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## **ACCEPTED MANUSCRIPT**

Techniques for blood volume fMRI with VASO: From low-resolution mapping towards sub-millimeter layer-dependent applications

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#### **Abstract**

Quantitative cerebral blood volume (CBV) fMRI has the potential to overcome several specific limitations of BOLD fMRI. It provides direct physiological interpretability and promises superior localization specificity in applications of sub-millimeter resolution fMRI applications at ultra-high magnetic fields (7 T and higher). Non-invasive CBV fMRI using VASO (vascular space occupancy), however, is inherently limited with respect to its data acquisition efficiency, restricting its imaging coverage and achievable spatial and temporal resolution. This limitation may be reduced with recent advanced acceleration and reconstruction strategies that allow two-dimensional acceleration, such as in simultaneous multi-slice (SMS) 2D-EPI or 3D-segmented-EPI in combination with CAIPIRINHA field-of-view shifting. In this study, we sought to determine the functional sensitivity and specificity of these readout strategies with VASO over a broad range of spatial resolutions; spanning from low spatial resolution (3 mm) whole-cortex to sub-millimeter (0.75 mm) slab of cortex (for cortical layer-dependent applications). In the thermal-noise-dominated regime of submillimeter resolutions, 3D-segmented-EPI-VASO provides higher temporal stability and sensitivity to detect changes in CBV compared to 2D-EPI-VASO. In this regime, 3Dsegmented-EPI-VASO unveils task activation located in the cortical laminae with little contamination from surface veins, in contrast to the cortical surface weighting of GE-BOLD fMRI. In the physiological-noise-dominated regime of lower resolutions, however, 2D-SMS-VASO shows superior performance compared to 3D-segmented-EPI-VASO. Due to its superior sensitivity at a layer-dependent level, 3D-segmented-EPI VASO promises to play an important role in future neuroscientific applications of layer-dependent fMRI.

#### **Abbreviations**

BOLD = blood oxygenation level dependent; CAIPIRINHA (CAIPI) = Controlled Aliasing in Parallel Imaging Results in Higher Acceleration; CBV = cerebral blood volume; CNR = contrast-to-noise ratio; CSF = cerebrospinal fluid;  $\Delta$ CBV = change in CBV; EPI = echo planar imaging; fMRI = functional magnetic resonance imaging; FOV = field of view; GE = gradient

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