Volumetric Blood Flow Rate Measurement by Flow ENhancement of Signal Intensity (FENSI)

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Introduction: Flow-based methods to examine brain function with magnetic resonance imaging (MRI) have been studied extensively as an alternative to the blood oxygenation-based (BOLD) approaches. Arterial spin labeling (ASL) technique offers quantitative information relating bulk flow of blood from a tagging plane into a slice, classical perfusion [1]; Time-of-flight and phase-contrast MR acquisition techniques mainly measure functional changes in blood flow of large arteries and veins. In this work, we applied the method Flow ENhancement of Signal Intensity (FENSI) [2] that gives quantitative information on volumetric flow rates or flux along with high spatial localization and directional sensitivity. Firstly a flow phantom was evaluated by this method, and then the technique was used to quantify microvascular (arterioles, capillaries, and venules) flow at rest and active states.

Theory:

FENSI is based on the MR microscopy method of DESIRE (Diffusion Enhancement of SIgnal and REsolution) proposed by Paul Lauterbur in 1992 [3]. The concept of this method is to saturate the spins within a thin plane as illustrated in Fig.1. By repeatedly saturating this region over a period of time, the signal void region grows proportional to the perpendicular component of the flow rate through the saturation plane. Thus images obtained by subtracting images with and without saturation, i.e., M_1-M_N as in Eq.1, contain blood flow information, where M_i stands for the image acquired after tagging for i repetition of tagging module. Normalizing by the magnetization of static tissue, i.e., $(M_0\text{-}M_1)/V_{tag}$, we can obtain the volume of moving spins during tagging interval Δt, therefore, the equation of blood volumetric flow rate Q *(ml/min)* per voxel can be expressed by Eq.1, and this flow rate is a flux through the cross-sectional area (CSA) of the imaging voxel area. λ is the brain-blood partition coefficient of water (0.9*ml/ml*) [4].

$$Q = \frac{M_1 - M_N}{(M_0 - M_1)/V_{tag}} \cdot \lambda \Big/ \Delta t \cdot 60 \quad (1)$$

Methods:

In experiments**,** we applied FENSI on a 400*um* saturation plane inside a 1*cm* imaging slice, with 30 tags applied at 11*ms* spacing and ignoring T1 effects. FENSI saturation sequence was combined with a spin-echo EPI imaging sequence with a TE of 40*ms*, a matrix size of 64x64, a field of view of 22*cm*, and a TR of 2*s*. It was implemented on a 3T Siemens Allegra headscanner.

In vitro A phantom was constructed to evaluate the method using a water-filled bottle and a 5% volume fraction of tubing of 0.86 mm inner diameter with flow rate 0.35*ml/min*. The scanning plane was set up perpendicular to the tubing flow.

In vivo Functional imaging was performed on six healthy subjects presented with blocked visual stimuli. Pairs of images from FENSI acquisitions were subtracted resulting in an effective TR of 4s. Z statistic images were thresholded using clusters determined by Z>2.3 and a cluster significance threshold of P=0.05. After obtaining the activated voxels, the region of interest (ROI) mask was used to average flow rate images under rest and activated states (Fig.2).

Results and Discussion:

In vitro The location of the tube segments could be easily determined by visual inspection of collected flow images. The average flow rate in the tubing was estimated 0.33±0.07*ml/min/voxel* with Eq.1. Compared with the set value 0.35*ml/min/voxel*, FENSI provides an accurate way to measure volumetric flow rate along with excellent localization and directional information.

In vivo The volumetric blood flow rates at baseline and visual stimulation estimated by FENSI are shown in Table 1. The average flow rate at rest is 1.52±0.16*ml/min*, while the average flow rate with visual task is 1.69±0.17*ml/min*. Since the CSA of each voxel is known (A_0) and the average cerebral microvasular flow velocities (v) are normally less than or equal to 2cm/s [5], we can compare the FENSI flow to the upper limit of volumetric flow (Q_{up}) of each voxel could be estimated as 0.709*ml/min* ($Q_{up} = A_0 \times CBV \times v$) by assuming a typical CBV as 5% [6]. Compared with the upper limit, the absolute blood flow rates measured by FENSI appear as two times overestimated. The apparent overestimation can be explained for two main reasons: (1) the tagging slice is within the imaging slice, thus FENSI actually detects the summation of two-directional flows through the tagging slice rather than one; (2) fast blood flows in large vessels may cause artifacts. To assess the contribution of fast flowing blood, we applied a flow suppression preparation (crusher level: 2cm/s) in FENSI for subject 6, resulting in a lower measured flow. According to the vascular response during functional activation, the increase of blood flow at microvascular level may result mainly from the CBV increases rather than blood velocity [7]. Therefore, attributing the percentage change (12.9±1.9%) of blood flow rate measured by FENSI as reflecting mainly the CBV change, the estimated flow change agrees well with literature reports of CBV increases [8].

Conclusion:

This work applied FENSI technique to image microvascular circulation and to reveal blood flow rates both at resting and activated states. This method has unique capability and benefits to measure blood flow: different from ASL and other perfusion techniques measuring bulk blood delivery to tissue, FENSI measures directional flow rate; compared with other flow measurement methods, FENSI gives high spatial localization at microvascular (arterioles, capillaries, and venules) level rather than large ateries or veins, thus it is expected that FENSI might provide more direct information about the physiology of brain activation and hemodynamic control. This method will be improved and utilized to measure microvascular flux change associated with disease, flow difference with ages and as a tool for examining hemodynamic coupling of functional responses.

References:

1. Williams *et al.* PNAS(89):212-216, 1992; **2.** Sutton *et al,* MRM(58):396-401, 2007; **3.** Lauterbur *et al.* XIISMR 1992; **4.** Herscovitch *et al.* JCBFM(5): 65-69, 1985; **5.** Guyton, *The Systemic Circulation,* 218-220, 1986; **6.** Buxton, Intr. to fMRI 8-10, 2002. **7.** Moonen *et al.* fMRI, 2000; **8.** Gu *et al.* NeuroImg(30):377-387, 2006.

Fig. 1

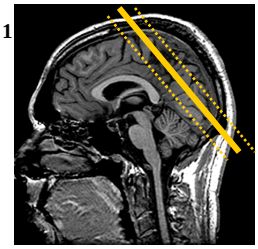

Fig. 2

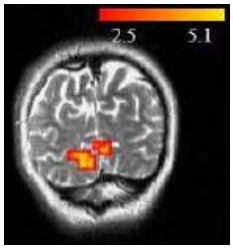

Table 1: Measured visual cortical volumetric blood flow rates per voxal CSA

Subjects	Baseline (ml/min) (SD)	Visual Stimulation (ml/min) (SD)	PercentageChange (%) (SD)
1	1.644 (0.013)	1.840 (0.048)	11.9 (3.03)
2	1.548 (0.004)	1.744 (0.044)	12.6 (2.84)
3	1.400 (0.072)	1.628 (0.040)	16.2 (5.91)
4	1.644 (0.048)	1.852 (0.060)	12.7 (4.70)
5	1.556 (0.024)	1.728 (0.044)	11.0 (3.21)
6	1.200 (0.052)	1.396 (0.048)	16.6 (6.02)

Fig.1: Illustration of tagging and imaging slices of FENSI functional imaging in a blocked visual paradigm. The solid line within the two dash lines stands for the thin tagging slice; and the area between dash lines is the imaging slice. **Fig.2:** The activated voxels in Z-score map located by FENSI are used as mask image for flow rate images.