Practical Considerations of Arterial Spin Labeling MRI for Measuring the Multi-slice Perfusion in the Human Brain

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In this work practical considerations of a pulsed arterial spin labeling MRI are presented to reliable multi-slice perfusion measurements in the human brain. Three parameters were considered in this study. First, in order to improve slice profile and inversion efficiency of a labeling pulse a high power inversion pulse of adiabatic hyperbolic secant was designed. A 900° rotation of the flip angle was provided to make a good slice profile and excellent inversion efficiency. Second, to minimize contributions of a residual magnetization between interleaved scans of control and labeling we tested three different conditions which were applied 1) only saturation pulses, 2) only spoiler gradients, and 3) combinations of saturation pulses and spoiler gradients. Applications of both saturation pulses and spoiler gradients minimized the residual magnetization. Finally, to find a minimum gap between a tagged plane and an imaging plane we tested signal changes of the subtracted image between control and labeled images with varying the gap. The optimum gap was about 20 mm. In conclusion, in order to obtain high quality of perfusion images in human brain it is important to use optimum parameters. Before routinely using in clinical studies, we recommend to make optimizations of sequence parameters.

Key Words: Arterial spin labeling, Cerebral perfusion, MRI, Human brain, Optimization

INTRODUCTION

Although positron emission tomography (PET) and single photon emission computer tomography (SPECT) are using most perfusion measurements in the human brain, magnetic resonance (MR) perfusion measurements can be performed with contrast agents (exogenous tracer)[1] or arterial spin labeling (ASL, endogenous tracer) without radiation injection.[2,3] The ASL method is a perfusion measurement technique by using signal differences between with (tag) and without (control) arterial blood inversion, which is called the perfusion-weighted imaging (PWI). Advantages of the ASL method compared to the MR perfusion measurement with contrast agents are totally noninvasive and easily repeatable. However, the ASL methods are still under the developing stage because of limitations of several intrinsic and extrinsic MR properties.

One of the major problems of the ASL method is to design an adiabatic hyperbolic secant (HS) inversion radio-frequency (RF) pulse with a good slice profile and excellent inversion efficiency. The RF imperfections on tag and/or control are caused in under- or over-estimations of the perfusion measurement in the human brain.[4,5] One proposed way to improve the perfusion measurement was by increasing both the RF power B_1 and the gradient strength G_1.[6] However, the increase of G_1 is limited by the tagging width in pulsed ASL labeling methods, for examples, echo-planar imaging (EPI) and signal targeting with alternating RF (EPISTAR),[7] flow- sensitive alternating inversion recovery (FAIR),[8,9] proximal inversion with a control for off-resonance effects (PICORE),[10] transfer insensitive labeling technique (TILT),[11] and double inversions with proximal labeling of both tag and control images (DIPLOMA).[3] Therefore, the most effective case for

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improving the perfusion signals may be related to adjusting the amplitude of the B1 of the HS inversion pulse to produce the total inversion with a nice slice profile. To increase tagging efficiency of a HS inversion pulse, the pulse duration can be made relatively short to minimize relaxation effects.[4] Previously, Edelman RR and Chen Q used 360° HS pulse to generate adiabatic double inversions. However, the transit bandwidth of the pulse was wide and the corresponding slice profile was degraded. The first goal of this study, therefore, was to make an adiabatic HS inversion pulse to improve the slice profile and inversion efficiency.

Because of tiny perfusion signals (about 1~2%) at 1.5 Tesla MRI, the perfusion measurement needs to repeat the increasing signal intensities by average. To minimize inter-scan movements of subjects, the perfusion measurement is also performed on an interleaved way. The second major limitation to measure perfusion accurately using an ASL-MRI is residual magnetizations.[12] During the interleaved scan with a short repeated time, both transverse and longitudinal magnetizations may still be existed between repeating acquisitions and perfusion values without suppressing the residual magnetizations, therefore, could over- or under-estimate. The contributions of the residual magnetization should be minimized on an ASL method. The second goal was to investigate the application of saturation pulses and/or spoiler gradients to suppress the residual magnetization.

The third major problem of an ASL method is an arterial transit time,[13] which is the time that the tagged blood is flowing into the imaging voxel. In order to obtain PWI, we separated a tagged region and an imaging region. The distance between two regions was called as a gap between a tagged plane and an imaging plane. The ideal way to measure perfusion using the ASL-MRI is without using the gap. In practically, however, the gap is necessary because slice profiles of inversion pulses and excitation pulses are not perfectly squared. The arterial transit delay can cause under-estimations in perfusion. Although this time can be measured in a human brain, it takes a long time to measure repeating different inversion times. It is impractical to apply it in all clinical patients. To minimize the transit delay time, the gap has to be as short as possible because this time is introduced to perfusion errors in the human brain. Also, the gap is depended on the applied inversion pulse. Whenever a new inversion pulse is developing, an optimum gap should be found to minimize the arterial transit time. The third goal, therefore, was to find an optimum gap to minimize the arterial transit time and to minimize the influence of the applied RF pulses in PWI data. The overall goal of this study was to understand the practical problems of the pulsed ASL and to make the pulsed ASL parameters for multi-slice perfusion imaging in the human brain.

MATERIALS AND METHODS

1. Slice profiles of the adiabatic HS inversion pulse

To improve the slice profile and inversion efficiency, a high power of an adiabatic HS pulse was designed, but the maximum power of the HS pulse was limited by the MRI system. Simulations of longitudinal magnetization with respect to different flip angles were performed by using the MATPULSE program[14] to show slice profiles and tagging efficiency. Two parameter sets were used: one parameter set was chosen from the Reference,[15] which is popularly used in perfusion measurements with two different low powers of adiabatic HS pulses (360° HS pulse). Another parameter set was obtained from an optimum HS pulse (900° HS pulse) designed by the author in this study using the MATPULSE program to use the current work for the tagged and the control pulses. Longitudinal magnetizations of three different powers (180°, 360°, and 900°) of adiabatic HS pulses were compared to show the slice profile of the pulse and achievements of inversion. To demonstrate the improvement of the slice profile, we measured the transit bandwidths for the three adiabatic HS pulses.

2. Minimizations of the residual magnetization

To evaluate residual magnetization effects,[12] a water phantom was used with 5 mm of a single slice and a 25 mm gap between the tagged plane and the imaging plane to get rid of effects in the slice imperfections in the tagged and/or control RF pulses. A cylindrical plastic bottle (diameter=12 cm and height=18 cm) was filled by tap water with doping by 0.89 mMol/liter of copper sulfate to maintain T_1=1,224.4±6.5 ms for a large water phantom.[16] The T_1 value was reasonable to demonstrate tissue T_1 in the human brain. Four different experiments were performed by turning on and off the spoiler gradients and/or saturation pulses, which were located at between tagged and control acquisitions, as

1) No saturation pulses and spoiler gradients between the interleaved acquisitions for using a reference image.

2) Only with spoiler gradients.

3) Only with saturation pulses.

4) Both saturation pulses and spoiler gradients.

Two saturation pulses were applied on an imaging region by a Sinc pulse of 2.56 ms durations. Spoiler gradients were applied on three axes with 10 mT/m of the gradient amplitudes and 20 ms of durations. Four experiments for the above four conditions were run by the same parameters except the four conditions. Percent signal changes with respect to reference image (experiment A) were evaluated in tagged and control images for each experiment to demonstrate suppression of residual signals.

3. Optimizing the gap between the tagged plane and the imaging plane

To get the optimized gap between the tagged plane and the imaging plane, the water phantom was primarily used. With a fixed slice position, the tagging position was moved further from 5 mm to 25 mm gaps with 5 mm intervals. Total 5 slices with 2 mm gaps between slices were scanned. In the most proximal slice of subtraction images, the average signal and its standard deviation were measured at noise regions and phantom regions. The Z-score, $(S_{noise}-S_{phantom})/STD_{noise}$, analysis was performed to further evaluate the statistical difference between the noise and phantom regions. The noise signal and its standard deviation were measured from the outside of the objects.

4. Perfusion measurements in the human brain

Thirteen healthy volunteers with mean ages of 45 years old with standard deviations of 14 years (range 29 to 64 years) were studied to test overall performances of the optimized parameters. An official consent form approved by the Committee on Human Research at the University of California in San Francisco VA Medical Center was used for all subjects. The protocols for this study were following after scout images. T1-weighted scan with the sagittal plane to set up the position of the PWI sequence; T1-weighted with transverse plane to obtain anatomical information; perfusion measurements by DIPLOMA.[3] The transverse T1-weighted scan was set to the same slice positions as the perfusion measurement. Five slices were acquired with 8 mm slice thicknesses and 2 mm gaps between slices. An oblique slice orientation was used to minimize susceptibility artifacts on the frontal region of brain. Perfusion values were averaged in all subjects per each slice to demonstrate perfusion uniformities across slices.

5. Overall structures of the PWI sequence

An optimized DIPLOMA with the QUIPSS II with thin-slice TI1 periodic saturation (Q2TIPS) sequence[3] was applied to obtain perfusion images in the phantom and the human brain studies. Detailed explains of the overall structure of the perfusion sequence were published in elsewhere.[3] Simply, the PWI sequence was: First, two pre-saturation pulses (Sinc with 2.56 ms durations) at the imaging region were applied to reduce the subtraction errors of static tissues. Second, the HS tagged/control pulse designed in this study was applied to label in-flowing blood at the inferior to the imaging region. Third, after the first labeling delay time (TI1), fourteen periodic saturation pulses were applied on the tagged and the control regions to saturate the tail of the tagged region in order to provide a sharp edge of tagged blood (20 mm widths and 2.56 ms durations for each Sinc pulse).[17] Fourth, after the second delay time (TI2), an excitation pulse was applied to obtain images with EPI acquisitions. Finally, two saturation pulses with spoiler gradients on an in-plane region were also applied in right after data acquisitions to fast dephase remainder spins in the in-plane region investigated in this study.

In all phantom study, imaging parameters were used in $TR/TE/TI_1/TI_2$=2,500/15/780/1,500 ms with exciting slices on the descending order, 48×128 of matrix, 280 mm of the field of view (FOV), 30 of averages, and 90 mm of the tagged width. The saturation width was 20 mm of the periodic saturation and 60 mm of the in-plane saturation. In the human brain study, the measurement parameters for the perfusion measurement were the same as the phantom study except 60 averages. Other sequence parameters, which were the HS inversion pulse, the saturation pulses and spoiler gradients, and the gap distance, were used from the optimized results of the current study. All experiments were performed on a 1.5T MR system, equipped with actively shielded gradients (Siemens Vision, Erlangen, Germany). A circularly polarized head coil was used for RF transmissions and signal receptions. In order to obtain PWI images from the control and the labeled data, a prost-processing was performed with home-built software using the MATLAB program (The MathWorks Inc, Natick, USA). The labeled image was subtracted from the control image in voxel-by-voxel pattern.

RESULTS AND DISCUSSION

1. Slice profiles of the adiabatic HS inversion pulse

Fig. 1 shows the slice profiles of the HS pulses with different flip angles. The HS pulse with 180° of flip angles was bad inversion efficiency. The HS pulse with 360° of flip angles was relatively better inversion efficiency than that of 180° flip angles, but was still bad, which looked like the saturation pulse. Note that two different flip angles had different slice profiles. The transit bandwidths of the pulse, which is explained in the slice profile of the pulse, were 483 Hz, 713 Hz, and 575 Hz for the flip angles of 180°, 360°, and 900°, respectively. Although the transit bandwidth of the 180° pulse was smaller than that of the 360° pulse, the inversion efficiency of the 180° pulse was so poorer than that of the 360° pulse. The transit bandwidth of the 900° pulse was narrower than that of the 360° pulse. Therefore, the mismatch

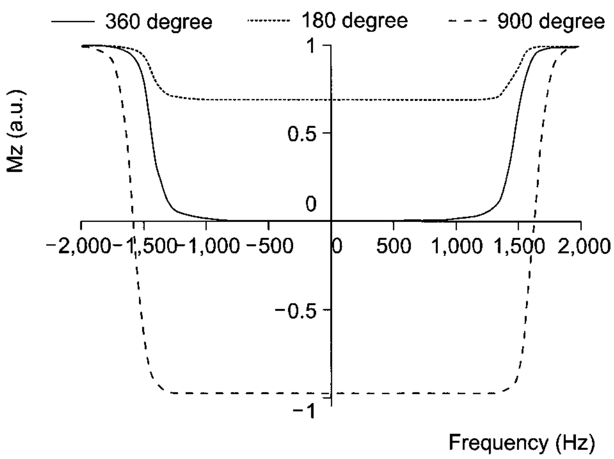

Fig. 1. Slice profiles of the adiabatic hyperbolic secant inversion pulse with different radio-frequency powers. Data were used from the multi-slice EPISTAR arterial spin labeling method proposed by Edelman et al[15] for 180° and 360° and used from the current work for optimizations of the pulse for 900° flip angle.

between two pulses can be affected on errors of perfusion measurements, which were used in EPISTAR.[15] The HS pulse with 900° of flip angles showed a nice inversion and a good slice profile. Therefore, the optimum flip angle used in this perfusion measurement in the human brain was used on 900°, which were provided in the total inversion with the minimum power. The increased power by increasing the flip angle was provided in a better slice profile, but the maximum power was limited in the MR system. The parameters for the HS pulse in the phantom and subject studies were 12.8 ms of the pulse duration, 2 kHz of the bandwidth, 10 of the side-to-width parameter (μ), 630/s of the pulse bandwidth factor (β), 14 μT of the RF field strength (B_1) with 900° of the flip angle, and 0.41 mT/m of the magnetic field gradient (G_1) in the 90 mm wide tagged regions. With the good slice profile, the slab position for tagged and control pulses can be designed as close in the imaging region as possible without interactions of the imaging pulse.[4] To minimize the MT effect on PASL, the inversion pulse has to be the same power and the same polarity for the tagged and the control pulses like as PICORE[10] and DIPLOMA.[3]

2. Minimizations of the residual magnetization

Table 1 lists the experiment results of minimizing the residual magnetization on the water phantom expressed by the percent signal suppression on tagged and control images. Applications of spoiler gradients only were not enough to suppress the residual magnetization. However, applications of two saturation pulses only[12] were good to minimize residual signals, which were about 13% suppressed on tagged and control images. However, we found from this study that the

Table 1. The experiment results of minimizing the residual magnetization on the water phantom expressed by the percent signal suppression.

Experiments	Tagged images	Control images
Spoiler only	−0.07%	−0.03%
SAT only	12.94%	13.07%
SAT and spoiler	13.14%	13.17%

a. Percent signal changes were calculated from the reference image, which was measured without using a spoiler gradient and a saturation pulse, b. SAT stands for a saturation pulse.

best results were gotten from applying two saturation pulses with spoiler gradients to suppress the transverse and longitudinal residual magnetizations, which were applied on the current optimum PWI sequence. When the interleaved scan is used to measure perfusion, it is clear to apply some saturation pulses to minimize interferences of the residual magnetization.

3. Optimization of the gap between the tagging plane and the imaging plane

Fig. 2 shows the results of gap effects in perfusion signals in the most proximal slice, which was the closest slice on the tagged plane, expressed by the Z-scores. The Z-score was very high at the 5 mm and 10 mm gaps in the water phantom. However, the Z-scores at the 20 mm gap were as low as the noise level. Further increasing the gap was not affected on reducing the Z-score. Therefore, the optimum gap used in this perfusion measurement in the human brain was 20 mm, which was provided in the minimum gap between the imaging plane and the tagged plane. Further increasing the distance has no advantage because the arterial transit time can be increased in the human brain.[13)]

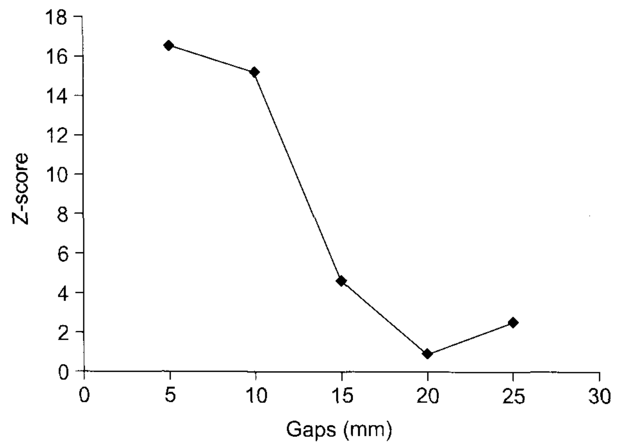

Fig. 2. The optimal gap between the imaging plane and the tagged plane in a water phantom. At the most proximal slice, the Z-score was calculated by using $(S_{noise}-S_{phantom})/STD_{noise}$. The noise signal and its standard deviation were measured from the outside of the objects.

The bandwidth, the slice profile, and the power of the HS pulse are affected on determining the minimum gap. The larger the bandwidth, the larger the gap because the most proximal slice can be affected by the pulse. The frequency offset of the inversion pulse must be greater than the half-bandwidth of the pulse plus the transition band of the pulse. The good slice profile with the sharp transition can be advantages with a small gap. Therefore, when a new labeling pulse is designed to use perfusion measurement, it is important to measure the corresponding minimal gap to minimize the arterial transit time in human study.

4. Perfusion measurements in the human brain

A representative set of PWI in a subject is shown in Fig. 3. The top row is T_1 weighted images to show anatomical information and the bottom row is PWIs. Fig. 4 shows

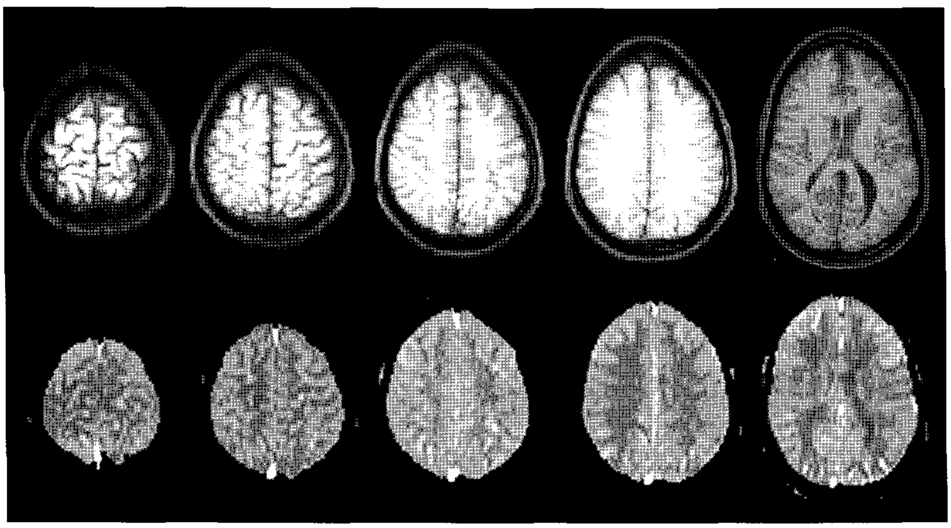

Fig. 3. A representative set of perfusion weighted images in a subject. The top row is the high resolution FLASH images and the bottom row is the corresponding perfusion weighted images.

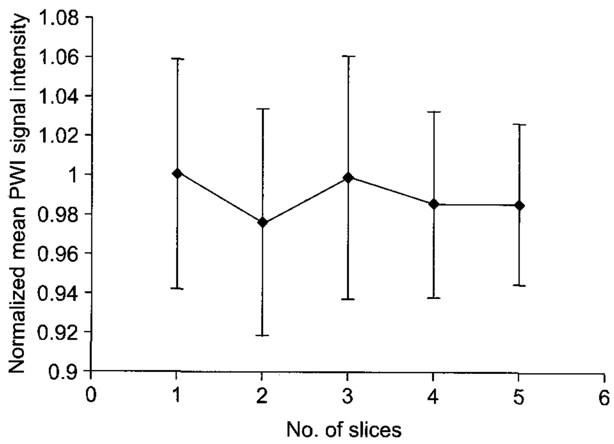

Fig. 4. Variations of mean signal intensities of perfusion weighted images in five slices averaged on 13 subjects. Signal intensities of the second to fifth slices were normalized by the signal intensity of the first slice. The error bars were used from the standard deviations for each slice in thirteen subjects. Slice 1 was the most distal slice (top of head) and slice 5 was the most proximal slice (bottom of head).

variations of mean signal intensities of PWI in five slices averaged on 13 subjects. Signal intensities of the second to fifth slices were normalized by the signal intensity of the first slice. The error bars were used from the standard deviations for each slice in thirteen subjects. Slice 1 was the most distal slice (top of head) and slice 5 was the most proximal slice (bottom of head). Variations of mean PWI signals of 5 slices were less than 3%. Excellent uniformities across slices can be achieved by the DIPLOMA labeling method. The previous study showed that variations of perfusion signals between slices were depended on the tagged method.[3] Perfusion signal intensities at the most proximal slice was especially varied in the PICORE ASL method and overall slice uniformities were worst in the EPISTAR ASL method.[3]

CONCLUSION

In conclusions, the good slice profile and the inversion efficiency of the tagged and control pulses were required to obtain reliable perfusion images and to minimize the distance between the imaging region and the tagged region. To minimize contributions of the residual magnetization between interleaved scans, combinations of the saturation pulse and the spoiler gradient were recommended. The gap between the tagged plane and the imaging plane needed to measure at least in a phantom and to optimize before using in the human brain. With using optimum parameters and the optimum perfusion sequence, high qualities of perfusion images can be obtained with an excellent contrast and uniform signal intensities across slices in the human brain. This must be helpful to obtain perfusion images in clinical patients, such as Alzheimer's disease or other types of dementia.

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스핀 라벨링 자기공명영상을 이용한 사람 뇌에서의 뇌 관류영상의 현실적 문제점을 향상 시키는 방법 연구

경희대학교 의과대학 동서신의학병원 영상의학교실

장 건 호

본 연구의 목적은 비침습적 동맥스핀라벨링(arterial spin labeling) 자기공명영상을 이용하여 다편(multislice) 뇌 관류영상(perfusion-weighted images)을 얻을 수 있는 최적화 방법을 연구하는 데 목적이 있다. 본 연구에서는 세가지 인자를 최적화하는 데 초점을 두었다. 첫째, 뇌로 흘러 들어오는 혈액을 최적으로 라벨링할 수 있는 펄스를 만드는 것이다. 시뮬레이션 결과 900도의 각을 이루는 반전펄스(adiabatic hyperbolic secant inversion pulse)는 반전을 효과적으로 할 수 있고 반전을 이루는 형태가 직각에 가깝게 할 수 있는 최적이었다. 둘째, 영상을 얻고 난 후에 계속하여 남아있는 자화(residual magnetization)을 최소화하는 것이다. 이를 최소화하기 위해서는 포화 펄스(saturation pulses)와 자화를 손상 시키는 자장(spoiler gradients)을 동시에 사용하는 것이 최상의 방법임을 알았다. 마지막으로, 라벨링하는 영역과 영상을 얻는 영역 사이의 거리를 최소화할 수 있는 방법을 연구하였다. 두 영역 간의 최소 거리는 약 20 mm 정도가 최적임을 발견하였다. 위에서 얻은 최적화된 인자들을 바탕으로 13명의 정상인의 뇌에서 관류 영상을 얻은 결과 매우 좋은 대조도의 영상을 얻을 수 있었다.

중심단어: 동맥스핀라벨링, 뇌관류, 자기공명영상, 사람의 뇌, 최적화