Arterial cerebral blood volume (CBVa) weighted functional MRI using pseudocontinuous arterial spin labeling

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Introduction: Functional magnetic resonance imaging using physiological parameters such as cerebral blood perfusion or cerebral blood volume (CBV), unlike BOLD fMRI, provides a quantifiable contrast and is also more closely related to neural activity [1]. Current Perfusion-based fMRI techniques, however, suffer from poor sensitivity and low temporal resolution. It has recently been shown that the change in CBV during neural activation mainly originates from arterial rather than venous blood volume [1], but CBV-based fMRI methods (such as VASO [2] and MOTIVE [3]) are also limited by their low signal to noise ratio. We propose a novel method based on pseudocontinuous arterial spin labeling (pCASL) technique [4] to achieve a contrast that depends on arterial cerebral blood volume (CBVa) and can be used for functional imaging experiments. The method proposed here offers sensitivity to brain activation that is on par with BOLD imaging and superior to perfusion ASL, while maintaining most of the advantages of perfusion ASL imaging.

Methods: The proposed method tailors the timing parameters of pCASL technique so that the parenchymal contribution to the observed signal is negligible, while the arterial compartment provides the bulk of the signal. To find the desired timing parameters (tagging duration and TR), we measure the perfusion signal at the resting condition using flow crusher gradients while varying TR and the tagging duration as proposed in [5] and find the TR and tagging duration leading to zero perfusion signal. Figure 1 shows a simulation of the continuous ASL signal at different TRs without any delay between tagging and image collection. We note that there are several TRs for which the tissue contribution to the ASL signal is zero. We chose the "zero-crossing" of the tissue signal in which the largest contribution of arterial signal in the ASL signal exists (indicated by a dashed rectangle in Figure 1). Using these parameters, the collected ASL image will be proportional to the arterial cerebral blood volume (CBVa) rather than cerebral perfusion.

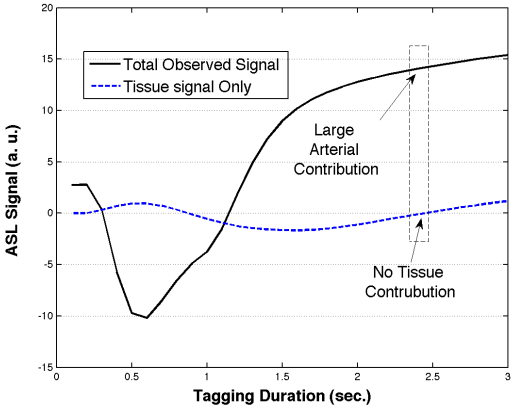

Fig 1. Simulated ASL signal (control minus tagged images) as a function of Tagging duration. TR was adjusted dynamically to accommodate the increasing tagging time.

The location of the crossing points is determined by each subject's specific arterial and tissue transit times relative to the image acquisition parameters. Therefore, the best selection of parameters will vary from subject to subject, although our simulations (not shown) indicate that the technique is not very sensitive to errors in transit time. We identify the timing parameters that produce CBVa images by testing a range of TRs with arterial suppression gradients (similar to the blue curve in Fig. 1) in order to find the null point of the perfusion signal contribution. We use these parameters to carry out a CBVa based functional MRI experiment. 10 subjects were scanned using a 3.0 T Signa Excite scanner (General Electric, Waukesha, WI. We employed pseudocontinuous tagging pulses [5] using the parameters suggested in [6]. After correcting for the field off-resonance using the method proposed in [6], desired timing parameters were estimated by varying TR (1500 to 2500 ms, steps of 100 ms) keeping the tagging time 500 ms shorter than TR to allow the acquisition of 16 slices using a 3D spiral acquisition (TE = 11 ms, slice thickness = 6 mm) [7]. To determine tissue contributions, arterial signals were suppressed by using a pair of crusher gradients (b = 4 s/mm2). The images of this experiment were reconstructed, pairwise subtracted and averaged (8 pairs for each TR). The TR and tagging that yielded minimal ASL contrast in the presence of flow crushers, but largest contrast without crushers (usually in the range from 1900 to 2500ms) was selected as optimal for CBVa. Next, subjects performed a simultaneous motor (sequential finger opposition) and visual (8Hz flashing checkerboard) activation task while being scanned once using the standard pCASL approach (TR = 4000 ms, tagging duration = 2000ms, post-tagging delay = 1500 ms), and again with the proposed CBVa fMRI method (TR and tagging duration estimated from previous experiment, post-tagging delay = 1 ms). A BOLD fMRI study was also conducted (TE=30 ms, TR = 2 s) for comparison purposes. The activation paradigm consisted of five cycles of alternating rest (30 seconds) and activation (30 seconds). All datasets were reconstructed and analyzed by estimation of standard general linear model (GLM) using home written software FASL01 [8].

Results: All experiments produced activation in visual and motor cortices. Figure 2 shows a slice of the activation maps in one the subjects obtained using perfusion-based fMRI (conventional pCASL), the proposed CBVa-based fMRI and BOLD fMRI. Mean Z score of the top 2% voxels averaged over all subjcets for perfusion-based fMRI, CBVa-based fMRI and BOLD were 4.25, 5.14 and 7.87 respectively. It indicates that the proposed method outperformed perfusion-based fMRI in terms of sensitivity. The average overlap of the activated voxels between Perfusion-CBVa, perfusion-BOLD and CBVa-BOLD were 25%, 31% and 36% respectively, which was expected considering the different physiological origin of each signal.

Discussions and Conclusions: We have presented a novel method using pseudocontinuous arterial spin labeling technique providing an arterial cerebral blood volume weighted signal suitable for functional imaging experiments. Our preliminary results suggest that the proposed CBVa-based fMRI method provides superior sensitivity and temporal resolution over the conventional Perfusion-based fMRI methods, closer to those of the BOLD technique, while retaining the statistical advantages of arterial spin labeling techniques.

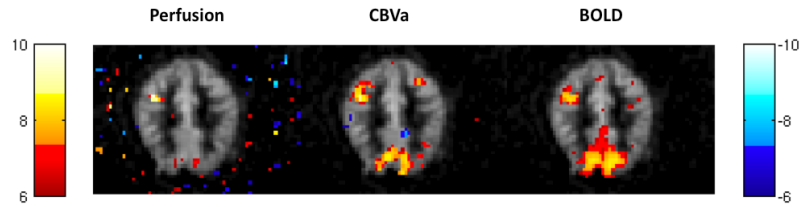

Fig 2. Activation maps obtained using: (left) standard ASL imaging (center) arterial CBV weighted imaging and (right) BOLD contrast fMRI during visual and unilateral motor stimulation. The color bars show the Z value of the activated area.

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References: [1] Kim et al. NeuroImage 49:1340–1349, 2010. [2] Lu et al. MRM 50:263-274, 2003. [3] Kim et al. JCBFM 27:1235–1247, 2007. [4] Dai et al. MRM 60(6):1488-97, 2008. [5] Hernandez-garcia et al. MRM 51:577–85, 2004. [6] Jahanian et al. NMR Biomed doi: 10.1002/nbm.1675, 2011. [7] Nielssen and HernandezGarcia, Proc. ISMRM 2012, (in review). [8] http://fmri.research.umich.edu/resources/software/shared_code.php#fasl.