Rapid MR Microscopy of the Mouse Inner Ear structures *in vitro* using True-FISP at 7.0T

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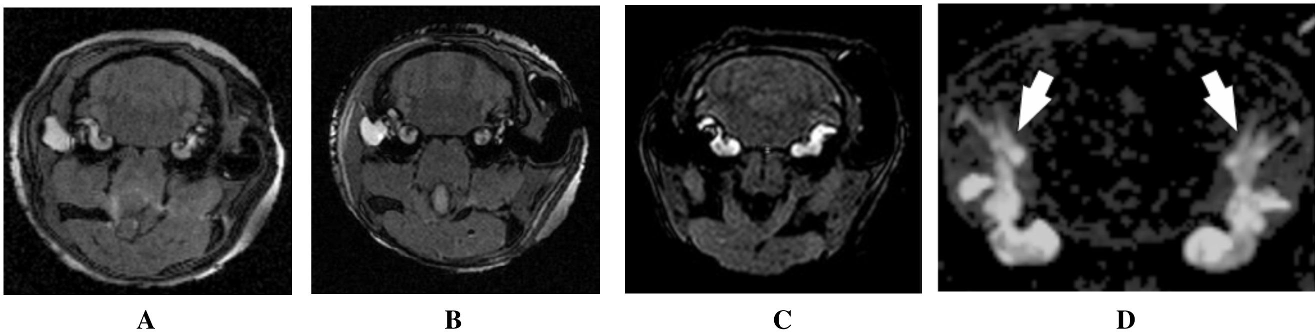
Introduction. An outgrowth of the progress in genome research is the need to evaluate the expression of a genetic modification in the developing or adult animal. MRI has been shown to be an excellent method for phenotyping the mouse, the mammalian genomic model of choice. Certain mouse mutations find phenotypic expression in the structure and function of the inner ear which are evident to the investigator via morphology and animal behavior.[1] 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. 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 True-FISP (also know as FIESTA or balanced-SSFP) 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 can be limited by banding artifacts in regions of magnetic susceptibility. [2] We describe the application of a steady-state imaging technique, True-FISP, as a method of rapidly obtaining high-resolution MR images of the inner ear spaces of the mouse.

Methods. The MRI examinations were carried out on a Bruker 7.0T NMR spectrometer equipped with microimaging apparatus (Bruker Biospec, Inc., Billerica MA, USA). The microimaging apparatus included a 7.05T wide bore vertical magnet with Microspec 2.5 gradients (1.5T/m with a slew rate of 12 kT/m/s) and 15 mm birdcage RF coil. The isolated mouse head was immersed and immobilized in an immiscible fluorinated liquid (Fomblin, Solvay-Solexis, Thoroway NJ USA) to reduce magnetic susceptibility induced gradients with minimal background signal. The imaging sequences compared are True-FISP and RARE. The 3D True-FISP imaging parameters are TR/TE=2.9/1.45 ms, flip angle 50°, 4 NEX, FOV 20x20x10 mm, 128x128x64 for a resolution of 156 microns in plane and through plane, with a total acquisition time of 98 seconds. The RARE imaging parameters were TR/TE=4000/100 with 32 echoes, 1 NEX, FOV 20x20x10 mm, 128x128x64 data matrix for a resolution of 156 microns, for a total acquisition time of 1024 seconds.

Results. Figure 1 below shows two representative coronal slices for the True-FISP (A) and RARE (B) sequences through the cochlea of a normal wild-type (WT) mouse. The SNR in the images of the inner ear lymphatic fluid is comparable for the two techniques however the signal for the surrounding brain and muscle tissue is less intense in the True-FISP image which is an aid in isolating the cochlear space and determining it's volume and geometry. The level of image detail is seen in the resolution of the structures within the inner ear, though care must be taken to minimize signal loss due to localized gradients originating from air filled spaces as seen in Figure 1A. Figure 1C is a coronal slice from a True-FISP image of the Pds knockout (KO) mouse. The Pds KO mouse has an enlarged and modified inner ear labyrinth.



A **B** **C** **D**

Figure 1. **(A)** True-FISP coronal image of WT mouse with resolution of 156 um. **(B)** RARE image of WT mouse comparable to A in CNR and resolution but substantially longer in imaging time. **(C)** A True-FISP coronal image of the Pds KO mouse with enlarged cochlear spaces are evident. **(D)** A cropped enlargement of a MIP projection generated from the image used in 1C shows the extent of the lymph filled inner ear of the Pds KO mouse. The arrows point to the dilated endolymphatic sacs of the Pds KO mouse.

Conclusion. High-resolution images of the mouse inner ear were acquired using 3D True-FISP and 3D RARE sequences. The extraordinary SNR per unit time of the True-FISP sequence allows rapid acquisition of microscopic MR images of tissues with long T2 relaxation times, such as endolymph and perilymph. 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.

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)** A. Opplelt et al. "FISP: eine neue schenell Pulssequenxae fur die Kernspintomographie.", Electromedica **54**, 15-18 (1986).