Multicomponent Relaxometry (mcDESPOT) in the Shaking Pup Model of Dysmyelination

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Introduction: Multi-component Driven Equilibrium Single-Pulse Observation of T1 and T2 (mcDESPOT) [1] is a recently proposed technique which provides two-component relaxometry using steady-state imaging. By modeling signal contributions from both slow and fast relaxing spins, the relative fraction of water in two microstructural compartments may be estimated via the myelin water fraction (MWF) map. Such maps have been applied to investigate white matter (WM) changes in clinical multiple sclerosis (MS) patients [2-3]. In this abstract, we report initial results from the mcDESPOT technique on the *shaking (sh)* pup myelin mutant. The *sh* pup is a canine model which suffers from dysmyelination without the confounding effects of inflammation or edema [4], and is thus an excellent model for investigating the sensitivity and specificity of mcDESPOT parameters to myelin content in the brain.

Materials and Methods: Two *sh* pups (27 & 29 months of age) and one age-matched control dog were scanned on a 3.0T GE Signa MR750 (GE Healthcare; Waukesha, WI) using an HD knee coil. Spoiled gradient echo (SPGR) scans were acquired with TR/TE=6.3/2.9 ms, NEX=0.75 over a range of flip angles α = [3 4 5 6 7 9 13 18].° The matrix size was 256x256x48. Fully-balanced steady-state free precession (SSFP) scans were acquired with TR/TE=6.0/3.0 ms, NEX=0.60 over a range of α=[12 16 21 27 33 40 51 68].° The matrix size was 512x512x48, and was down–sampled to 256x256x48 for subsequent processing. Two SSFP scans were acquired with rf phase cycling φ=0° and 180° to remove the effects of SSFP banding artifacts and provide an estimate of the B0 field [5]. An additional inversion recovery IR-SPGR scan was acquired to estimate the transmit B1 field using the DESPOT1-HIFI technique [6]. All scans used full echo readout, and an FOV of 14x14x9.6 cm.

The resulting images were smoothed with a 3x3 Gaussian kernel (σ = 1), and parameter maps were computed using a custom MATLAB implementation of the mcDESPOT algorithm described in [1]. Modified parameter bounds for free T1 were used, based on previously reported single-component values [7]. For analysis, WM regions of interest (ROI) were drawn bilaterally over the corticospinal tracts using a T2-weighted SSFP image as a reference.

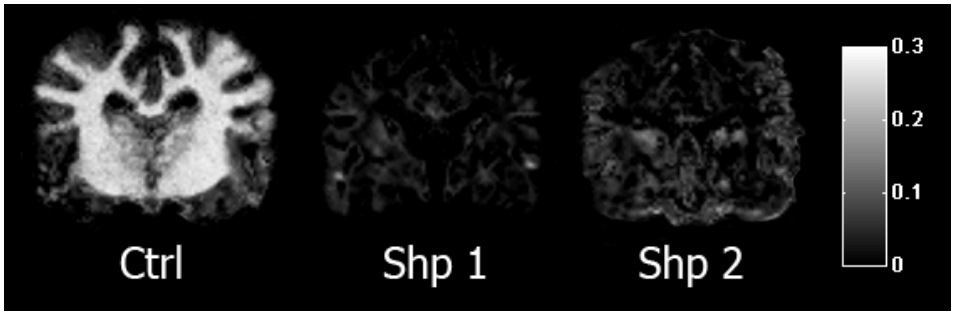

Figure 1: Myelin water fraction maps of a control (left) and two *sh* pups (middle and right). The *sh* pups demonstrate a significant lack of myelin water, as well as a spatial distribution that does not follow the typical appearance of healthy white matter in the canine.

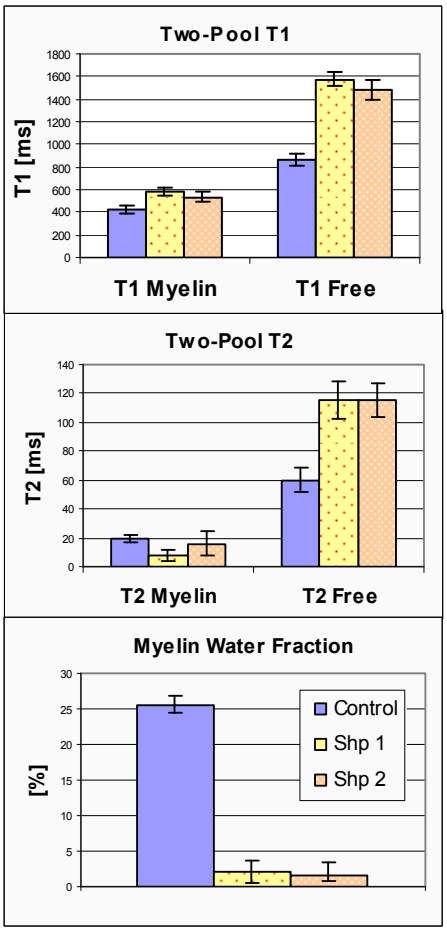

Figure 2: Mean mcDESPOT parameter values from WM ROIs for one control (left) and two *sh* pups (middle and right). Error bars represent ± 1 standard deviation. The *sh* pup shows an increase free T1 and T2, myelin T1, as well as a marked decrease in myelin water fraction.

Results: Figure 1 shows representative coronal slices of myelin water fraction maps for a control and two *sh* pups. Table 1 and Figure 2 present the data from corticospinal tract ROIs. The MWF of the *sh* pups is drastically decreased compared to control, and also exhibits a lack definition between WM and gray matter that is seen in healthy animals. Both free and myelin T1 values in WM are elevated in the diseased animals. This is consistent with previous single component *sh* pup results [7], although the measured value for free T1 from mcDESPOT is lower than the previously reported single component value. This is possibly explained by the use of a very short TR and excitation pulse length in the mcDESPOT acquisition compared to previous measurements, which may induce additional MT effects that bias T1 estimates [8].

	Ctrl	Shp 1	Shp 2
$T1_m$ [ms]	421 ± 39.6	584 ± 40.4	534 ± 42.4
$T1_f$ [ms]	857 ± 51.8	1579 ± 63.9	1483 ± 85.9
$T2_m$ [ms]	19.45 ± 2.26	7.60 ± 3.75	16.19 ± 7.86
$T2_f$ [ms]	60.16 ± 8.88	115.1 ± 12.6	115.4 ± 11.8
MWF [%]	25.58 ± 1.14	2.09 ± 1.66	1.55 ± 2.00
τ [ms]	82.9 ± 10.4	89.8 ± 19.3	101.2 ± 18.8

Table 1: Mean ± standard deviation mcDESPOT parameters from WM ROIs. T1 and T2 for myelin and free components, as well as the myelin water fraction (MWF). Mean residence time τ is the inverse exchange rate between the two components.

Discussion: The MWF is clearly reduced in the *sh* pup white matter relative to control, which is consistent with the profound lack of myelin characteristic of this model. This study is the first clear confirmation that MWF measurements using mcDESPOT appear to be specific to myelin. *Sh* pup 1 showed a lower value of myelin T2 than *sh* pup 2 or control. This may indicate a case where axonal myelination is not only reduced but also atypical where present. Previous mcDESPOT studies have not investigated the effects of parameters besides myelin water fraction; however histopathology in dysmyelinationg and demyelinationg animal models presents an excellent opportunity to study how microstructural changes contribute to individual mcDESPOT parameters.

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