Improving the reproducibility of labeling-efficiency measurements *in vivo* in pseudo-continuous arterial spin labeling

Kathrin Lorenz[1,2], Toralf Mildner[1], Torsten Schlumm[1], & Harald E. Möller[1,2]

[1]*Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany*
[2]*Faculty of Physics and Earth Sciences, University of Leipzig, Germany*

klorenz@cbs.mpg.de

Introduction

pCASL has become the recommended choice for non-invasive measurements of human cerebral blood flow (CBF) [1]. Nonetheless, CBF quantification is a challenge because the perfusion models depend on physiological and experimental parameters. Among these parameters is the labeling efficiency, α, which is defined as the degree of arterial spin inversion achieved by pCASL at the labeling site. CBF estimates depend on it linearly. Due to the lack of a robust and fast experimental procedure to directly measure α inside the brain-feeding arteries, it is typically estimated by simulations [2-4]. This work introduces a method for α measurements inside the large arteries. To address the impairing influences of field inhomogeneity and pulsatile flow, we investigated the stability of EPI time series obtained from voxels inside the internal carotid arteries (ICAs) depending on TE, the position of the imaging slice, and the sampling interval (TR).

Methods

- Single-slice gradient-echo EPI readout with a nominal resolution of 2x2x5 mm³ acquired between the base of cerebellum and the horizontal segment of the petrous part of the ICA.
- Labeling position 15 mm below the base of cerebellum; cf. Ref. [1].
- Partial Fourier 6/8 & GRAPPA with acceleration factor 3.
- Shimming parameters copied from a preceding whole-brain EPI volume to mimic a typical perfusion measurement.
- Balanced pCASL sequence with Hanning-shaped RF pulses (duration 0.5 ms, nominal flip angle $FA_{pCASL} = 22°$, inter-pulse interval 1.4 ms), average labeling gradient $G_{ave} = 0.6$ mT/m.
- Acquisition of raw data time series in a three-fold interleaved fashion, i.e. at equilibrium (S_0), control (S_C) and labeling (S_L) conditions, cf. Fig. 1 (top).
- Determination of a series of labeling-efficiency values α_i, cf. Fig. 1 (bottom), from the complex signals of S_0, S_C and S_L by:

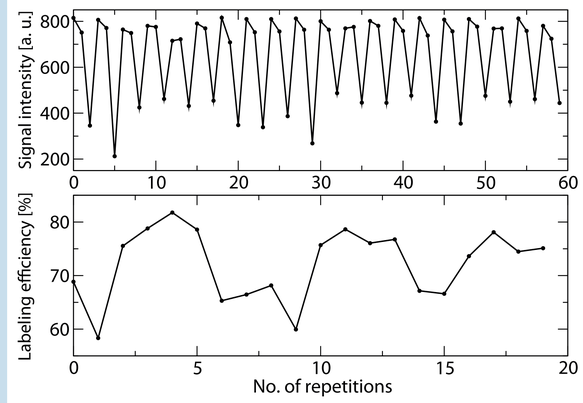
$$\alpha_i = \frac{\mathrm{abs}(S_{C,i} - S_{L,i})}{2 * \mathrm{abs}(S_{0,i})} \qquad (1)$$

- Significant voxels of a particular vessel identified in a three-step selection process by:
  - i) their average absolute signal difference S_C-S_L: select 4 voxels with the highest values (specific to a 2x2 mm² voxel size and an ICA diameter of 4 mm).
  - ii) their expected contamination by partial volume effects: exclude voxels possessing less than 70% of the maximum S_C-S_L.
  - iii) their time course stability: further exclude voxels violating the empirical quality criterion

$$\mathrm{E}(\alpha) - \frac{\mathrm{E}(\mathrm{abs}(S_C - S_L))}{2 * \mathrm{E}(\mathrm{abs}(S_0))} \leq 0.15 * \mathrm{SD}(\alpha) \quad (2)$$

- Averaging of finally remaining voxels.

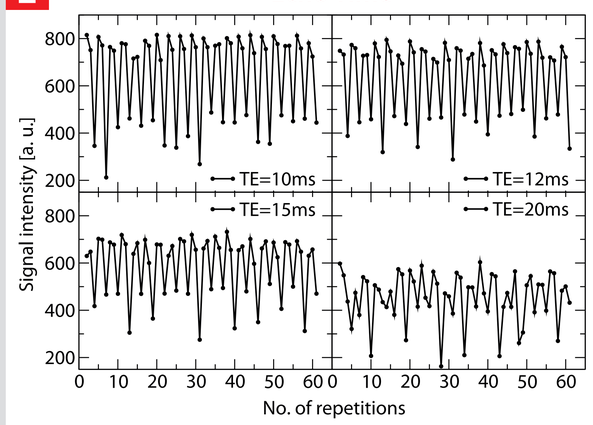
1



Top: Raw time series consisting of the equilibrium (S_0), the control (S_C), and the labeling (S_L) signals.
Bottom: Corresponding time series of α calculated from consecutive triplets of S_0, S_C and S_L by means of Eq. (1).

Results & Discussion

2 *Echo Time*



Raw time series obtained in a single subject from consecutive scans with variable TE as indicated.

Echo Time:

- Increasing TE reduces the mean signal level and augments the irregularities found in the signal courses (Fig. 2).
- Deterioration at longer TE due to effects like outflow of excited spins in slightly tilted or branching arteries and the increased dephasing due to the flow through existing field gradients.
- All further experiments conducted with minimum TE of 10 ms.

Imaging Position:

- Improved robustness of the α measurement found for an imaging position at the base of the cerebellum.
- At more superior positions, a high-resolution 3D field map indicates a strong magnetic field variation; example (inset of Fig. 3): up to 50 Hz at a z-position about 5 mm below the petrous part of the ICA, where the left ICA penetrates the image plane (white arrow).

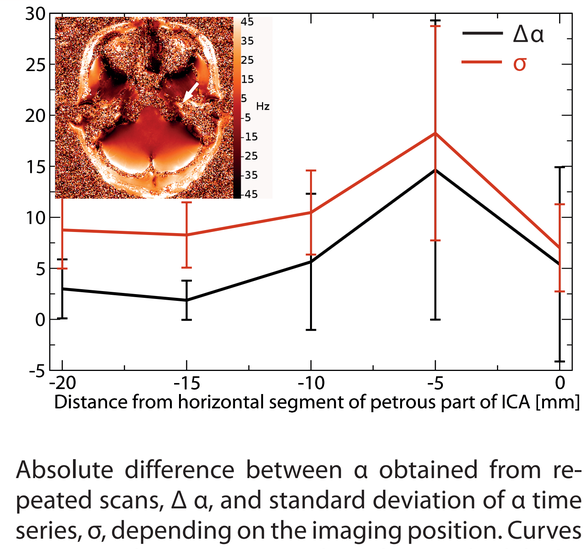
Sampling Rate:

- Comparison of α measurements at TR values of 1000 and 150 ms with corresponding labeling durations of 962 and 112 ms, and 60 and 150 repetitions, respectively.
- Enhanced intra (Table 1) and inter-subject (Fig. 4) reliability of α estimates found for the higher sampling rate due to better suppressed extra-arterial background signal (reduced partial volume effects) and reduced influence of the cardiac cycle (6-fold rise of sampled points).
- Bias towards higher α values of the order of 3% found for the high sampling rate and explained by oppositely phased slow travelling blood.
- Additionally, considerably reduced scan time (from 1 min to 23 s) for high sampling rate.

Comparison to Bloch Simulation:

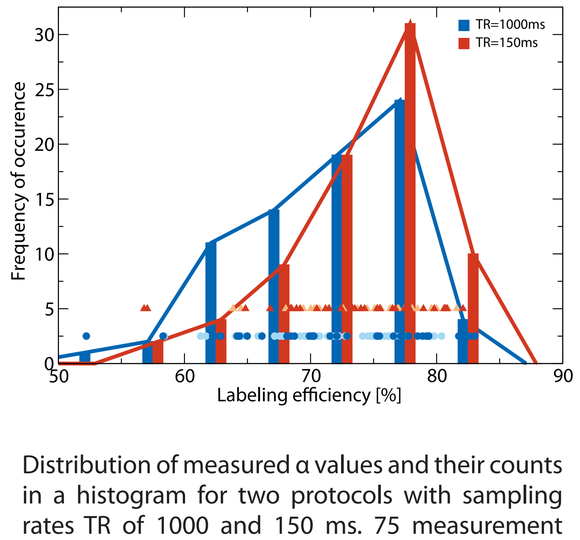
- Variation of the parameters of the pCASL labeling train: G_{ave} between 0.1 and 1.5 mT/m, and FA_{pCASL} between 10° and 30°.
- Bloch simulation by recursive application of kinetic Bloch matrix (time step = 0.5 µs) and averaging over an assumed laminar velocity distribution from 5 to 50 cm/s.
- Excellent agreement between experiment and simulation (Fig. 5) indicates the feasibility of α measurements by a short and robust prescan.
- Measured α values in agreement with Ref. [4].

3 *Imaging Position*



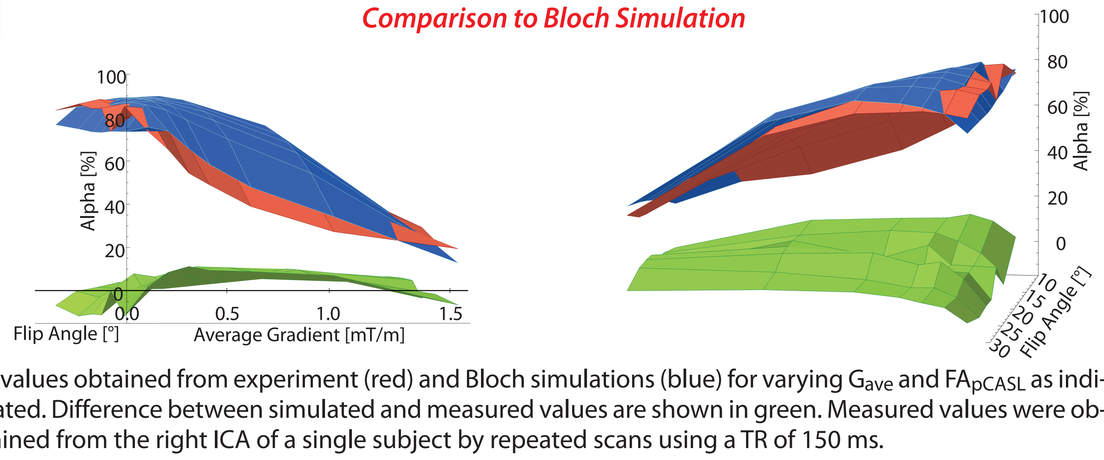
Absolute difference between α obtained from repeated scans, Δ α, and standard deviation of α time series, σ, depending on the imaging position. Curves represent the average, error bars the standard deviation over experiments from six subjects.

4 *Sampling Rate*



Distribution of measured α values and their counts in a histogram for two protocols with sampling rates TR of 1000 and 150 ms. 75 measurement points acquired in 12 subjects were included per TR value.

5 *Comparison to Bloch Simulation*



α values obtained from experiment (red) and Bloch simulations (blue) for varying G_{ave} and FA_{pCASL} as indicated. Difference between simulated and measured values are shown in green. Measured values were obtained from the right ICA of a single subject by repeated scans using a TR of 150 ms.

Table 1

α [%] ± SD	Subject 1		Subject 2	
	Left ICA	Right ICA	Left ICA	Right ICA
TE/TR/τ = 10/150/112 ms	75.0 ± 1.9	71.8 ± 3.4	80.2 ± 0.9	76.7 ± 1.5
TE/TR/τ = 10/1000/962 ms	74.7 ± 1.4	67.1 ± 3.7	72.8 ± 3.6	79.7 ± 2.3

α values (mean±SD) determined from 10 repeated measurements (voxel size of 2x2x5 mm³) with two TRs.

Conclusion

Estimating the labeling efficiency in pseudo-continuous ASL experiments by a short and robust prescan is feasible if some requirements are met. Firstly, TE should be as short as possible to ensure stable signal courses. Secondly, the robustness of the α measurement can be improved considerably by optimizing the position of the imaging slice. Best results were obtained if the position to measure the labeling efficiency was set at the base of the cerebellum and the labeling position 15 mm below. Thirdly, a high sampling rate emerged to enhance both the intra and inter-subject reliability of α estimates due to a better suppression of the extra-arterial background signal and a reduced influence of the cardiac cycle. This was confirmed by the excellent agreement between experiments using this protocol and Bloch simulations for varying FA_{pCASL} and G_{ave}.

References

[1] D.Alsop et al.; *Magn Reson Med* 2015; 73: 102-116.
[2] WC. Wu et al.; *Magn Reson Med* 2007; 58: 1020-1027.
[3] W. Dai et al.; *Magn Reson Med* 2008; 60: 1488-1497.
[4] H. Jahanian et al.; *NMR Biomed* 2011; 24: 1202-1209.

Acknowledgement

This work was funded by the International Max Planck Research School (IMPRS) "NeuroCom".