In vivo MR Imaging at 21.1 T

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INTRODUCTION

In vivo magnetic resonance (MR) imaging and spectroscopy are expanding our capability to observe and investigate many biomedical processes without invasive interventions. The unique 900-MHz ultra-wide bore (UWB) 21.1 tesla magnet built at the Magnet Lab in Tallahassee provides unprecedented opportunities to examine living systems. In this report, we present our first experiences and the results of *in vivo* MR imaging at the highest field available for such studies.

The ability to conduct *in vivo* MR imaging experiments was achieved as a result of multiple steps taken over the past few months. This work comprised designing and fabricating coils and probes, certifying facilities for animals, and gaining institutional approval for animal research. It also included the installation of an anesthesia station and animal physiological monitoring system. The Magnet Lab now has its own animal facility conveniently located in close proximity to the MR scanners and consists of animal housing rooms and animal procedural spaces. These accomplishments afford opportunities for internal and external users to run a variety of MR imaging experiments using the Magnet Lab world-record 900 UWB magnet.

EXPERIMENTAL

Testing the *in vivo* MRI capabilities of the 900 UWB system was performed using two animal models, C57BL/6J mice and zebra finch birds. The animals were anesthetized during MR scanning through the use of either a gaseous isoflurane/oxygen mixture or anesthetic injections.

The MR imaging experiments were carried out using a Bruker Avance console operated by PV4.0 and TopSpin 1.5 software. Currently, the 900 UWB system is equipped with a Bruker Micro2.5 gradient set

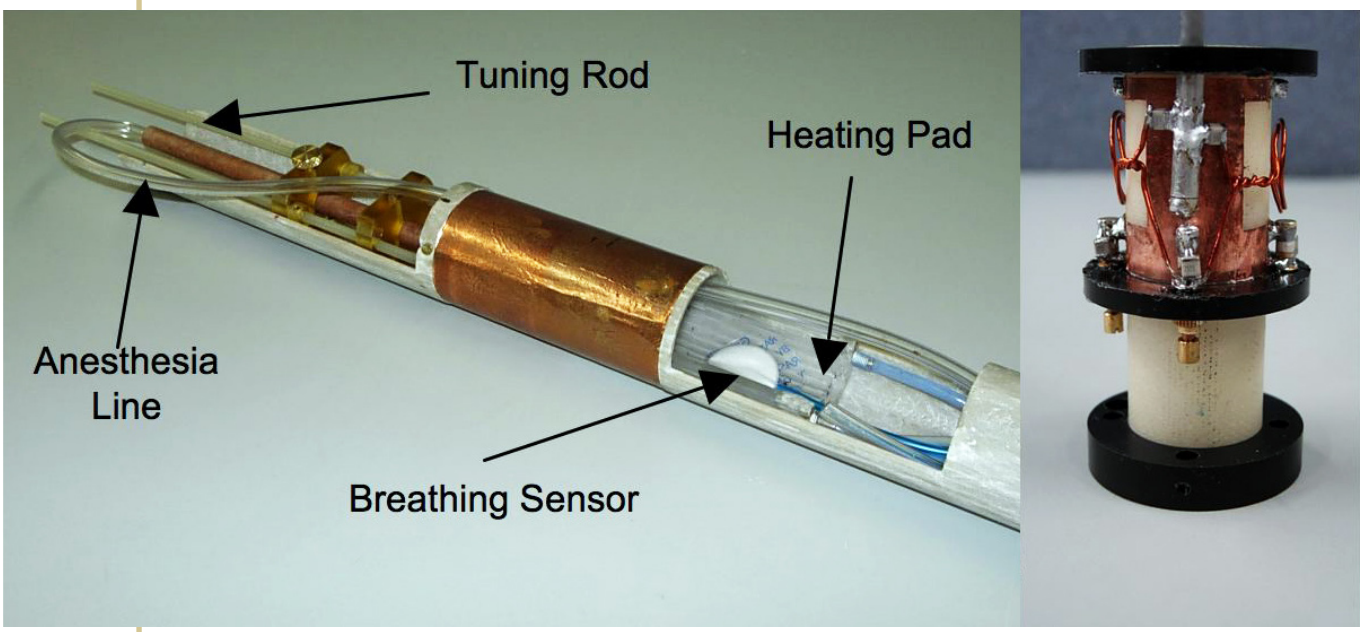

Figure 1.
Mouse *in-vivo* MRI probe and proton RF coil for the UWB 900 MRI scanner.

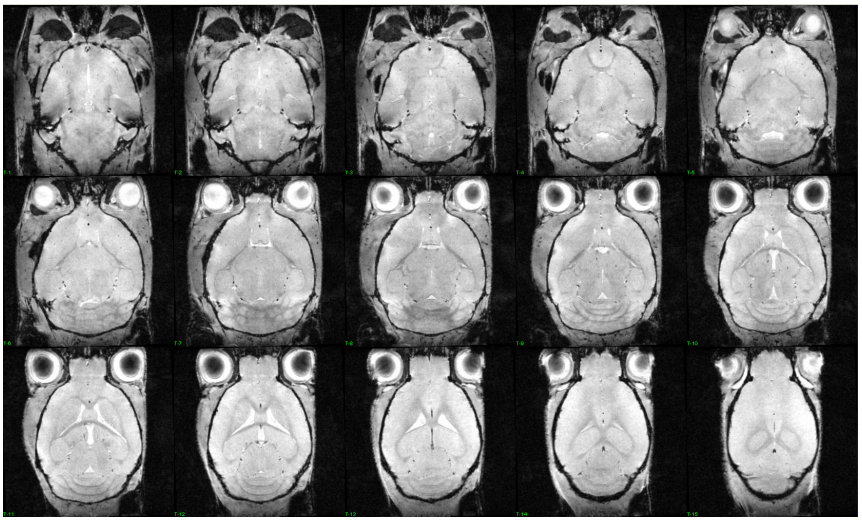

Figure 2.
Proton *in-vivo* MR images of mouse head acquired on the UWB 900 MRI scanner. Resolution in coronal plane was 62x62 µm, slice thickness was 150 µm.

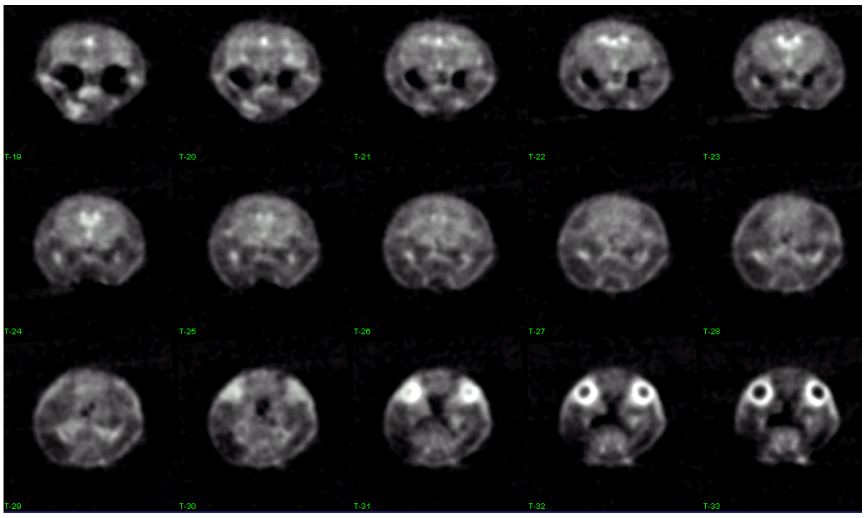

Figure 3.
Sodium *in-vivo* MR images of mouse head acquired on the UWB 900 MRI scanner. Resolution in axial plane was 500x500 µm, slice thickness 500 µm.

(ID =40 mm) and GREAT60 gradient amplifiers allowing maximum gradient strength of up to 1.5 T/m.

New RF probes were specifically developed for *in vivo* mice MR proton/sodium imaging at 21.1 T by Nathaniel Falconer and William Brey at the Magnet Lab. The RF coils were designed as single frequency Alderman-Grant coils with ID/OD = 17/25 mm (Figure 1). Both ^{1}H and ^{23}Na *in vivo* probes have an animal positioning system and a water-heated blanket to maintain body temperature inside the magnet. The probes have incorporated ECG, breathing and temperature control sensors that are connected to the Small Animal Monitoring and Gating System (Model 1025, SA Instruments, Inc.).

Gradient shimming is a well-established tool for MR imaging. For the 900 UWB system, the incorporation of FASTMAP proved more challenging because the magnet is equipped with a customized power supply and shim set (RRI, Inc.) to take advantage of the 105-mm size of the magnet bore. Recently our staff, Ashley Blue and William Brey, designed and constructed an interface for the Bruker power supply. This interface permits users to utilize Bruker software and hardware to control shimming through our customized shim coils. The FASTMAP technique has since been tested for both imaging and localized spectroscopy and is now available to users.

RESULTS AND DISCUSSION

In vivo Mouse Proton MR Imaging

The first brain ^{1}H MR images of the living mouse obtained at 21.1 T are presented in Figure 2. Fifteen images of the head of a normal mouse (C57BL/6J) were acquired using a Fast Low Angle Shot (FLASH) gradient recalled-echo sequence with TR/TE = 1000/4.3 ms, FOV = 16x16 mm and matrix = 256x256. The in-plane resolution was 62.5x62.5 µm with a slice thickness of 150 µm. The total accumulation time was ~ 18 min. The resolution of the MR images was sufficient to identify blood vessels in the mouse brain with diameter of ~100 µm, which can be seen throughout the images as the black dots in different parts of the brain.

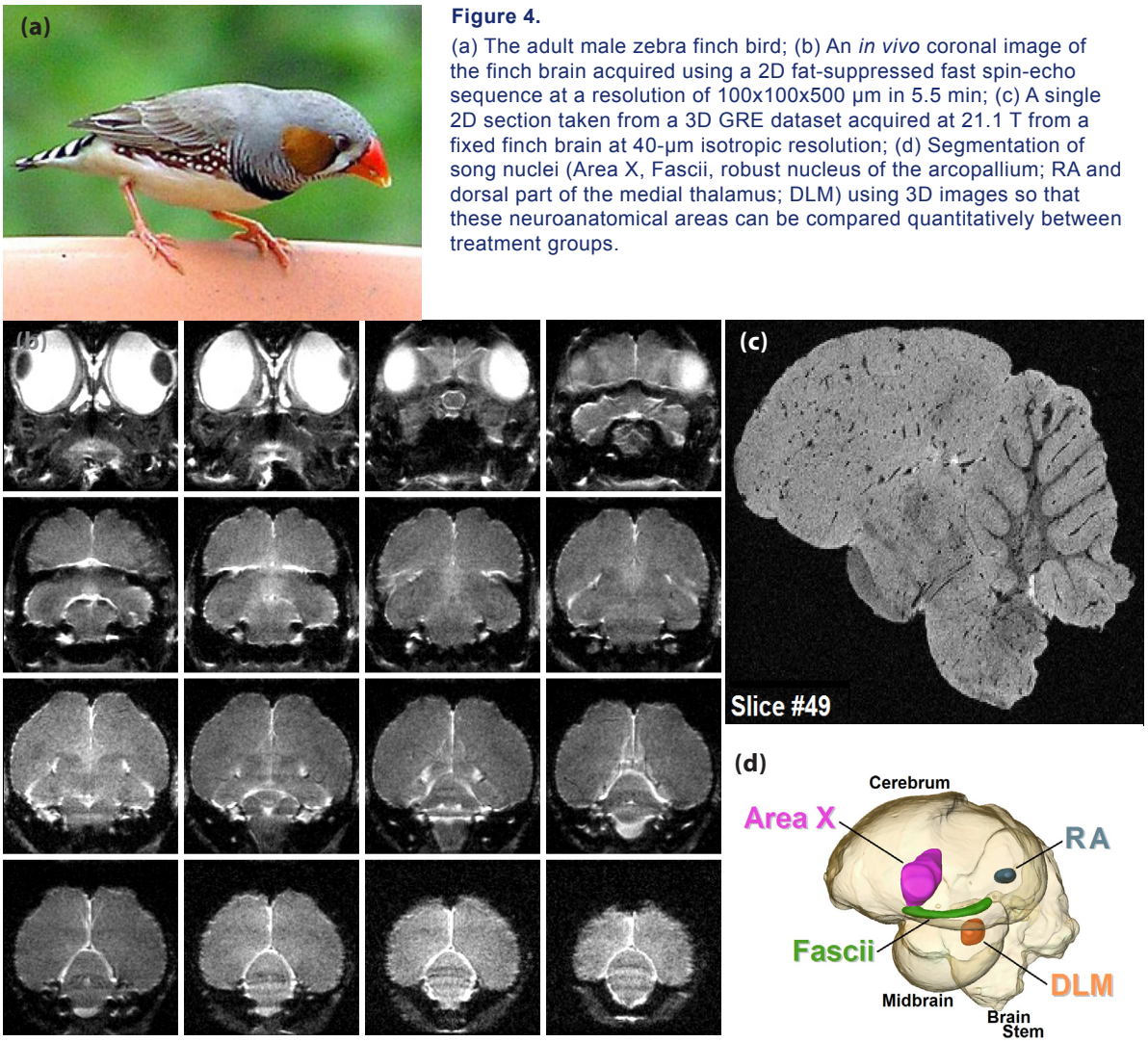

Figure 4.
(a) The adult male zebra finch bird; (b) An *in vivo* coronal image of the finch brain acquired using a 2D fat-suppressed fast spin-echo sequence at a resolution of 100x100x500 µm in 5.5 min; (c) A single 2D section taken from a 3D GRE dataset acquired at 21.1 T from a fixed finch brain at 40-µm isotropic resolution; (d) Segmentation of song nuclei (Area X, Fascii, robust nucleus of the arcopallium; RA and dorsal part of the medial thalamus; DLM) using 3D images so that these neuroanatomical areas can be compared quantitatively between treatment groups.

***In vivo* Mouse Sodium MRI**

The first *in vivo* ^{23}Na images of the mouse brain were acquired at 21.1 T (frequency = 237.4 MHz) with isotropic resolution of 0.125 µL (Figure 3). A custom-designed 3D back-projection pulse sequence was used with the following parameters: TE = 1.5 ms, matrix = 64x64x64, FOV = 32 mm, TR = 50 ms, NA = 16 and a total acquisition time of 55 min. High resolution *in vivo* sodium and proton MR imaging is a very important tool for upcoming studies that seek to use sodium content and diffusion changes as early biomarkers for tumor response to therapy (NIH grant R21 CA119177-01).

Zebra Finch Brain MR Imaging

Recent *in vivo* work on the 900 UWB system also included a unique animal model. Susanne Cappendijk of the FSU College of Medicine uses zebra finches (Figure 4) to examine the neurochemical and behavioral effects of nicotine and Ecstasy (3,4-methylenedioxy-N-methylamphetamine, MDMA). The zebra finch model presents the opportunity to evaluate the mechanisms of memory and learning, as well as the biochemical impact of these drugs of abuse by monitoring their ability to employ songs.

Complementing these biochemical and behavioral assays, high resolution MR imaging on the 900 UWB system provides a means of assessing the pharmacological impact of nicotine and Ecstasy on brain morphology both in the living animal and the excised brain. For *in vivo* studies, imaging sessions were restricted to a total time of less than 60 minutes to limit stress on the bird. However, the sensitivity afforded by the 900 UWB permitted multiple images to be acquired with high signal-to-noise ratios at high

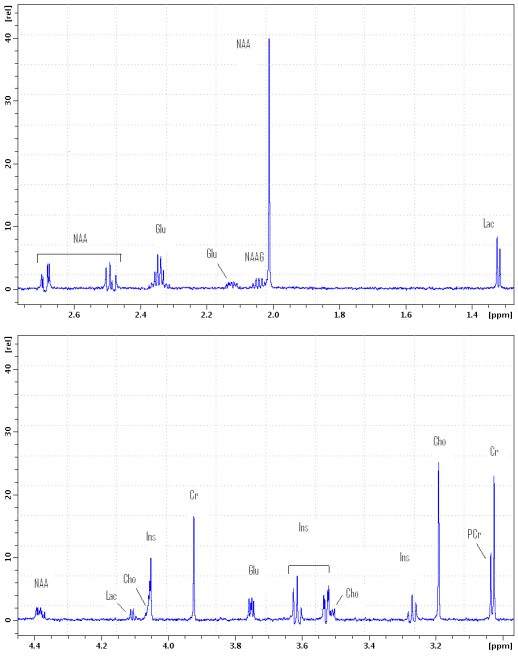

Figure 5..
Test of MR localized spectroscopy in brain phantom solution performed at UWB 900. The voxel volume was 8 µL, TR/TE = 4000/ 19 ms, accumulation time was 18 min.

Total acquisition time was 18 min.

resolutions within that timeframe (Figure 4b).

Once the longitudinal study was completed, the zebra finches were sacrificed for standard biochemical assays. However, because MR imaging is a non-destructive technique, the excised brains from these animals were first re-imaged on the 900 UWB system to achieve even higher resolutions. True 3D gradient recalled-echo (GRE) images were acquired from *ex vivo* brains at a 40-µm isotropic resolution (Figure 4c). Under the guidance of Biomedical Engineering Graduate Student Parastou Foroutan, Summer 2007 Research Experience for Teachers participants Stan Cutler and Mark Johnson assisted in segmenting regions in the song pathway of the finch brain for these studies (Figure 4d).

Localized Spectroscopy in Brain Phantom Solution

The high magnetic field of 21 T brings an extreme separation of MR spectral lines. Performance of the Point Resolved Spectroscopy (PRESS) was tested using a model brain solution (Figure 5 A, B). The solution was placed in 15-ml vial, and a localized 1D proton MR spectrum was acquired using a voxel size of 2x2x2 mm. Acquisition parameters were: TR/TE = 4000/19 ms, SW = 5 kHz. The FASTMAP shimming procedure allowed us to achieve a water line width of 18 Hz from the whole 15-ml sample.

Future Directions

Currently, we are in the process of purchasing a Bruker Mini 0.75 gradient coil. It will provide a peak gradient strength of 450 mT/m using the existing GREAT60 amplifiers. The installation of this gradient set and construction of the new large probes (now in progress) will permit numerous large rodent models to be evaluated at 21.1 T. In terms of RF coil advancements, we regularly receive valuable support from our AMRIS colleagues in Gainesville: Dan Clark, Barbara Beck, David Peterson, Steve Blackband and Art Edison. Their first proton single tuned 18-mm RF coil with remote tuning for 900 MHz is currently being evaluated. Further work is underway pursuing future MRI studies utilizing MR signals beyond proton.

CONCLUSIONS

The first *in vivo* mouse and zebra finch bird MR images have been acquired using the 900 UWB magnet system. The novel *in vivo* MR imaging capabilities create new opportunities for Magnet Lab users around the country to investigate a host of animal models and to conduct biomedical research using proton and non-proton nuclei with sensitivity and contrast afforded by this special instrument.

ACKNOWLEDGEMENTS

Our *in vivo* MR program and Magnet Lab user's support is strongly dependent on the skill and effort of our staff. In addition to those mentioned above, Richard Desilets, Kiran Shetty and Peter Gor'kov have made valuable contributions to *in vivo* RF probe development. The *in vivo* mice studies were supported by NIH grant R21 CA119177 (PI Schepkin). Zebra finch research was supported by the State of Florida through the James and Ester King Foundation (06-NIR2) awarded to Cappendijk. The MR imaging program at the Magnet Lab is supported by Cooperative Agreement (DMR-0084173) and the State of Florida.