# Artifact-suppressed Alternating SSFP fMRI in Human Subjects Using a Breath Hold Paradigm

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**Introduction** Pass-band Balanced Steady-State Free Precession (pbSSFP) methods are promising alternatives to Gradient-Recalled Echo Echo-Planar Imaging (GRE-EPI) for functional MRI (fMRI) studies due to advantages such as reduced signal dropout and image distortions[1]. Although pbSSFP images exhibit banding artifacts, these artifacts can be removed by combining multiple (e.g. two) acquisitions acquired with different RF phase-cycling angles to recreate a high-signal image. However, this requires repeating two runs of the fMRI paradigm sequentially. For most neuroscientific applications, repeating runs produces confounding effects from cognitive habituation to stimuli and is not ideal[1]. Results from a rat hypercapnia study suggests that by using RF catalyzation to alternate between two RF phase-cycling steady states, whole-brain BOLD activation from a single run of the functional paradigm is possible. This approach has been coined "alt-SSFP" [2]. Our overall goal was to investigate these possibilities in human studies for the first time. Using human breath holding experiments to perturb BOLD signal, the objectives of our study were to show that alt-SSFP (1) recovers functional sensitivity in regions that suffer signal dropout in GRE-EPI, and (2) exhibits functional sensitivity comparable to the pbSSFP two-acquisition method, but using a single functional run.

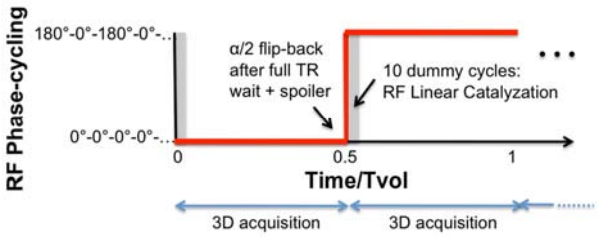


**Figure 1** Catalyzation scheme to transition from the 0° RF phase-cycling steady state (0°-0°-0°-…) to the 180° RF phase-cycling steady state (180°-0°-180°-0°…). For each steady state, a complete 3D volume was acquired. Ten dummy cycles were used for RF linear flip-angle catalyzation. At the end of each phase-cycling 3D acquisition, an α/2 flip-back pulse after a full TR wait was applied, followed by gradient spoiling.

**Methods** *Acquisition*: Measurements were made on a GE Discovery MR750 3T scanner using a 32-channel head coil. A 3D multi-shot flyback EPI sequence with an echo train length of 4 was used with the following parameters: TR = 10.26 ms, FOV = 240 x 240 x 130 mm$^3$, flip angle = 30°, receiver bandwidth = ±83.3 kHz. Echo-time shifting was used to reduce ghosting artifacts[3]. Data was acquired with an isotropic in-plane resolution of 3 mm and a slice thickness of 5 mm. Each 3D volume was fourfold uniformly undersampled in the in-plane phase encode direction to achieve a volume time of less than 3 s. These images were reconstructed using GRAPPA[5], for which the weights were calculated from the central region of a fully encoded reference volume acquired at the beginning of the time course. This resulted in an equivalent volume time of 2.9 s, defined as the time to acquire both RF phase-cycled alt-SSFP 3D acquisitions.

Ten linear ramp dummy cycles were used to catalyze the transient signal into steady state for each RF phase-cycled acquisition (see Figure 1)[6]. Slice phase-encodes were acquired centric-inward so that the center of k-space was acquired at the end of each 3D volume readout train. This scheme was used to ensure signal stability and to allow sufficient BOLD contrast to develop[4].

*Paradigm:* Breath-hold paradigms were performed on 4 human subjects. Subjects performed 5 repetitions of alternating 20 s blocks of self-paced breathing and end-expiration breath holding for each run. Trial timing was cued by visual stimulus using PsychoPy[7].

*Analysis:* Maximum Intensity Projection (MIP) was used to combine the alternating phase-cycling images[1] (Fig 2). FSL[8] was used for fMRI data statistical analysis. Activation was modeled as a boxcar function (representing the functional paradigm) convolved with a Gaussian function. A 2-sided f-test (to include frequency shifts on either sides of the transition bands) was included to detect activation, and z-scores were calculated using a cluster-level correction for multiple comparisons ($z > 2.3$, $p < 0.05$).

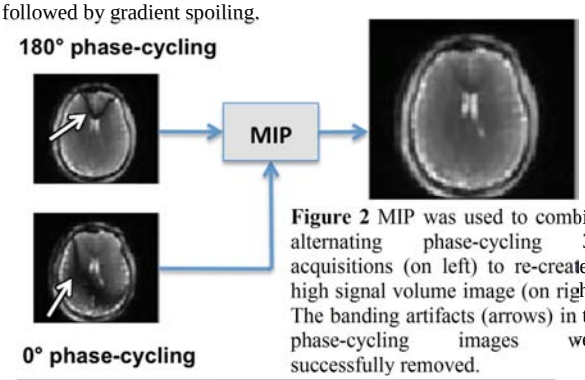


**Figure 2** MIP was used to combine alternating phase-cycling 3D acquisitions (on left) to re-create a high signal volume image (on right). The banding artifacts (arrows) in the phase-cycling images were successfully removed.

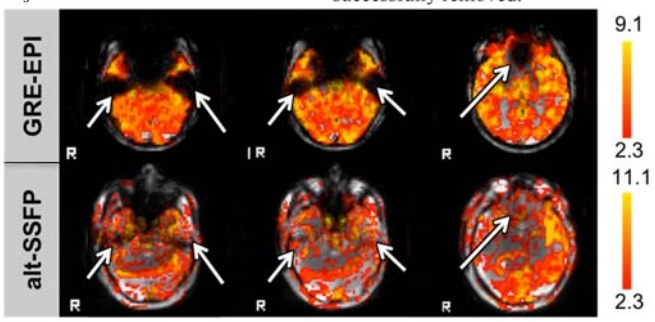


**Figure 3** Alt-SSFP recovers functional sensitivity in susceptibility regions that suffer signal dropout from GRE-EPI (see arrows).

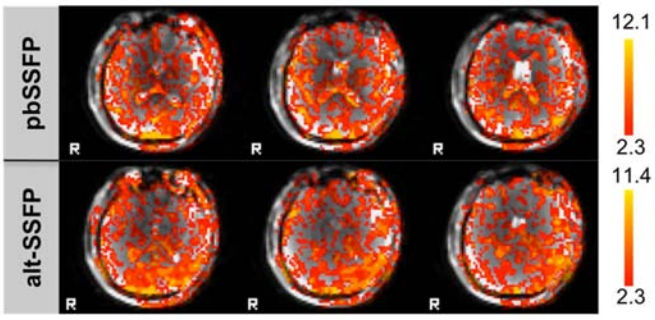


**Figure 4** Alt-SSFP exhibits comparable functional sensitivity to the pbSSFP two-acquisition method, but accomplishes this using a single paradigm run.

**Results and Discussion** The catalyzation scheme used to transition between steady states resulted in better stability across all frequencies, reduced oscillation significantly, and, with parallel imaging acceleration, allowed the possibility to alternate between steady states within temporal resolution limits. The MIP results show that the banding artifacts were removed successfully in the raw images. The functional sensitivity of the alt-SSFP sequence was compared to conventional GRE-EPI and conventional pbSSFP two-acquisition method with the same total volume times of 3 s. Figure 3 shows that alt-SSFP (bottom) recovers functional sensitivity in susceptibility regions that suffer from signal dropout in conventional GRE-EPI (top) images. Alt-SSFP was also found to fill in signal in banding regions of the individual phase-cycled pbSSFP images. Figure 4 shows that the functional sensitivity maps of alt-SSFP (bottom) are comparable to those acquired with conventional two-acquisition pbSSFP (top), but using a single functional run with matched volume times.

**Conclusion** We have shown that alt-SSFP allows the possibility for whole-brain fMRI in human subjects from a single functional run. Alt-SSFP may allow investigation of brain regions currently inaccessible to GRE-EPI, due to signal dropout, and two-acquisition pbSSFP, due to the requirement of repeat functional runs.

**References** [1] Lee, et al. MRM (2008), 59:1099; [2] Patterson, et al. ISMRM (2012), p2309; [3] John, et al. ISMRM (2010), p1084; [4] Patterson, et al. ISMRM (2011), p3112; [5] Griswold, et al. MRM (2002), 47:1202; [6] Deshpande, et al. MRM (2003), 49:151; [7] Peirce, Front Neuroinform (2009), 2:10; [8] Jenkinson, et al. NeuroImage (2012), 62:782.