Detecting focal changes in CBF independently from tissue content using arterial spin labeling (ASL) fMRI

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Introduction: Quantification of inter-subject differences in cerebral blood flow (CBF) separately from respective differences in tissue content presents a known challenge in analysis of group data[1]. Recently, our group has developed an algorithm which corrects for partial volume effects (PVE) in arterial spin labeling (ASL) imaging and also yields tissue specific flow 'density' maps (CBFd) which are, theoretically, independent of tissue content[2]. The PVE correction (PVEc) algorithm uses linear regression to estimate gray matter (GM) and white matter (WM) CBFd by modeling the voxel magnetization as a weighted sum of m_{GM}, m_{WM} and m_{CSF} (i.e. GM, WM and CSF magnetization) contributions and the ASL control-label difference signal as a weighted sum of d_{GM} and d_{WM} (i.e. GM and WM control-label difference) contributions[2]. The weighting coefficients in both cases are tissue's fractional volumes obtained from segmentation of subject's high-resolution structural image[2]. The algorithm assumes local homogeneity of tissue specific magnetization and CBFd over a small region surrounding each voxel (i.e. voxel's regression kernel)[2]. The goals of the present work are to (1) optimize the PVEc algorithm for applications where focal differences in CBFd (ΔCBFd) occur (e.g. in functional imaging) and (2) demonstrate how segmentation can affect accuracy of CBF and CBFd estimation.

Methods: *Optimizing PVEc method for detection of focal ΔCBFd:* Noise-free CBFd images were obtained via simulation of ASL control and label EPIs as: $M_{CONTROL}=(P_{GM}\cdot m_{GM})+(P_{WM}\cdot m_{WM})+(P_{CSF}\cdot m_{CSF})$, and $M_{LABEL}=(P_{GM}\cdot(m_{GM}-d_{GM}))+(P_{WM}\cdot(m_{WM}-d_{WM}))$. d_{GM} and d_{WM} were back-calculated from ASL 2-compartment formula[3] with the assumptions that CBFd = 107 and 28 mL/100g·min for GM and WM, respectively, and $m_{CSF}/m_{GM}/m_{WM}=1.7/1.2/1.0$[4]. P_{GM}, P_{WM}, and P_{CSF} denote voxel fractional tissue content obtained from segmentation of a subject's high resolution structural image[4] (acquisition detailed below). A 15% ΔCBFd activation was simulated on a 5x5x1 voxels region centered at [-35, 4, 8] mm MNI coordinate. EPIs were analyzed to yield CBF using both, the standard PVEc method[2] and the novel, fMRI-optimized method (referred to as 'selective-kernel PVEc') which modifies the regression kernel shape based on hypothesized activation ROI, as schematically detailed in Fig. 1. *Effect of image segmentation on quantification of CBF:* Spin Echo (SE) EPI CASL images (n=65) were acquired on a 22 y.o. male subject using 3T Philips, Achieva with: labeling duration=1.9 s, post labeling delay=1s, TR/TE= 4300/29 ms, FOV = 240 x 210 mm^2, in plane resolution= 3.75 x 3.75 x 8 mm^2, 13 slices. To test the effect of image modality on tissue segmentation, P_{GM}, P_{WM} and P_{CSF} images were obtained from SPM5 segmentation of (1) a magnetization prepared rapid gradient echo (MPRAGE) image (TR/TE=6.7/3.1ms, FA=8°, TI=0.8s, in plane resolution =.9 x.9 x.9 mm^3) and (2) a spoiled gradient recall (SPGR) image (TR/TE=25/1.94ms, FA=30°, in plane resolution =.9 x .9 x.9 mm^3). To test the effect of image segmentation algorithm, MPRAGE image was also segmented using SPM2 segmentation algorithm. PVEc regression method[2] was used to estimate CBFd using same set of ASL images and each tissue segmentation variant.

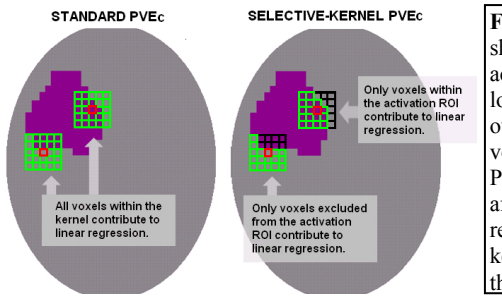

Fig. 1: The standard PVEc algorithm (left) was modified to adjust the shape of the regression kernel based on its overlap with hypothesized activation ROI (right). As the regression kernel is positioned at various locations throughout the image, the algorithm checks whether it also overlaps with the activation kernel (purple). If there is no overlap, all voxels within the kernel contribute to linear regression as per the standard PVEc method. Otherwise, the algorithm checks whether the overlap affects the center voxel. If the center voxel is affected, the linear regression includes only the voxels which are also within the activation kernel. Conversely, if the center voxel is not within the activation kernel, the linear regression excludes all voxels within the activation ROI.

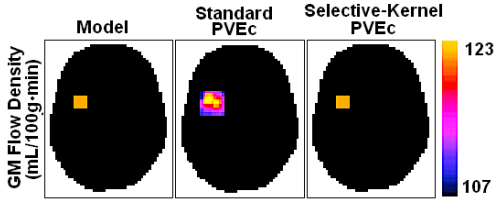

Fig. 2: Modeled GM ΔCBFd representing a 15% increase in baseline CBFd over a 5x5x1 voxels activated region (left) and ΔCBFd retrieved using standard PVEc method (center) and new, selective kernel, method (right).

Results: Fig. 2 illustrates that, while the standard PVEc method causes dilution of ΔCBFd signal, selective-kernel PVEc can retrieve activation with 100% efficiency in terms of both, magnitude and spatial localization. The signal dilution in standard PVEc method is caused by inherent spatial smoothing of the regression kernel[2]: ΔCBFd within activation ROI is under-estimated when non-activated voxels also contribute to the regression kernel; ΔCBFd in non-activated voxels surrounding the activation ROI is over-estimated when voxels within the activated region contribute to linear regression. The effect of tissue segmentation on quantification of CBF is illustrated in Fig. 3. Both, image modality and segmentation algorithm used, affect estimation of P_{GM} (1st row) and, in turn, estimation of CBFd using PVEc algorithm.

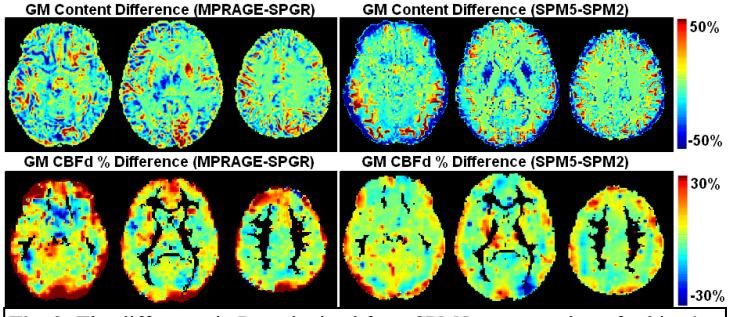

Fig. 3: The difference in P_{GM} obtained from SPM5 segmentation of subject's MPRAGE and SPGR (1st row, left) causes difference in GM CBFd (2nd row, left) estimation using PVEc. Similarly, the difference in P_{GM} obtained using two different (SPM5 and SPM2) segmentation algorithms (1st row, right) causes differences in estimated GM CBFd (2nd row, right).

Discussion: Selective-kernel PVEc ASL can, theoretically, detect focal changes in CBFd (e.g. due to stroke or functional activation) with 100% efficiency in magnitude and spatial localization. In case of stroke, the hypothesized 'activation' ROI can be selected by tracing the stroke lesion on subject's structural. In case of activation, the ROI can be obtained by parcelating functional brain regions based on standard atlas. Use of CBFd, rather than net CBF images, has potential to isolate inter-subject differences in CBF (or ΔCBF) from differences caused by inter-subject variation in tissue content. However, CBFd estimation is dependent on accuracy of tissue segmentation algorithm, and further work is necessary to evaluate which segmentation algorithm and image modality yield most accurate segmentation results. Importantly, net CBF using conventional, PVE-uncorrected method also depends on tissue content maps and is therefore also affected by segmentation differences.

References: [1]Momenan et al, NeuroImage 21(3) 2004; [2] Asllani et al, MRM 60(6) 2008; [3] Wang et al, MRM 48(2) 2002; [4] Asllani et al, HBM 30(9) 2009