

HIGH-RESOLUTION MURINE BRAIN IMAGING AT 15.2 TESLA

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INTRODUCTION The increasing number of available murine models for preclinical imaging generates a demand for high spatial resolution and high sensitivity of MRI systems. Recently, the advantages of cryogenic RF coils for enhancing the signal-to-noise ratio were reported [1,2]. Now, such coils have also become available for ultra-high magnetic field strength systems ($B_0 > 11.7$ T). The aim of this study was to test the limits of high-resolution *in vivo* mouse brain imaging within scan times consistent with standard measurement protocols (< 30 minutes each) on a 15.2 T scanner equipped with a cryogenic RF coil.

METHODS Scans were performed on a 15.2 T / 11 cm bore scanner (Bruker, Ettlingen, Germany) equipped with a closed-cycle helium-cooled cryogenic quadrature transceive surface coil and preamplifier ($T_{\text{coil}} = \text{about } 30$ K, $T_{\text{preamp}} = 77$ K, Bruker, Fällanden, Switzerland). For optimization of contrast, mouse brain T1 and T2 relaxation times were determined using a multi-echo, multi-TR sequence and non-linear least-square fitting of four regions of interest (RAREVTR, 5 echo images, TE: 7–63 ms, 10 TR times: 200 ms–15 s). Gradient echo images (FLASH) were acquired with an in-plane resolution of $(19.5 \mu\text{m})^2$ and a slice thickness of $150 \mu\text{m}$ within 21 minutes. The flip angle was set to 60 deg. 5 mm below the surface of the brain. An additional phase image reconstruction including phase unwrapping was obtained using the included SWI software package. Spin echo images (RARE) were acquired with an in-plane resolution of $(29 \mu\text{m})^2$ and a slice thickness of $200 \mu\text{m}$ within 26 minutes. The pulse power was optimized to the imaging plane. For both methods, four acquisitions were averaged to enhance the signal-to-noise ratio. Three adult female mice were anesthetized using Isoflurane (FLASH images: C57Bl/6, RARE / RAREVTR images: CD-1), and fixated with a stereotactic holder. Physiological conditions were monitored throughout all sessions.

RESULTS AND DISCUSSION Measured mouse brain T1 and T2 relaxation times at 15.2 T are summarized as a reference in Table 1. The FLASH image in Figure 1 demonstrates very high spatial resolution while maintaining good contrast and signal-to-noise ratio. The spatial resolution is greatly improved as compared to gradient echo imaging results in rat brain at 14.1 Tesla with a room temperature coil [3]. Signal intensity and contrast exhibit good homogeneity. Very small features of the murine brain become visible in the enlargements Figure 1 (b,c). The phase image reconstruction makes use of internal tissue frequency shifts that may be attributed to different iron or fat contents [3]. This enables the depiction especially of small venules with diameters of the order of one pixel. In addition, small structures close to the corpus callosum such as the cingulum and the dorsal fornix may be distinguished, and details of the hippocampus become visible (clear identification of the hippocampal fissure, alveus, and dorsal hippocampal commissure). The RARE image in Figure 2 shows excellent details of the hippocampus and the caudate putamen, as well as cortical sub-structures.

Region	T1 / ms	T2 / ms
frontal cortex	1870	33
hippocampus	1922	26
cerebellar WM	2115	26
cerebellar GM	1748	26

Table 1: T1 and T2 relaxation times in four different regions of the murine brain at 15.2 Tesla.

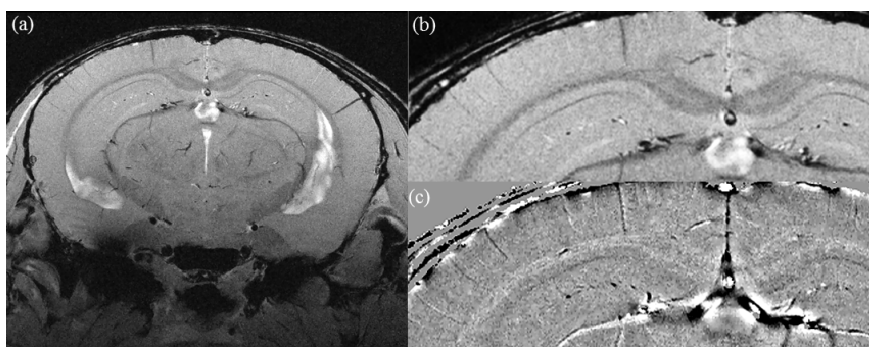


Figure 1: Images located approximately at position Bregma -2.7 mm. On the left a full field of view FLASH image is shown. Image (b) shows an expanded area and image (c) a phase image of the very same FLASH image. Acquisition details: Matrix: 768×768 , field of view: $(1.5 \text{ cm})^2$, TR: 550 ms, TE: 4.4 ms, slices: 7.

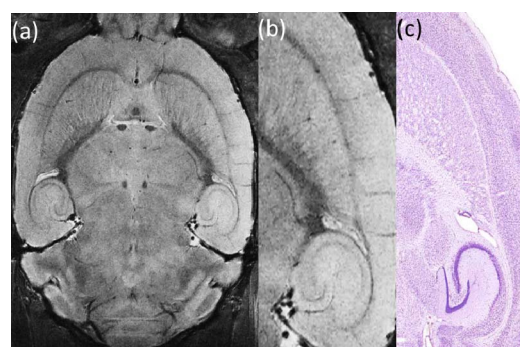


Figure 2: (a) Full field of view coronal RARE image, image (b) shows an expanded view of the hippocampal area, and image (c) a corresponding Nissl stained plate from [4]. Acquisition details for (a,b): Matrix: 660×660 , FOV: $(1.9 \text{ cm})^2$, TR: 3.5 s, TE: 25 ms, echoes: 6, slices: 7.

In conclusion, *in vivo* murine brain micro-imaging with resolutions slowly approaching cellular levels becomes feasible at high magnetic field strengths (15.2 T) using a cryogenic RF coil. This may open up new possibilities for research on microstructural changes in genetically modified mice as well as changes in tissue composition such as myelination or demyelination, vascularization, and specific defects in neurodegenerative brain diseases such as Alzheimer's.

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