Multi-Parametric qBOLD Approach for Robust Oxygen Extraction Fraction Quantification in Clinical Use

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Purpose

The quantitative blood oxygenation level-dependent (qBOLD) approach, based on the tissue model [1], has facilitated promising in-vivo results using Magnetic Resonance (MR). Thereby, the oxygen extraction fraction (OEF) is of great clinical interest providing a parameter for brain tissue viability [2] or monitoring radio and chemo therapy [3]. However, the qBOLD approach has not become clinically established yet due to numerous unknown fit-parameters in the tissue model requiring high signal-to-noise ratio (SNR) [4] or long measurement times clinically not available. In this work, a multi-parametric qBOLD (mp-qBOLD) approach is proposed to obtain robust OEF maps within clinical acquisition times by using separate MR sequences to reduce the number of fit-parameters. The mp-qBOLD method was validated in healthy volunteers and one tumor patient.

Methods

Theory: According to the tissue model, the long term regime ($|t\text{-}TE|>10$ms) of a gradient echo sampled spin echo (GESSE) signal is given by:

$$S(t\text{-}TE) = S_{SE} \cdot \exp(\lambda) \cdot \exp(-R_2 \cdot (t\text{-}TE) - R_2' \cdot |t\text{-}TE| + c \cdot (t\text{-}TE)^2) \qquad (1)$$

Here, TE describes the echo time and S_{SE} the signal of the spin echo at $t=TE$. R_2 and R_2' refers to the irreversible and the reversible transversal relaxation rate, respectively. The quadratic term in Eq. 1 accounts for the effects of macroscopic field inhomogeneities. The OEF is given by:

$$OEF = R_2'/\lambda \cdot 3/(4 \cdot \pi \cdot \gamma \cdot B_0 \cdot \Delta\chi_{do} \cdot Hct) \qquad (2)$$

Here, λ is the venous blood volume, γ the gyromagnetic ratio, B_0 the magnetic field strength, $\Delta\chi_{do}$ the susceptibility difference between fully oxygenated blood and tissue, and Hct the hematocrit level. In this study, $\Delta\chi_{do}$, was set to 0.27 ppm and Hct to 0.34. *Measurements:* Data from 5 healthy subjects and one postoperative tumor patient with a diagnosed glioblastoma was acquired at 3 Tesla. The protocol consisted of a GESSE, a Carr-Purcell-Meiboom-Gill (CPMG), a multi-slice multi-echo gradient echo (MMGE), and a high resolution T_1-weighted sequence. The slice position, the field of view (FOV=256x256mm^2), the matrix-size (128x128), and slice-thickness (Δz=6.0mm) was the same for the GESSE (TA=21,1min), the CPMG (TA=3,4min), and the MMGE sequence (TA=3,4min). To compare the temporal stability of both methods, the GESSE datasets of 66 averages were subdivided into four datasets of 65, 30, 15, and 5 averages prior to OEF estimation. *OEF Computation:* With qBOLD, R_2, R_2', and λ were estimated simultaneously from the GESSE data using Eq. 1. With mp-qBOLD, R_2' was determined prior to fitting the GESSE signal by estimating R_2 and R_2* using the CPMG/MMGE data applying a monoexponential model. Adjacently, $R_2'=R_2^*-R_2$ was used as input parameter for Eq. 1. The OEF was finally estimated using Eq. 2.

Results

Figure 1 shows a comparison of the OEF maps in a representative healthy volunteer and one tumor patient. Using qBOLD, the volunteer (i.e. sub. 4) exhibits multiple regions where OEF estimation apparently failed (Fig. 1b). In contrast, the OEF values were uniformly distributed when the mp-qBOLD technique was used (Fig. 1c). In the tumorous brain area of the patient (Fig. 1d), increased OEF values were found in the mp-qBOLD but not in the qBOLD dataset (Fig. 1e-f). Averaged over all subjects, the mean OEF was 41±5% (qBOLD) and 29±1% (mp-qBOLD) (Tab. 1). With the mp-qBOLD technique, the intersubject variability (i.e. std. between subjects / mean) was reduced from 12% to 3% and the intrasubject variability (i.e. the average relative error in all subjects) was reduced from 34±12% to 15±3%. For continuously reduced GESSE acquisition times, the mp-qBOLD OEF remained stable and the inter- and intrasubject variability remained clearly smaller at all acquisition times compared to the qBOLD OEF (Fig. 2a). Further, the OEF variability within each subject remained nearly constant while a continuous increase was observed in the qBOLD datasets (Fig. 2b).

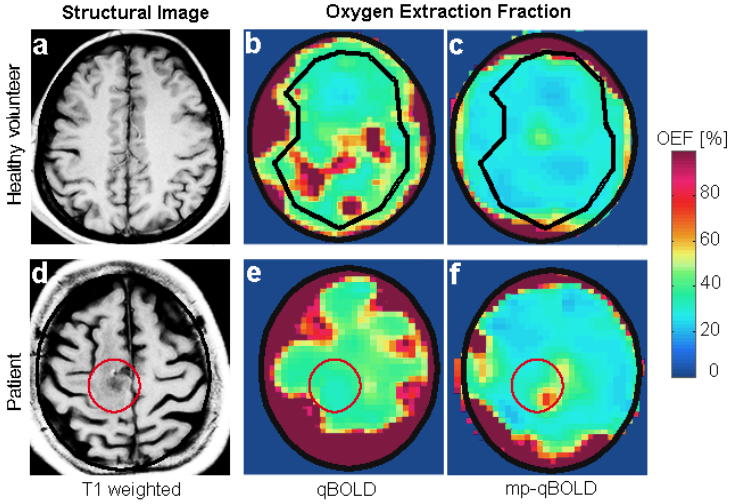

Figure 1. OEF maps in a representative volunteer and a postoperative tumor patient. *(**a**) High resolution T1-weighted image from a healthy volunteer (subject 4) and (**b**) corresponding OEF maps using the qBOLD and (**c**) the proposed mp-qBOLD method. (**d**) High resolution T1-weighted image from a postoperative tumor patient and (**e**) corresponding OEF maps using the qBOLD and (**f**) the mp-qBOLD method. OEF values from both methods were measured in the black ROI (polygon). For the patient, the tumorous brain area is marked by the red ROI (circle). The GESSE data was acquired in 4.8 min.*

	qBOLD method OEF [%]			mp-qBOLD method OEF [%]		
Subject	**Mean**	**Std.**	**Rel. Error**	**Mean**	**Std.**	**Rel. Error**
1	35	6	17	29	4	14
2	42	17	40	30	5	17
3	39	11	28	30	5	17
4	47	22	47	28	4	14
5	41	15	37	27	3	11
Mean ± Std.	**41 ± 5**	**15 ± 7**	**34 ± 12**	**29 ± 1**	**4 ± 1**	**15 ± 3**

Table 1. OEF results using the qBOLD and the proposed mp-qBOLD method. *The relative error was computed as the respective standard deviation (Std.) divided by the mean OEF. The GESSE data was acquired in 4.8 min.*

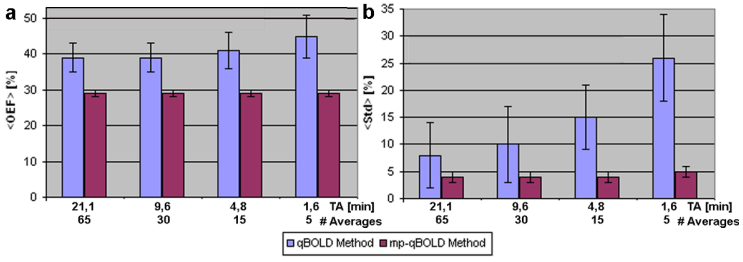

Figure 2. OEF in dependence of the GESSE measurement time. *(**a**) Mean OEF in five healthy subjects. (**b**) OEF standard deviation inside ROI averaged over all subjects. Note that the mp-qBOLD method used an extra measurement time of 6.8 min to acquire CPMG and MMGE data for R_2'-estimation.*

Discussion and Conclusion

In healthy subjects, the mean OEF values of both qBOLD methods were in the range of OEF values reported in the literature [5-6]. A uniform distribution of OEF values, well known from ^{15}O-PET studies [7-9], was only observed in the mp-qBOLD datasets and has also been found in previous MR studies [5, 10]. In the patient, the increased OEF values in the tumorous brain area are highly plausible since glioblastoma are highly aggressive and consume more oxygen compared to healthy tissue. In healthy subjects, we found that the intra- and the intersubject variability were clearly reduced using mp-qBOLD. Moreover, the OEF estimates remained stable when the data acquisition time was reduced to be clinically feasible. In conclusion, the proposed mp-qBOLD technique allows robust OEF mapping within clinical acquisition times. Hence, the proposed technique could be used to assess tumor aggressiveness or to monitor the success of radio and chemo therapy.

References

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