Single Line Multiple Echo Diffusion Tensor Acquisition Technique: feasibility of dynamic diffusion tensor parameters in a flow phantom and in vivo muscle tissue on a 3T clinical scanner

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Target audience Scientists and clinicians interested in the study of dynamic changes in Diffusion Tensor parameters in muscle tissue and elsewhere.

Purpose To demonstrate the feasibility of dynamic diffusion tensor acquisitions in clinical scanners *in vivo* in muscle tissue.

Diffusion Tensor Imaging (DTI) uses multidirectional diffusion sampling to provide biomarkers of tissue anisotropy and microstructure [1]. Following exercise, muscle tissue properties (metabolism, perfusion, myofiber structure) change dynamically, as has been captured in some imaging biomarkers (e.g. [2-6]), However, regarding the full diffusion tensor, traditional methods lack sufficient temporal resolution to resolve the dynamics of the DTI parameters. In contrast, the Single Line Multiple Echo Diffusion Tensor Acquisition Technique (SL-MEDITATE) is able to measure transient changes in biomarkers such as Mean Diffusivity (MD), λ_{axial}, λ_{radial} and Fractional Anistropy (FA) at a high temporal resolution [7] though with a lower spatial resolution. This is facilitated by compressing the necessary multidirectional diffusion acquisitions through modulation of multiple echoes, generated by a train of RF-pulses, with different diffusion weightings and directions [8-9] (Figure 1) and by limiting the readout to a single line volume, selected by applying slice selection gradients along two directions. In this work, we demonstrate the feasibility of dynamic diffusion tensor acquisitions in a flow phantom and in human muscle following exercise.

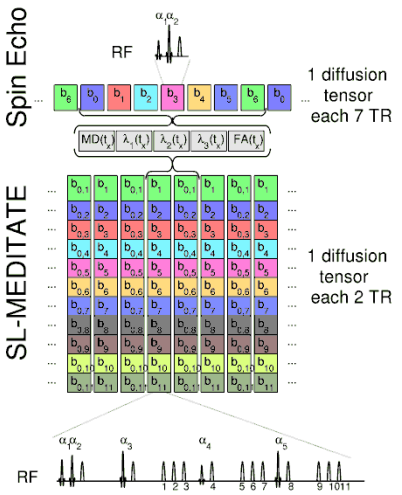

Fig. 1 Two Single Line-MEDITATE repetitions acquired with different diffusion gradients suffice to calculate the diffusion tensor, a dynamic advantage over traditional spin echo diffusion tensor measurements which need 7 repetitions.

Methods The SL-MEDITATE pulse sequence, which uses 5 RF-pulses to generate 13 echoes and a pattern of diffusion gradients on three axes, was implemented on a 3T full body Siemens Skyra scanner [10](Fig. 1). To isolate diffusion contrast, scans were alternately acquired with two different diffusion weighting strengths. DTI-analysis was performed using the difference in b-matrices (calculated in the standard way [1,8,9], condition number of 4.42 [11]).

Dynamic SL-MEDITATE measurements (the latter 11 echoes: TE: 90-245ms, isotropic B-values: 167-790 s/mm^2, flip angles $\alpha_1/\alpha_2/\alpha_3/\alpha_4/\alpha_5$ 61°/73°/85°/45°/85°, TR = 2000 ms (phantom)/ 1000 ms (in vivo) (hence, one DTI measurement per 4s/2s), single line dimension 30x30x190mm) were performed on a flow phantom (cellulose sponge, Fig 2a, [12]) and in *in vivo* muscle tissue (3 male/4 female, age 27.5 ± 4.3 y/o, BMI 23.2 ± 5.0; ECG-triggered, trigger delay of 600 ms from the R-wave) in a 15 channel knee coil. In the flow phantom, the flow speed was stepwise increased every 2 min, as indicated by the pressure differences over the sponge (Fig. 2b). In the healthy volunteers, SL-MEDITATE datasets of the right calf muscles were collected before and after a 2 min period of repeated moderate plantar-flexion against an exercise rubber band. For both cases, the line volume was oriented anterior-posterior, placed using a gradient echo localizer and a ROI volume was selected for further processing. The datasets were processed offline (Matlab, Mathworks) to extract time-resolved diffusion parameters. Outliers were rejected (> 30% deviation from a smoothed time curve, ±5% of the points) and the time-curves were smoothed temporally (Gaussian filter, width 5 time-points = ± 10s). In addition, the averaged *in vivo* time-courses were fitted using an empirical model function [13], previously applied to post-exercise BOLD-responses in skeletal muscle. Comparisons of accuracy were performed in the *in vivo* case with standard twice-refocused spin echo (TRSE) DTI (TR/TE = 7400/59 ms, 3×3×10 mm resolution, 6 directions, b = 0, 500 s/mm^2, 3 averages, 2:59 min) collected at the beginning and end of the time course.

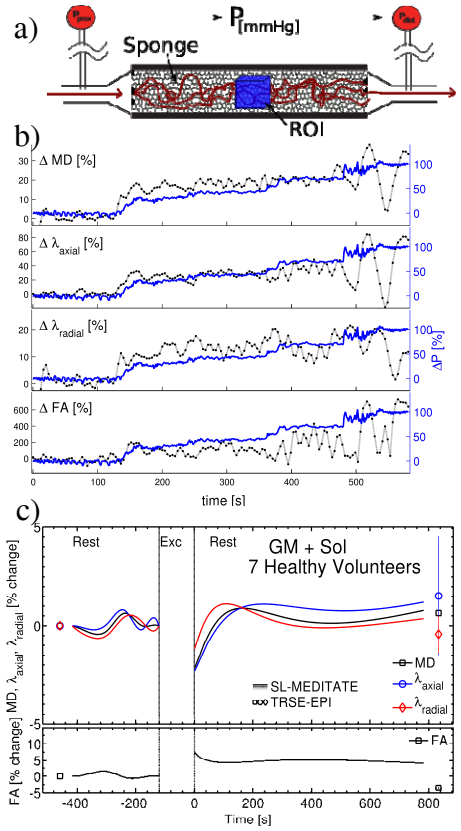

Fig. 2 (a) Schematic of a flow phantom displaying diffusion magnitude changes (cellulose sponge in a PVC pipe, flow regulated with a peristaltic pump). Time-courses of Mean Diffusivity (MD), axial and radial eigenvalues and Fractional Anisotropy (FA) as measured with SL-MEDITATE in (b) the sponge of the flow phantom (pressure-difference time-courses (gray lines, right Y-axis) show the stepwise increase of the water flow through the phantom); (c) the Gastrocnemius Medialis (GM) and Soleus (Sol) muscle of 7 healthy volunteers (averaged fitted time-courses, lines). In (c) SL-MEDITATE measurements are compared to TRSE EPI measurements (symbols) before and after the dynamic time-course.

Results and Discussion The dynamic time-courses of diffusion tensor parameters (Fig. 2b) illustrate the stepwise increases of MD, λ_{axial}, λ_{radial} and FA upon increments of the flow through the sponge. Moreover, SL-MEDITATE also identifies the oscillations due to increasingly non-linear flow in the sponge at higher pressure differences. Fig. 2c summarizes the *in vivo* results, the transient changes in diffusion tensor parameters agree with the low temporal resolution results in the literature (e.g. [2-4]) and the static DTI. The higher temporal resolution allows to better resolve the delayed exercise response [4] (initial decrease of λ_{axial} and MD and delayed increase of λ_{radial}) which is not typically observed since traditional DTI methods lack temporal resolution.

Conclusion The dynamic diffusion tensor measurement method, SL-MEDITATE, can be used to measure transient changes in tissue anisotropy and microstructure in phenomena such as muscle fatigue, exertion or reperfusion at higher temporal resolution than previously possible. In a next step, the compressed diffusion encoding of MEDITATE might allow for dynamic DTI imaging when combined with an appropriate k-space trajectory employing self-navigation and compressed sensing reconstruction.

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