

## T2-weighted imaging and stimulated echo diffusion tensor imaging in chronic exertional compartment syndrome calf muscle

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**Background:** Diffusion tensor imaging (DTI) provides quantitative markers of tissue microstructure and anisotropy, and as such can probe pathologies in oriented skeletal muscle fibers [1,2]. Pathologies such as ischemia [3], inflammation, and injury [4] can involve microscopic damage or disorganization in the myofibers or their substructure and are therefore detectable via DTI metrics such as mean diffusivity (MD) and fractional anisotropy (FA). In chronic exertional compartment syndrome (CECS) [5-7], certain muscle compartments retain excess fluid following exercise leading to elevated pressure, reduced perfusion, and pain. Standard diagnoses (e.g. intracompartmental pressure (ICP)) as well as surgical interventions (e.g. fasciotomy) can be invasive and/or debilitating, and noninvasive MRI markers are attractive alternative or supplemental diagnostic tools. This work shows preliminary results of stimulated echo DTI in suspected CECS patients at 3 T.

**Materials and Methods:** Nine patients with clinical suspicion of CECS and two healthy volunteers underwent comparative MR imaging of the legs along with a diffusion protocol approved by the local institutional review board (IRB). T2-weighted (T2w) imaging and DTI results were obtained both at rest and after 10 minutes of treadmill exertion. Images were collected in either a Siemens TIM Trio 3 T or wide-bore Siemens Verio 3 T scanner. Bilateral axial T2w images used a 2D TSE sequence with SPAIR fat suppression (TR / TE = 5380 / 62 ms, 256 x 116 x 50 matrix, 1.3 x 1.3 x 3 mm resolution, 2 avgs.) and a combination of anterior body matrix coil and posterior spine array elements using 5-6 elements total. Axial DTI used a stimulated echo (STE) diffusion sequence [8] with echo-planar imaging (EPI) readout and adjustable mixing time TM (TR / TE / TM = 12400 / 31 / 1000 ms, 64 x 64 x 10 matrix, 3 x 3 x 5 mm resolution, 6 directions, b = 0, 500 s/mm<sup>2</sup>, 3 avgs.) and a unilateral multi-channel knee coil. The mixing time flexibility allows high diffusion times, which increase structural contrast. Increased T2w signal on post exercise images was evaluated both subjectively and as a percent increase on ROI values. DTI data were processed offline (Igor Pro, Wavemetrics) to generate maps of MD, FA, and diffusion eigenvalues ( $\lambda_1, \lambda_2, \lambda_3$ ). Regions of interest (ROI) were manually segmented to estimate diffusion metrics and T2w signal changes in anterior tibialis (AT), extensor digitorum longus (EDL), posterior tibialis (PT), peroneus longus (PL), soleus (SOL), gastrocnemius lateralis (GL) and gastrocnemius medialis (GM). Group averages were calculated for all DTI metrics and muscle groups, and for the exercise response ratios of each parameter and muscle group. In the group T2w analysis, a 20% or greater change for a particular muscle group was defined as positive for CECS. Comparisons were made between metric results before and after exercise and in normal and CECS-positive muscle groups.

**Results:** Figure 1 shows example T2w and DTI results from a CECS patient. T2w images show clearly elevated signal intensity in the lateral and medial gastrocnemius muscles following exercise. MD values are elevated across all muscle groups following exercise, but increase more strongly in the same GM and GL groups. Similarly, FA values decreased in the GM, GL areas. 6 of 9 patients showed elevated T2w signal intensity both subjectively and based on ROI values in one or more muscle compartments after exercise. A total of 16 muscle groups (1 EDL, 1 PL, 2 AT, 3 SOL, 4 GM, 5 GL) were identified as CECS positive by this T2w criterion. MD and eigenvalues  $\lambda_1, \lambda_2, \lambda_3$  increased in all subjects and muscle groups by an average of 10.3% for unaffected groups, while FA decreased by an average of 4.2%, following exercise. In 4 of the 6 cases showing T2w increases, at least one CECS muscle group showed larger diffusion changes (>20%) in at least one diffusion metric. Figure 2 shows group results of the exercise response factor (i.e. the ratio of index values after and before exercise) of all DTI indices for the normal and CECS muscle groups. Statistically, a two-sided t-test with equal variance showed significant differences ( $p < 0.05$ ) between the unaffected groups (N = 61) and the CECS affected groups (N = 16) for mean diffusivity MD, primary eigenvalue  $\lambda_1$ , and tertiary eigenvalue  $\lambda_3$ .

**Discussion:** The observed changes in muscle tissue microstructure/function following exertion may have multiple contributions. One strong contributor is elevated temperature with exercise which increases the water diffusion rate isotropically. However, if temperature alone changed without a structural modification, apparent anisotropy would not change (or possibly increase), which is inconsistent with the observed FA decrease following exercise. Thus, some structural dilation of the myofibers is also likely occurring, and may be exaggerated in CECS. Such microscopic dilation would also parallel the well-known macroscopic engorgement of skeletal muscle groups following exertion. Beyond microstructure, functional changes such as permeability may also play a role. Further experiments and modeling of the muscle DTI metrics in CECS, particularly as a function of diffusion time [9] via stimulated echo sequence protocol, may shed further light on the CECS pathophysiology and its detection.

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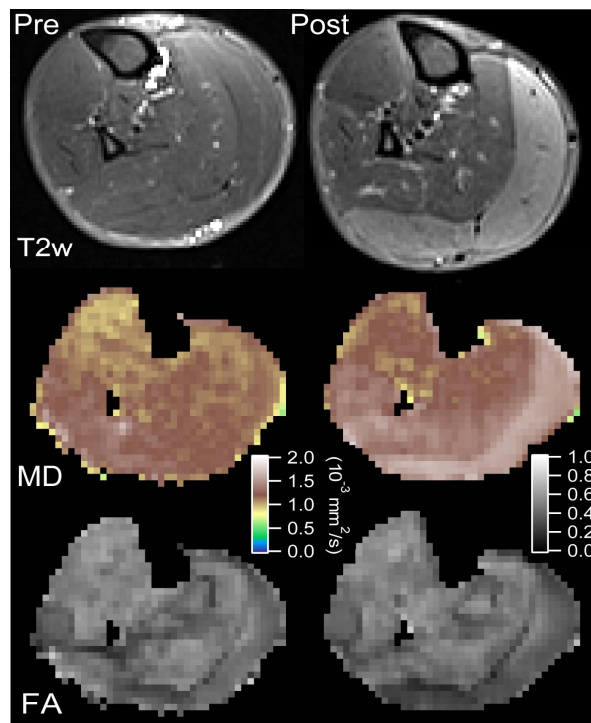


Figure 1: T2w-MRI and DTI in a CECS patient right calf muscle before and after exercise.

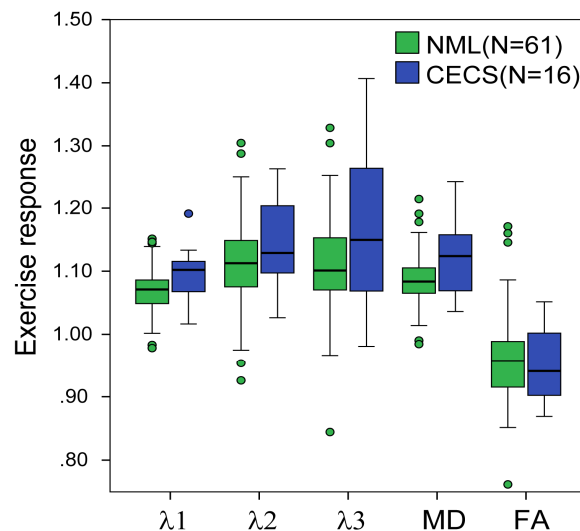


Figure 2: Group results of DTI index exercise response factors in a unaffected muscle groups (N = 61) and T2-identified CECS compartments (N=16) from 11 subjects.

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