A theoretical model describing the Cine-ASL perfusion mapping technique: steadily-pulsed labeling provides better acquisition efficiency than FAIR

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Introduction:
Arterial Spin Labeling (ASL) is a powerful, fully non-invasive, quantitative, and repeatable method for the assessment of perfusion. ASL of the mouse myocardium has been successful in the past (1-4), despite key limitations regarding acquisition efficiency due to cardiac motion, which leads to lower signal-to-noise ratios or longer acquisition times than in brain studies. A crucial issue in the widely used FAIR-ASL method is that it is based on a dynamic relaxation measurement, during which the labeled bolus magnetization also relaxes, leading to a vanishing ASL signal over time. We propose a new experimental scheme, which allows maintaining the magnetization in tagged state along the measurement, to benefit from increased sensitivity compared with FAIR in a similar way as continuous ASL. We provide a theoretical description of such a scheme and show close agreement with the magnetization behavior observed in a proof-of-concept *in vivo* experiment in the mouse heart.

Theory and methods:
The Cine-ASL technique relies on a fast cine-FLASH imaging scheme repeated over several cardiac cycles for each line of k-space. Replacing one single gradient-echo readout in each cardiac cycle by a selective labeling pulse in the basal heart, we are able to maintain continuous tagging of the arterial blood feeding the coronaries, while keeping the cine-readouts of the remaining cardiac phases (Tag scan). A Control scan is performed to compensate for Magnetization Transfer effects.
Here, we present a theoretical model for the magnetization behavior, based on Bloch equations. The model takes into account a constant tagging efficiency of the labeling scheme. The solutions provide a continuous and compact description of the magnetization time evolution M(t) in this experiment. The evolution predicted by the model was compared with experimental results of the Cine-ASL technique performed in healthy C57Bl6J mice on a Bruker Biospec 4.7T animal scanner.

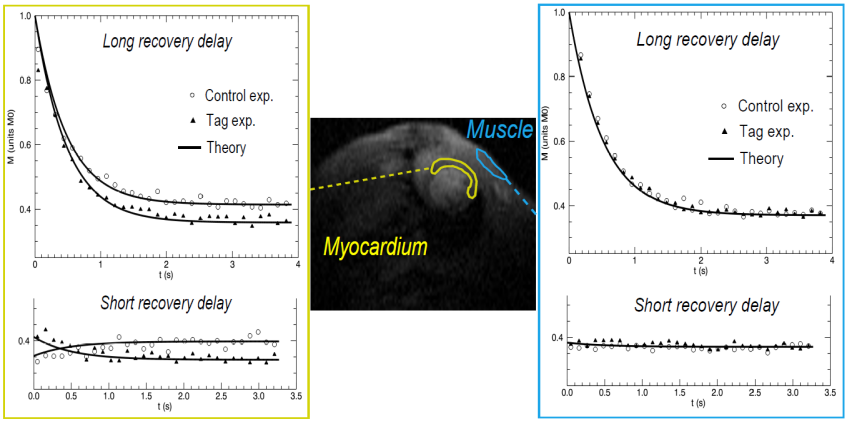

Figure 1: Magnetization time evolution for Control and Tag scans in different ROIs in mouse heart. Recovery delay between the two scans was taken long (6 s) and short (30 ms) for comparison.

Results:
Theory predicts that combination of the cine-readout with steadily-pulsed arterial labeling leads to a stationary regime for the magnetization, which depends on perfusion f. Figure 1 shows the magnetization M(t) obtained experimentally in a region of the mouse myocardium and in a ROI within the chest muscle. The magnetization difference between Control and Tag scans is due to perfusion, and clearly visible in the myocardium, whereas it is undetectable in the chest muscle, where perfusion is almost zero. In both cases, the theoretical predictions (with f≠0 and f=0) closely match the experimental magnetization behavior.
A major result from the theory is that the asymptotic regime reached by the magnetization is independent of the dynamic details of the experiment (heart rate variations, arterial input function...). Importantly, it is also independent of the recovery delay chosen between Control and Tag scans (figure 1). In this stationary regime, we found that the magnetization difference is proportional to f, and that a map can thus be extracted by applying the model pixel by pixel to raw images (figure 2-inset). Quantification of perfusion with this model and sequence was found consistent with values obtained with a FAIR-Look-Locker technique (1).
With persistent perfusion-dependent signal difference and an arbitrarily short recovery delay, the method allows for efficient data accumulation. Applying the theory in this setting, we calculated the acquisition efficiency (defined as the signal-to-noise ratio divided by the square root of the acquisition time) of the steadily-pulsed method compared to that of FAIR Look-Locker (figure 2), with typical parameters for the mouse heart. The model predicts an up to three times higher efficiency than FAIR. An experimental analysis done with up to four seconds of averaging per tag/control block well confirmed the theoretical findings.

Conclusion:
We have presented a theoretical description of a new "steadily-pulsed" acquisition strategy in cardiac ASL, designed for the assessment of myocardial perfusion. The model was shown to describe well the observations made in a proof-of-concept experiment in the mouse heart. While allowing for a reliable measurement of perfusion in small rodents, the acquisition efficiency of the cine-ASL technique was found significantly higher than FAIR Look-Locker.

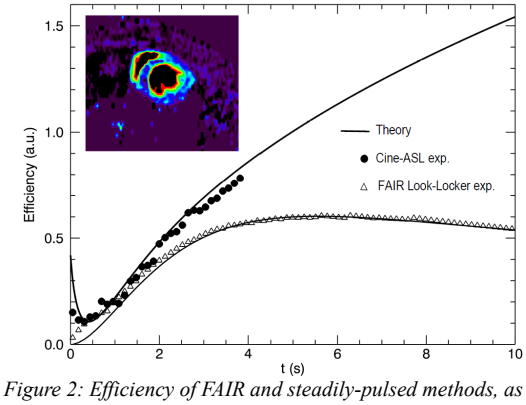

Figure 2: Efficiency of FAIR and steadily-pulsed methods, as a function of scan time.

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