Spin-lattice and spin-spin relaxation of water and lipids in human vastus lateralis m. measured by 1H-MRS at 3T

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Introduction: Quantitative evaluation of relaxation times (T_1 & T_2) is important for accurately determining absolute metabolite concentrations and for optimizing measurement protocols in MR spectroscopic sequences. Relaxation correction is necessary for comparing different populations and assessment of metabolic flux rates under in vivo conditions (1). A large number of proton magnetic resonance spectroscopy (^{1}H-MRS) studies involving skeletal muscle metabolites relaxation time measurements have been performed on soleus and tibialis anterior muscles but not on vastus lateralis (VL) at 3T, due to flexibility in manipulating orientation of the lower leg in the scanner and the parallel muscle fiber orientation of these muscles, which produces optimal separation of intramyocellular (IMCL) and extra-myocellular (EMCL) lipids (3-4). In the current study, we measure the relaxation times of water, IMCL and EMCL lipid methylene and methyl resonances in the human VL muscle using single-voxel stimulated acquisition mode (STEAM) sequence at 3T. In physiological studies, involving normal and diseased states, investigation of VL through ^{1}H-MRS is important as biopsies are generally performed on it and absolute units of IMCL & EMCL measured can be compared with results obtained from electron microscopy and biochemical assays(6).

Methods: ^{1}H-MRS were performed on five healthy subjects (2 male, 3 female, 20-38 yo, BMI = 22-28 kg/m^2) on a 3T MRI/MRS system (Magnetom TIM Trio, Siemens. Malvern PA). A four-channel flex coil (receive-only) was positioned over the right thigh of each subject. Exact positioning of the voxel ~2mL (10 x 10 x 20mm^3) was performed using T_1-weighted localizer images. The volume of interest was positioned, choosing tissue from the VL muscle and avoiding inclusion of large vessels, inter-muscular fat and bone. For each voxel placement, gradient shimming was performed and water linewidth (FWHM) was adjusted to ~20-35Hz. The relaxation times, T_1 and T_2, of water and lipid resonances (0.9-1.5ppm) were measured using unsuppressed ^{1}H-muscle spectra and suppressed STEAM MRS respectively. Parameters for evaluation of the transverse relaxation time T_2 measurements are: TM = 10 ms, 16avg, BW=2kHz, TR=3s and varying TE=30, 60, 90, and 150ms. Longitudinal relaxation time (T_1) data was acquired with a TM=10 ms, 16avg, BW=2kHz, TE=30 ms and varying TR=0.5, 1, 3, 5s. Water pre-saturation was used for the lipid spectrum acquisitions, with fixed water suppression BW =50Hz.

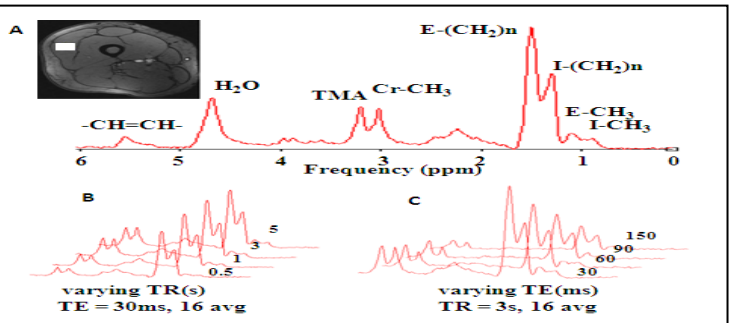

Fig 1: ***A.*** **Representative ^{1}H-MRS water-suppressed fat spectrum obtained at TR/TE=3s/30ms(16avg), of a 27 yo female subject with the selected voxel superimposed on vastus lateralis (VL) muscle** ***B.*** **Spin-lattice relaxation behavior in human VL** ***C.*** **Spin-Spin relaxation behavior in VL.**

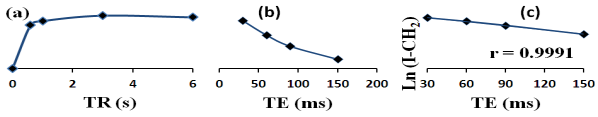

Fig 2: (a) Mono-exponential T_1 fit of VL muscle I-CH_2 peak (1.3ppm) as a function of TR (b) T_2 fit of I-CH_2 as a function of TE (c) Semi-logarithmic plot of I-CH_2 as a function of TE.

Peak	Freq (ppm)	T_1 (ms)	T_2 (ms)
H_2O	4.7	1687.81 ± 208	28.28 ± 3
EMCL-CH_2	1.5	462.50 ± 185	76.78 ± 8
IMCL-CH_2	1.3	580.16 ± 103	78.57 ± 19
EMCL-CH_3	1.1	462.06 ± 183	72.67 ± 12
IMCL-CH_3	0.9	579.96 ± 104	67.89 ± 17

Table 1: T_1 and T_2 relaxation times of water and lipids in human vastus lateralis m. at 3T expressed in mean ± SD.

Data Analysis: All ^{1}H-MRS data were processed using the AMARES fitting algorithm in the jMRUI 4.0 software package. One subject dataset was excluded from the analysis due to poor spectral quality. Each spectrum was apodized to a Gaussian 2.5Hz line function and a first order phase correction was fixed to zero to estimate the zero-order phase correction. An HSLVD filter was used to remove the residual water peak in the water-suppressed spectra. The methylene $(CH_2)_n$ and methyl (CH_3) peaks of intramyocellular (I) and extramyocellular (E) lipids and water peaks were fitted to Lorentzian line shapes. Prior knowledge was developed considering the theoretical molar ratio $(-(CH_2)_n-/-CH_3 = 62/9)$ to adjust the amplitude and linewidth of the methyl and methylene peaks at 3T, and a fixed frequency shift of 0.2ppm with respect to methylene : methyl peaks ($CH_3 = CH_2 - 51.1$Hz) was applied(2). Area under the peak for each signal was calculated as a product of linewidth and amplitude. T_1 & T_2 relaxation times of water and lipid resonances (0.9 - 1.5ppm) were calculated with two-parameter non-linear least-squares fitting procedure using R 2.15.0 statistical software.

Results and Discussion: Well resolved water suppressed spectra from the VL muscle measured by varying TR and varying TE are shown in Fig.1. Relaxation behavior of methylene IMCL lipid peak signal is shown in Fig 2(a-b). Non-linear least-squares curve fitting for spin-lattice relaxation behavior $M_z(t)=M_0(1-e^{-TR/T1})$ vs. TR and spin-spin relaxation $M_{xy}=M_{xy(0)}(e^{-TE/T2})$ vs. TE produced strong correlation for each subject. Fig 2(c) shows the r value of 0.9991 for semi-logarithmic IMCL-$(CH_2)_n$ peak fit as a function of TE. The mean values of T_1 and T_2 obtained through the non-linear least-squares fitting approach for water and lipid peaks are summarized in Table 1. Limitations in this study include the limited number of subjects which limits the statistical power. In this study we did not evaluate any diseased states and the specific orientation of the muscle fibers are not taken into account. Orientation of the muscle fibers potentially can alter the measurements in VL muscle, since all fibers may not be aligned parallel to the magnetic field which could result in shifting of the center of the resonance lines and EMCL line broadening(5). Future studies will concentrate on the influence of muscle fiber orientation on ^{1}H-MRS data as a means to gain insight into muscle function and physiology in normal and diseased states.

Conclusion: This study reports proton relaxation times of water, lipid methyl and methylene resonances in the vastus lateralis of healthy subjects at 3T. The results obtained are in agreement with data reported for studies conducted at 1.5T, showing a steady increase of spin-lattice relaxation with B_0 and no effect on spin-spin relaxation. These data can be applied to relaxation correction for the absolute quantification of VL muscle lipid concentrations.

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