Flow-based arterial spin labeling: from brain to body

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Chapter 6

B_0 and B_1 influence on velocity selective inversion arterial spin labeling and background suppression efficiency

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INTRODUCTION

Arterial Spin Labeling is more and more used outside of the brain [19], [97], [176]. For applications in the body, flow-based ASL techniques are particularly suited, because of the easier planning procedure due to non-spatially selective labeling, and transit time insensitivity. These techniques thus enable, or simplify, ASL measurements in organs which are fed by multiple feeding vessels, and organs with relatively slow flow. In brain[53], [148], velocity selective inversion ASL (VSI-ASL) has demonstrated the highest SNR of flow-based ASL techniques thus far.

In the body, however, magnetic field inhomogeneity will start to play a role in optimization of the ASL-sequences. In a previous study we have demonstrated severe subtraction errors of VSI-ASL in some volunteers, when applied in the kidneys[148]. The subtraction errors are likely due to B_0/B_1-inhomogeneity of both the VSI-ASL module and the background suppression (BGS) pulses.

In the original implementation of VSI-ASL[53], the label module is velocity-sensitive, containing bipolar motion-sensitizing gradients, and the control module is velocity-compensated, containing unipolar gradients, see Figure 1A and B. The velocity-compensated control module prevents subtraction errors because it compensates for the diffusion contribution to the signal[53]. The downside, however, is that the velocity-compensated control module is associated with a relatively high B_1-sensitivity, which already limits inversion of static tissue for B_1-ranges encountered in brain[53]. This B_1-sensitivity is expected to lead to even more degradation of image quality in body applications, probably to the level that clinical interpretation is hampered. In addition, the velocity-selective inversion pulse train consists of hard pulses, which are increasing the sensitivity to B_1 imperfections even further[53].

Besides the B_1-sensivity of the VSI-ASL modules, B_1-sensitivity of the BGS pulses also plays a role when applying VSI-ASL in kidneys[148], and as such, likely also in other abdominal applications. The purpose of BGS is to minimize the static background signal intensity in both the label and control image, while conserving the difference in magnetization between label and control due to labeled blood[13]. BGS reduces fluctuations in the ASL-signal, which are cause by e.g. patient motion and physiological noise. BGS consists of a certain number of inversion pulses, which causes all signal to undergo T_1-recovery based on the tissue's T_1 value. Image acquisition is timed close to the zero-crossing of the dominant background tissue signals[13]. Dixon et al. first proposed the use of multiple inversion pulses to minimize signal of tissues with a range of T_1's[181]. However, the BGS pulses do not have a perfect inversion efficiency, resulting in transverse relaxation of the signal, and corresponding signal loss. Thus, the choice for the number of pulses creates a trade-off between signal loss and the width of the

suppressed T_1-range[13]. For most body ASL methods, two BGS pulses are used, but VSI is typically used with three. In VSI-ASL, static tissue is inverted, so to prevent inversion of the static tissue signal during image acquisition, VSI-ASL is employed with an odd number of BGS pulses. The higher number of BGS pulses in VSI-ASL, makes the sequence particularly sensitive to the inversion efficiency of the BGS pulses.

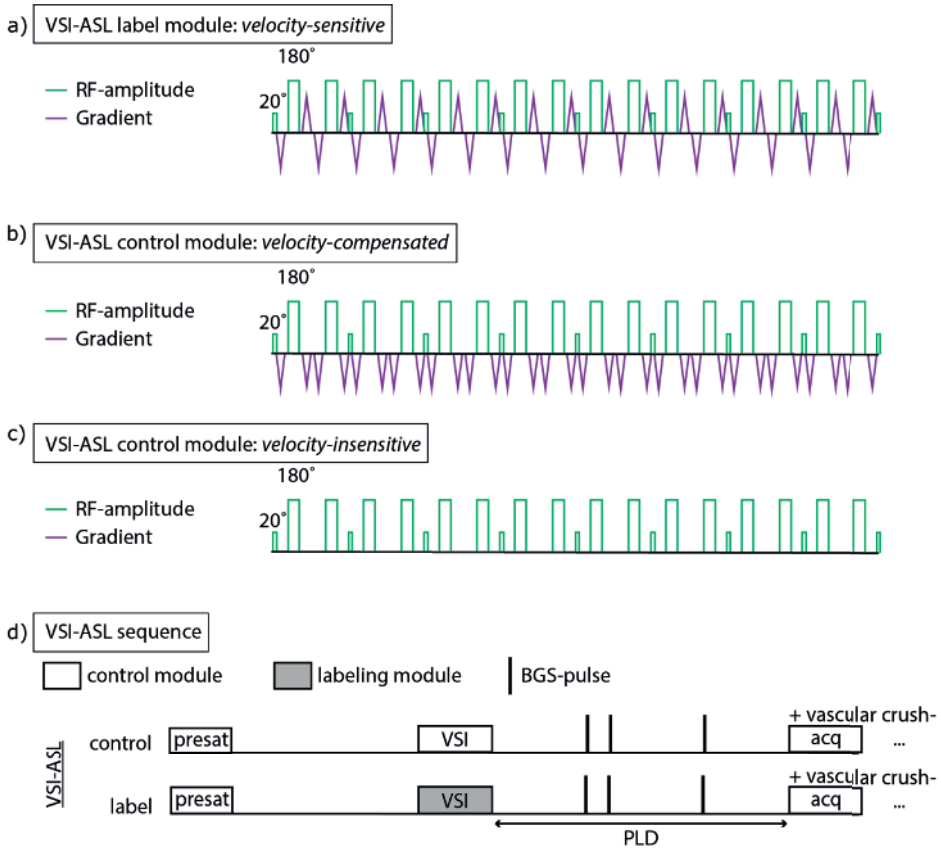

Figure 1. Velocity-selective inversion arterial spin labeling (VSI-ASL) label and control modules. A) The VSI-ASL label module is velocity-sensitive pulse train; containing alternating motion-sensitizing gradients. B) The traditional implementation of the VSI-ASL control module is velocity-insensitive and does not contain any gradients. C) The velocity-compensated VSI-ASL control module contains solely unipolar gradients. D) The VSI-ASL sequence, including presaturation of the imaging volume (presat) and three background suppression (BGS-) pulses.

The hyperbolic secant pulse (HS) is an adiabatic pulse frequently used for BGS[182]. Besides the HS, multiple other adiabatic inversion pulses exist[183], each with varying sensitivity to B_0 and B_1. B_1 insensitive rotation (BIR)-4[184] is for example an often used pulse, which has been developed to perform non-selective inversion in a B_1-inhomogenous environment[184]. Frequency offset corrected inversion (FOCI)[185] is another often used inversion pulse, which

has been developed to be robust for off-resonance effects[185], and has since e.g. been used as spatially-selective inversion pulse in ASL-applications[186].

The goal of the current study was to first gain insight into the sensitivity of the different parts of the VSI-ASL sequence to B_0-/ and B_1 inhomogeneity, specifically including BGS, evaluated for B_0-/ and B_1 conditions representative for abdominal application at 3T. Secondly, we aim to investigate whether adjustments can be made to improve the robustness to field inhomogeneity. Simulations were performed of the VSI-ASL label and control modules under realistic B_0 and B_1 field conditions, where a distinction was made between velocity-compensated and velocity-insensitive control modules. In addition, the inversion efficiency of the traditionally used BGS pulse, HS, as well as two possible alternatives, BIR-4 and FOCI, was investigated for the same range of field conditions, at two maximum B_1-levels, to find out which BGS pulse is most suitable for abdominal applications at 3T.

METHODS

All simulations were performed based on 3T conditions, using a T_1 = 1650 ms[187] and T_2 = 150 ms[188] of arterial blood. The B_0 and B_1 range were based on the field inhomogeneity that can be expected for anatomies in the vicinity of the lungs[127], [128], [145]. The B_0 was varied between -300 and +300 Hz, the B_1 was varied between 0.4 and 1.2 (= 40%/120% of the intended B_1).

First, Bloch-simulations for the inversion efficiency of VSI-ASL label and velocity-compensated/ velocity-insensitive control modules were performed at a velocity range of -20 cm/s to 20 cm/s.

Second, optimization of BGS pulse parameters was done based on a constrained nonlinear optimization algorithm, with sum of squares as loss function. The optimization parameters were pulse duration, maximum B_1 and maximum frequency offset for all pulses. BIR-4 additionally had the phase-step (defining the flip angle) and β (defining the shape)[184] as parameters.

The BGS pulse optimizations were performed for two different maximum B_1-conditions: 13.5 μT, which is the maximum B_1 that can be used on our 3T Philips system with a body transmit coil, and 23 μT, as has been used in previous implementations of BIR-4[57]. The other constraints included a maximum duration of 30ms, maximum frequency offset of 1 MHz, a maximum phase-step of π, and a maximum β of 200.

Starting values of the HS pulse were set to the standard values as implemented by the vendor on our 3T Philips system, see Table 1. For the BIR-4 pulse, the starting values were set to the

settings used by Guo et al[57]. For the FOCI pulse, the starting values were set to the settings that were used previously by our group when implemented as labeling pulse in a flow-sensitive alternating inversion recovery (FAIR) ASL-sequence[108], [145]. The starting values of the maximum B_1 were always set to the maximum available B_1, i.e. either 13.5 μT or 23 μT.

	Standard setting	Optimized with max B_1 of 13.5 μT			Optimized with max B_1 of 23 μT		
Parameter	**HS**	**HS**	**BIR-4**	**FOCI**	**HS**	**BIR-4**	**FOCI**
Max B_1 (μT)	13.5	13.5	13.5	13.5	23.0	23.0	23.0
Max frequency (Hz)	597	597	42.5E3	6.40E3	597	42.5E3	6.40E3
Duration (ms)	13.3	13.1	4.90	13.9	11.3	3.60	14.3
Phase step (rad)	-	-	1.63	-	-	1.64	-
□	-	-	189	-	-	164	-

Table 1. Sequence parameters of the standard hyperbolic secant (HS), and HS, B1 insensitive rotation (BIR)-4, and frequency offset corrected inversion (FOCI) pulse optimized for two maximum B1 conditions.

RESULTS

The traditionally implemented VSI-ASL label module shows reduced labeling efficiency at B_1-levels < ~0.7, while there is only a very limited effect of B_0-inhomogeneity, see Figure 2. The traditionally implemented VSI-ASL control module is motion-compensated, this module shows severe sensitivity to both B_0- and B_1-inhomogeneity. In contrast, the motion-insensitive control module is robust to B_0 inhomogeneity, and only shows reduced inversion efficiency for B_1-levels < ~0.7.

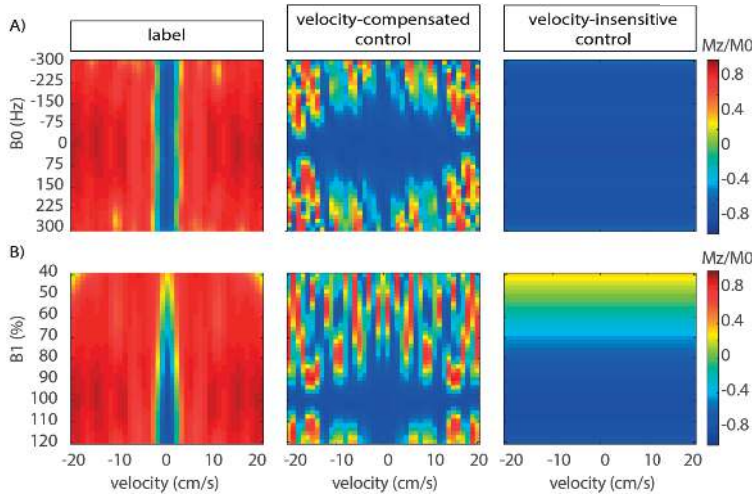

Figure 2. Effect of A) B_0 and B) B_1 inhomogeneity on the VSI labeling module, velocity-compensated module (traditionally used), and velocity-insensitive module. Reduced labeling efficiency due to B_1-sensivitiy can lead to subtraction artefacts in poor B_1 conditions, as was previously observed in kidneys[145].

Optimization of the BGS pulses, for the two maximum B_1 constraints, resulted in the sequence parameters shown in Table 1. Comparing the results for the two different B_1 constraints, it is clear that all optimized pulses use their maximum B_1. Besides B_1, the optimized settings for the two B_1-constraints differ in their duration, while the other parameters stayed relatively constant. Note, that optimizing the HS pulse for B_0 and B_1 inhomogeneity expected in the abdomen, did not result in any significant changes to the pulse parameters at a maximum B_1 of 13.5 µT, compared to the standard settings. The resulting amplitude and frequency diagrams of the optimized sequence parameters for maximum B_1 of 13.5 µT are shown in Figure 3.

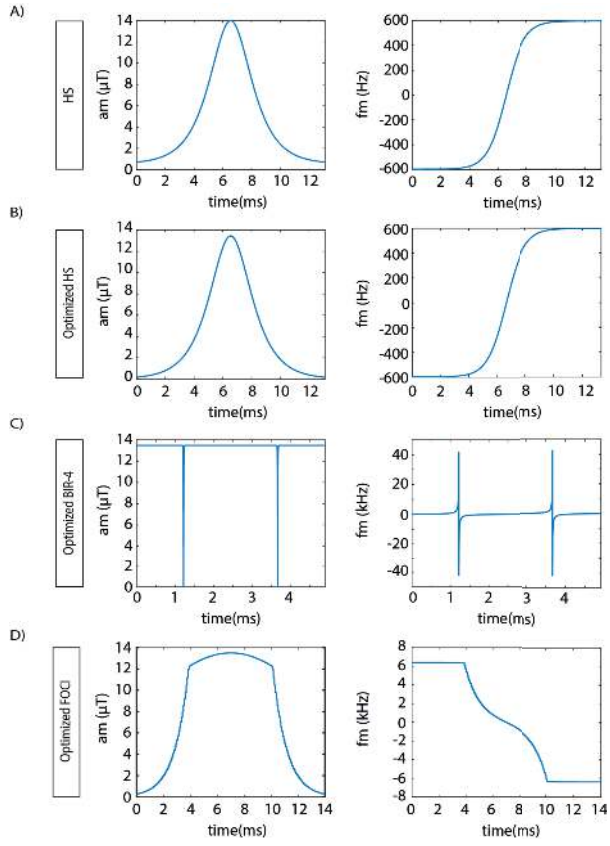

Figure 3. Pulse sequences of A) standard hyperbolic secant (HS), B) HS, C) B_1 insensitive rotation (BIR)-4, and D) frequency offset corrected inversion (FOCI) pulse optimized with a maximum B_1 of 13.5 µT.

Comparing the four pulses at maximum B_1 of 13.5 µT, reveals that the optimized HS pulse overall shows the highest robustness to B_0 and B_1, see Figure 4. For a maximum B_1 of 13.5 µT, there is no visible improvement in inversion efficiency of the optimized HS compared to the standard one, see Figure 3, as expected from Table 1. Only in cases where solely B_1-

inhomogeneity plays a role, while the B_0 homogeneity is near perfect, and the maximum available B_1 is 13.5 µT, BIR-4 could show a better inversion efficiency than HS, see Figure 4.

Having a maximum B_1 of 23 µT, instead 13.5 µT, available improves inversion efficiency considerably, see Figure 5. Also in this condition, the optimized HS pulse shows the best performance.

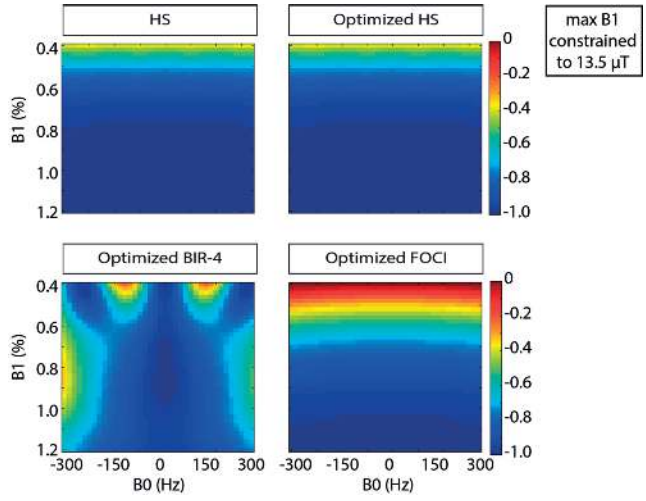

Figure 4. Inversion efficiency, for a range of B_0/B_1-levels corresponding to anatomies in the vicinity of the lungs, of the standard hyperbolic secant (HS) and HS, B_1 insensitive rotation (BIR)-4, and frequency offset corrected inversion (FOCI) pulse. These pulses were optimized with a maximum B_1 of 13.5 µT. Pulses correspond to the pulse shapes shown in Figure 3.

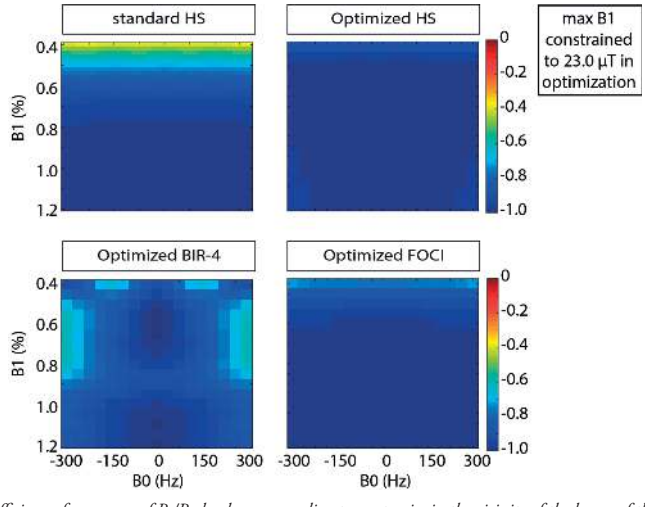

Figure 5. Inversion efficiency, for a range of B_0/B_1-levels corresponding to anatomies in the vicinity of the lungs, of the standard hyperbolic secant (HS) and HS, B_1 insensitive rotation (BIR)-4, and frequency offset corrected inversion (FOCI) pulse. These pulses were optimized with a maximum B_1 of 23 µT.

DISCUSSION

In this study B_0/B_1-simulations were performed to gain insight into which parts of the VSI-ASL sequence require further optimization, and to explore possible solutions, to eliminate subtraction errors in body applications, such as in kidneys. First of all, the B_0 and B_1 sensitivity of the VSI-ASL sequence was considered. Simulations show that there is a severe sensitivity to B_0 and B_1 inhomogeneity with the default implementation of the VSI-ASL sequence, especially due to the motion-compensated control. Secondly, simulations were performed to study the B_0 and B_1 sensitivity of various BGS pulses. The standardly used BGS pulse (HS) shows B_1-sensitivity, but no remarkable B_0-sensitivity. Optimized versions of the HS, BIR-4, and FOCI, do not show an overall improved performance when considering both B_0 and B_1-field inhomogeneity at a maximum B_1 of 13.5 μT. The BIR-4 could provide an improved performance, only in cases where there is only B_1-inhomogeneity and where the maximum available B_1 is 13.5 μT. Allowing a maximum B_1 of 23.0 μT, and using optimized settings for HS would improve the inversion efficiency under B_1-inhomogeneity considerably.

These results confirm the previously found B_0- and B_1 sensitivity of the motion-compensated VSI-control module described by Qin et al. [53]. In the current study, a broader range of B_0 and B_1 were employed, to simulate the field conditions in the abdomen. In these field conditions there is an even more severe disturbance of the inversion efficiency of the motion-compensated VSI-control module. In contrast, the motion-insensitive control module is robust to these field conditions. The motion-insensitive control module does introduce an imbalance in diffusion-weighting between the label and control module, potentially leading to an overestimation of the blood flow due to a diffusion-related signal contribution. Although, this effect was previously found to be negligible[122]. For abdomen, the tradeoff likely favors the motion-insensitive control with increased inversion efficiency, and consequently fewer subtraction artefacts, including a possible diffusion contribution, over the subtraction artefacts associated with motion-compensated VSI-control module. In a more recent study in the myocardium, a motion-insensitive control module was employed for these reasons[125]. This study further improved labeling efficiency by optimizing the amplitudes of the VSI-sub pulses, based on the expected off-resonance and B_1 condition in the heart, as well as the intended velocity field of view[125]. A separate study has demonstrated a reduction in eddy currents and B_1-sensitivity by replacing the hard refocusing pulses in the VSI-module to composite pulses[189]. Optimizing the amplitudes and/or pulse shape of the VSI-sub pulses would, in addition to using a velocity-compensated control module, also for other body applications be an interesting approach to reduce the sensitivity for field inhomogeneity even further.

The BGS simulations show that there is no clear alternative to the HS pulse for applications in challenging B_0- and B_1-conditions, both in case of a maximum B_1 of 13.5 μT and of 23

μT. BIR-4 only has a better inversion efficiency when solely the B_1-field is disturbed, without perturbation of B_0 (at a maximum available B_1 of 13.5 μT), which is not realistic for abdominal applications with the current B_0-shimming possibilities. Furthermore, results have shown that the inversion efficiency improves drastically when a higher B_1 (23.0 μT) is available, as is the case in ref[57], or can be achieved by using local transmit coils. In those cases, an optimized implementation of the HS-pulse has the best performance.

To reduce the effect of field inhomogeneity on the ASL-measurements, going to a lower field strength could also be considered. Magnetic susceptibility effects halve at 1.5T[61]. In addition, the B_1-field is also more homogenous[61]. For example, a B_0 of ±80 Hz and B_1-levels of 0.8-1.1 have been measured in liver at 1.5T[190]. However, future studies could indicate whether the improvement in field conditions at 1.5T outweigh the expected reduction in SNR[61] and shortening in T_1[61], and how the performance compares to spatially-selective techniques, such as flow-sensitive alternating inversion recovery (FAIR)[148], at 3T.

This study also has some important limitations. First, the study only consisted of simulations. In-vivo studies, showing the performance of the different VSI-ASL modules and BGS pulses in-vivo would be very valuable and would enable inspection of the ASL subtraction artefacts. Second, this study only considered the field conditions at 3T. In-vivo studies comparing 1.5T and 3.0T could provide more insight in what the optimal setting would be for abdominal VSI-ASL. Third, only a limited number of inversion pulses have been considered for BGS in this study. Multiple other adiabatic inversion pulses exist and should be considered, although differences in performance were mostly shown to be subtle[191]. Lastly, this study solely performed simulations for the traditional VSI-ASL sequence. Previously, specific optimizations for myocardium of the amplitudes of the hard pulses that make up the VSI-ASL pulse train, have shown promising results[125]. The concept of optimizing the VSI-ASL pulse train for specific organs should be considered for other body applications.

In conclusion, this study has shown that there is a B_0- and B_1-sensitivity of both the VSI-module and the BGS pulses for VSI-ASL. Several improvements of the VSI-sequence should be considered in future body applications of VSI-ASL, to prevent subtraction errors as demonstrated in ref[145]. For example, our simulations have shown that using a velocity-insensitive instead of a velocity-compensated control module will increase labeling efficiency considerably. Furthermore, optimization of the VSI sub-pulse amplitudes under the expected field conditions, and/or usage of composite refocusing pulses could potentially make VSI-ASL labeling efficiency less dependent on field homogeneity, and thus further improve robustness. In terms of BGS pulses, no superior alternative to HS pulses were found. In vivo studies investigating the effect of these recommended adjustments to the VSI-sequence, and possibly investigating other alternatives to BGS-pulses, at 1.5T and 3.0T are warranted.