

Evaluation of a new qBOLD approach to map local blood oxygen saturation in non human primates

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Introduction

Tissue oxygenation can be characterized by local oxygen saturation (ISO₂), which may be mapped by quantitative Blood Oxygen Level Dependent (BOLD) approaches [1]. An approach that combines separate estimates of T₂, T₂*, BVf, and B₀ inhomogeneities has recently been proposed and validated in rats [2] and a preliminary study has been realized in humans [3]. The aim of this study is to evaluate this approach in non human primates under two depth of anesthesia.

Materials and Methods

Groups. Studies were performed on 6 male non human primates (NHP) (*Macaca fascicularis*) weighing 6-12 kg. All Animals were anesthetized with an intramuscular Ketamine (30 mg/kg) / Xylazine combination using two depths of anesthesia: Group 1 received 2mg/kg of Xylazine and Group 2, 10mg/kg.

Acquisition. The imaging protocol was carried out on a 3T TX Achieva MR scanner (Philips Healthcare®) using a whole-body RF transmit and 8-channel head receive coils. In addition to a 3DT₁ sequence used for tissue segmentation (TR/TE=9.8/4.6ms, resolution=0.5x0.5x1mm), three sequences were acquired with a FOV of 160x160x20 mm: a 3D multi gradient echo (GE) sequence to obtain a T₂* estimates (10-25 slices, 17 echoes, TR=180msec, ΔTE=7.57ms, resolution= 0.5x0.5x0.8mm); a multiple spin-echo to map T₂ (2-5 slices, TR=1200 ms, 32 echoes, ΔTE=9ms, resolution=1x1x4mm); a perfusion sequence with injection of a bolus of Gadolinium-DOTA (0.1mmol/kg, Guerbet, France) to map BVf using a first passage approach (TR=500ms, dynamic scan time= 500 msec, resolution=1x1x4mm).

Data Analysis. To correct for macroscopic magnetic field inhomogeneities, the 3D gradient echo sequence was spatially averaged. The final spatial resolution was that of the multiple sin-echo sequence. T₂ and T₂* maps were obtained by fitting a monoexponential decay to the corresponding MR images. Relative BVf maps were obtained by fitting a gamma-variate function to the change in 1/T₂* over time during Gd-bolus passage. To obtain quantitative BVf maps, the mean brain blood volume was normalized to 5%. ISO₂ maps were eventually calculated pixelwise using [2]:

$ISO_2 = 1 - (4/3 \cdot \pi \cdot \gamma \cdot B_0 \cdot \Delta\chi_0 \cdot Hct \cdot T_2 \cdot BVf)^{-1}$ where $1/T_2' = 1/T_2^* - 1/T_2$, $\Delta\chi_0 = 0.264$ ppm is the difference in magnetic susceptibilities between fully oxygenated and fully deoxygenated hemoglobin, Hct=0.42 is the hematocrit fraction, γ is the gyromagnetic ratio, B₀=3T is the strength of the magnetic field.

Then, using SPM8, gray (GM) and white matter (WM) masks were obtained from the 3DT₁ images [3]. The masks were realigned and resliced to match the T₂ map (1b). Significance between groups was evaluated with a Student t-test (<0.05).

Figure 1. Maps obtained in one primate at 3T.

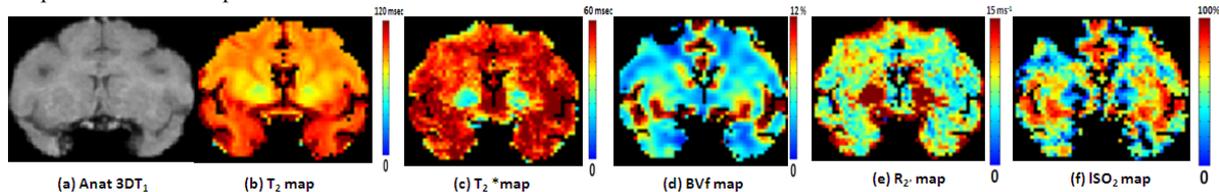
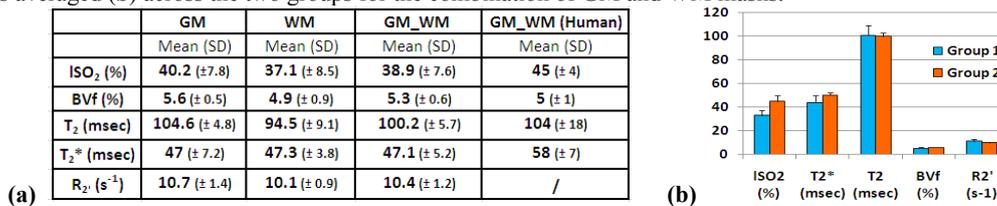


Figure 2. T₂*, T₂, BVf, R₂' and ISO₂ values averaged (a) across the six primates for GM mask, WM mask and the combination between GM and WM masks. Corresponding human estimates obtained in [3] are given for comparison purposes (mean±standard deviation); T₂*, T₂, BVf, R₂' and ISO₂ values averaged (b) across the two groups for the combination of GM and WM masks.



Results

Fig. 1 shows representative maps obtained from one NHP. The noise level in each maps is low. Maps reflect the gray/white matter anatomy. Average T₂* and T₂ values measured in GM were 47±7.2ms and 104.6±4.8ms and in WM 47.3±3.8ms and 94.5±9.1ms, respectively. BVf was 5.6% in GM and 4.9% in WM. T₂* values in GM and WM are comparable, conversely to what was observed in human [3]. As expected, BVf is lower in WM than in GM. ISO₂ values in GM and in WM were 40.2±7.8% and 37.1±8.5%, respectively, lower than what has been observed in humans [3] (Fig 2a). ISO₂ values are significantly lower in group 1 than in group 2 (33.0±4.4% and 44.9±4.5%, respectively).

Discussion / Conclusion

ISO₂ values obtained by MR in NHP appear reproducible and correspond to what has been reported in the MRI and positron emission tomography literature [4, 5], i.e. lower values than in human. As expected, the depth of anesthesia had an effect on ISO₂ and the proposed MR approach appears sensitive enough to detect this change. The deeper anesthesia yielded a higher ISO₂, in line with a reduced electrical activity in the brain. Note that in our study, we considered the BVf stable (the same normalization value was used for the two groups). The next experiments, such as gaseous challenges to further validate the approach, should use a fully quantitative technique to map BVf (e.g. with a steady-state approach and iron oxide nanoparticles [6]).

In conclusion, this study shows that local blood oxygen saturation may be measured in a single MR exam from three MR sequences with good spatial resolution in non-human primate. This technique may be applied to monitor primate model of diseases such as glioma, stroke or Parkinson.

References

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