Slow Magnetization Transfer Dominates Inefficiency of Suppressed Arterial Spin Labeling

D. M. Garcia[1,2], G. Duhamel[1], D. Alsop[1,3]

[1]Radiology, Beth Israel Deaconess Medical Center, Boston, MA, United States, [2]Electrical Engineering and Computer Science, Massachusetts Institute of Technology, Cambridge, MA, United States, [3]Harvard Medical School, Boston, MA, United States

Introduction: Arterial Spin Labeling is a noninvasive technique that provides quantitative maps of blood perfusion. Background suppression techniques using additional inversion pulses during the labeling of arterial spins greatly reduce the background signal intensity and improve sensitivity and reproducibility (1, 2, 3). Imperfect inversion by these pulses, however, can attenuate the ASL signal and 17% signal loss with 2 pulses was previously reported (3). Such large signal loss is not consistent with that expected for optimized adiabatic inversion pulses applied to tissues with the T_2 and T_1 of blood or brain tissue(4). Here we compare experimental measurements of adiabatic inversion efficiency in-vivo and in in-vitro blood with simulations and measurements in phantoms.

Methods: Simulations. Numerical integration of the Bloch equations was performed as previously described (4, 5). Simulations of a 3.21 ms hyperbolic tangent (tanh) pulse (6) were performed for a peak B_1 of 0.18 G and also over a range of B_0 offset up to ±400 Hz and a range of B_1 errors of ±20%. T_1/T_2 of 1.4/0.25 ms for blood and 1.2/0.08 ms for tissue were assumed for the purpose of the simulations.

In Vivo Measurements. Experimental measurements of inversion efficiency were performed on a 3.0 Tesla GE VH/i scanner using the product head coil. The FAIR labeling method (7) was used with a single-slice echoplanar imaging acquisition, carried out with a TI of 1.8 s, a TR of 7 s and a TE of 25 ms in a 7 mm thick axial slice through the superior part of the lateral ventricles. The long TR was selected to minimize any effects of the inversion pulses on blood magnetization for the next repetition. A 2 cm slab was inverted for the control image and a 40 cm slab was inverted for the label rather than traditional non-selective FAIR label inversion in order to assure that labeled blood was all well within the head coil during the application of the later inversion pulses. ASL images were acquired with and without added inversion pulses to assess inversion efficiency. Acquired images were interleaved in the following order: label without inversion pulses, control without inversion pulses, label with inversion pulses, control with inversion pulses, repeated 10 times for an approximately 5 minute scan. The signal intensity of the difference (label-control) images without the applied pulses over that of the difference images with pulses applied was used as an indicator of efficiency.

Eight normal adult volunteers were studied. Two different sets of images were acquired. One set was acquired with four tanh inversion pulses applied 20 ms apart ending 100 ms before image acquisition. A second set was acquired with the four inversion pulses applied at optimal times for background suppression, 1510, 876, 376, and 96.6 ms before acquisition.

In Vitro Measurements. Blood samples gathered from a healthy 40-year-old male were scanned within three hours of collection employing the tanh pulses as in the in-vivo studies. The selective/non-selective FAIR was replaced with inversion/no inversion because the blood is not moving. Samples were imaged within an array of phantoms containing MnCl doped deionized water in varying concentrations. The imaging sequence was replaced by a single shot fast spin echo sequence with nonselective inversions that otherwise mimicked the in-vivo sequence. In between each scan, the tubes of blood were temporarily removed from the phantom and slowly rotated to avoid separation.

Results: Figure 1 shows representative difference images for one volunteer. The tanh pulses caused observable attenuation that was much higher for the optimally timed inversions during background suppression (BS) than for the closely spaced (CS) inversions. Average whole slice ASL difference signal results are shown in figure 2. These average results support the qualitative appearance in figure 1. Within subject fractional standard deviation of the ASL signal was more than 2 times higher without suppression despite the attenuation. Also shown are the efficiencies measured in the in-vitro blood specimens. The blood specimens showed qualitatively similar but weaker attenuation. In the MnCl phantoms, only those with T_2 less than 40 ms showed comparable inefficiency, figure 3.
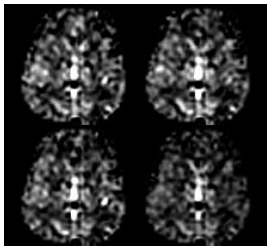

Figure 1. ASL perfusion sensitive images from one slice acquired without (top row) and with (bottom row) four 3.21 tanh pulses applied during labeling either rapidly 100 ms before acquisition (left) or optimally spaced for background suppression (right).
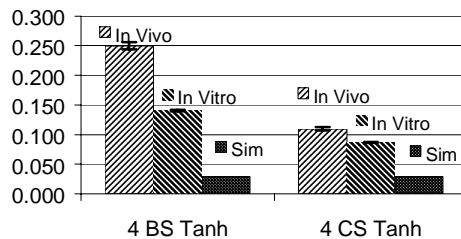

Figure 2. Fractional signal loss of in vivo, in vitro, and blood simulation measurements with 0.18 G B_1 and ± 0 Hz offset are shown. Results are presented both for four pulses optimally timed for background suppression (BS) and for four pulses closely spaced (CS) applied rapidly 100 ms before imaging.
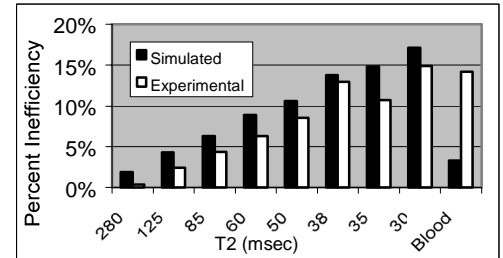

Figure 3. Simulated and experimental inversion inefficiency for phantoms and blood samples. Phantoms are presented by T_2 values. The final bars are for the blood vials. Four 3.21 ms tanh pulses optimally timed for background suppression were employed for the experimental set.

Discussion:

In vivo ASL inversion efficiency is much lower than can be explained by T_2 and T_1 relaxation. The higher attenuation when the pulses are applied more widely spaced and at times when the labeled spins are certainly still in blood support a slow magnetization transfer within blood as a mechanism for the attenuation. The lower attenuation in in-vitro experiments may be due in part to reduced hematocrit from settling and aggregation in whole blood. Evidence for a slowly exchanging spin pool in whole blood with approximately 5% concentration and 250 ms exchange time has been previously reported (8) and such a phenomenon could easily explain our findings. Despite the 25% attenuation observed, the more than two fold decrease in fractional error of whole brain ASL measurements provides continuing evidence of the benefits of background suppression.

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