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

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Purpose. Pseudo-continuous arterial spin labeling (pCASL) has become the recommended choice for non-invasive perfusion measurements in the human brain [1]. Nonetheless, perfusion quantification is a challenging enterprise because it depends on physiological conditions, such as transport of the label to the imaging slice, and on experimental parameters, such as the labeling efficiency, α. Here, we investigated how results from *in-vivo* measurements of α depend on slice position and sampling rate (TR) to address the impairing influences of field inhomogeneity and pulsatile flow. Another goal was to improve the reproducibility of α measurements towards a procedure for measuring α robustly in one additional pre-scan.

Methods. The experiments were performed on a 3T scanner (TIM Trio, Siemens) using the built-in body coil for transmission and a 32 channel head coil for reception. For labeling, a balanced pCASL module was used, which consisted of a train of Hanning-shaped RF pulses (duration 500 µs, flip angle 22°, inter-pulse interval 1.4 ms), each applied with a labeling gradient of 9 mT/m. The average labeling RF magnetic field and the labeling gradient over the entire pCASL pulse train were 2.1 µT and 0.6 mT/m, respectively. The labeling efficiency α was measured by a series of single-slice EPI images (TE 10 ms; PAT factor 3; partial Fourier factor 6/8) with sequential acquisition of 3 signals: at equilibrium (S_0), during control (S_C), and during labeling condition (S_L). Preparation pulses for fat saturation were applied prior to the image acquisition. The labeling duration τ was set to its maximum value at a given TR, that is, the difference of TR and the 38ms-long readout duration. To investigate pulsatile flow effects on the α measurement, different TR values (1000 and 150 ms) were used. The labeling position was set consistently 15 mm below the base of cerebellum, and the slice for the α measurement was shifted over a distance of 20 mm between the base of cerebellum and the horizontal segment of the petrous part of the internal carotid artery (ICA). To mimic the conditions of a typical perfusion measurement, shimming at the imaging slice was omitted. Instead, the shimming parameters were copied from a preceding whole-brain EPI volume. In order to spatially resolve the signal in the ICA (diameter 4-5 mm [2]), a voxel size of 2×2×5 mm^3 was chosen. The reproducibility of the α measurement was explored by repeating an experiment 2-10 times for the auxiliary conditions slice position and TR. Voxel-wise evaluation was performed by converting the complex ASL time series into a series of α values according to $\alpha_i = \mathrm{ABS}((S_{C,i} - S_{L,i})/2S_{0,i})$, and by calculating its mean and standard deviation. The α value in a particular vessel was obtained as the average of the two most significant voxels identified by the maximum absolute signal difference $S_C - S_L$ in the averaged single-voxel time series.

Results & Discussion. The reproducibility of α measurements was found to significantly depend on the slice position (Fig. 1). Optimum values were obtained with a slice position directly at the base of the cerebellum and the labeling plane 15 mm below. The reproducibility was reduced for slice positions approaching the petrous part of the ICA, i.e. the transition between extra and intracranial regions. This is due to the passage of the excited blood magnetization through strong field gradients (~ 50 Hz difference, Fig. 1) with concomitantly rapid T_2^* decay, an effect which also amplifies the susceptibility to pulsatile flow. Although the conditions improved again for superior locations (horizontal segment of petrous part), decreased α values were found there due to contributions possessing different transit times. We therefore recommend the base of the cerebellum for measuring α. At this position, the ICA is also relatively straight and parallel along the *z*-axis.

Pulsatile flow has a major effect on both the achieved labeling and its downstream measurement. To study this influence, protocols with different sampling rates were used. In the first protocol, 60 repetitions (20 for each condition) were acquired with TR = 1000 ms and τ = 962 ms in a total scan time of 1 min. For the second (fast) protocol, 150 repetitions (50 each) were recorded with TR = 150 ms and τ = 112 ms in 23 sec. Figure 2 shows the series of all 50 α values obtained with this protocol. Surprisingly, the fast protocol yielded better reproducibility of α in repeated scans in the same volunteer (Fig. 3). However, a comparison of the results from multiple measurements indicated excellent agreement of both protocols in the estimated mean α (Tab. 1). The standard deviation was smaller in three out of four cases for the fast protocol. Due to the need of acquiring the signal under three conditions, the effective sampling interval of the α time series is 3 TR. Thus, each condition is acquired at a different phase of the cardiac cycle. For the long TR, this effect might lead to additional variance if single measurements of α are repeated. For the short TR, temporal delays between the three conditions are reduced, and can even be partly corrected by interpolating the complex time series from each condition on a common grid. Therefore, the corresponding protocol provides more consistent values in single runs, which is a prerequisite for a use as a routine protocol. Additionally, partial volume effects are reduced because the background is more effectively suppressed at short TR. A drawback could be the short labeling duration of only 112 ms, which goes along with a lower possible distance between the labeling plane and the slice position. For the proposed distance of 15 mm, blood traveling faster than 14 cm/s contributes. This is supposed to yield a valid estimate of α for the mixture of blood arriving in the brain at the position of the perfusion maps. In summary, the robustness of labeling-efficiency measurements can be improved considerably by optimizing both the slice position of the α measurement as well as the sampling rate.

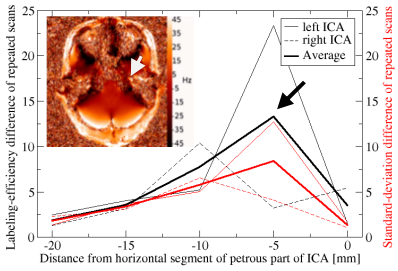

Fig. 1: Absolute difference between the mean α (black lines) in repeated scans depending on the slice position (average over six volunteers). Red lines illustrate analogous curves for the standard deviation of α. The region of increased field inhomogeneity, ~5 mm below the petrous part of the ICA, is marked by a white arrow in the B_0 map (inset).

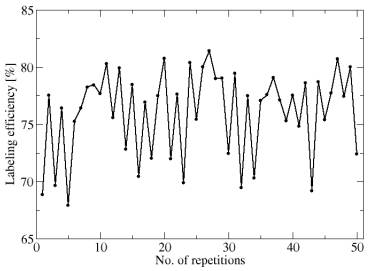

Fig. 2: Exemplary α time series (mean 76.1%; SD 3.7%) obtained in the right ICA with TR = 150 ms and τ = 112 ms. Complex signals acquired during S_0 and S_L conditions were interpolated on the grid of the S_C condition in order to reduce the influence from the cardiac cycle.

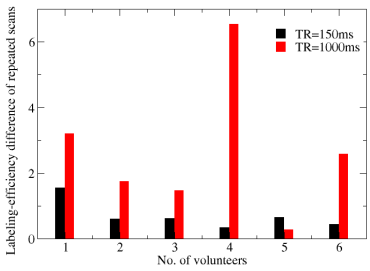

Fig. 3: Absolute difference of α measured in repeated scans for six healthy volunteers, and averaged over hemispheres. The data were acquired at the base of the cerebellum 15 mm above the labeling plane using two protocols (TR 150/1000 ms; cf. text).

Labeling efficiency [%] ± SD	Volunteer 1		Volunteer 2	
	Left ICA	Right ICA	Left ICA	Right ICA
TR/τ = 150/112 ms	74.8 ± 3.5	69.3 ± 2.9	81.3 ± 3.3	76.4 ± 1.6
TR/τ = 1000/962 ms	74.6 ± 1.8	67.2 ± 3.5	79.7 ± 4.7	78.8 ± 4.8

Tab. 1: α values (mean ± SD) determined from 10 repeated measurements in two volunteers using two protocols.

References. [1] D. Alsop et al. Magn Reson Med 2014; DOI 10.1002/mrm.25197. [2] R. Albayrak et al. J Clin Ultrasound 2007; 35: 27–33.

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