Functional MRI with SWIFT

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Introduction

Despite the large utilization of the Blood Oxygenation Level Dependent (BOLD) contrast [1], intense theoretical and experimental efforts are currently devoted to design novel methodologies for fMRI in an effort to more directly access cellular (rather than hemodynamic/metabolic) events. Available models predict that the BOLD signal change approaches zero when data acquired at different echo times (TE) are extrapolated to TE~0 [2]. This implies that a technique that generates no echo has the potential to detect phenomena other than T_2 or T_2^* changes related to deoxyhemoglobin (dHb). Here, we applied in fMRI a novel methodology, sweep imaging with Fourier transformation (SWIFT) [3], which provides 3D coverage of the brain in a few seconds without producing an echo. Also, since SWIFT is a 3D method, the in-flowing blood signal can be minimized when using a volume coil. SWIFT is also compelling for fMRI applications because it drastically minimizes the acoustic noise associated with the scanning procedure. We performed experiments on the human brain at 4 T during visual stimulation. In addition, with the goal of characterizing the origin of the SWIFT functional contrast, we performed experiments on the rat brain during respiratory challenges and on phantoms containing arterial or venous blood at 9.4 T.

Methods

Four healthy subjects were scanned at 4 T. One-hundred 3D-SWIFT volumes were acquired with TR=1.5 ms, flip angle=3°, spatial resolution=2.7 mm (isotropic), temporal resolution=5.2 s. For anatomical reference, T_1-weighted images were collected with MPRAGE (spatial resolution=2x1x2 mm^3). The functional protocol consisted of a block-design paradigm (20 off–20 on–20 off–20 on–20 off), employing a radial red/black checkerboard flickering at 8 Hz and covering the entire visual field. One rat was scanned at 9.4 T. One-hundred 3D-SWIFT volumes were acquired with TR=1.5 ms, flip angle=2°, spatial resolution= 0.5 x 0.5 x 2 mm^3, temporal resolution=3 s. At scan #20 and #60 the ventilator for the animal was switched off for 20 s. Finally, SWIFT and gradient echo (GRE) images were acquired on a phantom containing two 5-mm tubes filled with arterial or venous blood obtained from a rat.

Results and Discussion

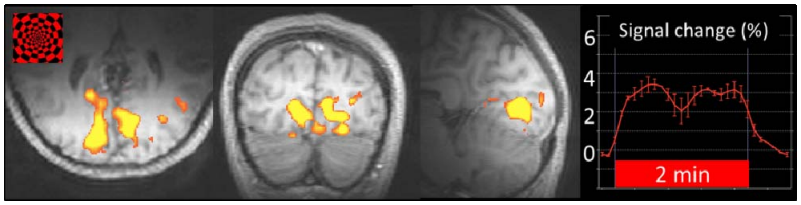

Figure 1. Activation maps obtained with SWIFT (TR=5.2 s) during a visual stimulation paradigm from one representative subject, threshold $p<3.3e^{-10}$

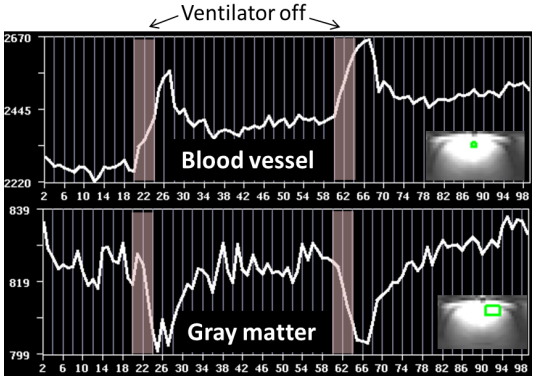

Figure 2. SWIFT signal time course (as a function of scan #, TR=3s) acquired on the rat brain at 9.4T. Shaded bars indicate when the ventilator was off.

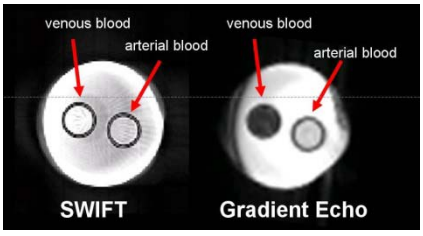

Figure 3. 5-mm tube samples containing venous/arterial blood, imaged with SWIFT or GRE at 9.4T.

Robust activation during a visual stimulation paradigm was detected over the primary visual cortex including the gray matter areas (Fig. 1). The signal change was in the same range of what is observed with GRE-EPI (~3-4 %), and the signal time course resembled the dynamics of what is typically observed with BOLD. Interestingly, no MRI contrast was observed with SWIFT between venous and arterial blood *in vitro* (Fig. 3) demonstrating that SWIFT, unlike GRE-EPI, is not sensitive to the shorter T_2^* of the former. During respiratory challenges in the rat, the expected CBF increase was detected (Fig. 2, top panel) as a signal increase in the large vessels with SWIFT implemented with a local surface coil that renders the 3D acquisition inflow sensitive; conversely signal decreased in the cortex (Fig. 2, lower panel). Taken together, these findings suggest that blood oxygenation might significantly influence the SWIFT signal *in vivo*, through mechanisms which are not mediated by T_2 or T_2^* changes which dominate GRE-EPI BOLD fMRI. A possible explanation is that the SWIFT sequence, which is known to generate a chemical shift or frequency dependent phase during excitation/acquisition has an inherent intravoxel phase dispersion and hence signal cancellation in the presence of magnetic field inhomogeneities around blood vessels containing dHb; modulation of the dHb content then modulates this signal cancellation, thus providing a measure of the BOLD effect at zero TE. Alternatively or in addition, other cellular events associated with spins which are not visible at normal (finite) TE due to their ultrashort T_2s but detectable at TE~0 in SWIFT may contribute through T_1-changes, induced possibly by alterations in trans-membrane ion fluxes and coupled H_2O and/or H^+ exchange between different tissue and cellular compartments. Regional tissue water content changes, such as changes in local blood volume, neuronal and/or glial swelling [4] and changes in arterial pressure [5] also have the potential to generate functional signals with SWIFT. However, such proton density changes might explain only signal changes < 1%. In conclusion, robust brain activation maps can be detected with SWIFT despite the absence of an echo. The development of fMRI protocols with SWIFT will likely have significant impact for brain mapping, thanks to the increased comfort for the subject, minimization of the acoustic noise, and less sensitivity to susceptibility artifacts typical of GRE-EPI techniques.

References [1] Ogawa et al (1990) PNAS 87:9868-72. [2] Uludag et al (2009) NeuroImage 48:150-65. [3] Idiyatullin et al (2006) JMR 181:342-9. [4] Le Bihan (2007) Phys Med Biol 52:R57-90. [5] Stroman et al (2002) MRM 48:122-7. **Acknowledgments:** KECK Foundation, NIH Grants: BTRR-P41 RR008079, P30 NS057091, R01 NS061866, R21 NS059813, S10 RR023730, S10 RR027290.