Evaluation of multiparametric qBOLD in white matter: a simulation study

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Introduction
Quantitative estimates of the tissue blood oxygen saturation (StO2) may be obtained using a multiparametric quantification of the blood oxygen level dependent effect (multiparametric qBOLD) [1, 2]. This method, based on a model of the MR signal, yielded promising experimental results on rodents [2]. However, the first estimates of StO2 obtained in humans with this method matched those reported in the literature for gray matter only [3, 4]. To obtain reliable StO2 estimates in white matter, this study evaluates a solution to account for the bias on StO2 estimates induced by myelin, a paramagnetic substance, using a numerical simulation approach.

Materials and Methods
Numerical simulations were conducted for B0=4.7T using Matlab and the following parameters: the gyromagnetic ratio for proton: γ; hematocrit: Hct=0.4; Blood Volume fraction: BVf=3%; StO2=60%; difference in magnetic susceptibilities between fully oxygenated and fully deoxygenated hemoglobin: Δχ0=0.264ppm; difference in magnetic susceptibilities between tissue and myelin: Δχmyelin=-0.02693sin2(θ)-0.013 ppm, assuming a tensor susceptibility [5], and where θ is the angle between B0 and the myelin fibers. In the simulated matrix, vessels were considered as filled cylinders (diameter: 5μm) and myelin fibers were considered as hollow cylinders (diameter/wall thickness: 7/0.7 or 2/0.2μm).

To evaluate the impact of the Myelin Volume fraction (MVf), the porosity, the extravascular space between the myelin fibers, took 6 different values between 0.35 and 0.85. The angle between B0 and myelin fibers θ took 6 different values between 0 and π/2. A total of 36 conditions were thus simulated. Simulations were conducted as described in [6]. Briefly, the magnetic field was computed, water diffusion was accounted for, T2 and T1* were derived from the spin-echoes and the free induction decay (FID) obtained from the simulated matrix, respectively. To account for the presence of myelin, T2* was obtained by fitting to the FID the following new equation:

\[ s(t) = Cst e^{-\beta t} - BVf \gamma^3/3 \pi^2 \Delta \chi_{Hct} + (1-StO2)B0 \beta t + (K* MVf \gamma^4/3 \pi^2 \Delta \chi_{myelin} + B0 \beta t) \]

Eq. [1]

where K is a parameter that accounts for the porosity and θ. K was optimized (non-linear fit) to obtain a simulated StO2 as close as possible to the theoretical StO2, computed as described in [2, 6]. Two approaches were evaluated: a fixed K value for all conditions and a variable K.

Results
In absence of myelin, the StO2 estimates obtained with the simulation were within 1% of the theoretical value. The presence of myelin had small impact on T2 estimates (less than 10%). However, myelin had a strong impact on StO2 estimates (errors beyond 400%). Using a constant coefficient K in Eq. [1] (optimal K was found to be K=0.31) had a limited impact (errors up to 200% of the theoretical values). Using a variable K coefficient yielded better results. For θ below π/4, the error between the simulated and the theoretical StO2 was less than 10%. This error increased to 50% for θ=π/3 and 100% for θ=π/2. The coefficient K increased with increasing angle and porosity (Fig. 2).

Discussion / Conclusion
This study shows that myelin has a strong impact on the determination of StO2 using the BOLD effect. A practical model is proposed to account for the susceptibility of myelin in the determined of StO2 using multiparametric qBOLD. This model requires two additional estimates: the myelin volume fraction, which may be estimated using magnetization transfer sequences and the myelin fiber orientations, which may be obtained with diffusion tensor sequences. This model appears valid when the angle between the fibers and the magnetic field is below π/4.

References

Figure 1. Example the simulated geometry and of the correspond magnetic field. (a) Distribution of capillaries (filled red disks) and myelin fibers (large and small red circles) for a porosity of 25%. (b) Distortions of the magnetic field with a porosity of 45% and θ =π/2.

Figure 2. (a) Dependence of the coefficient K on the myelin volume fraction (MVf) and the angle θ between the fibers and B0. (b) Simulated StO2 for 6 porosities and 6 fiber angles. The coefficient K is the one that gives the closest simulated StO2 to the theoretical StO2.

The coefficient K increased with increasing angle and porosity (Fig. 2).