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Dynamic Diffusion Tensor Imaging in Calf Muscle with MEDITI

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A. Introduction

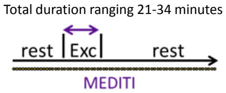
- Muscle tissue properties change dynamically following exercise [1-3]
- Diffusion Tensor Imaging (DTI): Multidirectional diffusion sampling to provide biomarkers of tissue anisotropy and microstructure [4].
- **Traditional DTI methods lack sufficient temporal [1,2] or spatial resolution [5] to resolve muscle tissue dynamics in sufficient detail.**
- MEDITI (Multiple Echo Diffusion Tensor Imaging)
  - Able to image transient changes in biomarkers (Mean Diffusivity (MD), λ_{axial}, λ_{radial} and Fractional Anisotropy (FA)) at a high temporal resolution
  - Compresses the multidirectional diffusion acquisitions by using multiple echoes [9,10], each echo modulated with a different diffusion encoding
  - Accelerates the spatial encoding by acquiring a highly efficient k-space trajectory (STAR) and reconstructing the images with a multidimensional compressed sensing approach which exploits sparsity along both echo and time dimensions.
- Here, we demonstrate the **feasibility of dynamic diffusion tensor imaging in vivo in lower leg muscles of volunteers and chronic exertional compartment syndrome (CECS) patients following exercise**.

C1. Methods : Subjects and Acquisition

- Subjects
- 2 healthy volunteers
- 4 chronic exertional compartment syndrome (CECS) patients
  Previously observed to show anisotropic diffusion changes [11-13] with exercise in compartments with edema and elevated pressure, but kinetics not mapped out

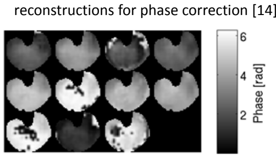
- MEDITI Sequence parameters
- Siemens 3T Skyra, Unilateral 15-channel knee coil
  - flip angles: 61°/73°/85°/45°/85°
  - TE = 90-245 ms (latter 11 echoes), isotropic b-values = 167 – 790 s/mm²
  - TR = 2000 ms
  - 5-petal STAR-trajectory ([9], Single TrAjectory Radial)
  - Reconstructed spatial resolution 3 x 3 x 10 mm
  - 4 shots (weighted and unweighted) for each frame → 16 s spatial resolution

Exercise protocol
- Custom MR-compatible ergometer providing plantar flexion resistance
- MEDITI data captured continuously before, during and after plantar flexion
- Baseline period > 5 minutes, 3 minutes exercise,> 15 minutes recovery
- Total duration ranging 21-34 minutes



C2: Methods : Reconstruction and Analysis

- Reconstruction: Matlab (Mathworks), NYU High performance Cluster (HPC)
  - For each individual echo k-space, phase maps are calculated from low level reconstructions for phase correction [14].



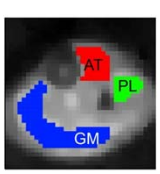
Low resolution phase maps for each echo acquired in a single TR; phase errors removed from each shot prior to compressed sensing reconstruction.

- Readouts from 4 consecutive TRs with the same diffusion weighting are combined and a time series is formed.
- Sparsifying transforms exploit similarities between diffusion weighted images along the echo (t_{echo}) and time (t)-dimensions

$$\hat{X} = \arg min_X\{\|EX - Y\|_2^2 + \lambda_{PCA}\|PCA^{t_{echo}}X\|_1 + \lambda_{PCAt}\|PCA^{t}X\|_1 + \lambda_{TV}TV^{xy}X\}$$

- ***X*** is the time-series of images to be reconstructed, ***Y*** its k-space, ***E*** the multicoil encoding matrix, including coil sensitivities [15] and the NuFFT-transform, *PCA* is the Principal Component Analysis and TV^{xy} the in plane total variation
- λ_{PCA}, λ_{PCAt} and λ_{TV} are regularization parameters chosen as (2.5,2.5,5)10^{-5}
- Solutions are found using a non-linear conjugate gradient method
- In selected subjects, 'high and low' values of regularization parameters are selected in a range of reconstructions

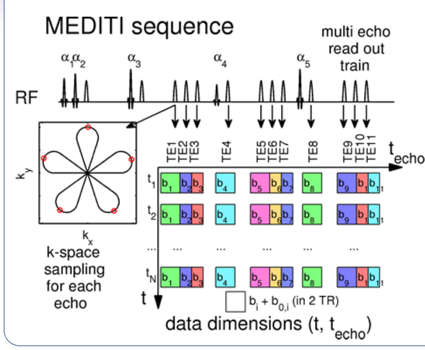
$*10^{-5}$	Low	High	Variable
λ_{PCA}	0.25	2.5	echo
λ_{TV}	0.5	5	space
λ_{PCAt}	2.5	7.5	time



- Data during exercise excluded from reconstruction
- Post-hoc temporal median filter (5 frames) applied

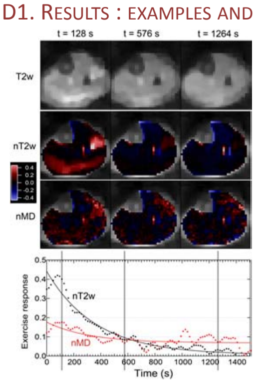
DTI analysis
- Using calculated b-matrices for weighted / unweighted series, a cylindrical DTI model is fit to every time point ($\lambda_1 > \lambda_2 = \lambda_3 = \lambda_{rad}$) [8]
- Time series of parametric maps generated and normalized to average of pre-exercise period; Response maps generated of deviation from rest
- Unweighted Echo #8 of MEDITI series adopted as T2-weighted series
- 4 regions of interest (anterior tibialis (AT), peroneus longus (PL), gastrocnemius medialis (GM), and soleus (SOL)
- Post-exercise recovery fit of T2w and DTI metrics to exponential decay

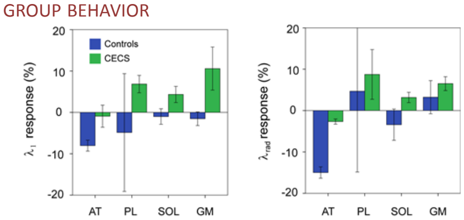
B. MEDITI: Multiple Echo Diffusion Tensor Imaging



- Based on MEDITATE sequence [7,8]
- 5 RF-pulses → 13 echo producing coherence pathways
- Each echo encodes a different diffusion weighting and direction [6,7,8], hence the diffusion tensor can be calculated from two scans, alternatingly acquired with different diffusion gradient strengths (b and b0)[4,6].
- Each echo is captured by a 5-petal STAR-trajectory [9]
- k-space coverage is optimized by rotating consecutive STAR-trajectories (GRASP-scheme: Golden Ratio Angle Sparse Parallel [10]) in both echo (t_{echo}) and time (t)-dimensions.
- Reconstruction exploits similarities between diffusion weighted images along both echo (t_{echo}) and time (t)-dimensions.
- Dynamic acquisitions: **full DTI maps are calculated every 16s**

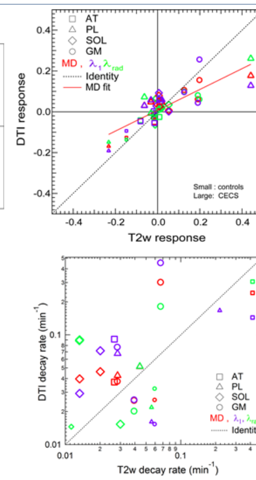
D1. Results : Examples and Group Behavior





DTI metric response levels (error bars ± 1 standard error). CECS responses (green) were typically positive, while those in controls (blue) were negative.

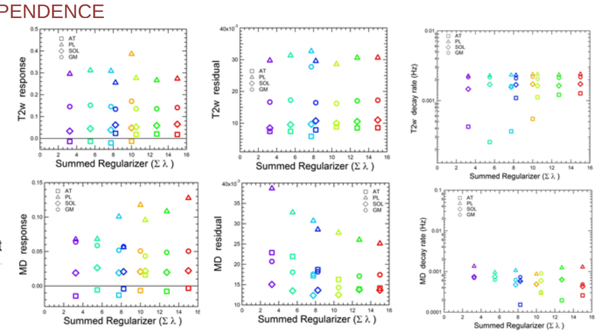
Crossplots of DTI and T2w responses show general correlation but also anisotropic response. Decay rates between T2w and DTI metrics are far less correlated.

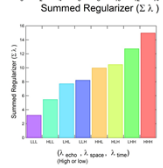


MEDITI images and normalized response maps (nT2w and nMD) of the post-exercise recovery in a chronic exertional compartment syndrome (CECS) subject. nT2w and nMD maps show activation of peroneous longus (PL) and gastrocnemius medialis (GM) muscle compartments with different kinetics.

D2. Results : Regularization Dependence

- 8 configurations executed on selected datasets
- Sum of λ parameters adopted to approximately represent degree of regularization
- T2w and DTI metric responses show different dependence on regularization
- In example shown in D1, T2w response level, fit residual and decay rate are largely independent regularization, but MD response level and fit quali both increase with regularization
- DTI metric maps possess lower SNR than raw T2wimages and are therefore more sensitive to regularization
- Optimal regularization required to avoid reconstruction bias while maximizing contrast





Dependence of response level, fit residual, and decay rate for post-exercise recovery analysis of T2w or MD data from a CECS patient on the regularization parameters of the compressed sensing reconstruction. The sum of three λ parameters approximates the degree of regularization employed.

E. Discussion

- Multiple Echo Diffusion Tensor Imaging (MEDITI) acquires DTI-parameter maps dynamically by simultaneously accelerating both diffusion and spatial encoding. The combination of rapid encoding and compressed sensing reconstruction enables continuous dynamic resolution for in vivo muscle DTI at a temporal resolution of ~15s.
- Activated compartments in plantar flexion, particularly those in compartment syndrome patients, can be dynamically monitored with DTI
- Activation kinetics of DTI metrics are correlated with T2w response but also show patient-dependent anisotropic behavior
- DTI metrics generally more sensitive to regularization than raw MEDITI images; full optimization of regularization is warranted
- Incorporation of the DTI-model in the reconstruction [16] might improve SNR; controlled exercise regimens may also reduce variability.

- MEDITI can be used for imaging transient changes in tissue anisotropy and phenomena such as muscle fatigue and exertion in more detail than previously possible, allowing detection of early symptoms of compromised muscle function

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