# Arterial Spin Labeling without control/label pairing and post-labeling delay: an MR fingerprinting implementation

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**TARGET AUDIENCE:** Researchers and clinicians interested in novel ASL techniques.

**PURPOSE:** Magnetic Resonance Fingerprinting (MRF) [1] is a recently developed technique that can estimate multiple MR parameters simultaneously using dynamic signal patterns. One important feature of MRF is that it takes advantage of the signal dependence on events occurred earlier in time, thus the signal intensity obtained in the present TR is modulated by spin history during the prior period up to several TRs ago. This concept is highly similar to the Arterial Spin Labeling (ASL) techniques [2] in which the MR signal is affected by the incoming blood spins that are labeled a few seconds ago. Therefore, ASL may be an ideal application for the MRF principle. ASL also meets other requirements of typical MRF applications in that the signal is influenced by multiple parameters and, as a matter of fact, ASL researchers are often frustrated by the fact that there are too many unknown parameters (e.g. tissue T1, arterial transit time) in the kinetic model. The goal of the present work is therefore to develop a MRF-based ASL sequence that can provide a voxel-by-voxel (i.e. map) estimation of multiple perfusion and MR parameters in a single scan. We conducted simulations, healthy control studies, and a clinical demonstration in a patient with cerebrovascular disease.

**METHODS:** ***Theory and pulse sequence design:*** The schematic diagram of our proposed sequence is depicted in Fig.1. Compared to conventional ASL, there are four main differences in this MRF-based ASL sequence. One is that there is no post-labeling delay (PLD) in our sequence. PLD is necessary in conventional ASL to allow labeled spins to reach the imaging slice. However, it is inefficient since it is a completely idle time. In MRF-ASL, the spins labeled in one TR will actually manifest their effects in images acquired several TRs later. Thus, delays to allow the spins labeled in the present TR to influence signal acquired in the same TR is not necessary. The second difference is that there is no strict pairing of label (red) and control (blue) scans. Since the CBF estimation is based on signal pattern matching rather than control-label subtraction, such pairing is no longer needed. In fact, the strict pairing (i.e. label-control-label-control order) may be detrimental for MRF-ASL, as their influence on signal (acquired several TRs later) may be canceled out. Thus, in our sequence, the control and label scans are randomly assigned. The third difference is that the labeling duration is now varying. The final difference that is not apparent in the diagram is that the excitation flip angle is no longer 90˚, as we want to preserve some effects of the incoming spins to influence the signal of next TR. In this study, we used a constant 70˚ as our flip angle, but it could be further optimized.

***Simulation:*** We used a single compartment perfusion General Kinetic Model (GKM) [3] to simulate the signal evolution for our pulse sequence. For each set of a four dimensional variable combination (T1, CBF, δ, B1), we could generate a time course of 1000 time-points. By sampling the 4D parameter space as following, T1 (500:10:2000, 2000:50:3000, 3000:100:3500ms), CBF (0:6:198ml/100g/min), arterial transit time δ (300:50:2000ms), and B1 power (50%:1%:120%), we generated a 4D dictionary of signal evolution which can be used for dictionary matching of experimental data.

***Experiment in healthy volunteers:*** Feasibility of our methods was investigated in two healthy subjects (1m/1f, 26 and 33 yrs.). All scans were studied on a 3T MRI scanner (Philips) and the imaging parameters were: 2D gradient echo EPI; single-slice, SENSE factor = 2.3; matrix size = 64×64; resolution = 2.81mm×2.81mm; TE = 8.1ms; flip angle = 70°, 1000 dynamics, the duration of the label/control periods varied from 72 to 450ms; total scan duration = 6 min 39 s. Reproducibility was accessed by repeating the protocol for three times. For data analysis, a correlation-based pattern recognition algorithm was used to identify a signal entry in the dictionary that best matches the observed signal evolution. All parameters, i.e. T1, CBF, δ, B1, of this signal entry can then be retrieved simultaneously.

***Experiment in a patient with Moyamoya Disease:*** Moyamoya Disease [4] is a vascular stenotic disease that is known to cause a change in arterial transit time δ. We applied the MRF-ASL sequence in one patient (m, 32 yrs.) with Moyamoya Disease who was diagnosed with right supraclinoid internal carotid artery (ICA) and middle cerebral artery (MCA) occlusion and poor distal branches. TOF MR angiography scan was also acquired.

**RESULTS and DISCUSSION:** ***Simulation:*** Five entries in the dictionary corresponding to five different parameter sets are shown in Fig. 2. It can be seen that the general curvature is primarily affected by the T1, while CBF and arterial transit time only have small effects. However, by zooming into the curves, one can still see a clear difference (note: noise was not added in these simulations, thus the difference reflects the real effects).

***Experiment in healthy volunteers:*** Maps of T1, CBF, and δ from a healthy volunteer are shown in Fig. 3a. The CBF map has an excellent quality and expected image contrast. The δ map is noisier but the white matter clearly manifests longer transit time compared to the gray matter. Figure 3b shows the test-retest reproducibility of another slice. It can be seen that both CBF and δ maps have good reproducibility. It can also be seen that the large vessel regions in the Sylvian fissure (arrows) have shorter transit time.

***Experiment in patient:*** The patient's results are shown in Fig. 4. From the angiogram image (Fig. 4a), it is evident that the right middle-cerebral-artery (MCA) has severe stenosis (red arrow). Accordingly, asymmetry in the δ map could be observed (green circle in Fig. 4b), with the right side showing prolonged bolus arrival compared to the left side. No such deficit could be seen in the MRF-derived CBF map (Fig. 4c), presumably due to collateral perfusion, which is confirmed in conventional ASL-CBF map (Fig. 4d).

**CONCLUSIONS:** We developed an MRF-based ASL sequence that does not use post-labeling delay or control/label pairing, but can provide an estimation of multiple perfusion and MR parameters in a single scan. Preliminary testings in healthy volunteers and in vascular disease patient showed promises of this novel technique.

**REFFERENCES:** [1]Ma et al, Nature 2013;495:187–192. [2]Wong et al, MRM 2007;58:1086–1091. [3]Buxton et al, MRM 1998;40(3):383-96. [4]Scott et al NEJM 2009;360:1226-1237.

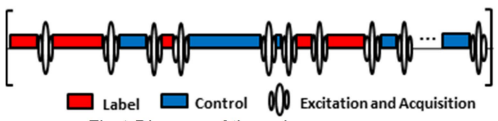


Fig.1.Diagram of the pulse sequence.

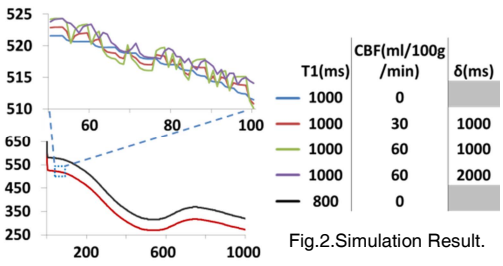


Fig.2.Simulation Result.

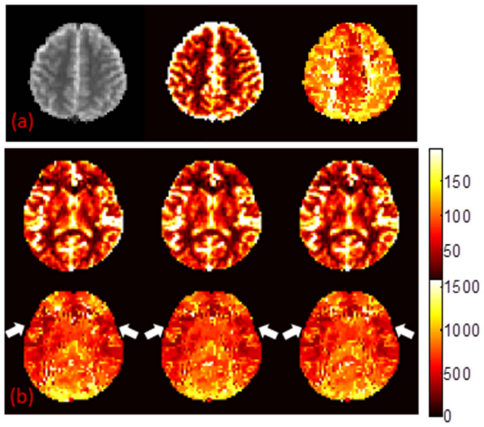


Fig.3 Health subject: a) T1, CBF, δ. b) Top row: CBF(ml/100g/min); Bottom row: δ(ms).

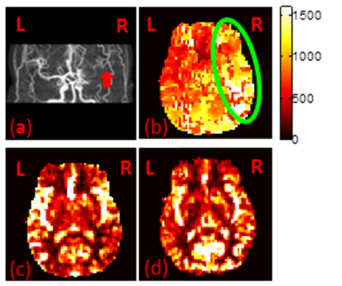


Fig.4. Patient result: a)Angiography;b) δ(ms); c) MRF-derived CBF; d) conventional ASL-CBF.