Evaluation of a new quantitative BOLD approach to map local Blood Oxygen Saturation

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Introduction

Quantitative mapping of brain oxygenation levels using MR would be of considerable interest for numerous pathologies. Recently, He and Yablonskiy proposed an *in vivo* MR approach – quantitative BOLD – to obtain blood volume fraction (BV_f) and local blood oxygen saturation level (lSO_2) maps **[1] [2]**. To analyze the difference observed between T_2 and T_2* (i.e.T_2'), they distinguished two effects: a macroscopic effect due to large-scale B_0 inhomogeneity (non-ideal shim), and a mesoscopic effect, due to the susceptibility gradients between blood vessels and tissue. The mesoscopic effect depends on both BV_f and lSO_2, but these two contributions are difficult to separate during data analysis **[2]**. To improve the accuracy on the determination of lSO_2, we introduce in this study a different measurement scheme. We propose to combine a steady-state BVf/Vessel size index (VSI) measurement scheme **[3]** with standard B_0 and T_2 mapping techniques. This new approach should provide quantitative maps of BVf, VSI and lSO_2 and improve the accuracy on lSO_2 estimates.

In this study, we evaluate the proposed acquisition scheme in healthy rats while varying the inspired oxygen fraction.

Theory

The gradient echo MR signal decay can be described by (assuming that the effect of water diffusion can be neglected):

$$S(t)= Cte.\ F(t).\exp(-t.R_2).\exp(-t.R_2') \quad \textbf{[Eq. 1]}$$

where Cte is an proportionality constant, F(t) represent the contribution to signal attenuation caused by macroscopic field inhomogeneities **[1]** and $R_2= 1/T_2$, $R_2'= 1/T_2'= 4/3.\pi.\Delta\chi_0.Hct.(1-lSO_2).B_0.\gamma.BVf$. $\Delta\chi_0$ stands for the change in magnetic susceptibility between oxy and deoxy-haemoglobin (0.264 ppm), Hct for hematocrit (%), and γ for magnetogyric ratio.

Material and methods

Experiments were performed at 4.7 T on a Bruker Avance 3 console using volume/surface cross coil configuration. Wistar rats (n=12) were anaesthetized using isoflurane (2%) in air. The tail vein was equipped with a catheter. lSO_2 was monitored over time using MR. For 6 rats, the inspired gas were switched from Air to Air+O_2 (O_2 fraction ~80%) during 10 min (O_2 challenge).

All data were acquired with the same geometry (7 contiguous, 1mm-thick slices, FOV=30x30mm; matrix=64x64 or 128x128), except for B_0 mapping (3D GE sequence, FOV=30x30mm, matrix=128x128x40, TR=100ms, TEs=4 and 12ms). Acquisition protocol was: brain shimming, B_0 mapping, T_2 mapping (TR=1500ms, 20 spin-echoes, ΔTE=12ms), T_2* mapping (TR=1500ms, 30 gradient echoes, ΔTE=2.5ms), BVf/VSI mapping (multiple gradient-echoes spin-echo sequence, before and 3min after injection of 200µmol/kg of iron oxide particles (USPIO: Combidex®/Sinerem®, Amag Pharmaceuticals/Guerbet): TR=6000ms; ΔTE_{GE}=3ms; TE_{SE}=60ms). The entire MRI protocol lasted 1h15 per animal.

Processing was performed within the Matlab environment and using home-made software. B_0 map was obtained by unwrapping the phase maps of the 3D GE sequence **[4]**. This B_0 map was used to compute the contribution to signal attenuation caused by macroscopic field inhomogeneities (denoted as F(t) in **[1]**). T_2 was computed using a non-linear fit algorithm and a two-parameter exponential decay. BVf and VSI were obtained with the formula given in **[3]** using 700µm²/s for the apparent diffusion coefficient and 0.28ppm for the increase in intravascular magnetic susceptibility due to the injection of USPIO **[3]**. To compute lSO_2 maps, **Eq [1]** was fitted to the MR gradient-echo data. Since maps of BVf, R_2, and F(t) were available (assuming a stable BVf during O_2 challenge), the fitted parameters were Cte and lSO_2.

Results

Fig. 1 shows examples of T_2*, T_2, B_0, VSI, BVf and lSO_2 maps acquired in a single animal. Red pixels correspond to rejected values (outside the range of validity). Table 1 summarizes quantitative results obtained in all rats. BVf≈3% and VSI≈6µm values are consistent with previous studies using vessel size imaging **[3]**. During air inspiration, lSO_2 was about 60%. After inspiring Air enriched in O_2 for 10min, lSO_2 increased to about 70%. Figure 2 shows an example of lSO_2 time course obtained in the striatum of one animal during O_2 challenge.

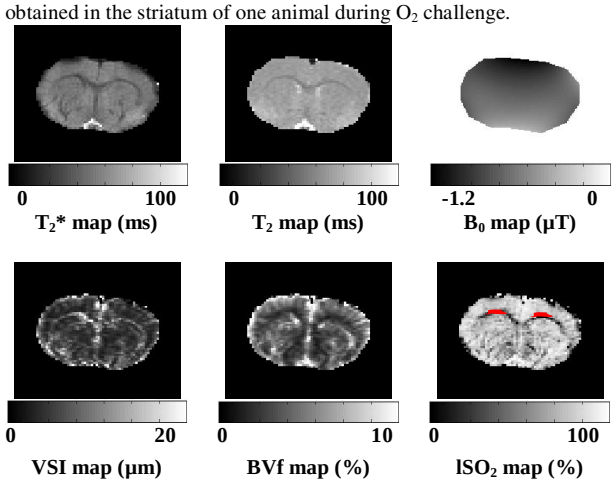

Fig. 1. Example of maps acquired in one rat at 4.7T. Red pixels correspond to rejected values (out of boundaries pixels).

	VSI (µm) n=12	BVf (%) n=12	lSO_2 in air (%) n=12	lSO_2 in (air+O_2) (%) n=6
Whole brain	**6.2±1.2**	**3.0±0.6**	**59.8±4.8**	**69.3±3.4**
Striatum	**5.7±1.1**	**3.0±0.6**	**60.9±4.0**	**71.8±3.3**

Table 1. VSI, BVf and lSO_2 (mean±standard deviation) across all animals.

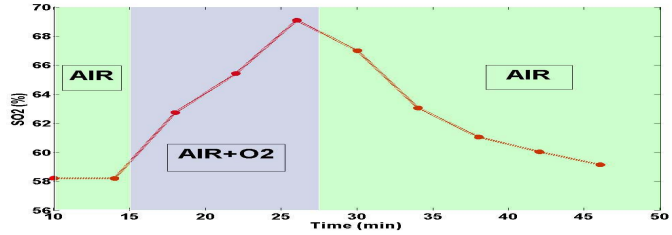

Fig. 2. Example of mean local oxygen saturation (lSO_2) obtained in the striatum of one rat during inspiration of Air, Air enriched in O_2 and Air.

Conclusion

Value of lSO_2 obtained while breathing air are similar to those reported by **[1]** and are consistent with SO_2 measured by Near InfraRed Spectrometry (NIRS) in the brain **[5]**. The increase in lSO_2 is consistent with the increase in inspired oxygen fraction. Standard deviations on lSO_2 estimates are relatively small (<5%). Corrupted values in corpus callosum could be explained by its microvascular network which might not be adequately described by the mathematical model used in this study. This study shows that microvascular characteristics (blood volume fraction and vessel size index) and blood oxygen saturation can be collected within a single MR exam, with good spatial resolutions. Comparison with blood gases, qBOLD **[1]** or optical fiber pO_2 measurements should provide further insights on the physiological meaning of lSO_2.

References

[1] X. He and D. A. Yablonskiy, *Magn Reson Med*, 2007. [2] H An and W Lin, *JCBFM*, 2000 [3] I Troprès et al, *Magn Reson Med*, 2001.[4] M. Jenkinson, *Magn Reson Med*, 2003. [5] Y Chen et al, *Phys Med Biol*, 2003.