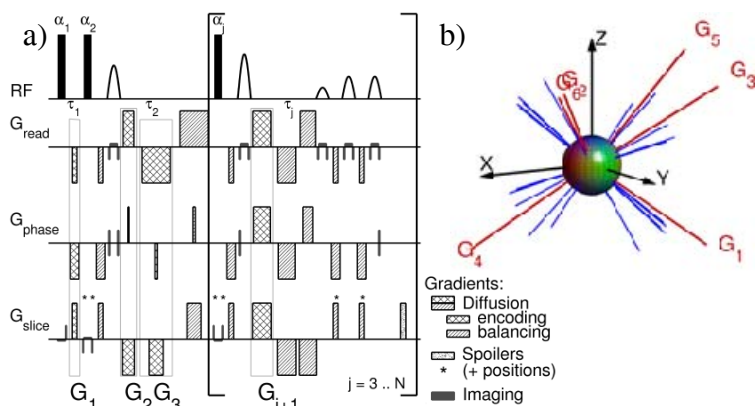


## Two-scan Multiple Echo Diffusion Tensor Acquisition Technique on a 3T clinical scanner with application to skeletal muscle

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**Fig. 1** (a) Multiple-Modulation-Multiple-Echo Diffusion Tensor Imaging Sequence. Five RF pulses ( $N = 5$ ) generate 13 echoes, each of which encodes a diffusion weighting and direction in three dimensions as determined by the diffusion gradient vectors  $G_1$ - $G_6$ . (b) Diffusion gradient vectors  $G_1$ - $G_6$  and effective diffusion sensitizing directions of the 13 echoes (blue lines).

coupled with spoiler adjustment for signal fidelity, and flip angle optimization guided by the target tissue of skeletal muscle.

**Methods** The MEDITATE pulse sequence, which uses 5 RF-pulses and a pattern of diffusion gradients on three axes, was implemented on a 3T full body Siemens Skyra scanner (Fig. 1). The diffusion gradients were optimized to minimize the error on the diffusion tensor estimates, giving a condition number [5] of 4.42. Besides diffusion weighting, the echo amplitudes are also weighted by the RF flip angles and spin relaxation [1,2]. To isolate diffusion contrast, DTI-analysis is performed on the ratio of equal timing acquisitions with different diffusion weighting strengths and analyzed by the difference in B-matrices, computed in the standard way [2,3,6]. Fully segmented Cartesian encoding is used for image encoding in this phase of optimization.

MEDITATE datasets of the right calf muscle were collected in five healthy volunteers (3 male and 2 female, age  $33.0 \pm 3.4$  y/o) with cardiac-gating (ECG, trigger delay of 600ms from the R-wave; 15-channel knee coil, TR = 4000 ms,  $3 \times 3 \times 10$  mm resolution, scan time 4:16 per diffusion gradient set). Flip angles  $\alpha_1/\alpha_2/\alpha_3/\alpha_4/\alpha_5$  of  $61^\circ/73^\circ/100^\circ/45^\circ/60^\circ$  were chosen in order to maximally equalize the magnitudes of the relaxation weighted echoes [1] (human muscle  $T_1 = 1420 \pm 40$ ms and  $T_2 = 32 \pm 2$ ms at 3T [7]). For the latter 11 echoes, echo times were 90 – 245 ms (timing parameter  $\tau = 9$  ms) and isotropic B-values were 167 to 790  $s/mm^2$  (median 388  $s/mm^2$ ). The datasets were processed offline (Matlab, Mathworks) to generate maps of diffusion tensor parameters. Comparisons of accuracy and directional diffusion sensitivity were performed with standard twice-refocused spin echo (TRSE) DTI (TR/TE = 7400/59 ms,  $3 \times 3 \times 10$  mm resolution, 6 directions,  $b = 0, 500$   $s/mm^2$ , 3 averages, scan time 2:59).

**Results and Discussion** Figure 2 illustrates the agreement (2a, quantitative, 5 healthy volunteers; 2b, qualitative, one healthy volunteer) between the diffusion tensor parameters of *in vivo* skeletal muscle estimated with a standard TRSE-DTI and MEDITATE. The eigenvalues and FA of *in vivo* calf muscle estimated with both methods are in good quantitative agreement, despite the different diffusion time, relaxation and diffusion weighting of each of the echoes in MEDITATE. In this comparison, the diffusion eigenvalues and FA are estimated slightly higher with MEDITATE, possibly due to a residual ghosting artifact in the segmented Cartesian sampling, or higher variance due to the different conditioning of the MEDITATE diffusion encoding.

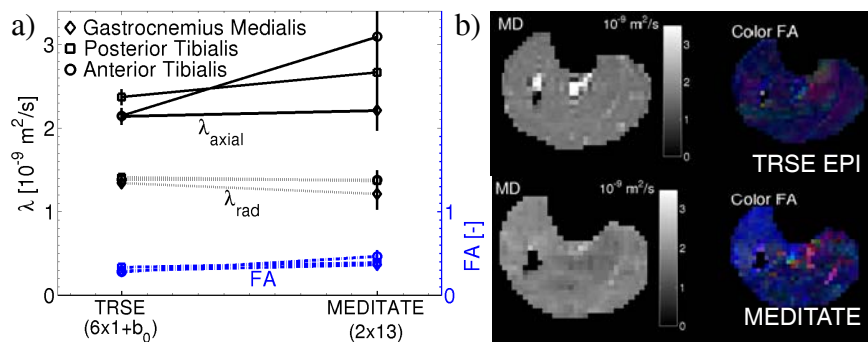
**Conclusion** The two-scan MEDITATE method of accelerated diffusion encoding is feasible on the clinical scanner platform. When combined with an appropriate k-space trajectory employing self-navigation and view-sharing, which improves on the slow fully segmented image encoding, this technique may be used in clinical applications requiring time-sensitive acquisition of DTI parameters such as dynamical DTI in muscle.

**Funding** We acknowledge NIH support (R21EB009435-01A1), SB is a Fellow of the Belgian American Educational Foundation. **References** [1] Sigmund et al. MRI 24:7-18,2006. [2] Song et al. JMR 170:136-48,2004. [3] Cho et al. J Chem Phys 126:154501,2007. [4] Baete et al. Proc ISMRM Melbourne, p121, 2012. [5] Skare et al. JMR 147:340-52,2000. [6] Basser et al. JMR B 103:247-54,1994. [7] Gold et al. Am J Radiol 183:343-351,2004.

**Target audience** Scientists and clinicians interested in the technical development of novel diffusion MRI pulse sequences.

**Purpose** To describe the concepts and implementation of an MRI method capable of accelerated acquisition of apparent diffusion tensor maps in two scans. The method is demonstrated in *in vivo* skeletal muscle.

Diffusion Tensor Imaging (DTI) uses multidirectional diffusion sampling to provide biomarkers of tissue anisotropy and microstructure. This multidirectional diffusion encoding is accelerated in the Multiple Echo Diffusion Tensor Acquisition Technique (MEDITATE) sequence by encoding multiple echoes with each a different diffusion weighting and direction, together sufficient to estimate the 3D diffusion tensor (Fig. 1). Earlier versions of MEDITATE required more than two scans to accurately estimate DTI-parameters of fibrous phantoms [1-4]. The present work extends the original MEDITATE-approach, which is limited by the low SNR in materials with short  $T_2$  [1-4], to a two-scan *in vivo* method, by exploiting longitudinal magnetization storage. This modification is



**Fig. 2** (a) Average  $\lambda_{axial}$ ,  $\lambda_{radial}$  and FA-values of *in vivo* calf muscle of 5 volunteers sampled over a ROI's in DTI parameter maps and (b) sample MD and Color FA-maps of the right calf muscle of a single volunteer obtained with a TRSE EPI and the MEDITATE sequence.