Quantitative MR estimates of blood oxygenation based on T2*: a numerical study of the impact of model assumptions.

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Introduction: Several MR methods have been proposed over the last decade to obtain quantitative estimates of the blood oxygen saturation (StO2) using quantification of the blood oxygen level dependent (BOLD) effect [1-3]. These quantitative BOLD approaches are all based on mathematical models describing the time evolution of the MR signal in a gradient echo experiment. Although the experimental results are very encouraging, possible biases induced by the model assumptions have not been extensively studied. In this study, we use a numerical approach to examine the influence on T2*, blood volume fraction (BVf), and StO2 estimates of possible confounding factors such as the water diffusion or the presence of arterial blood in the voxel. To evaluate the impact of the vessel geometry, the use of straight cylinders and realistic data from 2-photon microscopy for microvascular geometry is compared.

Material and methods: All simulations were performed on a Dell Precision computer with double quad 2.33GHz Intel Xeon processors and 8 GB of RAM. Calculations were performed in the Matlab (Mathworks Inc. Natick, MA, USA) environment using homemade software.
We considered a tridimensional matrix Pxyz that describes a voxel containing a tissue compartment (Pxyz=0) and vessels (Pxyz=1). Two types of microvascular networks were considered: (i) an ensemble of straight cylinders, classically used for numerical simulations, and (ii) real microvascular networks (n=11 mice), acquired using a two-photon microscope as previously described [4]. In both cases, a reference BVf (BVf,ref) was derived as the ratio between the number of points in a vessel and the total number of points in the voxel: $\sum(Pxyz=1)/\sum Pxyz$.
A diffusion coefficient ($D=10^{-9}\ m^2s^{-1}$) and a magnetic susceptibility – that of blood ($\Delta\chi=\Delta\chi 0.Hct.(1-StO2)$, where Hct=0.4 is the hematocrit and $\Delta\chi 0=0.264$ ppm is the difference between the susceptibilities of fully oxygenated and deoxygenated hemoglobin) or of tissue ($\Delta\chi=0$) – were assigned to each matrix point. The magnetic field distribution was computed at B0=3T using a Fourier based approach [5]. Relaxation and diffusion of water were accounted for using a deterministic approach [6]. The MR signal (i.e. the gradient echo transverse magnetization as a function of echo time) was then computed.
T2* was obtained using a non linear exponential fit of the signal. BVf,MR was estimated by simulating the presence of a contrast agent (CA) inside the vessels (difference of magnetic susceptibility $\Delta\chi_{USPIO}=0.231$ppm) and using $BVf,MR=3/(4\pi)\ \Delta R2^*/(\gamma\ \Delta\chi_{USPIO}\ B0)$, where $\Delta R2^*$ represents the change of R2* induced by the CA [7]. StO2,MR was computed following the previously proposed quantitative BOLD approach and by fitting the simulation signal to the equation $s(t) = Cte\ \exp(-1/T2.t - BVf,MR.\gamma.\Delta\chi.Hct.(1-MR\_StO2).B0.t)$.

Results

Fig 1: Effect of water diffusion on T2 estimates as a function of vessel radius and oxygenation.*

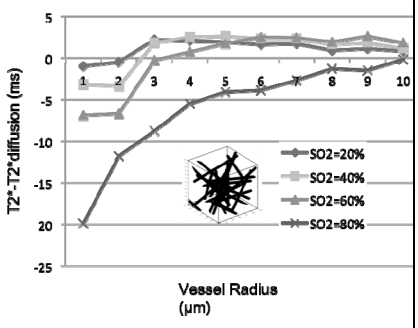


Fig 2: Effect of the presence of arterial and venous compartments on StO2,MR estimates.

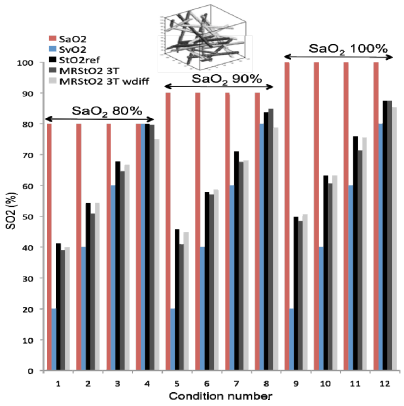
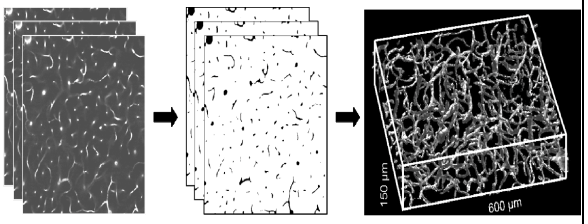


Fig 3: Impact of vessel geometry on BVf,MR and StO2,MR estimates.



Mice n°	01	02	03	04	05	06	07	08	09	10	11	Average
BVf,ref (%)	7.8	2.8	3.2	3.1	6.4	8.1	1.1	1.2	6.5	4.0	3.6	4.3
BVf,MR(%)	9.5	4.4	4.9	4.0	8.9	10.1	1.7	1.8	9.9	2.8	5.4	6.0
SO2,MR (%) SO2,Ref=60	65.4	63.6	64.5	62.8	60.3	58.9	63.8	65.3	66.2	62.1	65.0	63.5

Effect of water diffusion: We considered voxels with homogenously oxygenated cylindrical vessels of identical radius. T2* was estimated for various vessel radii (from 1 to 10 µm) and for several SO2 levels (from 20 to 100%) with (T2*diffusion) or without (T2*) taking into account the process of water diffusion. It can be seen in Fig 1 that water diffusion has a large effect on T2* estimates for small and well-oxygenated vessels at 3T. However, this effect is greatly reduced and tends towards zero when the vessel radius increases.
Presence of arterial and venous compartments: In voxels containing 5 µm-radius straight cylinders, we considered two types of vessel: arteries, occupying an arterial blood volume fraction (BVfa) of approximately 1% and veins, occupying a venous blood volume fraction (BVfv) of approximately 3%. Three arterial SO2 (SaO2) 80-90-100%), and four venous SO2 (SvO2) (SvO2=20-40-60-80%) were considered. For all conditions of oxygenation, the simulated MRStO2 (with and without diffusion) and StO2ref (computed as (BVfa/BVf)*SaO2+(BVfv/BVf)*SvO2) were very similar (the MR estimate was, however, always lower than the reference one).
Impact of vessel geometry: To analyze the impact of the geometrical assumption only, neither the water diffusion nor the intravascular signal was considered. The vascular networks placed in the voxels were derived from the high-resolution microscopic data (Fig 3). BVf,ref and BVf,MR estimates are given in the table in Fig 3. BVf,ref varied from 1% to 8% (average 4.3%) which is consistent with data from the literature [7]. BVf,MR always overestimates BVfref. However an excellent correlation (R2=0.98) was obtained between the two BVf estimates. We assigned an homogeneous SO2,ref=60% to the microvascular network and then simulated the MR protocol to obtain an StO2 estimate (note that this includes the BVf,MR estimates previously obtained). A mean StO2,MR of 63±2% was obtained suggesting that the precise vessel geometry does not significantly impact in the StO2 estimates.

Conclusion: Using numerical simulations, we analyzed the influence of three assumptions of a mathematical model on the estimates of BVf and SO2 obtained at 3T using MR techniques. Our results suggest that the static dephasing regime (water diffusion neglected) is a good approximation at 3T as long as the vessel radii are above 3 µm and SO2 is below 80%. The MR estimates of SO2 will represent the SO2 averaged over the arterial and venous compartments. According to the results obtained using microscopy data, the assumption of using straight cylinders to simulate blood vessels seems appropriate. However the reasons for the overestimation of BVf,MR still require further investigation.

References: [1] X. He et.al, *MRM*, 2007. [2] H An and W Lin, *JCBFM*, 2000 [3] T Christen et.al, NMR in biomed, 2010 [4] T Christen et al, Proc ISMRM 2009, #830. [5] J. P. Marques and R. W. Bowtell, *NMR Biomed*, 2007. [6] L. M. Klassen and R. S. Menon, *Biophys J*, 2007. [7] I Troprès et al, *MRM*, 2001.