In vivo ^{31}P diffusion tensor spectroscopy of human calf muscle

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Introduction. Diffusion-weighted imaging (DWI) is a common technique in the probing of the diffusion properties of water in several tissues including skeletal muscle. DWI and diffusion tensor imaging (DTI) have been applied in a number of studies in skeletal muscle for information on microstructure in healthy individuals, but also after muscle injury (1; 2) and in muscle disease (3) The information content of DWI results is limited, however, by the lack of compartment specificity of water. In addition, in skeletal muscle, adipose tissue can lower the diffusion coefficient estimations in skeletal muscle (3; 4). In contrast, diffusion tensor spectroscopy (DTS) of metabolites, which are mainly located in the intracellular space, can yield microstructural information that is more specific to cellular geometry (5). ^{31}P DTS of the phosphocreatine (PCr) signal provides a useful method to probe intracellular space, as it is almost exclusively present in the muscle cells, and not in adipose tissue or collagen structures. To our knowledge, ^{31}P diffusion MRS has only been applied in animal studies (6), probably due to limited signal-to-noise ratios. Therefore, the aim of the present study was to show the feasibility of applying DTS chemical shift imaging (CSI) on PCr signals in human skeletal muscle, by using bipolar gradients for diffusion weighting, accounting for phase fluctuations caused by the diffusion gradients and exploiting the higher SNR that can be obtained at a field strength of 7T.

Methods. All experiments were performed on a 7T scanner (Philips Achieva) equipped with a custom-built double-resonant ^{31}P and ^{1}H birdcage coil. Data were obtained from healthy volunteers with the following scan parameters: TR 5000ms, TE 50ms, TM 440ms, VOI 160x160mm^2, readout bandwidth 3kHz, 2048 sample points, matrix size 8x8 and voxel size 20x20x100mm^3. The STEAM-based 2D-DW-CSI pulse sequence is shown in Figure 1. The bipolar diffusion gradient scheme was employed here to minimize eddy-current effects. The phase-encoding gradients were applied just before signal acquisition to allow navigator data to be collected preceding the echo acquisition to obtain phase information required for signal post-processing. Diffusion weighting was applied in six standard non-colinear diffusion directions with g=3.5 Gauss/cm, Δ=465ms and δ=12ms, resulting in b=1885 s/mm^2. One set of data was also collected without diffusion (b=0). Navigator data were obtained using 30 complex data points, zero-filled to 64 points and then Fourier transformed (FT). The FT of the navigator signal for each phase encoding step yielded a coarse spectrum in which, due to the high SNR at 7T, the PCr peak could be easily identified and used for phase measurement and correction for the corresponding phase-encoded FID. Fractional anisotropy (FA) and apparent diffusion coefficients (ADC) were calculated using the integrated values of the PCr signal.

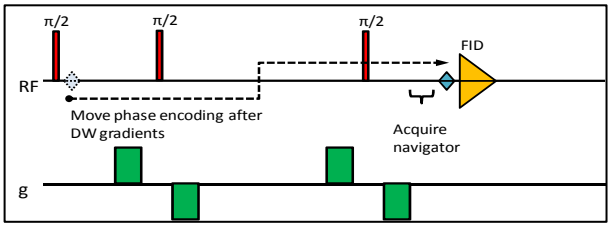

Fig 1. STEAM-based 2D-DW-CSI sequence diagram

Results. A total of 12 voxels located in different muscles of the lower leg had sufficient SNR to calculate FA and ADC values. Average values over these voxels were FA=0.48±0.12 and ADC=3.66x10^{-4} ± 0.57x10^{-4} mm^2/s.

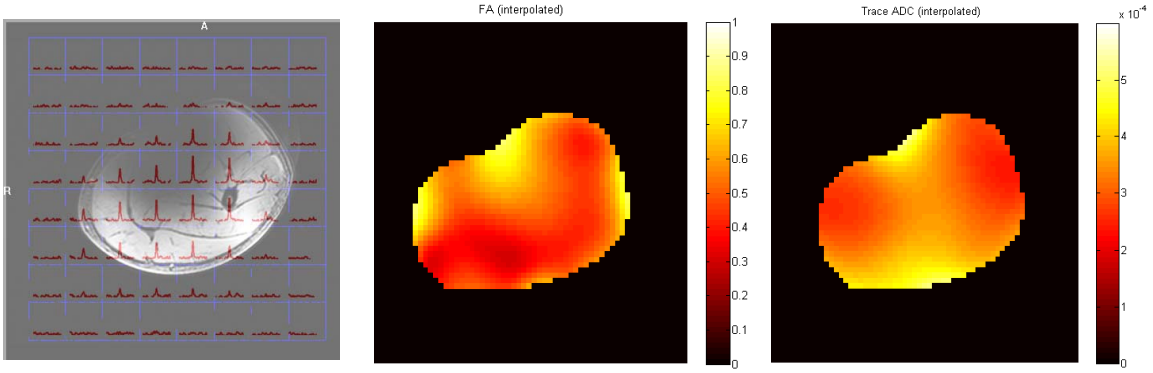

Fig 2. ^{31}P CSI spectra at b=0 overlaid on a ^{1}H gradient echo image (left), and FA (center) and ADC (right) maps. FA is similar between muscles and an apparent increase is present near the tibia bone, likely due to increased noise. Trace ADC values vary differently, with higher values near the extensor digitorum region, as well as the medial gastrocnemius region.

Conclusion. In this study we show, for the first time in humans, that it is feasible to obtain ADC and FA values of PCr in different skeletal muscles in the human calf using ^{31}P 2D -DT CSI and a newly developed coil design for 7T. The values we obtained for FA are similar between different muscles, which is in line with values from ^{1}H DTI studies (7). The ADC values for PCr are very close to those reported in previous animal studies for these mixing times (8; 9). Application of ^{31}P DWS and DTS could be especially important in muscle disease, such as Duchenne muscular dystrophy, where heavy fat infiltration is present, and could complement other approaches that reduce the effects of adipose tissue in DTI measurements, such as Dixon based DTI (10). This combination of DTI and ^{31}P 2D-DT CSI could also provide independent measures of cellular diffusion, which could be useful to elucidate the role of diffusion in compartments adjacent to skeletal muscle, like the endomysium. In the future, signal to noise can be increased even further by optimizing the pulses and reducing the echo time, as well as by using multiple receive coils.

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