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Theoretical and experimental evaluation of multi-band EPI for high-resolution whole brain pCASL Imaging

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ABSTRACT

Multi-band echo planar imaging (MB-EPI), a new approach to increase data acquisition efficiency and/or temporal resolution, has the potential to overcome critical limitations of standard acquisition strategies for obtaining high-resolution whole brain perfusion imaging using arterial spin labeling (ASL). However, the use of MB also introduces confounding effects, such as spatially varying amplified thermal noise and leakage contamination, which have not been evaluated to date as to their effect on cerebral blood flow (CBF) estimation. In this study, both the potential benefits and confounding effects of MB-EPI were systematically evaluated through both simulation and experimentally using a pseudo-continuous arterial spin labeling (pCASL) strategy. These studies revealed that the amplified noise, given by the geometry factor (g-factor), and the leakage contamination, assessed by the total leakage factor (TLF), have a minimal impact on CBF estimation. Furthermore, it is demonstrated that MB-EPI greatly benefits high-resolution whole brain pCASL studies in terms of improved spatial and temporal signal-to-noise ratio efficiencies, and increases compliance with the assumptions of the commonly used single blood compartment model, resulting in improved CBF estimates.

Introduction

Arterial spin labeling (ASL) perfusion imaging makes use of arterial blood water as an endogenous tracer to estimate tissue perfusion and evaluate tissue viability (Detre et al., 1992). The non-invasive and non-contrast enhanced characteristics of ASL imaging make it an attractive approach for both neuroscience research and clinical applications (Detre et al., 1998; Detre and Wang, 2002). High-resolution studies are desired in order to reduce partial volume effects on cerebral blood flow (CBF) quantification, increase the ability to identify small focal lesions (Bokkers et al., 2012) and improve perfusion quantification in small sub-cortical structures such as the hippocampus (Li et al., 2011, 2013). However, obtaining high-resolution ASL based perfusion measurements is challenging due to the intrinsically low signal-to-noise ratio (SNR) and increased acquisition times when using standard acquisition strategies. Decreased perfusion SNR for high-resolution imaging is a consequence of multiple factors including; 1) increased in-plane resolution, 2) increased through-plane resolution and 3) the need for more slices to cover the same volume resulting in prolonged delay times between labeling and signal acquisition during which labeled spins experience longitudinal relaxation. The necessity of increasing the number of label/control image pairs for sufficient perfusion SNR greatly increases the total imaging acquisition time, thus limiting, if not prohibiting, the practice of acquiring high-resolution whole brain ASL perfusion data.

To overcome such challenges, different strategies have been previously proposed to increase perfusion SNR of ASL methods. Continuous arterial spin labeling (CASL) (Alsop and Detre, 1998), one of two major types of ASL methods, can provide better perfusion SNR than pulsed arterial spin labeling (PASL) (Kim and Tsekos, 1997; Wong, 2005), but requires a dedicated transmit/receive coil with the capability of continuous transmission of radiofrequency (RF) energy. More recently, an intermediate approach, pulsed- or pseudo-continuous arterial spin labeling (pCASL), has been shown to provide higher labeling efficiency than CASL without the need for a dedicated transmit/receive coil (Wu et al., 2007; Dai et al., 2008). The use of a body coil for RF transmission and a separate phased-array coil for signal reception makes pCASL amenable for applications on current clinical scanners. Therefore, pCASL has become the preferred ASL approach for whole brain ASL perfusion imaging (Alsop et al., epub ahead of print).

Abbreviations: ASL, arterial spin labeling; CBF, cerebral blood flow; EPI, echo planar imaging; FA, flip angle; FAIR, flow-sensitive alternating inversion recovery; FOV, field of view; GRAPPA, generalized autocalibrating partially parallel acquisitions; GRE, gradient recalled echo; LEADS, lead evaluation via acquired dummy slices; MB, multi-band; MPRAGE, magnetization prepared rapid acquisition gradient echo; MR, magnetic resonance; MRI, magnetic resonance imaging; PASL, pulsed arterial spin labeling; pCASL, pseudo-continuous arterial spin labeling; ROI, region of interest; SB, single-band; S.D., standard deviation; TE, echo time; TLF, total leakage factor; TR, repetition time.

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To increase the SNR of whole brain ASL imaging studies, 3D imaging methods have also been explored (Gunther et al., 2005; Dai et al., 2013). In this approach, a 3D slab, rather than a single slice, is excited by the RF excitation pulse. The excited spins are continuously refocused by using spin echo refocusing RF pulses between phase encoded slices and spatially encoded in plane with rapid k-space sampling strategies such as echo-planar imaging (EPI) (Gunther et al., 2005) or spiral (Dai et al., 2013) trajectories. Recently, to overcome the adverse T_2 blurring effects of 3D acquisition on perfusion imaging, alternative imaging acquisition strategies have been proposed and demonstrated (Gai et al., 2011; Tan et al., 2011; Nielsen and Hernandez-Garcia, 2013).

In contrast to 3D imaging methods, 2D EPI does not suffer T_2 blurring, but requires a longer total imaging acquisition time to cover the same volume. The imaging slices, typically acquired in an ascending slice order, experience widely varying post-labeling delay times, during which longitudinal relaxation of the labeled spins occurs. The total acquisition time is lengthened with increasing encoding matrices and slices as required in high-resolution whole brain studies. In such studies, the most inferior slices and superior slices are acquired at extremely short and long post-labeling delays, respectively. Short delay times have the potential problem of not allowing sufficient time for labeled spins to perfuse the target tissue and long delay times suffer from poor SNR. Particularly, the validity of the standard single-blood compartment model for CBF quantification can be compromised as the range of post-labeling delay times expands, which arises from using the T_1 of the blood for the longitudinal relaxation decay correction of the perfusion signal (Wang et al., 2003).

Multi-band imaging, or simultaneous multi-slice imaging, provides an attractive and alternative solution to reduce the total acquisition time of high-resolution whole brain imaging with 2D EPI, especially when increased spatial or temporal resolution is desired (Moeller et al., 2010; Setsompop et al., 2012b). Multi-band EPI imaging (MB-EPI) uses multi-banded radiofrequency (RF) pulses to simultaneously excite multiple spatially distributed slices, where the superimposed signals acquired from the multiple slices are unwrapped via anti-aliasing reconstruction. The simultaneous acquisition of multiple slices can greatly reduce total imaging acquisition time for whole brain applications with EPI, and particularly has the potential to improve whole brain ASL perfusion studies where high in-plane and through-plane resolution is desired, necessitating the use of a large number of thin imaging slices to achieve the desired coverage. MB-EPI has been successfully demonstrated in functional magnetic resonance imaging (fMRI) (Moeller et al., 2010) and resting state fMRI (Feinberg et al., 2010; Koopmans et al., 2012; Smith et al., 2012), showing improved detection of resting state networks, as well as diffusion-weighted imaging (DWI) (Feinberg et al., 2010; Setsompop et al., 2012a) for dramatic reductions in imaging time. As such, MB-EPI has become an essential data acquisition strategy for both fMRI and DWI in the Human Connectome Project (Van Essen et al., 2012).

MB-EPI has been recently demonstrated (Kim et al., 2013) and compared to 3D GRASE (Feinberg et al., 2013) for PASL perfusion imaging in the brain using flow-sensitive alternating inversion recovery (FAIR) (Kim and Tsekos, 1997). By using a standard low imaging resolution, these studies found that perfusion signal differences between single-band (SB) and MB-EPI are minimal. While an important initial finding, these studies did not explore the potential of MB-EPI on ASL imaging in high-resolution whole brain applications where the slice dependent effects become pronounced. On the other hand, MB-EPI introduces confounding factors that may reduce the reliability of CBF estimation, including spatially varying noise amplification as characterized by geometry factor (g-factor) due to slice-GRAPPA (generalized autocalibrating partially parallel acquisition) reconstruction (Robson et al., 2008) and leakage contamination resulting from imperfect anti-aliasing of simultaneously acquired multiple slices (Cauley et al., 2013; Xu et al., 2013). These potential confounding effects and their slice dependence were not directly and systematically investigated in the previous studies.

In this study, the potential benefits and confounding factors of MB-EPI for high-resolution whole brain ASL perfusion imaging are explored through both systematic experiments and theoretical simulations.

Materials and methods

MR imaging

Imaging studies were performed on a 3 T Siemens Trio whole-body scanner (MAGNETOM Trio, Siemens Healthcare, Erlangen, Germany). The body coil was used for RF transmission, and the Siemens 32-channel phased array head coil for signal reception. High-resolution 3D anatomic images were acquired by using an MPRAGE (magnetization-prepared rapid acquisition with gradient echo) sequence with 1.0 mm isotropic resolution after a multi-plane scout localizer. These high-resolution images were used as the reference to prescribe imaging slices for the following ASL studies.

MB-EPI pCASL sequence

The pCASL preparation modules used the balanced gradient approach (Wu et al., 2007; Dai et al., 2008) (Fig. 1a). The implemented pCASL EPI imaging sequence consisted of labeling/control RF pulse trains, post-labeling delay (PLD) and SB- or MB-EPI readout (Fig. 1b). MB-EPI image slices are divided into a number of groups or bands equivalent to the MB factor (Fig. 1c). Slices within each band can be collected in an ascending, descending or interleaved fashion, and slices across bands are acquired simultaneously in a spatially interleaved fashion. The applied MB-EPI method employed a blipped-CAIPI approach (Setsompop et al., 2012b) and aliasing constrained slice-GRAPPA algorithm to reduce leakage contamination (Cauley et al., 2013). In addition, a phase-scrambling strategy was applied for the MB RF pulses to reduce RF pulse peak power and/or duration (Goelman, 1997; Wong, 2012). The MB-EPI acquisition was preceded by a calibration scan for training the anti-aliasing reconstruction kernel without pCASL preparation. Additional EPI images could be optionally collected after the pCASL series with all RF pulses turned off for estimating thermal noise and calculating g-factor maps. Blipped CAIPI MB-EPI used a field of view (FOV) shift factor of 1/3, and MB-EPI reconstruction used a GRAPPA kernel size 5 for all studies.

To minimize B_0 off-resonance effects on pCASL labeling efficiency, EPI ghost artifacts and leakage contamination resulting from the EPI ghosts, Siemens' advanced B_0 shimming was applied in a targeted region covering both the imaging volume and the pCASL labeling plane (Fig. 1c). B_0 shimming was performed twice, one after the other, by using sequentially acquired B_0 maps.

MB RF pulse manipulations and LEADS

To understand the impact of MB leakage contamination on CBF quantification, various studies were performed which involved manipulating components of the complex MB excitation RF pulse. Specifically, to estimate leakage signal contamination in a targeted slice, the MB RF pulse component exciting this specific slice was turned off (given zero amplitude) during imaging acquisition while all other simultaneously acquired slices were still excited, denoted as MB-RF_{out}. With such an RF pulse manipulation, MB reconstruction of the aliased slices would reveal the total signal contamination from all other simultaneously excited slices within the unexcited slice (dummy slice). This measured total leakage contamination was used to estimate the total leakage factor (TLF) described below. In a similar fashion, experimental measurement of the traditional leakage factor (LF) (Xu et al., 2013) can be also obtained by only exciting a single slice in the MB acquisition and measuring the resulting contamination within the other (MB-factor)-1 slices which are not excited (i.e. dummy slices). Such an RF