

# Temporally flexible tracking of Neuro-progenitor stem cells using Golden Angle incremented Linear combination Steady-State Free Precession (LCSSFP) imaging for artifact reduction.

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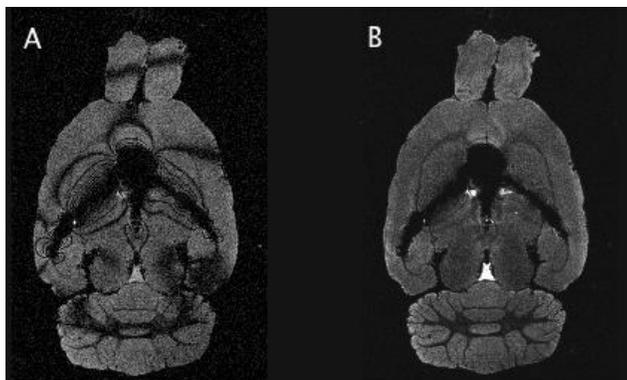
**Introduction.** MRI has proven to be an excellent tool for cell tracking via magnetic nano- or micro-particles. It is possible to track individual single cells via magnetic particles greater than 1 micron diameter using high resolution MR microscopy. This technique relies on the magnetic field distortion of the particle to produce a local artifact in the image many times larger than 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] High concentrations of the magnetic label such as in the ventricles generate 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 weighted or linear combination of SSFP images (LCSSFP).[4] Previously, these techniques require a fixed parsing of the offset bandwidth of the field distortions. We describe a technique based on the Golden Angle to parse the offset bandwidth without a fixed set of acquisitions as applied to the LCSSFP technique. Using the Golden angle increment in the RF phase, the banding artifacts do not appear in the same position twice no matter how long the cycle is projected forward. This is analogous to the use of Golden Angle selected projections in back-projection MRI.[5] We demonstrate the utility of this method for rapidly obtaining MR images of a 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 25 mm ID SAW RF coil. The 3D SSFP imaging parameters are  $TR/TE=2.0/1.0$ ms, pulse angle  $60^\circ$ , 1 NEX, FOV  $30 \times 18 \times 13$  mm,  $512 \times 340 \times 168$  for a resolution of  $50 \times 50 \times 75 \mu\text{m}$ , with a total acquisition time of 1min 45 seconds per image. The LCSSFP images were formed by the complex summation of the individual images with a minimum of 3 phase precession sequences. The minimum time required for each LCSSFP image is at least 3 times that of a single SSFP image. Six-week-old Sprague-Dawley rats (Charles River Laboratories, Inc., Wilmington, MA) were stereotactically injected with  $1.4 \times 10^8$  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 three separate SSFP images with different RF pulse phase progression cycles: (0-0-0), (0-137.51-275.02-52.53), and (0-275.02-190.04-105.06). 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 ( $50 \times 50 \times 75 \mu\text{m}$ ) images of a rat brain injected with iron oxide particles were acquired using SSFP sequence at high field in approximately 2 minutes. Banding artifacts were successfully suppressed by golden angle LCSSFP using the 3 phase cycles, resulting in a 3-fold increase in acquisition time. Additional, SNR and artifact suppression can be obtained by incremented the phase cycles and acquiring the additional images. Since each Golden-Angle SSFP image is independent of the others this can be used to provide a sliding window reconstruction of any of the images. This can be exploited to provide rapid MR microscopy for investigating the position of magnetic particles in the rodent brain even with local field distortions. The use of golden-angle RF phase advance makes it possible to add to the artefact progression without any need to worry about overlap.

**References.** 1) Shapiro et al. MRI detection of single particles for cellular imaging. Proc Natl Acad Sci USA **101**(30) 10901-6 (2004). 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. Opplert et al. FISP: eine neue schnell Pulssequenz für 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). 5) Winkelmann et al. An optimal radial profile order based on the Golden Ratio for time-resolved MRI. IEEE Trans Med Imag **26**(1), 68-76 (2007).



**Figure 1.** (A) A SSFP image with a one phase-cycle progression ( $50 \times 50 \times 75 \mu\text{m}$  resolution). Note the extensive banding artifacts throughout the entire visible brain image. Acquisition time is 1:54. (B) A Golden Angle LCSSFP image formed from 3 single SSFP images with 3 different RF phase progressions as detailed above. The artifacts are reduced to minimal variations in intensity. The acquisition time required for this image is 3 times more than (A) for a total of 5:42.