed in rat brain. Possible explanations could be the presence of iron or the anisotropy of the magnetic susceptibility that has been implicated as a source for the WM/GM contrast in phase maps [8]. Nevertheless the MR_SO2 values averaged over the entire brain (Fig 2) are in line with previously reported oxygenation values (MR_SO2=61±3%). A T2* of 53±2 ms and a T2 of 69±1 ms are also consistent with the literature. A mean correction factor of 3.0±1.0 was found in the 5 subjects leading to a corrected CBV of 4.1±0.6 %. An average of 15% voxels were excluded according to our criteria.

Conclusion: This study suggests that MR-SO2 maps can be obtained in human brain using a qBOLD approach. Although the global values are in agreement with prior reports, further insights are needed to understand (and possibly correct) the apparent WM/GM contrast. Applications to pathologies such as stroke or cancer will also help to elucidate the meaning and utility of such parameter.

References: [1] T Christen et.al, NMR in biomed, 2010. [2] T Christen, ISMRM09, #1353. [3] I Troprès et al, Magn Reson Med, 2001. [4] G Zaharchuk et al, MRM, 2010. [5] Dai et al., MRM, 2008. [6] Newbould et al., MRM 2007. [7] Straka et al., JMRI 2010. [8] Lee et al, neuroimage, 2010.
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