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Searching for an MR Fingerprinting sequence to measure brain oxygenation without contrast agent

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Synopsis

We propose to use numerical simulations and Monte Carlo approaches to test 40 MR fingerprinting sequences for their ability to quantify the BOLD effect and provide maps of baseline blood oxygen saturation without the need for contrast agent injection. Our results suggest that several sequences can produce SO₂ maps with less than 3% error on average even in the presence of B₁ and B₀ inhomogeneities. T₂ and blood vessel radius could also be estimated with the same acquisitions.

Introduction

The Magnetic Resonance Fingerprinting¹ (MRF) framework has opened the possibility to use unconventional MR sequences (such as random succession of FA and TR) for tissue relaxometry. This type of approach should also be suited to quantify the BOLD effect as it has been shown that balanced SSFP sequences and their transient-states are highly sensitive to magnetic fields inhomogeneities². Following our previous work on vascular MRF³, we propose to use these types of sequences to obtain blood oxygenation saturation maps without the need for contrast agent injection. We used numerical simulations and a Monte Carlo method⁴ to assess the efficiency of numerous MRF sequences based on 3 types of acquisitions (1) bSSFP with acquisition of transient-state (2) bSSFP with oscillations of RF phases (OSSIS⁵), in order to shift frequency offset patterns, and (3) succession of random TR and FA. Our numerical results suggest that several MRF sequences can produce SO₂ maps with less than 3% error on average. T₂ and blood vessel radius could also be estimated with the same acquisitions.

Materials and methods

All simulations were performed on Matlab (The MathWorks Inc., Natick, Ma, USA) with the MRVOX software⁶. Blood vessels were modelled in 2D with uniform oxygenation. Variations of Blood Volume fraction (BVF [1,10]%), mean vessel radius (R [2,10]µm), blood oxygen saturation (SO₂ [35,90]%) and T₂ ([40,110]ms) were considered to create the MRF dictionaries. For 2 particular sequences (see below), variations of B₁ ([0.7,1.3]) and B₀ offset frequencies ([0,75]Hz) were added.

3 types of sequences were tested (150 pulses each):

- Type 1 (transient-state/bSSFP): constant FA, TR, TE=TR/2, no phase cycling, Fig. 1a 1d.
- Type 2 (transient-state/bSSFP/phase OSSIS): constant FA, TR, TE=TR/2, no phase cycling for 40 pulses, followed by 110 pulses with a phase cycling⁵ to establish an oscillating steady-state, Fig. 1b 1e.
- Type 3 (transient-state/random pattern): Random FA, random TR, TE=TR/2, no phase cycling, Fig. 1c, 1f.

For the three sequence types, about 15 trials were made with different combinations of TR and FA (see Fig. 2). Sequence evaluation was performed in two steps with a Monte-Carlo method⁴ (thermal noise with a normal distribution ($\mu=0$, $\sigma=\text{Signal}/\text{SNR}$, with $\text{SNR} = 20$), parameter and error evaluations performed 2000 times on 50 entries equally distributed in the parameter space) to obtain mean error values on the estimation of each parameter of interest.

Results

Fig. 1 shows examples of sequence diagrams as well as signal evolutions for the 3 types of sequences tested. One can notice the different signal responses to different SO₂ baseline values (blue to red colors), highlighting the importance of the transient-state in terms of SNR and sensitivity. Amongst all the MR sequences tested (Fig. 2), several combinations of parameters seemed to provide acceptable (<10% average) errors on SO₂ estimates, and 2 particular candidates (Type2:Seq4 and Type3:Seq1) were chosen (based on overall error and signal evolutions) for further evaluation. Sequence diagrams and signal responses to SO₂ variations are shown in Fig. 3 for Type2:Seq4. The initial pattern was repeated 4 times in order to reduce the influence of low SNR in the steady-state part of the signal, leading to an acquisition time of 9s per slice. 3D plots of signal standard deviations under variation of SO₂, for different values of BVF and R, are also shown to highlight the cross-talk between the dimensions of the dictionary. Finally, it can be seen that the MC approach predicts low errors for SO₂ and T₂ estimates as well as acceptable estimates of blood vessel radius for this particular pattern. Similar results were obtained for the random pattern Type3:Seq1 (not shown). New simulations were performed in order to test the sensitivity of the 2 sequences to B₁ and B₀ offset artefacts. Results are presented in Fig. 4, where it can be seen that Type2:Seq4 still performs well under such conditions with only a small increase in SO₂ error due to B₀ offset. Signal variations (Fig. 4 d-e) are also shown to highlight the changes of patterns due to the 2 new dimensions. Results obtained with Type3:Seq1 were more impacted by B₁ artefacts with 10% average error on SO₂ estimates and concomitant increase in standard deviation.

Conclusion

According to numerical simulations, several MRF sequences should be able to provide accurate measurements of baseline blood oxygenation saturation without the need for contrast agent injection and in a clinically acceptable scan time. While it is not easy to automatically optimize vascular MRF sequences due to the computational load of the numerical simulations (magnetic susceptibility effects + water diffusion + relaxation in a fine microvascular geometry), new optimization approaches could further improve the sequence's efficiencies⁷. In vivo data are now required to eventually validate our findings.

Acknowledgements

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Figures

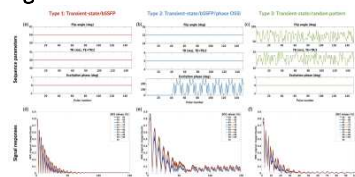


Figure 1: Example of pulse parameters for (a) one sequence of Type 1 Transient-state/bSSFP: FA = 60°, TR = 40ms (b) one sequence of Type 2 Transient-state/bSSFP/phase OSSIS: FA = 25°, TR = 5ms and phase cycling starting at the 41st pulse, (c) one sequence of Type 3 Transient-state/random pattern: 45° < FA < 90°, 11ms < TR < 15ms. (d),(e),(f) Respective signal responses for different values of SO₂.

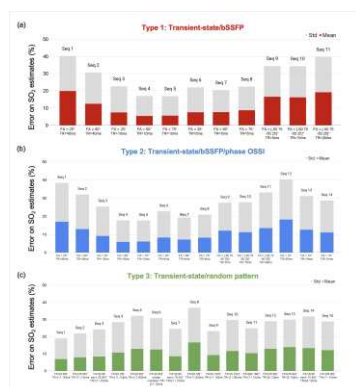


Figure 2: Monte-Carlo SO₂ error estimation (Mean and Standard deviation) for different (a) Transient-state/bSSFP sequences, (b) Transient-state/bSSFP/phase OSSI sequences, (c) Transient-state/random pattern sequences.

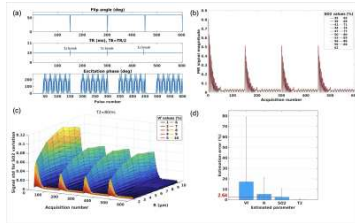


Figure 3: Detailed results obtained with the Type2:Seq4 sequence. (a) Sequence parameters. (b) MR signal responses for different SO₂ values. (c) 3D plots of signal standard deviations under variation of SO₂, for different values of cerebral blood volume (CBV) and vessel radius (R). (d) MC error estimation (mean and std) for different parameters of the model.

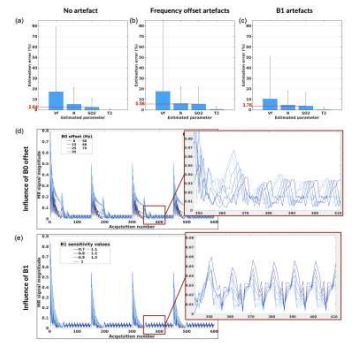


Figure 4: MC error estimation (Mean and Standard deviation) for different parameters of the model for the Type2:Seq4 sequence. (a) without artefact, (b) with B₀ frequency offset artefacts, (c) with B₁ artefacts. (d) Signal responses for one value of SO₂ and multiple B₀ offsets. Zoom on the steady-state part of the signal. (e) Signal responses for one value of SO₂ and multiple B₁ values. Zoom on the steady-state part of the signal.