Use of balanced SSFP MR microscopy for imaging endogenously labeled neuroprogenitor stem cells with Linear Combination Steady-State Free Precession (LCSSFP) for artifact reduction.

H. D. Morris[1], and J. P. Sumner[2]
[1]NIH Mouse Imaging Facility, National Institues of Health, Bethesda, MD, United States, [2]Laboratory of Functional and Molecular Imaging, National Institues of Health, Bethesda, MD, United States

Introduction. MRI has proven to be an excellent tool for cell tracking via magnetic nano- or micro-particles. In particular single cell tracking is possible via magnetic particles greater than 1 micron using high resolution MR microscopy. This technique relies on the magnetic field distortion of the particle to produce a local artifact in the image many times larger that the particle itself.[1] Consequently, cells can be tracked in tissue in 3D and *in vivo*. Recently, cell labeling techniques have been applied to *in vivo* labeling of endogenous cells in the rat brain.[2] Global magnetic field distortions prevent the use of high-SNR efficiency techniques such as steady-state free precession (SSFP) in such labeled tissue.[3] These field banding artifacts can be suppressed to good effect by use of a linear combination of SSFP images (LCSSP).[4] We describe the application of the LCSSFP technique as a method for rapidly obtaining MR images of the rat brain labeled with micron-sized magnetic particles.

Methods. The MRI images were acquired on a Bruker Avance III 14.0T NMR spectrometer with microimaging apparatus (Bruker Biospin, Inc., Billerica MA, USA) using a standard Avance RF console, Micro-5 gradients (G=1.5 T/m, SR=2500 T/m/s) and 30 mm ID SAW RF coil. The 3D SSFP imaging parameters are TR/TE=3.366/1.168 ms, pulse angle 60°, 4 NEX, FOV 30x18x13 mm, 256x172x128 for a resolution of 100µm isotropic, with a total acquisition time of 5:51min. The LCSSFP images were formed by the complex summation of the individual images with a minimum of 4 phase precession sequences. The minimum time required for each LCSSFP image is at least 4 times that of a single SSFP image. Six-week-old Sprague-Dawley rats (Charles River Laboratories, Inc., Wilmington, MA) were stereotactically injected with 1.4x108 MPIOs (Bangs Laboratories, Inc., Fishers, IN). Two-weeks post injection, animals were transcardially perfused with PBS followed by 10% buffered formalin solution. Intact brains were removed and stored in PBS.

Results. Figure 1 below shows two representative axial slices for a conventional SSFP (A) and LCSSFP (B) sequences through the midplane of a normal rat brain. Figure 1A demonstrates the banding artifact observed in SSFP images where the high concentration of magnetic particles in the ventricles produce local field gradients and move the resonant frequency out of the passband for the pulse sequence. Figure 1B is formed of four separate SSFP images with different RF pulse phase progression cycles: (0-0-0-0), (0-π/2-π-3π/2), (0-π-0-π), and (0-3π/2-π-π/2). The acquired images are squared, summed, and scaled. The reduction of banding artifacts is nearly perfect without the large distortions from the high concentration of magnetic particles in the ventricles and produces a high quality image.

Conclusion. High-resolution (100 µm isotropic) images of a rat brain injected with iron oxide particles were acquired using SSFP sequence at high field in approximately 5 minutes. Banding artifacts were successfully suppressed by LCSSFP using four phase cycles, resulting in a 4-fold increase in acquisition time. This feature can be exploited to provide rapid MR microscopy for investigating the position of magnetic particles in the rodent brain event with local field distortions.

References. 1) Shapiro et al. MRI detection of single particles for cellular imaging. Proc Natl Acad Sci USA (2004) vol. 101 (30) pp. 10901-6. **2)** Sumner et al. In vivo labeling of adult neural progenitors for MRI with micron sized particles of iron oxide: Quantitation of labeled cell phenotype. Neuroimage 44(3) 671-8 (2009) **3)** A. Opplelt et al. FISP: eine neue schenell Pulssequenxae fur die Kernspintomographie., Electromedica **54**, 15-18 (1986). **4)** SS Vasanawala et al. Linear Combination Steady-State Free Precession MRI, Magn Reson Med 43(1), 82-90 (2000).

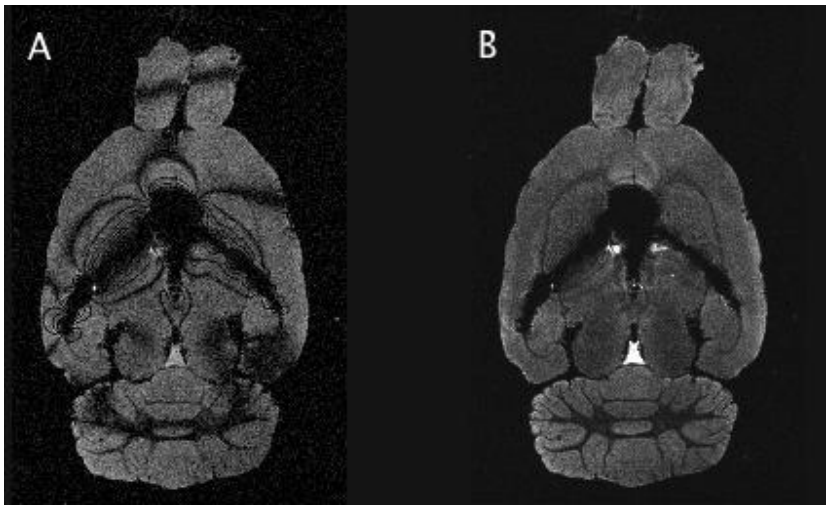

Figure 1. (A) A SSFP image with a one phase-cycle progression (100µm isotropic resolution). Note the extensive banding artifacts throughout the entire visible brain image. Acquisition time is 5:51. (B) An LCSSFP image formed from 4 single SSFP images with 4 different RF phase progressions as detailed above. The artifacts are reduced to minimal variations in intensity. The acquisition time required for this image is 4 times more than (A) for a total of 23:21.