Enhanced T_2 contrast for MR Histology of the mouse brain

A. A. Sharief[1,2], G. A. Johnson[2]

[1]Biomedical Engineering, Duke University, Durham, North Carolina, United States, [2]Center for In Vivo Microscopy, Duke University Medical Center, Durham, North Carolina, United States

INTRODUCTION: Magnetic resonance histology (MRH) has enabled high SNR images at resolutions of 50 microns and greater in the mouse brain [1]. The behavior of MR-associated tissue properties of T_1, T_2, and diffusion at high fields however, has made the optimum T_2 contrast difficult to achieve. Accurate T_2 measurements and T_2-weighted contrast are a challenge due to signal attenuation caused by the combined effects of diffusion-mediated losses and large susceptibility variations. Further, in the presence of paramagnetic contrast agents, tissue T_2s decrease significantly. Previous methods [2,3] have relied on lower resolution, multiple, single echo acquisitions with longer echo times that those reported in our work. We present the combination of a well balanced 3D Carr-Purcell-Meiboom-Gill (CPMG) sequence and a post-processing method for obtaining enhanced T_2 contrast in the actively stained (perfusion with fixative and contrast agent) mouse brain at 9.4 T.

METHODS: 1. C57BL6/J male mice approximately 9 weeks in age were perfused using a transcardial approach with an initial flush of saline/ProHance (ProHance®, gadoteridol, Bracco Diagnostics, Inc., Princeton. NJ) followed by a 10% buffered formalin/ProHance mixture as described in [4]. The fixed ex-vivo, in-situ specimens were imaged on a 9.4 T (400 MHz) vertical bore Oxford magnet with a GE EXCITE console (Epic 11.0).
2. A 3D CPMG sequence was implemented by stepping through successive phase-encoding gradients on two axes. Phase-encoding gradients were applied after each refocusing pulse and rewound after the echo readout. Crusher gradients alternating in polarity and increasing in amplitude were applied along the slice-encoding gradient to dephase stimulated echoes. Alternate halves of k-space were encoded in the odd and even echoes to make the gradients symmetric around each refocusing pulse. The sign of the crushers for a particular echo was kept identical to the current polarity of the slice-encoding gradient in an inter-pulse interval.
For the high-resolution 3D acquisition, actively stained specimens were imaged using an array size of $512 \times 256 \times 256$ over a FOV of $22 \times 11 \times 11$ mm yielding isotropic 43-micron voxels. The total acquisition time was minimized to 4 hours by encoding only 75% of the full Nyquist sample along the two phase-encoding axes.
3. 3D multi-echo data was fitted pixel-by-pixel with a non-linear least squares exponential decay function to derive T_2 estimates for the entire brain.
4. Using the 3D echo image sets, a complex Fourier transform (FT) was computed at each voxel along the echo dimension to generate the T_2-weighted image set with the multi-echo frequency domain image contrast (MEFIC) method [5].

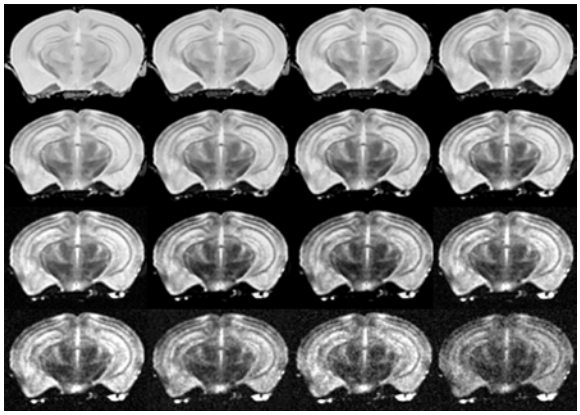

Figure1: Echo images of an axial slice from a 3D volume acquisition; FOV=$11 \times 11 \times 22$mm, matrix=$128 \times 128 \times 128$, TE=4, 8, 12...64 ms, TR=400ms.

CONCLUSIONS: 1. We have demonstrated that with the use of well-balanced crusher and imaging gradients, the 3D CPMG sequence is capable of generating true T_2-weighted contrast in the actively stained mouse brain at 9.4 T.
2. Even with the use of a volume excitation, we have succeeded in suppressing stimulated echo artifacts and harnessing the decaying signal up to the late echo images indicative of T_2-weighted contrast.
3. With the combined use of active staining, short inter-echo spacing, and the multi-echo frequency domain image contrast method, we are able to visualize mouse brain morphology such as multiple layers of the cortex, layers of the superior colliculus, and groups of thalamic nuclei with a high degree of definition and contrast not reported before in T_2-weighted acquisitions at high fields.

REFERENCES

1. Johnson et al. Magn. Res. Quarterly 1993 9(1), 1-30
2. Guilfoyle et al. MRM 2003 49, 576-580
3. Zhang et al. MRM 2004 51, 452-457
4. Johnson et al. JMRI 2002 16(4), 423-429
5. Yang, Q. X. et al. MRM 1999 41, 423-428

RESULTS: 1. Figure 1 shows 16 echo images of one slice in the axial plane through the midbrain region from a 3D multi-echo acquisition. The in-plane resolution is 86 microns with a slice thickness of 172 microns. These echoes range from 4 ms to 64 ms with an echo spacing of 4 ms. TR used was 400 ms since T_1 in the stained brain is < 100ms. At TR = 400 ms, the earlier echoes show high signal intensity depicting the proton density weighted contrast. The latter echoes are T_2-weighted with a successive decrease in signal, but an increase in contrast between structures with differing T_2 relaxation rates. The laminar structure of the cortex is more evident at longer echo times
2. T_2 values obtained in the actively stained mouse brain were compared with those previously computed for the formalin-fixed brain. In the case of active staining with ProHance, the T_2 relaxation times were reduced on an average by a factor of 2.
3. Figure 2 shows a coronal (a) and axial (b) slice of a T_2-weighted MEFIC image computed from an FT along all 16 echoes of a 3D volume acquisition. This image retains T_2-weighted contrast of the later echoes in combination with an increased SNR. The panels show among other structures, multiple cortical layers and thalamic nuclei in high definition.

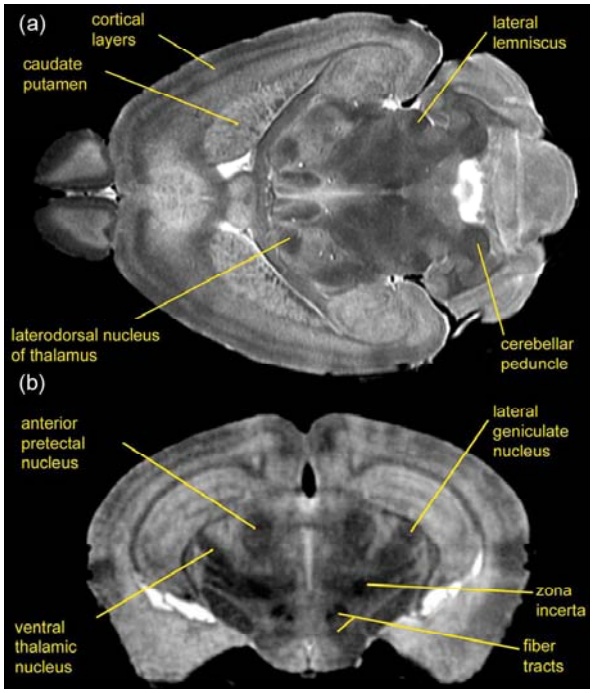

Figure 2 (a) Coronal and (b) Axial slice from a MEFIC computed T_2-weighted 43-micron isotropic resolution acquisition of an actively stained mouse brain. FOV=$11 \times 11 \times 22$, matrix=$256 \times 256 \times 512$, TE=7,14…112 ms, TR=400 ms.