

# Towards Whole Brain Myelin Imaging

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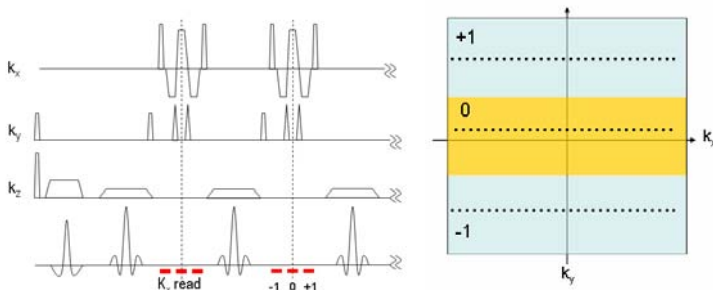
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## Introduction:

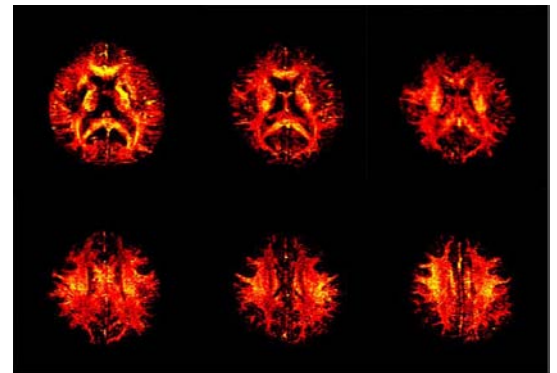
Imaging the short  $T_2$ -component of water trapped between the myelin sheaths of CNS-axons requires high accuracy and SNR on the multi-echo readout sequence. Significant progress has been made over the past years to either improve scan time, feasibility and, or scan resolution towards the application as a regular clinical protocol with acceptable brain volume coverage. The conventional multi-echo  $T_2$ -relaxation technique is based on a single slice CPMG-sequence with composite refocusing pulses and alternating crusher gradients around the refocusing pulses [1]. Only one k-space line is sampled at every TR-cycle, leading to excessively long scan times for only one slice (25 min / 4 NSA) [2]. Although MacKay et al. introduced a variable TR acquisition technique [3] to further reduce the overall scan time where phase encodings at higher  $k_y$ -values were repeated at shorter TR's, the final reduction in scan time was only about 20%. Interleaved multi-slice approaches introduced in the past three years [4,5,6] have highly improved scan-time efficiency but might either suffer from magnetization transfer (MT) between adjacent slices and therefore depletion of the small amount of signal deriving from the myelin-water or do provide suboptimal SNR. Samsonov's approach of segmented  $T_2$ -spin echoes in combination with a linear filter method [7] provides a very elegant method to reduce scan time but requires complex data manipulation and inherits loss in SNR. As previously introduced [8], 3D-CPMG methods combine multi-slice coverage, sufficient SNR and reasonable scan time without the disadvantage of intrusive MT-effects or sophisticated data processing methods. With the additional incorporation of blipped gradient echo readouts encoding the periphery of k-space, another 3-5 fold reduction in scan time is possible and therefore enables whole brain myelin water quantification in less than 15 min.

## Methods:

The modified 3D-CPMG-EPI sequence was derived from a conventional FSE-CPMG [8] on a Philips Achieva 3T system operating on release level 1.5.4. Imaging parameters: matrix 208x176, 32 echoes at  $\Delta TE=10ms$ ,  $TR=1500ms$ , receiver bandwidth=100 kHz (non-EPI) and 350 kHz (EPI-factor=3,5), NSA=1. All measurements were performed with a six-channel phased array head coil. High gradient performance (33mT/m at 200mT/m/ms) and large receiver bandwidth are essential for a three- to fivefold k-space readout enhancement (EPI-factor 3 to 5) between successive spin-echoes. For EPI-factor>3 the volume selective refocusing pulses had to be replaced by shorter, non-volume selective refocusing pulses. Only the central k-space lines (0) produce the desired spin-echo  $T_2$ -weighting, whereas the peripheral k-space lines (-1 | +1) and (-2,-1 | +1+2) respectively, are  $T_2^*$  weighted due to gradient echo rephasers. Imaging parameters were adjusted in such a way that the total scan time did not exceed 15min. The 32-echo decay curves were analyzed on a per-pixel base with a regularized non-negative least square algorithm (NNLS) for a  $\chi^2$  misfit between 1.02 and 1.025. The sequence was tested on 10 healthy volunteers and ROI-based results of Myelin Water Fraction (MWF) were compared to literature results as well as values obtained from a non-EPI sequence [8].



**Fig.1:** 3D-CPMG-EPI with segmented  $k_y$ -phase encodings per TR-cycle. The central echo (0) encodes the  $T_2$ -spin-echo (yellow area in k-space diagram), the other symmetric echoes (-1,+1) are gradient echoes encoding the peripheral k-space trajectories. This scheme allows a 3-fold decrease in scan time compared to the conventional 3D-CPMG [8]; (for EPI-factor>3 see text).



**Fig.2:** Example of Myelin Water Fraction (MWF) Images obtained with the 3D-CPMG-EPI sequence (EPI-factor=3) (MWF scale: 0 to 0.20).

**Results:** Table 1 summarizes scan parameters and various possible volume coverages with their associated total scan times. Whole brain myelin-imaging is realistically achievable in scan times less than 15 min.

Matrix: 208 x 156,  $TR=1500ms$ ,  $FOV=240mm$ , voxel size: (1.15 x 1.57 x 4)  $mm^3$

Sequence	EPI-factor	BW (kHz)	Echoes readout (ms)	Sense factor	Half Fourier	Num. Slices	Scan time (min:ss)
3D-CPMG [6]	-	100	2.1	1	Yes (2D)	5	17:10
3D-CPMG-EPI	3	320	3.1	1	No	8	14:48
	3	320	3.1	1	Yes	15	14:48
	3	320	3.1	1.5	Yes	22	14:36
	5	350	5.4	1	No	13	14:28
	5	350	5.4	1	Yes	26	15:06
	5	350	5.4	1.5	Yes	32	12:25

**Tab.1:** Summary of scan parameters for different speed-up options

## Conclusion:

Substantial scan time reductions by a factor of 3 to 5 can be obtained with segmented EPI-readout at the periphery of k-space for each spin-echo. The substitution of volume-selective refocusing pulse by non-volume selective pulses for EPI-factors>3 leads to better  $B_1$ -homogeneity profiles across the VOI but increases the susceptibility for flow and outer volume signal back-folding. Nevertheless, SNR is still sufficient in all cases to resolve the short  $T_2$  component associated with myelin water (Fig.2). We believe this technique could be a break-through for the routine application of quantitative myelin-imaging in the MR-examination of white matter diseases.

**References:** [1] Poon et al. JMRI 2(1992) ; [2] Whittall et al., MRM 37 (1997) [3] Laule et al. Proc. ISMRM 8 (2001); [4] Oh et al., Proc. ISMRM 13: 759 (2005); [5] Vidarsson et al. Proc. ISMRM 14 (2006); [6] Maier et al. JMRI 17 (2003); [7] Samsonov et al. Proc. ISMRM 14 (2006); [8] Mädler et al. Proc ISMRM 14: (2006)