

## Model-independent arterial transit time mapping using pseudo-continuous ASL

Toralf Mildner<sup>1</sup>, Kathrin Lorenz<sup>1,2</sup>, and Harald E. Möller<sup>1</sup>

<sup>1</sup>Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Saxony, Germany, <sup>2</sup>Faculty of Physics and Earth Sciences, University of Leipzig, Saxony, Germany

### Purpose

Previously, the Mapping of Arterial Transit time ( $\delta_a$ ) by Intravascular Signal SElection (MATISSE) was introduced (1) in order to obtain  $\delta_a$  directly from the temporal shift of an arterial spin labeling (ASL) time series without the application of a dedicated perfusion model. This was demonstrated both theoretically and experimentally in a dual-coil continuous ASL (CASL) approach. In particular, labeling was applied within short  $T_R$  intervals in an amplitude-modulated fashion. The current work shows that the basic principles of MATISSE can be transferred to pseudo-continuous ASL (2,3) by employing its strong  $B_0$  offset dependency for amplitude modulation (4). Similar to the common name convention to distinguish between CASL and pCASL, we refer to the novel MATISSE approach as 'pMATISSE'.

### Methods

All measurements were carried out on a 3T MRI scanner (TIM Trio, Siemens). For labeling, a balanced pCASL module was used which consisted of a train of Hanning-shaped RF pulses (duration 500  $\mu$ s, flip angle 22°, inter-pulse interval 1.4 ms) each played out in combination with a labeling gradient of 9 mT/m. The average values of the labeling magnetic field and the labeling gradient over the total pCASL labeling train were 2.1  $\mu$ T and 0.6 mT/m, respectively. In pMATISSE, the pCASL labeling train was applied during the first 383 ms of each  $T_R$  interval (500 ms), and four slices were acquired without further delay during the last 117 ms. In order to achieve a short readout duration per slice, a parallel acquisition technique (GRAPPA, PAT factor 3) was combined with 6/8 partial Fourier imaging. 12 slices ( $T_E$  7.2 ms; bandwidth 2368 Hz/Px; voxel size 3x3x4 mm<sup>3</sup>) were recorded in three single runs with the following slice subsets: 1+4+7+10, 2+5+8+11, and 3+6+9+12. Each run consisted of 210 repetitions during which the ASL labeling efficiency at the labeling plane (located at the base of cerebellum) was cyclically modulated in 21 steps; see below. The slice separation within each subset of 15 mm ensured that saturated blood from exciting the first slice was not affecting the next slice acquired only 29 ms later. Evaluation of the ASL time series was performed in the same way as in the original MATISSE (1).

### Results & Discussion

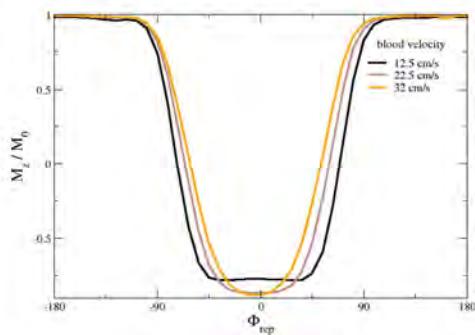


Fig 1.  $z$ -magnetization after passing the labeling plane ( $M_z$ ) relative to the equilibrium value ( $M_0$ ) obtained by Bloch simulations with pCASL parameters as described in Methods for varying  $\Phi_{rep}$  between  $-180^\circ$  and  $+180^\circ$ .

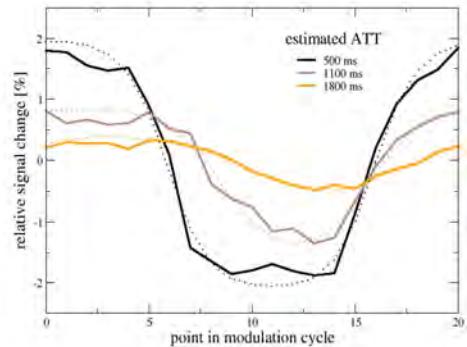


Fig 2. *In-vivo* pMATISSE time courses averaged over all modulation periods in three small ROI's differing in their mean  $\delta_a$ . Voxel-wise  $\delta_a$  values were estimated by fitting to an approximated Heaviside hat function (dotted lines).

principle with single-coil pseudo-continuous labeling, an advantage over the original MATISSE achieved in the current work is a more efficient image acquisition due to the implementation of GRAPPA. This may be straightforwardly expanded by employing simultaneous multi-slice (SMR) acquisition techniques in future work.

In the original MATISSE method, a smooth transition between zero and maximum ASL labeling efficiency  $\alpha$  was achieved by modulating the RF power applied to the neck labeling coil (1). In order to adopt this principle to the widely-used single-(transmit) coil pCASL, we have employed a modulation strategy that relies on the (mostly unwanted)  $B_0$  offset dependency of pCASL. By adding an additional repetition-dependent RF pulse phase term,  $\Phi_{rep}$ , to the nominal phase increment,  $\Phi_{nom} = (\Phi_{sys} + \Phi_{corr})$ , of pCASL, a smooth transition between zero and maximum  $\alpha$  is achieved.  $\Phi_{sys}$  and  $\Phi_{corr}$  are the systematic (due to the applied gradients) and the corrective (due to the  $B_0$  offset at the labeling plane) phase increments, respectively. Especially, if  $\Phi_{rep}$  is varied for successive repetitions between  $-180^\circ$  and  $+180^\circ$  this yields almost zero  $\alpha$  for  $\Phi_{rep} = \pm 180^\circ$  (corresponds to the control condition of pCASL) and maximum  $\alpha$  for  $\Phi_{rep} = 0$  (labeling condition) with a certain transition in between. Simulations based on the Bloch equations (Fig. 1) confirm that the requested smooth  $\alpha$  modulation is achieved in this way. The shape of the  $\alpha$  modulation created at the labeling plane (the so-called labeling function) does not only depend on the blood velocity in the labeled artery but also on the parameters employed in the pCASL labeling train. For example, the width of the labeling function can be adjusted by varying the average labeling gradient. This permits optimization of the labeling functions, e.g., for better time efficiency by the use of a narrower shape.

Figure 2 shows representative *in-vivo* pMATISSE time courses obtained in the human brain with RF phase modulation at the labeling plane. A corresponding map of the temporal shift of the time courses ( $\delta_a$  map; Fig. 3) shows reasonable patterns of human vascular territories including their border zones. The slight asymmetry observed in the time courses, with a shift of the signal minimum to later points in the modulation cycle with increasing mean transit times, can be attributed to an increasing spread in  $\delta_a$  (1, 5). This effect might be exploited for obtaining an estimate of the width of an underlying  $\delta_a$  distribution to characterize the dispersion of the labeling bolus.

Compared to RF power modulation, RF phase modulation inherently guarantees that the shape of the brain response is independent of magnetization-transfer effects, which is an essential feature in single-coil pMATISSE. An inconvenience is, however, the need to calibrate the labeling function with respect to zero  $\delta_a$ . This was performed in the current work by adjusting the corrective phase increment  $\Phi_{corr}$  based on a pCASL pre-scan with varying  $\Phi_{corr}$  for successive control/label pairs (4). pMATISSE data were then acquired with a  $\Phi_{corr}$  obtained from small ROI's in the left and right insula, and averaged. However, a more accurate calibration that includes a pMATISSE reference scan in the vicinity of the labeling plane, and corrective gradient blips parallel to the labeling plane (4) are desirable. Besides combining the MATISSE

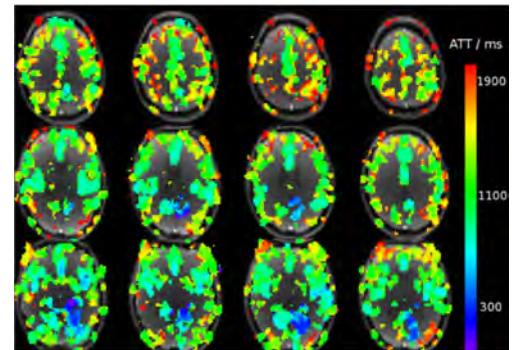


Fig 3.  $\delta_a$  map obtained with pMATISSE in a scan time of 5:15 min.

### References

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