Rapid MR microscopy of Mouse Inner ear structures *in vivo* using Linear Combination Steady-State Free Precession MRI

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Introduction. Progress in genome research requires characterization of the phenotypic expression of genetic modifications in developing and adult animals. MRI is an excellent method for phenotyping the mouse, the mammalian genomic model of choice, as it can be applied *in vivo* so that development can be monitored. Malformations of the inner ear are common phenotypic expressions of congenital deafness mutations , which may be quantified by microscopic imaging. [1] Previously we have shown that volumetric imaging of the fluid filled spaces of the inner ear is an ideal application for MRI particularly as histologic methods of evaluation require lengthy decalcification procedures. [2] Conventional techniques are spin-echo derived methods for selecting the long-T2 of the perilymph and endolymph. An alternative approach is to use steady-state refocused gradient echo techniques such as balanced-SSFP (also know as FIESTA, true-FISP, and balanced-FFE) to generate high SNR from fluid rapidly. This technique has been used in humans at lower fields such as 1.5T to good effect but is limited by banding artifacts in regions of magnetic susceptibility. Susceptibility effects are exacerbated in our application due to high $\mathbf{B_0}$ field strength as well as the location of the inner ear embedded within the air filled temporal bone. [3] The artefacts can be greatly reduced by the use of linear combinations of SSFP images (LCSSFP), which can cancel out the band artifacts from local magnetic field distortions. [4] We describe the application of the LCSSFP imaging technique, as a method of rapidly obtaining MR images of the inner ear of the mouse *in vivo* at high resolution.

Methods. The MRI examinations were carried out on a Bruker Biospec 7.0T MR scanner (Bruker Biospin, Inc., Billerica MA, USA) using an Avance RF console, BGA-9 gradients (G=0.3 T/m, SR=2500 T/m/s) and 35 mm ID birdcage RF coil. C57-Black 6 mice were anesthetized using isoflurane following an NIH OLAC approved protocol for MR imaging procedures. The SSFP imaging sequence used has a variable RF phase precession cycle to modulate the frequency of the passband for the SSFP image. The 3D SSFP imaging parameters are TR/TE=3.1/1.55 ms, pulse angle 60°, 2 NEX, FOV 60x30x15 mm, 256x128x64 for a resolution of 234 µm in plane and 234 µm through plane, with a total acquisition time of 52 seconds. 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.

Results. Figure 1 below shows two representative axial slices for a conventional SSFP (A) and LCSSFP (B) sequences through the cochlea of a normal Black-6 mouse. Figure 1A demonstrates the banding artifact observed in SSFP images where local field variations (due to susceptibility induced gradients from the air filled mastoid cavity and middle ear) move the resonant frequency out of the passband for the pulse sequence. Figure 1B is formed of 4 separate SSFP images with different RF pulse phase progression cycles: (0-0-0-0), (0-90-180-270), (0-180-0-180), and (0-270-180-90). The acquired images are complex summed and scaled. The reduction of banding artifacts is striking and permits determination of small structures and chamber volumes.

Conclusion. High-resolution (234 µm isotropic) images of the mouse inner ear were acquired using SSFP sequence at high field in under one minute. The extraordinary SNR per unit time of the sequence allows rapid acquisition of microscopic MR images of tissues with long T2 relaxation times, such as endolymph and perilymph. Banding artefacts 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 following phenotypic expression of genetic modifications in the structure of the mouse inner ear in living mice.

References. **1)** LA Everett et al., "Targeted disruption of the mouse Pds provides insight about inner-ear defects encountered in Pendred syndrome", Hum Mol Gen **10**(2), 153-161 (2001). **2)** HD Morris et al. "Rapid MR Microscopy of the Mouse Inner Ear structures in vitro using True-FISP at 7.0T", Proc. ISMRM 15:2138 (2007) **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).

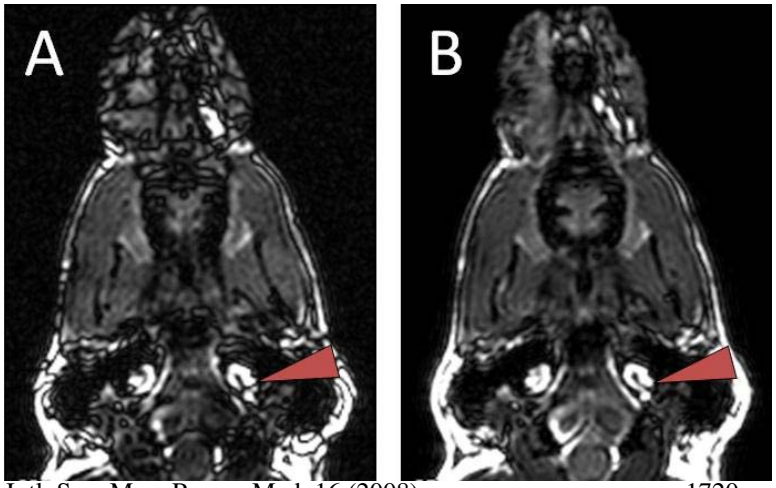

Figure 1. **(A)** A conventional SSFP image with a one phase-cycle progression (234 µm isotropic resolution). Note the extensive banding artifacts throughout the cochlea and the visible subcutaneous fat. Acquisition time is 0:52. **(B)** An LCSSFP image formed from 4 single SSFP images with 4 different 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 3:24.