High Resolution Quantitative Imaging of Rodent Brains at 7T

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Introduction: Quantitative MR measurements have numerous advantages over traditional T1 or T2-weighted images, such as permitting the direct comparison of images taken from different scanners or times. Advanced signal modeling techniques, such as breaking the signal into contributions from multiple discrete tissue compartments, can also extract interesting tissue parameter information from quantitative data, or allow for the correction of imaging artifacts. The DESPOT family of techniques has been repeatedly demonstrated at low and medium field-strengths, but has yet to be demonstrated at higher field strengths typical of pre-clinical imaging systems. We present here preliminary T1&T2 maps at 200 μm isotropic resolution over the whole rodent brain, reconstructed using both "classic" DESPOT1&2 [1] techniques and a modified DESPOT-FM [2] technique. We also present Myelin Water Fraction maps constructed using a 3-component mcDESPOT [3] technique.

MR Acquisition: 2 adult male Sprague-Dawley rats were sacrificed when approximately 6 months old and their tissues fixed by transcardial perfusion with heparinized saline followed by ice-cold 4% paraformaldehyde (PFA). Heads were removed from the body and post-fixed for 24 hours in 4% PFA. To minimize changes to T1&T2 by dehydration they were then rinsed in 0.1M Phosphate Buffer Solution and stored in the same solution with 0.05% sodium azide for a minimum of 2 weeks. Each head was then scanned with 7T Direct Drive (Agilent) system equipped with a quadrature birdcage RF transmit/receive coil. The magnet was shimmed using a 3D Gradient Echo (3d GE) technique and then Spoiled Gradient Recalled (SPGR) and balanced Steady-State Free-Precession (SSFP) images obtained with the parameters listed in table 1. Actual Flip Angle (AFI) images were interleaved with the SPGR and SSFP images to measure the $B1^+$ field ratio (by dividing the obtained flip angle maps by the nominal angle) [4].

Data Analysis: Classic DESPOT1&2 images were produced by using the standard linearization process and fitting using least-squares [1]. The measured $B1^+$ values were used to correct the nominal flip angles, and only used the 180° phase-cycling SSFP data. T1&T2 maps were then also produced using a modified DESPOT2-FM method [3]. Briefly, a global non-linear method was used to fit the full Bloch-McConnell expression for both the SPGR and SSFP (including off-resonance) signals to the acquired data. Instead of using the T1 calculated with the classic DESPOT1 technique and feeding this into the DESPOT2-FM calculation, we fitted for T1&T2 simultaneously.

The same data was then reanalyzed using a three-component mcDESPOT model [3]. This essentially consists of extending the DESPOT-FM technique to contain signal contributions from multiple discrete pools of water, each with their own T1&T2 value, in this case believed to correspond to intra-/extra-cellular water, cerebro-spinal fluid and water trapped between myelin bilayers. This last component, the Myelin Water Fraction (MWF), is a potential biomarker for any neurodegenerative disease that affects myelin. Suitable fitting ranges for the T1&T2 values of each component were chosen after reviewing the available literature on multi-component relaxometry studies [5].

Results: Figures 1 and 2 show example T1 and T2 maps processed with classic DESPOT and DESPOT-FM respectively. The T1 maps are substantially identical between the two techniques, as expected. The T2 map in figure 1b exhibits clear off-resonance banding artifacts, which have been removed in figure 2b. Figure 3 shows an example MWF map from the same data. The reported MWF fraction is high in the sub-cortical white matter tracts and lower in the grey matter. The T1, T2 and MWF values were found to be similar between the two subjects (data not shown).

Discussion: These images demonstrate the viability of DESPOT methods for quantitative pre-clinical MR imaging. Their only significant drawback is currently speed. Due to the need to collect many flip angles and multiple phase-cycling patterns with sufficient SNR, the current cumulative scan time is approximately 4 hours. Further work to prove repeatability and to enhance the SNR per unit time are ongoing to make these techniques suitable for *in vivo* scanning.

References:

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4. Yarnykh VL. Actual flip-angle imaging in the pulsed steady state: A method for rapid three-dimensional mapping of the transmitted radiofrequency field. *Magnetic Resonance in Medicine.* 2007;57(1):192–200.
5. Does MD, Gore JC. Compartmental study of T1 and T2 in rat brain and trigeminal nerve in vivo. *Magnetic Resonance in Medicine.* 2002;47(2):274–283.

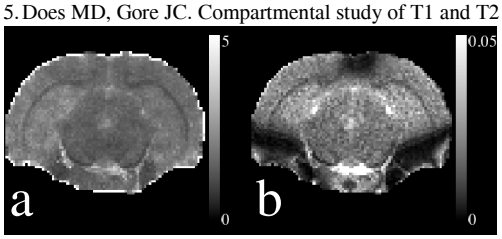

Figure 1 - (a) T1 and (b) T2 maps processed with classic DESPOT. Note the banding artifacts in the T2 image. Color bar units = seconds.

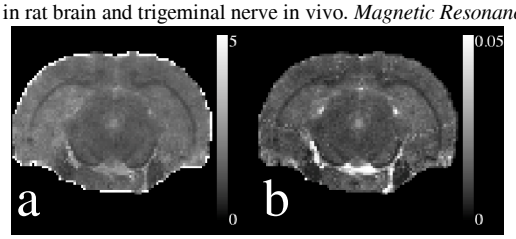

Figure 2 - (a) T1 and (b) T2 maps processed with the DESPOT-FM method. Note the absence of banding artifacts. Color bar units = seconds.

Sequence	Matrix Size	Field-of-View (mm)	TE/TR (ms)	Flip Angles (°)
SPGR	192x192x192	40x40x40	4.876/11.216	2,4,6,8,10,12,16,20,30,40,50
SSFP	192x192x192	40x40x40	1.76/3.52	2,4,6,8,10,12,20,30,40,50
AFI	96x96x96	40x40x40	2.816/7.096	55

Table 1 - Acquisition Parameters for the 3 scan types. The AFI had a TR1/TR2 ratio of 5, the SSFP was acquired with 3 phase-cycling patterns (90,180,270°), and all sequences were averaged 3 times.

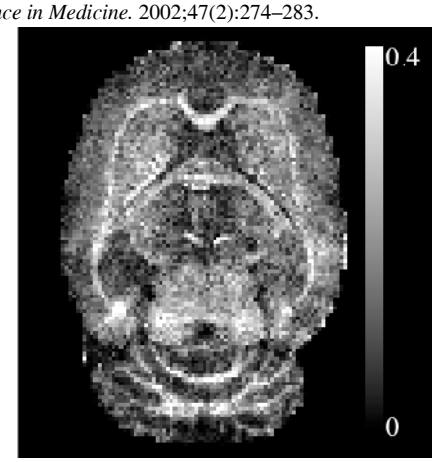

Figure 3 - Coronal section of a Myelin Water Fraction (MWF) Map from a 3-pool mcDESPOT model.