

## Application of the Extended Phase Graph Technique to Improve $T_2$ Quantitation Across Sites

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**Introduction:** The need for sensitive and non-invasive biomarkers of disease progression is becoming increasingly important as new Duchenne Muscular Dystrophy (DMD) therapies are being considered for clinical testing. Quantitative transverse relaxography ( $qT_2$ ) of  $^1\text{H}_2\text{O}$  MR signals has shown excellent sensitivity for the detection of muscle pathology associated with DMD<sup>1</sup> and holds significant promise in this regard. However, a significant challenge in any quantitative MRI application is standardization across sites since these are likely to involve multiple instrument vendors, radiofrequency (RF) coil configurations, and subtle differences in MRI pulse sequences. This is of particular relevance for  $qT_2$  applications since imperfect radiofrequency (RF) refocus pulses have significant potential to generate a multitude of coherence transfer pathways that may contaminate the desired primary echo decay. In MRI applications, single-shot gradient crushing schemes have been developed<sup>2</sup> but these schemes are difficult to implement in multi-slice acquisitions which are demanded when coverage is important. Post-processing methods that use prior knowledge are a promising approach to separate primary and stimulated echo pathways.<sup>3</sup> The purpose of this study was to investigate the Extended Phase Graph (EPG) post-processing method<sup>3,4</sup> to improve agreement and accuracy of  $qT_2$  mapping across multiple sites.

**Methods:** Data were acquired from two healthy adult male volunteers (35 y, 42 y) on whole-body 3T MRI instruments at three institutions; i) Site 1 - Philips Achieva 3T whole-body imaging system with a body RF coil transmit 8-channel extremity RF coil receive, ii) Site 2 - Siemens TIM Trio 3T instrument using an extremity quadrature transmit-receive RF coil, and iii) Site 3 - Siemens Verio TIM 3T instrument using a body RF coil transmit extremity receive only 8-channel array coil. Axial images of the lower leg were acquired using a multi-slice Carr Purcell Meiboom Gill (CPMG) sequence on each instrument with the following parameters; in-plane resolution was  $(0.75 \text{ mm})^2$  with 7 mm slices separated by 3.5 mm interslice gap; 16 echoes were acquired with echo times (TE) evenly spaced from 20 to 320 ms; and a repetition time (TR) of 3000 ms. The refocus pulse width was effectively 1.5 times the excitation pulse width. Excitation and refocus pulses were nominally 90 and 180 degrees, respectively. Fat saturation was achieved using a frequency selective inversion prepared module. Voxel wise fits were performed using two models: i) a single exponential function with three adjustable variables,  $A \cdot \exp(-TE/T_2) + \text{constant}$ , and ii) an EPG approach that incorporates  $B_1$  amplitudes, slice profiles, and tissue  $T_1$  values.<sup>3</sup>

**Results and Discussion:** Figure 1 shows a representative signal intensity decay across TE for the ROI indicated in the inset image (fat-suppressed TE20/TR3000, i.e. 1<sup>st</sup> CPMG echo). The evident intensity oscillation is a signature of mixing between transverse and longitudinal magnetizations due to imperfect refocus pulses and leads to inflated  $T_2$  estimates. The EPG method takes into account these pulse imperfections and is able to properly account for stimulated and primary echo pathways. The solid line in the Fig 1 plot was calculated using the EPG algorithm and nicely captures the signal oscillation. The  $T_2$  estimate from the EPG method is substantially reduced compared to fitting the echo train with a single exponential function (see Figure 2). In the Table we compare single exponential and EPG fits to ROI data for two muscle regions in two volunteers. The EPG method has significant promise for improving quantitative agreement in  $T_2$  measurement under a large range of acquisition conditions.

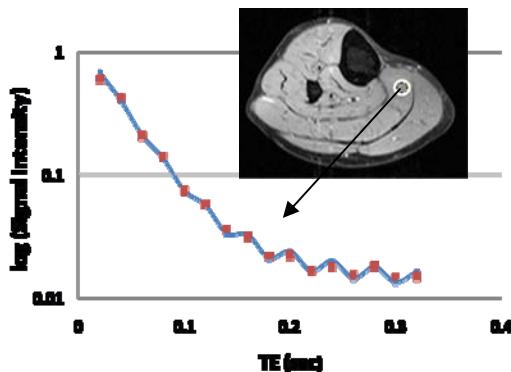


Figure 1. Soleus  $^1\text{H}_2\text{O}$  signal and TE. The solid line is the EPG fit to the data with  $T_2 = 29.1$  ms.

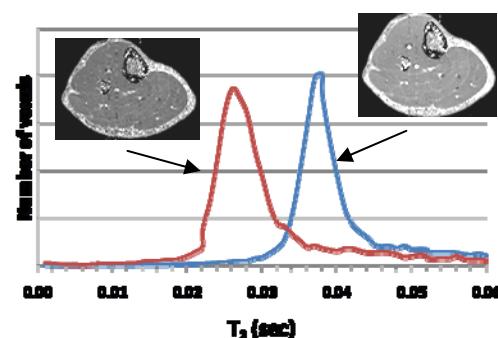


Figure 2. Whole-slice  $qT_2$  histograms and maps (inset). Blue curve from the single exponential and red curve from EPG fits, respectively.

	$T_2$ values in ms (std. dev.)							
	Tibialis Anterior				Soleus			
	Single Exponential		EPG		Single Exponential		EPG	
	Volunteer1	Volunteer2	Volunteer1	Volunteer2	Volunteer1	Volunteer2	Volunteer1	Volunteer2
Site 1 (Philips Achieva)	32.8(1.0)	28.9(0.6)	27.7(1.0)	28.7(1.0)	32.9(1.1)	29.9(1.5)	28.0(1.3)	29.1(1.5)
Site 2 (Siemens TIM Trio)	39.4(1.0)	39.9(1.5)	26.6(0.8)	31.9(0.6)	39.2(1.1)	40.2(1.0)	28.7(1.3)	34.5(1.1)
Site 3 (Siemens Verio)	37.4(0.9)	37.8(0.7)	27.9(1.0)	29.6(1.2)	39.7(0.9)	38.0(1.0)	29.1(1.0)	28.7(1.1)

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**References:** 1. Huang, Majumdar, Genant, Chan, Sharma, Yu, Mynhier, Miller. J Magn Reson Imaging;4:59-64 (1994). 2. Poon, Henkelman. J Magn Reson Imaging. 2:541-553 (1992). 3. Lebel, Wilman. Magn. Reson. Med. 64:1005-1014. (2010) 4. Hennig, J. Magn. Reson. 78 397-407 (1988).