Improved separation of tissue oxygenation extraction fraction and deoxygenated blood volume by using the qBOLD technique.

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Introduction: He and Yablonskiy introduced a quantitative BOLD method (qBOLD) for estimation of the oxygenation extraction fraction (OEF) and the deoxygenated blood volume (DBV) in brain tissue [1]. In qBOLD, the signal course of a spin echo scan is compared to tissue model curves. The model incorporates assumptions about the blood capillaries, parenchyma, interstitial/cerebrospinal fluid, and static macroscopic field inhomogeneities; OEF and DBV are a subset of all these model variables, they are estimated by fitting the modeled to the measured signal decay, and the best match between MR signal and respective model functions is assumed to exhibit the true OEF and DBV. It has been observed that the input variables OEF and DBV barely affect the magnitude or real part of the modeled complex MR signal; also several combinations of OEF and DBV may match the original signal and therefore introduce ambiguity (Fig. 1, left) [2]. The imaginary part of the signal is, however, decoupled from the signal of the model tissue matrix and could potentially better determine OEF and DBV parameters. Hence, in this work we focus on the imaginary part of the signal as compared to the real part and assess whether the root mean square error (RMSE), a quality measure of the fit to identify the best model parameters, delivers a clearer minimum with no ambiguity for OEF and DBV than the original qBOLD approach.

Methods: Signal time curves encompassing the time point of the spin echo were calculated for the tissue model according to the primary publication of qBOLD [1]. The following parameters were chosen: OEF=45%, DBV=2.5%, $R_{2,\,tissue}=0.1s^{-1}$, hematocrit=0.45, and $\Delta\chi_{do}$ =0.18ppm(cgs) which represents the difference in magnetic susceptibility between fully oxygenated and deoxygenated red blood cells [3]. All other model parameters, such as the fraction of the interstitial/cerebrospinal fluid and macroscopic static field inhomogeneities, as well as noise were set to zero in order to simplify the model. The signal time curves were calculated in steps of milliseconds starting 30ms before the actual spin echo and ending 70ms thereafter. RMSEs were determined between a reference curve which was calculated for an OEF/DBV pair of 45%/2.5% and other curves simulated with varying OEF and DBV parameters where OEF was varied between 0 and 100% and DBV between 0 and 5%.

Results: The real and imaginary part of the signal is shown in Fig.1 for a subset of different OEF and DBV parameters. The signal's real part shows similar curves with slightly higher or lower slopes whereas the imaginary part produces curves which differ significantly as a function of OEF and DBV when compared to the curves of the real part of the signal. Calculated RMSEs of the curves of all OEF and DBV combinations are shown with respect to the reference curve in Fig.2. The RMSEs of the real part of the signal show a wide range of OEF/DBV pairs that produce signal curves which well fit to the reference curve and produce low RMSEs. In contrast, the RMSEs of the imaginary part show a clear minimum which coincides with the correct parameter set of the reference curve.

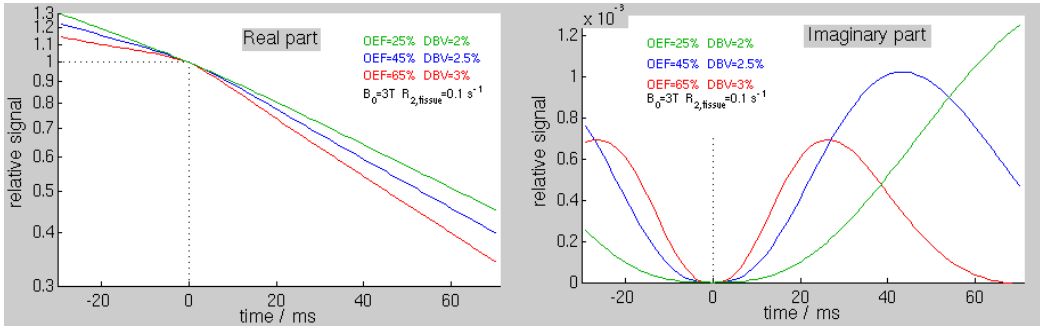

Figure 1: Signal curves obtained for different OEF and DBV parameters. Both signal curves are plotted relative to the total signal at the spin echo time point (t=0). Here the real part equals one and the imaginary part is zero. **Left:** Real part of the complex signal. A logarithmic scale was chosen for better visualization. **Right:** Imaginary part of the signal in a linear scale. Note the lower amplitude of the imaginary part compared to the real part.

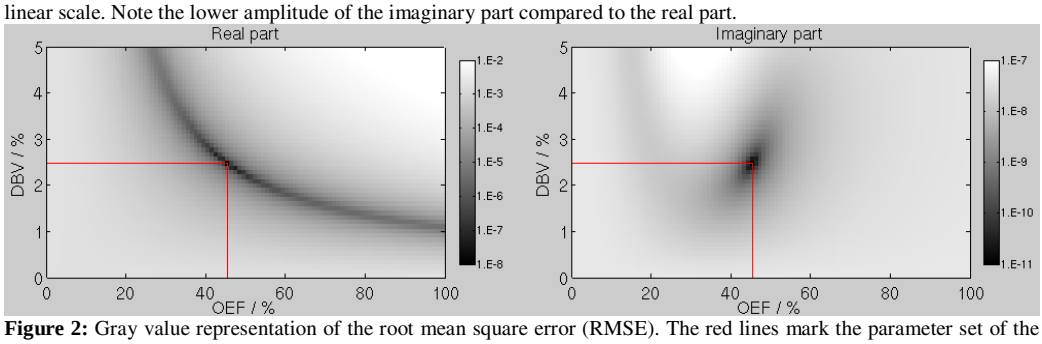

Figure 2: Gray value representation of the root mean square error (RMSE). The red lines mark the parameter set of the reference curve with OEF/DBV=45%/2.5% where the RMSE is zero. **Left:** RMSEs calculated from the real part of the signal curves. **Right:** RMSEs derived from the imaginary part of the signal curves.

Discussion/Conclusion: Our results suggests that a fitting routine which incorporates only the signal's real part could easily stop the optimization process if it hits an OEF/DBV pair which produces a low RMSE value but represents not the correct OEF/DBV combination. However, the imaginary part of the tissue model is more sensitive to independent changes of the OEF or DBV parameters which in turn better delineates the correct OEF/DBV pair in the RMSE plot as compared to the real part. Thus, we propose that a fitting routine which optimizes both the RMSEs of the signal curves' real and imaginary part estimates the model parameters OEF and DBV more reliably than one that fits the magnitude or real part only. However, the simplification of the model in our study limits its significance, since static field inhomogeneities and the frequency shift between the parenchyma and the interstitial/cerebrospinal fluid also introduce signal changes into the imaginary part and have to be corrected for or considered in the calculation. Further studies are needed to investigate the robustness of this approach in an *in vivo* setting.

Literature: [1] He X et al. MRM 57:115-26, 2007. **[2]** Sedlacik J et al. Proc. of ISMRM 3104, 2008. **[3]** Weisskoff RM et al. MRM 24:375-383, 1992.