Single Venule Multi-Echo Line-Scanning fMRI (MELS-fMRI)

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Target Audience Scientists developing fast acquisition sequence for fMRI or studying neurovascular coupling mechanisms.

Purpose Multi-echo EPI was previously utilized to measure BOLD fMRI signal for human brain mapping [1, 2]. The previous work indicated the T_2* signal could be more specific to neural signal with less temporal noise interference, and the T_2* decay signal acquired at different TE may be relevant to specific neuronal populations given certain tasks. In this work, we implement the multi-echo acquisition into the established line-scanning fMRI method [3], i.e. Multi-Echo Line-Scanning fMRI (MELS-fMRI). The single-vessel specific fMRI signal can be detected at different TEs ranging from 3 ms to 20ms with a 100ms sampling rate. This work allows us to analyze the BOLD fMRI signal spatial distribution pattern from individual penetrating venules at millisecond scale. Also noteworthy is the inflow effect due to short TR/TE-induced saturation, i.e. cerebral blood flow (CBF), may not directly elicit fMRI signal detected from individual vessels at short TEs.

Methods All images were acquired with a 14.1 T/26cm horizontal bore magnet (Magnex), interfaced to an AVANCE III console (Bruker) and equipped with a 12 cm gradient set, capable of providing 100 G/cm with a rise time of 150 us (Resonance Research). A transreceiver surface coil with 6mm diameter was used to acquire fMRI images. **Multi-Echo Line-Scanning fMRI (MELS-fMRI))**: A 2D MGE sequence was applied to map the fMRI signal with the following parameters: TE: 3 ms, 6.5 ms, 10 ms, 13.5 ms, 17 ms, 20.5ms; TR 100ms; matric 96x64, slice thickness, 400μm, in plane resolution, 100x100μm. As previously described [3, 4], the 2D MGE slice image was reconstructed from the reshuffled k space data with 100ms sampling rate. Using a conventional MGE sequence (TR: 50ms, TE, 2.5, 5, 7.5, 10, 12.5, 15ms; flip angle 40°, matrix: 192x128, in-plane resolution: 50μmx50μm), the single vessel map was acquired by averaging the MGE images acquired from the second echo to the forth echo, where the venule voxels showed as dark dots due to fast T_2* decay, but arteriole voxels remain bright dots due to the in-flow effect [5]. The image data were processed using AFNI software. T_2* values were calculated voxel-wisely by fitting the following two parameter equation: $S = M_0 \times \exp(-t / T_2^*)$, where S is signal acquired from each voxel, M_0 is the proton density constant estimated from baseline timepoints. Electrodes were placed on the forepaw to deliver a 2.5mA pulse sequence (2s, 300μs duration repeated at 3Hz). Total three rats were tested.

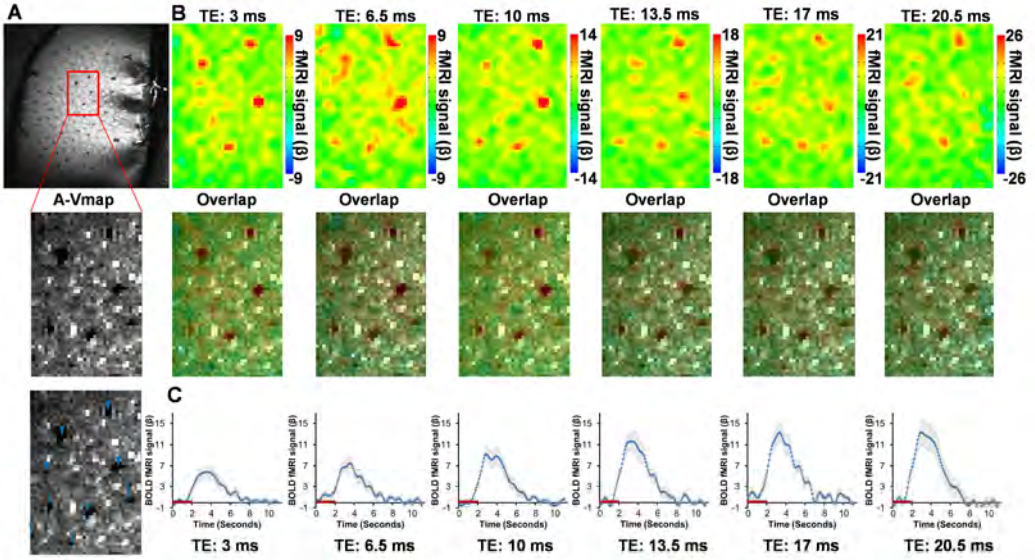

Fig 1. A. The A-V map shows the venules (dark dots) and arterioles (bright dots). Individual venules were characterized based on the signal intensity (blue arrowheads). B. BOLD functional maps overlapped on the A-V map at different TE from 3 ms to 20.5 ms. C. BOLD fMRI time courses of the selected venules (blue arrowhead) at different TE from 3 ms to 20.5 ms with 2s stimulation (red line)

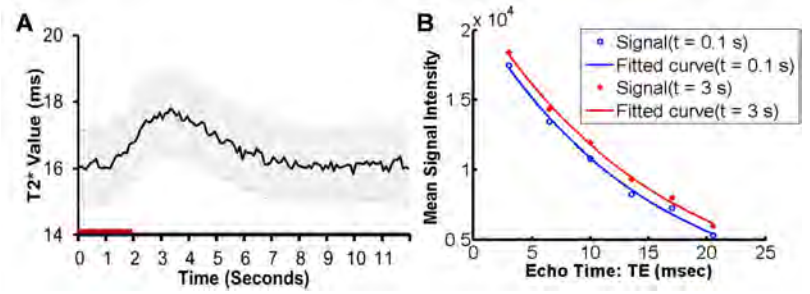

Fig 2. A. The T2* time course was averaged from nine venules (blue arrowheads in Fig.1A). B. Signal decay measured from the venules and the fitted curve based on the exponential model at different time points (0.1 s and 3 s) 2s stimulation (red line).

Result Fig 1.A shows the arteriole and venule map (A-V map) with venules in dark spots and arterioles in bright spots. The peak BOLD voxels were primarily overlapped with the venule voxels acquired at different TEs from 3 ms to 20.5 ms (1B), but not on the arteriole voxels, which could have been shown up if in flow effect contributed to CBF signal. The time course (100ms sampling rate) from nine venules characterized by A-V map was shown in Fig 1C, noting the higher BOLD signal at longer TE. In addition, besides T2*-weighted fMRI signal, we also acquired the T2* fMRI time course (Fig 2A), which is derived by FID fitting for the multi-echo MGE data reconstructed from each time point (Fig 2B).

Conclusion This work clearly demonstrates the single-venule BOLD fMRI pattern propagation using MELS-fMRI method. It is the first step to decipher the millisecond scale fMRI signal propagation across cerebrovasculature in the deep layer cortex.

Reference 1. Kundu et al. NI, 60:1759-70. (2011) 2. Kang etal. ISMRM, 3042, (2014). 3. Yu et al. Nature Method, 11:55–58, (2014). 4. Silva & Koretsky, PNAS, 99:15182-7 (2002). 5. Yu et al. ISMRM, 4360, (2014).