High temporal resolution sampling of tracer kinetic curves using time encoded pCASL with Look-Locker readout.

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Targeted audience: Researchers interested in measuring tracer kinetics and new developments in ASL.

Purpose: The aim of this study is to develop a method for sampling the tracer kinetics curve with high temporal resolution using time encoded pseudo Continuous Arterial Spin Labeling [1] (te-pCASL, a.k.a. Hadamard encoded pCASL) in combination with Look-Locker (LL) imaging. High temporal resolution sampling provides a tool to validate tracer kinetics modeling in vivo. This technique also demonstrates hemodynamic changes when subjects are exposed to a visual stimulus.

Methods: Five healthy female volunteers (age 19-25 y) were scanned at 3T (Achieva, Philips Healthcare) with a 32-channel head coil. The te-pCASL was applied with a total labeling duration of 4400 ms, a 12 x 11 encoding matrix (12 different encodings of the labeling period, rendering 11 sub-boli with 400 ms duration each). Minimum post labeling delay (PLD) was 25 ms and background suppression as proposed by Dai et al [2] was implemented with 2 FOCI pulses at 2400 and 3900 ms. To improve SNR 8 repetitions of the hadamard sequence were used leading to a scan time of 9 minutes. Single shot GREPI was used for imaging (single slice, 3.5x3.5x10 mm) with a Look-Locker read-out consisting of 8 images with 50 ms spacing. To establish equal signal level in subsequent LL images a flip angle sweep was applied with respective flip angles of 23, 26, 29, 32, 39, 50, 60 and 90˚. Furthermore, the PLD was increased 50 ms with each repetition, effectively creating an offset of the time line and shifting the image acquisition one position within the LL sequence. When repetitions are corrected for timing offset and then averaged in post processing the signal for each time point is the average of 8 LL images each acquired at a different position within the LL sequence. Scans were acquired during rest and during visual stimulation (watching Tom & Jerry cartoons), both with and without vascular crushing (c = 5cm/s). Crushed data was used for evaluation of tissue signal. For arterial signal the subtraction of non-crushed minus crushed was thresholded (signal > 0.05*$signal_{max}$) to exclude noisy voxels. In post processing arterial data was fitted taking bolus dispersion into account [3,4] while the model was adapted for pCASL labeling. The Buxton model [5] was used for fitting the tissue data and two approaches were followed: 1) no exchange from arteries to tissue, assuming no wash-out of label and using the T1 of blood, 2) immediate exchange incorporating label wash-out and T1 of tissue. In both approaches either the measured or fitted signal of the nearest arterial voxel was used as arterial input function (AIF). Goodness of fit was evaluated by taking the sum of squared differences (SoSD) between measured and fitted data. A region of interest (ROI) containing the visual cortex was defined and separated into an arterial and tissue component, based on the arterial map. The average ROI signals were fitted and fit parameters were used to compare rest and stimulated conditions.

Results and discussion: Figure 1 gives an example of arterial Cerebral Blood Volume (aCBV), Arterial Transit Time (ATT), dispersion coefficient and CBF maps for rest and stimulus condition in a single subject. On average, the visual cortex region showed an 8% and 10% decrease in ATT and dispersion resp. while CBF increased with 45% with visual stimulation, see table 1. In most subjects increased CBF was observed that extends well beyond the boundaries of the visual cortex. This is possibly caused by a stimulus that affects more areas than the visual cortex alone or due to quantification errors and is subject of further investigation. The sample density is demonstrated in figure 2 that shows measured and fitted signals in the visual cortex during stimulation. In the evaluation of the tissue fitting approaches the immediate exchange model yielded smallest SoSD and fitted AIF out-performed usage of measured AIF, see table 2. Shifting the Look-Locker images in subsequent repetitions greatly reduced instabilities in the averaged image intensity. However, individual images still showed fluctuating intensities. This is probably due to unwanted stimulated echoes and B1 inhomogeneities which will be reduced by implementation of RF phase spoiling and adding a B1 measurement for correction.

Conclusion LL-te-pCASL allows for tracer kinetic curve sampling with high temporal resolution and is suitable for in vivo perfusion model validation. Flip angle sweep combined with LL-shift is an effective way to limit signal variations in subsequent LL images. Brain activation results in a decrease of ATT and dispersion while CBF increases.

References 1. Günther, ISMRM 2007; 2. Dai et al, MRM 2012;
3. Hrabe et al, JMR 2003; 4. Ozyurt et al, ISMRM 2010;
5. Buxton et al MRM 1998

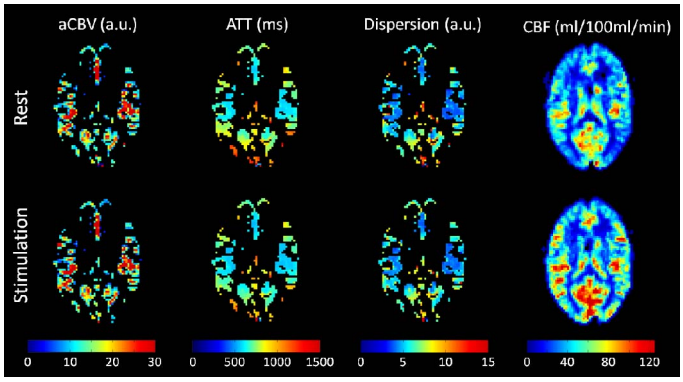

Figure 1. Maps of aCBV, ATT and dispersion in the arterial bed and brain CBF. Top row shows rest condition, bottom row visual stimulation.

	aCBV (a.u.)	ATT (ms)	Dispersion (a.u.)	CBF (ml/100ml/min)
Rest	18 (3)	917 (153)	10.0 (1.9)	93 (28)
Stimulus	18 (3)	843 (134)	8.8 (1.0)	132 (36)
Relative change (%)	-1	-8	-11	+45

Table 1. Hemodynamic characteristics of the visual cortex during rest and visual stimulation (average for 5 subjects). With stimulation the ATT and dispersion are reduced while CBF increases.

		Mean SoSD (sd)
Immediate exchange	Measured AIF	11 (4)
	Fitted AIF	10 (4)
No exchange	Measured AIF	19 (12)
	Fitted AIF	12 (5)

Table 2. Sum of squared differences between measured and fitted tissue signal. Values are average for 5 subjects, see text for details.

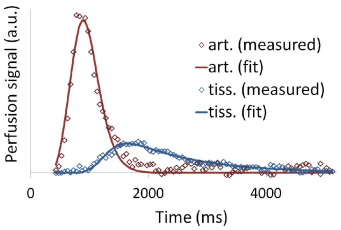

Figure 2. Measured and fitted signals in the visual cortex during stimulation. Dots represent individual sample points.