Theoretical Framework for MR Fingerprinting with ASL: Simultaneous Quantification of CBF, Transit Time, and T_1

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Target Audience: Those interested in ASL and novel quantitative MRI methods.

Purpose: The purpose of this study is to explore the use of the MR Fingerprinting framework for ASL-based parameter quantification. MRF has recently been introduced as an accurate and efficient approach for simultaneous quantification of multiple physical or physiological parameters[1]. Here we show how MRF can be extended to quantitation of ASL perfusion-related parameters, including cerebral blood flow (CBF) and transit time. Traditional ASL methods require long acquisition times and perfusion quantitation requires knowledge of several tissue properties. The goal of this work is to develop a theoretical framework that could overcome limitations in traditional ASL by providing a new approach to acquisition of ASL data and estimation of perfusion parameters.

Methods: In MRF, a unique signal timecourse for each pixel is generated based on interesting tissue properties. A dictionary of possible timecourses is generated by using Bloch simulations and knowledge of the sequence. Utilizing template matching algorithms, the obtained timecourse for each pixel is paired against the best dictionary match, which then identifies all underlying parameters used to generate the dictionary entry. For ASL MRF, unique signal timecourses are needed for tissues with different perfusion-related parameters (CBF, transit time, tissue T_1). This was achieved by modifying the pulse sequence with a PCASL labeling scheme such that a variable arterial input function of labeled spins was delivered to the tissue over time. A dictionary of possible signal evolutions that includes inflow and outflow of labeled spins was created using the Bloch equations[2]:

$$\frac{dM}{dt} = \frac{M_o - M}{T_1} + fM_a(t) - \frac{f}{\lambda}M,$$

and by modeling the arterial input:

$$M_a(t) = M_o\left(1 - 2\alpha e^{-\Delta t/T_{1,a}}\right) * k(t-\Delta t), \text{ if L(t)=1}$$

$$M_a(t) = M_o\left(1 - e^{-\Delta t/T_{1,a}}\right) * k(t-\Delta t), \text{ if L(t)≠1}$$

where M is the magnetization in brain tissue, M_0 is the equilibrium tissue magnetization, T_1 and $T_{1,a}$ are the T1 values for tissue and blood, $M_a(t)$ is the magnetization of labeled arterial blood, f is perfusion, Δt is the transit time of blood, k(t-Δt) is a Gamma-variate function to capture arterial dispersion[3], and L(t) is the labeling function that indicates the occurrence of inversion pulses (L(t)=1). Using this dictionary, a pattern recognition algorithm (maximum inner product[1]) was used to identify the dictionary entry that best matches the signal, yielding CBF, transit time, and T_1.

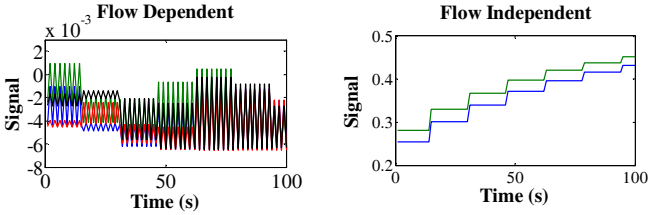

Figure 1. Simulated signal changes due to transit time and perfusion effects (flow dependent, f=0.01,0.02ml/s/g, Δt=1,1.2s) and T_1 of tissue (flow independent, T1=1.2,1.4s).

Sequence Design: For initial evaluation, we explored varying the tagging duration and TR. The labeling function (L(t)) was varied throughout the acquisition; L(t)=1 during labeling pulses, L(t)=-1 during control pulses, and L(t)=0 during the post-label delay and data acquisition. The labeling duration and TR were linearly increased, with alternating labeling/control pulses.

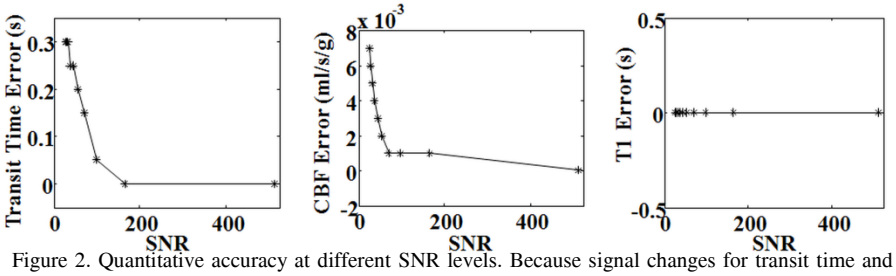

Figure 2. Quantitative accuracy at different SNR levels. Because signal changes for transit time and CBF are smaller, they are more sensitive to noise than T1.

***Simulations*:** Simulations were performed to evaluate the ability of MRF ASL to select the correct dictionary entry at different SNR levels. The dictionary was created by varying the T1 of tissue (0.4-1.6s, 0.05s step size), f (0.001-0.02ml/s/g, 0.001ml/s/g step size), and Δt (0.5-2.5s, 0.05s step size), yielding a total of 20500 entries. An ideal signal curve representing a time series of images was created by selecting a single entry in the simulated dictionary, and random noise was added to the curve for 10 different SNR values. SNR was computed by taking the maximum signal from the ideal curve and the standard deviation of the added noise.

Results: Figure 2 demonstrates simulation results of accuracy of parameter estimation at different SNR levels for the time series of images. Signal changes in the time-course related to T1 relaxation are fairly large, which results in accurate T1 estimation at all SNR levels tested. Signal changes in the time-course related to CBF and transit time are small, which results in increased error at lower SNR values. Figure 3 shows a simulated curve with an SNR of 98 and the matched dictionary entry, showing a good match between the noisy signal and dictionary entry. The errors in perfusion and transit time were 0.001ml/s/g and 0.05s, respectively.

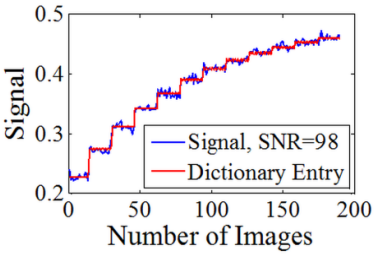

Figure 3. Signal generated with an SNR value of 98, and the best fit dictionary

Discussion: We present a theoretical, simulation based study exploring the feasibility of using MRF for estimating perfusion parameters from an ASL experiment. As with traditional MRF[1], MRF many degrees of freedom in sequence design can be used to generate a unique signal timecourse for each tissue. For example, label/control pulses no longer need to occur in pairs. The occurrence and tagging duration of each control/label pulse can be randomly selected. Other sequence parameters could also be randomized, including but not limited to: post labeling delay time, occurrence of background suppression pulses, acquisition TR, and acquisition flip angle. Future work will apply this technique *in vivo* to measure T_1, CBF, and transit time simultaneously. Previous studies have explored randomized labeling[4,5] and using a dictionary-based approach for quantitative anlaysis[5], and show promising results. With the potential added flexibility in sequence design in MRF ASL, efficiency and accuracy could be further improved.

References: [1]Ma D, et al. Nature 2013;495:187–192. [2]Buxton RB, et al. MRM 1998;40:383–396. [3]Gallichan et al, MRM 2008;60;53-63. [4]Taei-Tehrani M-R, et al. JMRI 2012;35:223–8. [5]Wong EC, Guo J. MAGMA 2012;25:95–101. **Acknowledgements**: Siemens Healthcare and NIH grants 1R01DK098503, 1R01EB017219.