MR Microscopic Imaging of Rodent Brain using Contrast Enhancement and Relatively Short Acquisition Times

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Introduction: High-resolution anatomical imaging of rodent brain can be a useful tool to study brain development and neurological disease models affecting brain structures. However, acquisition of high-resolution image is generally achieved with long acquisition times (6-12 h) that limit the applicability of the method, especially when the sample size is large. It has been reported that the scan time in high resolution imaging of mouse brain can be reduced by perfusing the brain with a fixative and contrast agent [1]. Furthermore, an increase in SNR and T_2 contrast can be achieved using the multiecho frequency domain image contrast method [2]. This study was performed to demonstrate the efficacy of a conventional 3D gradient echo sequence to achieve equivalent or better contrast between the white and gray matter. We show that this technique leads to imaging feature that match closely to myelin stained histological slides, indicating the potential of high-resolution MR microscopy.

Method: Three mice (nude, 22-24 g) and three female Fisher rats (approximately 130 g) were sacrificed for high resolution *ex vivo* imaging. Animals were deeply anesthetized by i.p. injection of ketamine/acepromazine and transcardially perfused with 4% paraformaldehyde (PFA)/phosphate buffered saline (PBS) fixative mixed with Gd-DTPA (Omniscan; Nycomed). The concentration of Gd-DTPA in the PFA was 0.125 mM. The extracted brain tissues were stored in the same solution at 4 °C for 2 days before the scan to allow even distribution of Gd-DTPA across the brain. High resolution imaging was performed on fixed brain tissues using a 9.4T, 89 mm vertical bore magnet with a home-built 20mm resonator coil. The 3D gradient echo pulse sequence was used with TR = 50 ms, TE = 5ms, number of acquisitions = 2, FOV=2 cm x 1 cm x 1 cm, and acquisition image matrix = 512 x 256 x 256, resulting in 39 μm isotropic acquisition resolution. The acquisition time for the 3D imaging was 1 hour and 50 minutes. T_1 and T_2 were measured using 2D gradient echo sequence with multiple flip angles (10, 20, 30, 40, 50, 60, 70, 80, and 90) and 2D spin echo sequence with TR=1 s and TE=9, 14, 19, and 24 ms. All animal studies were approved by the Institutional Animal Care and Use Committee.

Results and Discussion: Fig.1 shows the representative slices of a mouse brain. The images were linearly scaled to make the gray scale of the image from raw data without any image processing. Good contrast between the white matter (WM) and the gray matter (GM) can be observed. The branching structure in the caudate putamen is clearly seen in the lower right panel of Sag-2. This structure is often visualized by myelin stain histology slide as shown in ref. [2]. The directionality of myelin can also be observed through the pons, medulla oblongata, and the spinal cord, located below the cerebellum in the sagittal images. The GM/WM contrast-to-noise ratio, $(S_{GM} - S_{WM})/\sigma_{noise}$, is about 9.88 when the intensities of the gray matter, white matter, and noise were measured from the cortical area, genu of corpus callosum, and the background, respectively. SNR in GM and WM are 20.6 and 10.0, respectively. The T_1 and T_2 of the brain parenchyma were 126 ±18.9 ms and 6.7 ±1.5 ms, respectively. We were able to acquire similar quality images for rat brain as well, but with half the resolution because an FOV=4 cm x 2 cm x 2 cm was used to cover the larger size of the rat brain. We have also tested the same sequence with a shorter TR (25 ms) to further reduce the scan time and have achieved comparable results. The excellent contrast and signal to noise achieved in relatively short acquisition times allows for the possibility of increasing the resolution further or to acquire high-resolution imaging data from a large number of samples.

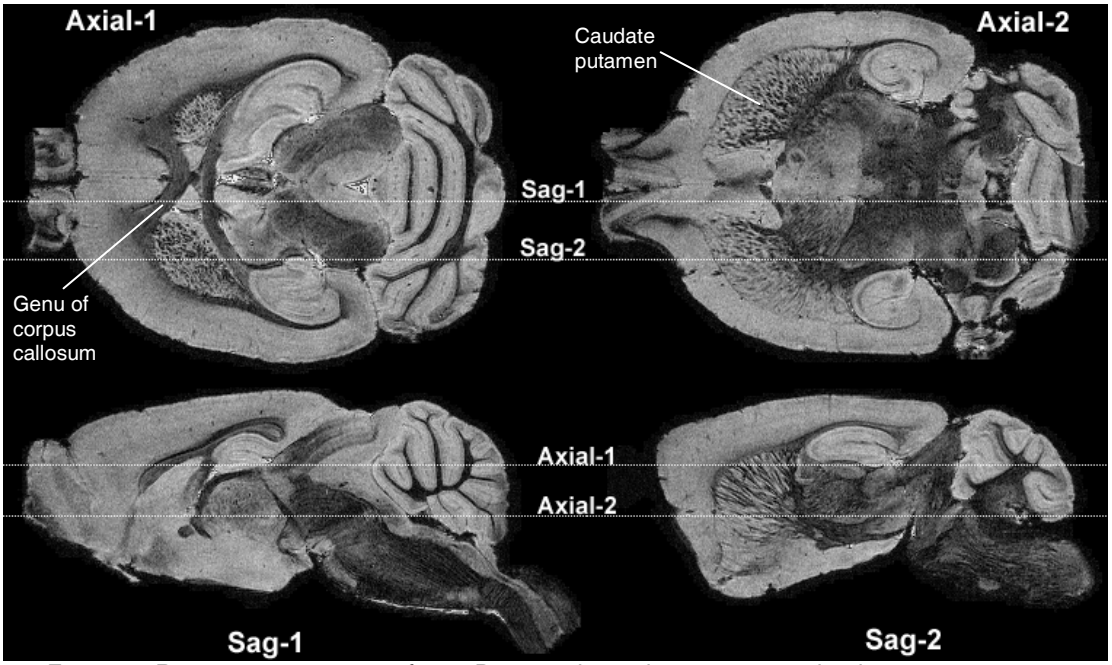

Figure.1. Representative images from 3D mouse brain data set acquired with an isotropic acquisition resolution of 39 microns

References:

[1] Johnson et al., JMRI 16:423-429, 2002.

[2] Sharief and Johnson, MRM 56:717-725, 2006.