Improved Perfusion Contrast and Reliability in MR Perfusion Images Using A Novel Arterial Spin Labeling

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ASTRACT

Neurodegenerative disorders, like Alzheimer's disease, are often accompanied by reduced brain perfusion (cerebral blood flow). Using the intrinsic magnetic properties of water, arterial spin labeling magnetic resonance imaging (ASL-MRI) can map brain perfusion without injection of radioactive tracers or contrast agents. However, accuracy in measuring perfusion with ASL-MRI can be limited because of contributions to the signal from stationary spins and because of signal modulations due to transient magnetic field effects. The goal was to optimize ASL-MRI for perfusion measurements in the aging human brain, including brains with Alzheimer's disease. A new ASL-MRI sequence was designed and evaluated on phantom and humans. Image texture analysis was performed to test quantitatively improvements. Compared to other ASL-MRI methods, the newly designed sequence provided improved signal to noise ratio improved signal uniformity across slices, and thus, increased measurement reliability. This new ASL-MRI sequence should therefore provide improved measurements of regional changes of brain perfusion in normal aging and neurodegenerative disorders

Keywords: Perfusion, blood flow, Alzheimer's disease, texture analysis, reliability

1. INTRODUCTION

Neurodegenerative disorders, like Alzheimer's disease are often accompanied by reduced brain perfusion (cerebral blood flow) [1][2]. Using the intrinsic magnetic properties of water, arterial spin labeling magnetic resonance imaging (ASL-MRI) can map brain perfusion without injection of radioactive tracers or contrast agents [3]. Several pulsed ASL (PASL) methods, including EPISTAR (echo-planar imaging and signal targeting with alternating RF) [4] and PICORE (proximal inversion with a control for off-resonance effects) [5] have been proposed to measure cerebral perfusion. However, perfusion measurements with ASL-MRI can be complicated by two major problems: 1) Stationary spins can also contribute a signal, increasing background noise in perfusion images. 2) Transient magnetic fields, induced by pulsed magnetic field gradients, can modulate the perfusion signal, resulting in measurement errors [6]. The first goal of this study was therefore to design a sequence for PASL that eliminates these problems. Most previous experimental comparisons of perfusion methods relied either on visual inspections of perfusion images or on first order statistics, such as mean intensity and standard deviations [5][7][8]. However, visual inspections are subjective and difficult to quantify and first order statistics is limited in reflecting the complexity of perfusion images. Therefore, the second goal was to test improvements of the PASL sequence using quantitative first and second order image texture analysis [9]. Reliability of ASL-MRI measurements is a critical issue in evaluating longitudinal and cross-sectional perfusion studies. Therefore, the third goal was to determine reliability of perfusion measurements with the new PASL method. Part of this data was presented at the 10th international meeting of the society of magnetic resonance in medicine (ISMRM) in Honolulu [10].

2. METHODS

2.1. Sequence Design

A diagram of the proposed method for PASL is sketched in Figure 1A. The new PASL sequence was doubted double inversion with proximal labeling of both tagged and control images (DIPLOMA). Tagging of blood protons (Tag in Fig.1) proximal to the PWI slices is accomplished by an off frequency inversion pulse ($\alpha_{off}=5\pi$), followed by a slab

selective inversion pulse (α=5π). A control scan (without tagging, Control in Fig.1) is achieved by applying two slab selective inversion pulses (α=5π). Subtraction of tagging and control scans yields perfusion images. Because the corresponding RF pulses in tag and control scans have identical flip angles (α=5π), slice profiles are the same and contributions of stationary spins should cancel out upon subtraction of tagging and control scans. In addition, slab-selective gradients are being used in both tagging and control scans to balance eddy-current effects. The perfusion imaging scheme (Fig. 1B) and the overall sequence (Fig. 1C) are also schematically shown in Fig. 1. . For comparisons, two previously proposed PASL schemes, EPISTAR[11] and PICORE[12], were incorporated into the same sequence structure.

2.2. Phantom Experiments to reduce noise from stationary spins

To compare the abilities of DIPLOMA, PICORE, and EPISTAR in canceling out signals from stationary spins due to magnetization transfer (MT) effects, experiments were performed on a 3% agarose phantom[13] with inversion pulses for spin tagging turned off in the reference mode and turned on perfusion imaging mode (PWI mode). Here, reference mode refers to turn off both tagged and control pulses to obtain reference signal and standard deviation in subtraction image. Differences in image intensity between experiments were expressed relative to the mean image intensity in reference mode (S_{ref}) and transformed into a Z score, according to $(S_{pwi}-S_{ref})/STD_{ref}$, where STD_{ref} is the standard deviation of the image intensity in the reference mode.

2.3 Texture Analysis and Reliability of Human Brain Perfusion Studies

In order to determine the improvements of DIPLOMA for perfusion studies of human brain, image texture analysis and reliability tests were performed on perfusion data from thirteen healthy volunteers (mean age: 45 ± 14 years, 29 to 64 years range, 9 women, 4 men). Volunteers were scanned using all three PASL schemes (DIPLOMA, EPISTAR, PICORE), while the rest of PWI sequence parameters were kept identical. Following an initial scout scan for anatomical orientation, PWI acquisitions with PICORE, EPISTAR, and DIPLOMA, were performed in rapid succession in a single session. Scans were repeated on each volunteer after approximately 30 minutes with the same conditions to evaluate reliability of perfusion measurement. Imaging parameters were used in TR/TE/TI_1/ TI_2 =2500/15/780/1500 ms with exciting slices on the descending order, 48x128 of matrix, 280mm of FOV, 60 of averages, and 90mm of tagging width. The saturation width was 20mm of Plane 3 and 60mm of Plane 1 in Fig. 1B. Quantitative assessment of PWI data was accomplished by image texture analysis using first order (Mean Signal intensity (MSI), Coefficient of variation of signal intensity (COVSI)) and second order (Contrast, Entropy, Correlation, Angular second moment (ASM)) statistical features. Differences between the tagging techniques were tested using ANOVA with image textures as dependent and tagging method as independent variables. Reliability tests were performed by relating variability of perfusion between subjects to within subject variations by means of an intra-class correlation coefficient (ICC)[14]. 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 transmission and signal reception.

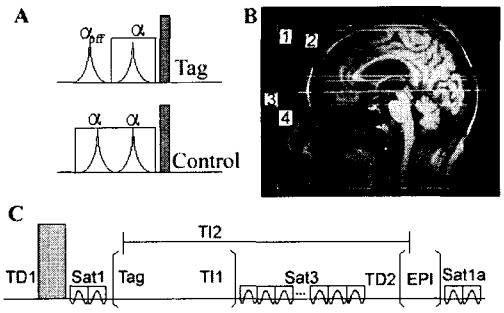

Fig. 1. The DIPLOMA tagging method and multi-slice perfusion MRI. Tagging and control method (A), perfusion imaging scheme (B), and entire perfusion sequence (C). Plane 1=Sat1 and Sat1a, Plane 2=EPI, Plane 3=Sat3, and Plane 4=Tag

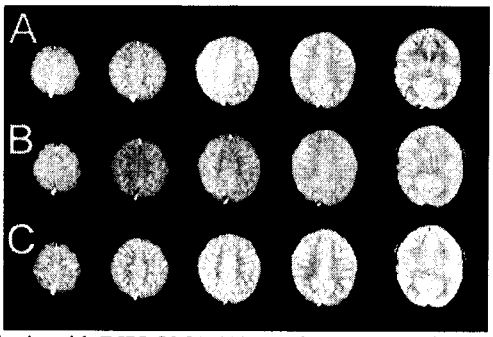

Fig. 2. Representative sets of PWI data obtain with DIPLOMA (A), EPISTAR (B) and PICORE (C) on a volunteer (Female, 28 years old). Images were scaled to the same brightness for better comparison.

3. RESULTS AND CONCLUSIONS

3.1. Phantom Experiments

Results from the phantom experiment for reduction of MT effects are listed in Table 1. Compared to the other PASL schemes sequences, DIPLOMA achieved the best MT compensation with the lowest MT noise.

3.2. Texture Analysis and Reliability

Representative sets of PWI data from a volunteer obtain with DIPLOMA (A), EPISTAR (B) and PICORE (C) (Female, 28 years old) are shown in Figure 2. Images were scaled to the same brightness for better comparison. This shows a higher perfusion contrast in regions of gray matter and white matter with DIPLOMA than with the other PASL methods. Results from an image texture analysis of PWI data from 13 volunteers are listed in Table 2. This shows that mean intensity of perfusion images increased by about 8% and contrast increased by about 23% with DIPLOMA compared to EPISTAR. PICORE yielded similar values for mean intensity and contrast than DIPLOMA. Uniformity across slices improved with DIPLOMA by 1.04 from 3.74 and 5.85 with comparing EPISTAR and PICORE, respectively, measured by a coefficient of variation (CoV = standard deviation divided by the mean intensity from 5 slices). Finally, measurement reliability was best for DIPLOMA, achieving an ICC of 0.92 compared to an ICC of 0.73 for EPISTAR and 0.82 for PICORE. In conclusion, pulsed arterial spin labeling using DIPLOMA improved compensation of magnetization transfer effects without sacrificing tagging efficiency, yielding especially a higher image contrast for perfusion images than previously published PASL methods. The new PASL scheme should improve accuracy of perfusion measurements with MRI, including improved differentiation between gray matter and white matter perfusion. This is of particular importance for studies of regional changes of cerebral perfusion[15] in normal aging and neurodegenerative disorders, such as Alzheimer's disease and other dementias, without requirement for radioactive tracers.

Table 1. Magnetization transfer (MT) effects for different PASL schemes measured on an agarose phantom expressed by Z-score.

PASL	Tagging $\Delta\omega$	PWI mode
DIPLOMA	550 Hz	1.1
EPISTAR	550 Hz	6.1
PICORE	550 Hz	3.8

$\Delta\omega$ = Frequency offset;
PWI mode (S_2) := MT measurements with tagging and control pulses *both on*

Table 2. Comparison of perfusion weighted images obtained with different PASL methods on 13 volunteers using first and second orders of texture analysis

FEATURE	DIPLOMA	EPISTAR	PICORE	DE (%)	DP (%)
MSI [a]	1.00 ± 0.05‡	0.92 ± 0.06	1.01 ± 0.08	**8**	1
COVSI	0.14 ± 0.03†‡	0.11 ± 0.03	0.18 ± 0.05	**21.4**	**-28.6**
Contrast	187 ± 126‡	144 ± 81	186 ± 129	**23**	0.5
Entropy	2.88 ± 0.15†	2.86 ± 0.13	2.83 ± 0.15	0.7	**1.7**
Correlation	0.63 ± 0.06	0.65 ± 0.07	0.64 ± 0.07	-3.2	-1.6
ASM	1.81 ± 0.87†	1.86 ± 0.72	2.08 ± 0.95	-2.8	**-14.9**

[a] MSI = Mean signal intensities, normalized to MSI of DIPLOMA;
[b] COVSI = Coefficient of variation of signal intensity;
[c] ASM = Angular second moment;
Data are means and standard deviations of 13 subjects and 5 slices per subject. Values of 2nd order textures (Contrast, Entropy, Correlation, ASM) are the average from 4 directions in the image plane (0°, 45°, 90°, 135°).
Difference in image textures between DIPLOMA and EPISTAR (DE) and between DIPLOMA and PICORE (DP) in percent relative to DIPLOMA;
† $p \leq 0.008$ Diploma vs. PICORE; ‡ $p \leq 0.008$ Diploma vs. EPISTAR

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