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ADVANCING ARTERIAL SPIN LABELING TOWARDS CLINICAL USE

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Abstract
Arterial Spin Labeling is an MR imaging method to non-invasively and quantitatively measure perfusion. Problems like long scan times and motion sensitivity prevent it as of yet from being in clinical use. We present a novel data acquisition sequence and reconstruction method for ASL to overcome these challenges. The introduced 3D GRASE sequence with time-dependent CAIPIRINHA undersampling pattern allows faster, single-shot imaging. The novel second—order, spatio-temporal TGV constraint in the reconstruction produces a better Signal-to-Noise ratio from fewer measurements by denoising the images. Both novel methods improve upon the motion sensitivity of ASL. Given all this progress, ASL becomes closer to being in clinical use.

Keywords— *MRI, Arterial Spin Labeling, Quantitative Imaging*

Introduction

MR Imaging is an invaluable tool in today's clinical environment. In many situations, an MR scan is the optimal path towards diagnosis or disease monitoring. Novel MRI methods are capable of measuring additional physiological parameters for supporting clinical diagnosis or treatment decisions. One of these techniques is Arterial Spin Labeling (ASL) which allows the non-invasive quantification of perfusion in organs. In contrast to other perfusion measurements (e.g. PET, DSC, DCE), ASL does not use an exogenous tracer, but magnetically labels blood flowing into the organ. The non-invasiveness of the procedure and the possibility of absolute quantification of perfusion makes it highly suitable for repeated measurements and longitudinal studies.
ASL works by acquiring a set of two images, a so-called 'label image' where the inflowing blood of the organ is magnetically labeled with special preparation pulses and a 'control image' without preparation. By calculating the difference between these two images, the signal from the static tissue cancels while the signal from the inflowing labeled blood remains. Through a physiological model, quantitative perfusion values can be calculated [1]. ASL was shown to yield promising results in stroke, arteriovenous malformation and tumor studies as early as 2000 [2]. The continued importance of ASL is shown by a recent consensus paper from the ISMRM study group summarizing state-of-the-art methods and recommending imaging procedures [3].
However, ASL faces many challenges before it can be adopted as a routine tool for clinical diagnosis. The perfusion signal is relatively small, leading to inherently low SNR. The intuitive solution, measuring multiple times and averaging, results in clinically unfeasible scan times and makes the scans prone to physiological noise (e.g. motion).

Methods

In this work we present and combine two novel methods that bring ASL beyond its current limitations and one step further into clinical routine. The first aspect to be addressed is the image acquisition. ASL images are commonly acquired with a multi-shot Gradient and Spin Echo (GRASE) or Stack-of-Spiral (SoS) sequence, where different parts of the data are acquired over several brief acquisition periods called 'shots' [3]. While this technique provides good SNR and image quality it is very susceptible to inter-shot motion which is a main source of physiological noise (see figure 1 below) [4].

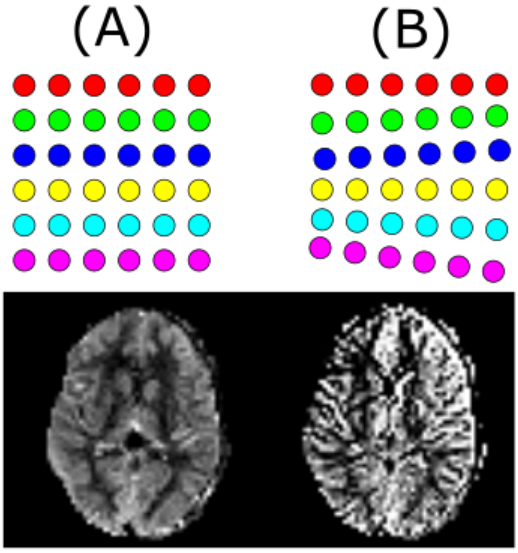

Figure 1: (A) A fully sampled, multi-shot acquisition of a 3D k-space of a stationary patient. Each dot represents one k-space line and each color represents one shot. (B) In case of motion between shots (here, rotation), the true coordinates of the acquired data do not align with the expected k-space coordinates [4]. Below the result of image acquisition of a stationary and a moving subject.

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To reduce the influence of inter-shot motion current recommendations [3] propose parallel imaging with acceleration factors of up to 3. This allows the acquisition of the k-space in two shots, which improves motion robustness but is insufficient for patients (e.g. stroke) who often move involuntarily. To overcome this limitation we developed a GRASE [6] sequence (see figure 4) whose acceleration can be increased up to 6 by using a time-dependent CAIPIRINHA undersampling pattern [5] (see figure 2), allowing a single-shot acquisition of each time frame. [11]

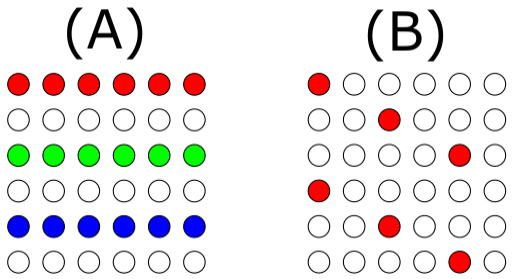

Figure 2: Comparison of GRAPPA and CAIPIRINHA undersampling patter: (A) 2x1 GRAPPA acceleration. (B) 1x6 CAIPIRINHA acceleration with a shift of 2

The developed time-dependent CAIPIRINHA pattern brings together the acceleration of common parallel imaging techniques like GRAPPA or SENSE while introducing additional spatial and temporal incoherence which is advantageous in the reconstruction. Also, over the course of several images a full dataset is acquired allowing easy calculation of coil sensitivities (see figure 3) which are needed in the reconstruction process.

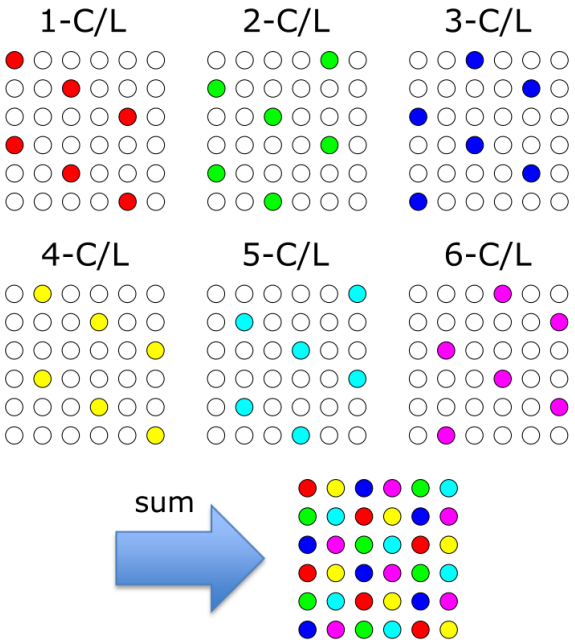

Figure 3: A time-series of 6 k-spaces with a 1x6(2) time-dependent CAIPIRINHA acceleration. Over the course of the series a full k-space is acquired. Still, a full image can be reconstructed from each undersampled k-space.

The readout sequence, GRASE, improves upon Echo-Planar Imaging (EPI). Over the course of any MR data readout, the signal decays due to T2 relaxation. The longer the readout lasts, the stronger is the decay. This decay leads to blurring in the image [7]. During an EPI readout, the signal decay happens with time constant T2*. In a GRASE sequence, EPI is combined with a Turbo-Spin Echo (TSE). This leads to a signal decay with a mix of time-constants T2* and T2, which is longer than T2*. This allows more data to be acquired while keeping the blurring at the same level.

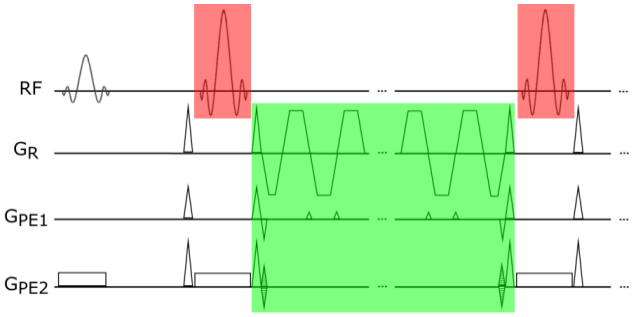

Figure 4: The GRASE readout of the sequence diagram. Prior to the shown section, a pulsed Continuous Arterial Spin Labeling (pCASL) [8] labeling module is applied in combination with background suppression pulses to improve SNR. In the shown section, a 3D slab is excited. Then, the TSE refocusing pulses reverse signal losses due to field inhomogeneities (red). In between two refocusing pulses, an EPI readout occurs (green). The shown section is repeated several times. The number of refocusing pulses and the length of the EPI readout determine how many lines of k-space are measured per shot.

The second aspect of the ASL process to be improved is the image reconstruction. As a baseline, the new, accelerated sequence necessitates parallel imaging reconstruction algorithms. In theory, this would suffice to get the images. Here, a second-order, spatio-temporal Total Generalized Variation (TGV) [9] regularization is added to constrain the reconstruction process for the control, the label and the difference images simultaneously [11]. TGV is a powerful regularization tool which enforces piecewise smooth images which has been shown to be an appropriate choice for MR image reconstruction [10]. All images are reconstructed simultaneously. Sparsity in both the spatial and temporal dimensions are exploited with TGV which inherently denoises the reconstructed images. The full reconstruction problem is stated in equation (1):

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$$(c^*, l^*) \in \operatorname{argmin}_{c,l} \frac{\lambda_c}{2}||Kc - d_c||_2^2 + \frac{\lambda_l}{2}||Kl - d_l||_2^2 + \gamma_1(w)TGV(l) + \gamma_1(w)TGV(c) + \gamma_2(w)TGV(c - l) \quad (1)$$

In equation (1) λ and ɣ are weighting parameters, *c* and *l* are the control and label images, K is the forward Operator from image space to the measurement space and *d* refers to the measured data. The definition of TGV can be found in [9].

To test this novel acquisition and reconstruction method data was acquired in-vivo to compare it to fully sampled multi-shot acquisitions. 5 healthy, consenting volunteers were measured on a 3T MR system (Prisma, Siemens Healthcare, Germany). All measurements were done using a pCASL sequence with a 3D-GRASE readout, once using 6 shots for a fully sampled acquisition and once using the above described CAIPIRINHA acceleration for single-shot acquisition. The parameters were: FOV: 200x200 mm^2, matrix: 64x64x38 voxels, 3.1x3.1x3 mm^3 resolution, 20% slice oversampling, TE/TR: 15/4100, EPI-factor: 21, Turbo-factor: 23, 180° refocusing pulses, labeling duration: 1800 ms, Post-Labeling Delay: 1800 ms. This results in an acquisition time of 4.5 min for 5 control/label pairs and one proton density image for the fully segmented acquisition. All scans were done with the patients being asked to remain still. For two volunteers the procedure was repeated with the subjects cued to move their head in a predetermined manner. All data was then reconstructed using equation (1). In post-processing, all images for each subject were registered to reduce motion artifacts in the averaging process, the perfusion weighted images were calculated and Cerebral Blood Perfusion (CBF) maps were created according to [3].

Results

Figure 5 shows a comparison between the motion-affected and the motion free data acquired with the standard multi-shot approach and the proposed single-shot method. The figure clearly shows visually that the multi-shot acquisition is much more prone to motion-induced errors than the accelerated single-shot sequence.

In figure 6, there is a comparison between the different acquisition types for different number of averages in. Visually, a significant noise increase is evident for the fully sampled image between 30 and 12 averages, especially in the white matter. For the novel acquisition and reconstruction method nearly the same image quality can be achieved although the acquisition time is reduced by more than half.

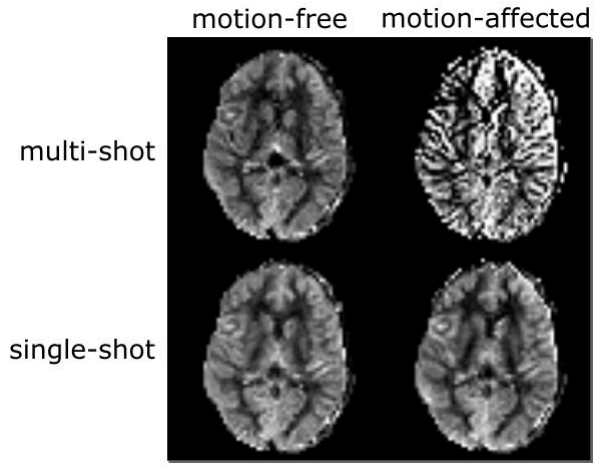

Figure 5: Comparing the effects of motion onto the CBF maps for the two tested acquisition methods.

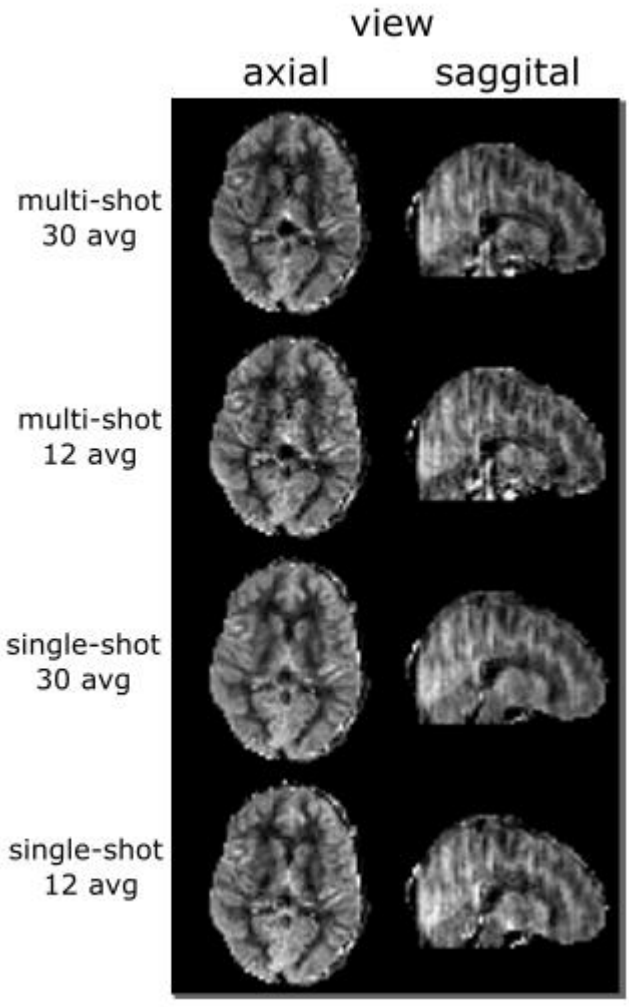

Figure 6: Comparison for a different number of averages for the two tested acquisition methods.

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A quantitative comparison confirms the visual analysis. The novel method increases temporal signal-to-noise ratio over the whole brain by 16% compared to the full acquisition. In addition the acquisition time can be reduced by a factor of 3 without the loss of information or image quality.

Discussion

The results show a clear improvement of the GRASE sequence with a time-dependent CAIPIRINHA pattern and TGV-constrained reconstruction compared to the recommended ASL acquisition as described by Alsop et al [3]. With this, the motion problem as well as the SNR problem are addressed.

With this new approach the current motion problems are reduced due to two factors. First, the single shot acquisition completely circumvents the problem of inter-shot motion. The only motion that can impact the data for one image is during the < 300 ms acquisition period. Second, the TGV constraints enforces smoothness in spatial and temporal directions. Thus, slight inconsistencies between subsequent images may be smoothed out in the reconstruction process.

The TGV constraint also reduces the problem of low SNR. Additionally, it allows the acquisition of less averages while maintaining details and image quality.

The proposed method is currently evaluated in simulations and patients with neurovascular diseases and compared to current gold standard methods.

Measuring perfusion non-invasively can be a great step forward in the clinical routine as well as in brain research areas e.g. for studying the neuronal activity in the human brain or for real-time interoperative guidance. Also, having increased the time resolution by a factor of 6, real-time ASL for psychological and neurological research becomes a possibility.

With the presented improvements ASL has come one step closer to a clinically, viable tool.

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