High Throughput Microimaging of Mouse Brain and Embryo

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Introduction

Anatomical abnormalities, especially in neuroanatomy, are important indicators of human disease and their respective mouse models. Using magnetic resonance imaging (MRI) and subsequent image analysis, minute abnormalities in the mouse brain can be detected. With growing interest in screening for anatomical abnormalities, new methods to rapidly assess anatomy need to be developed.

High-resolution, ex-vivo 3D datasets provide maximal flexibility in extracting quantitative information and allow for automated image analysis. However, with 12 hour scan times, high throughput of specimens has been problematic. Therefore, we present a method for the parallel acquisition of 16 high-resolution MR data sets of fixed in-skull mouse brains and mouse embryos in overnight scanning sessions.

Methods

A custom-built 16-coil solenoid array was created to image 16 samples concurrently within a 300 mm internal diameter (ID) gradient set (rise time = 840 μs, maximum gradient strength = 120 mT/m) (Fig. 1). Using a custom-made former, 13 mm diameter 8-turn solenoid coils were fabricated with over wound ends[1] provide uniform sensitivity to within 10% over a length of 26 mm. Each coil was individually shielded within a modular compartment to minimize cross-talk between coils and radiofrequency (RF) interference. Small wave guides located on the bottom of each compartment allows the coil cabling to pass through the RF shielding without compromising shield integrity and to facilitate access for coil servicing. The 16 coil compartments were assembled to a frame, which positions the coils in a 4 x 4 array and slides the coils into the gradient on fixed fiberglass rails. Once positioned inside the gradient, a pneumatic bladder is inflated to clamp the assembly within the gradient to minimize motion and vibration throughout the scan. Imaging was carried out on a multi-channel 7.2-T Varian INOVA scanner.

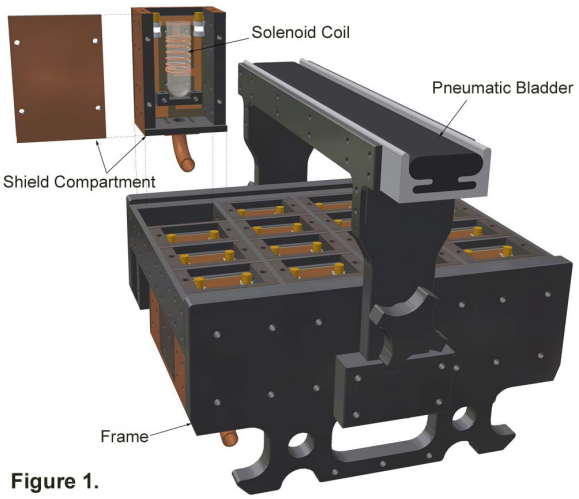

Figure 1.

Imaging

Parameters used for the MRI scan were optimized for grey/white matter contrast: A T2 weighted, 3D fast spin-echo sequence, with TR/TE = 2000/42 ms, NSA =1, field-of-view 14 x 28 x 25 mm and matrix size = 250 x 504 x 450 giving an image with 56 μm isotropic voxels. Total imaging time was 11 h and 45 minutes.

Results

16 mouse brains were imaged with an average SNR of 33. Figure 2 shows a slice taken from each of the 16 brains.

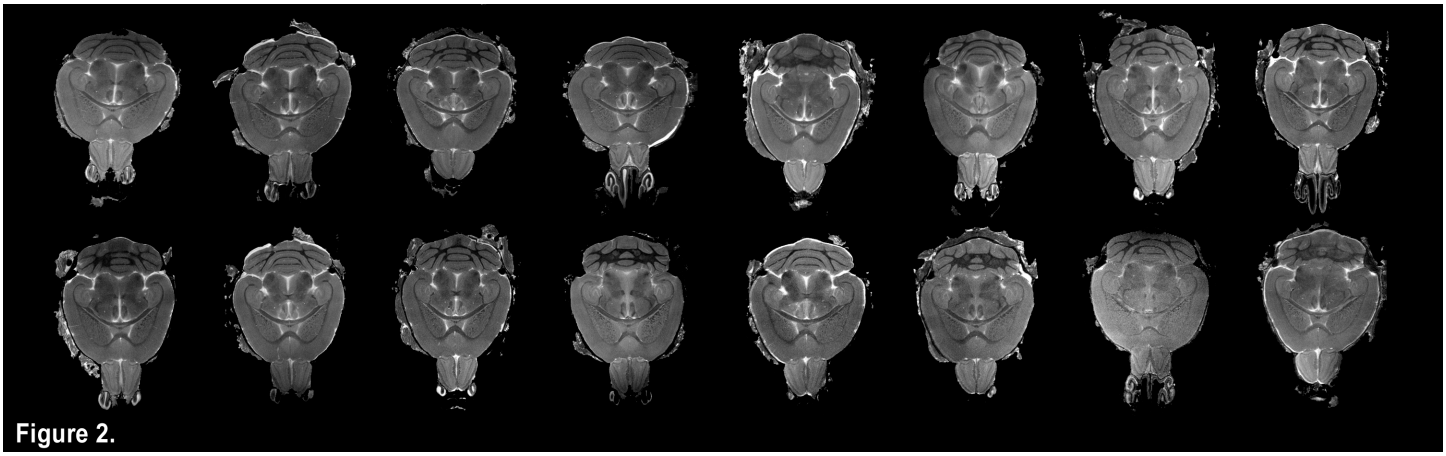
Figure 2.

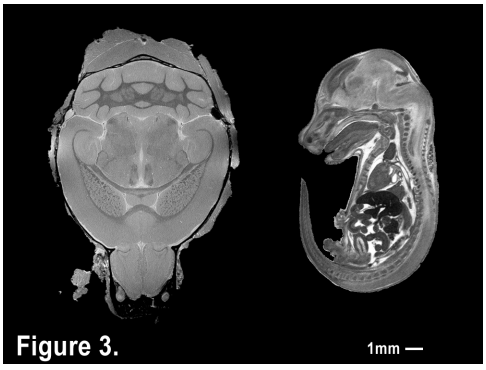

Figure 3.

Discussion

In order to improve resolution, we have also developed a three coil solenoid array to fit within a more powerful 60mm ID gradient set (rise time = 130 μs, maximum gradient strength = 1000 mT/m). This resulted in an effective throughput of four hours per sample with 32 μm isotropic resolution and an average SNR of 22 [2]. Figure 3 shows a slice taken from an embryo and a brain using this setup.

Hence, we are currently in the process of installing a new 205mm gradient set (rise time = 240 μs, maximum gradient strength = 600 mT/m) to use with our 16-coil array in hopes to achieve the same 32 μm isotropic resolution with an effective throughput of less than 45 minutes per sample.

References

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2 R. M. Henkelman et al., "High throughput microimaging of the mouse brain." Proc. Int. Soc. Mag. Reson. Med. 14, 2010 (2006).