Error analysis of qBOLD technique for measurement brain hemodynamics

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Introduction: qBOLD (quantitative Blood Oxygenation Level Depend) technique introduced in [1] and validated in [2] provides an MRI-based method to measure tissue hemodynamic parameters such as oxygen extraction fraction (OEF) and deoxyhemoglobin-containing (veins and pre-vinous part of capillaries) cerebral blood volume fraction (dCBV). It is based on a theory of MR signal dephasing in the presence of blood vessel network [3] and experimental method – Gradient Echo Sampling of Spin Echo (GESSE) previously proposed and validated on phantoms [4]. Herein, using Bayesian approach we present a comprehensive analysis of uncertainties in OEF and dCBV estimates thus allowing optimization of qBOLD technique for dCBV and OEF evaluation. We also test this analysis on phantom studies.

Methods: A phantom consisting of 0.5-mm diameter polyethylene filament strands (fish lines), threaded in parallel along a 75 mm length to form a matrix of 17 ×17 filaments is used in this study. The average volume fraction (ζ) occupied by the filaments is about 5~6%. The filament matrix was placed horizontally and immersed in a spherical container (fish ball) filled with a solution of $NiSO_4$ and NaCl in water. 2D GESSE images (128×128 matrix with resolution of 2×2×15mm^3 and gradient echo (GE) spacing δt of 2 ms) were acquired on a Siemens 1.5T whole body scanner Sonata with a 4-channel receive-only head coil. Resultant SNR was about 100. High resolution field map is also acquired and used to account for signal decay due to macroscopic field inhomogeneities $F(t)$. Data were fitted by an equation describing a time course of signal evolution in GESSE experiment $S(t) = S_0 \cdot F(t) \cdot \exp\left(-R2 \cdot t - \zeta \cdot f_c\left(t / t_c\right)\right)$ [4], where f_c is a function defining contribution of filament network to the water MR signal decay (Eq. A11 in [3]), $R2=1/T2$ of water, ζ is a volume fraction of filaments (analog of dCBV), $t_c^{-1} = 2\pi\gamma\chi B_0$, and χ is the susceptibility difference between filaments and solution (analog of OEF). χ, ζ and $R2$ are estimated as fitting parameters.

Bayesian approach similar to developed in [5], is used here to analyze the uncertainties $\Delta\chi$, $\Delta\zeta$ and $\Delta R2$ in parameter estimates.

Results and Discussion: The results of Bayesian analysis can be presented as follows:

$\Delta\chi = \frac{1}{SNR} \cdot \sqrt{\delta t / t_c} \cdot \frac{1}{\zeta} \cdot F_\chi\left(T/t_c, T0/t_c, T2/t_c\right)$, $\Delta\zeta = \frac{1}{SNR} \cdot \sqrt{\delta t / t_c} \cdot F_\zeta\left(T/t_c, T0/t_c, T2/t_c\right)$, where δt is the GE spacing, T – time between SE and the last GE, T0 is the time of the first GE in the GESSE sequence. Functions F_ζ and F_χ are plotted in Fig. 1.

Fig. 2 shows resultant maps of parameters χ and ζ for the fish line phantom in experiments when the first GE was at the positions indicated in Fig. 1: (a) starting 2 ms after SE; (b) starting at SE; (c) fourteen GE before SE.

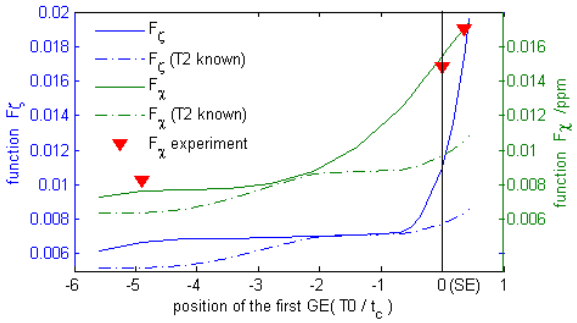

Fig 1. Functions F_ζ (green lines) and F_χ (blue lines). Solid lines represent results when T2 is fitting parameter. Dashed lines - when T2 is determined independently. Red triangles are measured F_χ from experiment.

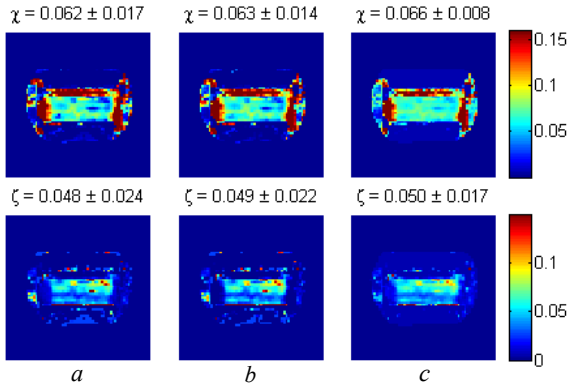

Fig 2. Maps of χ (upper row, in *ppm*) and ζ (lower row)

The maps show relatively same mean values of χ and ζ, but the standard deviations are decreasing significantly when signal is acquired earlier. The R2 value measured across the whole phantom is very homogeneous, with mean of 9.7 s^{-1} and STD 0.3 s^{-1}. The STD of χ maps are practically identical with theoretical calculations of the errors in parameter estimates based on Bayesian approach. The STD of the ζ maps on the other hand are substantially bigger than estimated fitting errors. These results should be expected because the filaments are not evenly distributed in space and their density varies. It is an intrinsic filaments density distribution that is mostly contributed to STD in ζ maps. On the other hand, χ is magnetic susceptibility difference between the filaments and water and it does not depend on filaments density. Our theoretical predictions also agree with previous phantom studies [3,6].

Conclusion: The developed herein analysis of uncertainties in OEF and dCBV estimates allows optimization of qBOLD technique for dCBV and OEF evaluation. It provides quantitative dependence of these uncertainties on SNR and main GESSE sequence parameters such as a position of initial gradient echo (T0) and a total sampling time (T). It shows that measurement accuracy can be substantially improved by starting sampling at $-2t_c$ before SE. However, it also shows that it is possible to measure dCBV and χ without using SE, though SNR in this case should be much higher.

References: **1.** He, X. and D.A. Yablonskiy, MRM 2007. 57: p115; **2.** He, X. Zhu, M. and D.A. Yablonskiy, MRM 2008. 60:p882; **3**. Yablonskiy, D.A. and E.M. Haacke, MRM 1994. 32: p749; **4.** Yablonskiy, D.A., MRM 1998. 39: p.417; **5.** Sukstanskii, A.L. et al, JMR 2006, 184:p62; **6.** Sedlacik, J. and Reichenbach, J.R, MRM 2010. 63: p910;