Identification of two myocardial lipid pools in muscular dystrophy patients by $^1$H MRS at 3 T

B. Rial $^1$, J. J. Sutton$^1$, S. Neubauer$^1$, M. D. Robson$^1$, and J. E. Schneider$^1$

$^1$Dept of Cardiovascular Medicine, University of Oxford, Oxford, Oxfordshire, United Kingdom

Introduction

In recent years, proton magnetic resonance ($^1$H MRS) has been successfully applied to study myocardial lipid metabolism in normal and diseased subjects (1,2) with the aim to clarify the potential link between myocardial lipid storage and myocardial function. The use of high magnetic field strengths (3 T) has facilitated a more detailed quantification of various fatty acid components in hepatic tissue and skeletal muscle (3,4). The separate observation of intra- (IMCL) and extramyocellular lipids (EMCL) has also become an important application of $^1$H MRS in skeletal muscle (5). In human myocardium, the additional EMCL resonance has been attributed to epicardial fat when the voxel was located on the anterior left-ventricular wall. The aim of this work was to assess the feasibility of $^1$H MRS at 3 T to differentiate EMCL and IMCL in a voxel of inter-ventricular myocardial tissue in patients with suspected high lipid myocardial content.

Methods

Patients with confirmed dystrophin mutations (Becker or Duchenne muscular dystrophies) were chosen for this study as these conditions are associated with elevated lipid levels in skeletal muscle (6) and also a high rate of cardiomyopathy. Five patients (age = 41±13 yrs; BMI= 24.5±2.7 kg/m$^2$) with impaired septal contractility (peak circumferential strain -11±2%; normal -18±2%; p<0.001) were scanned on a 3 T Siemens Tim Trio using the whole body coil in transmit mode and the 6-channel anterior and 24-channel posterior phased-array coils for signal receiving. Mid-ventricular long and short-axis cine series were acquired to determine the trigger delay for mid-diastole. A 22x18x32 mm (12.7 ml) STEAM voxel was planned on the corresponding cine frame (Figure 1A, B). Shimming was performed based on a GRE dual echo 3D imaging data set. A cardiac-gated water spectrum (3 averages; TR of at least 4 s) was acquired in a single breath-hold to use as internal reference. Next, five to six WET water-suppressed scans (5 averages each; TR of at least 2 s) were acquired at mid-diastole in a series of single breath-holds. The acquisition parameters were: TE = 10 ms, TM = 7 ms, BW = 2000 Hz, 2048 data points. Individual coil signals were combined within Matlab using purpose written modules. Following frequency correction, the 25 or 30 water-suppressed scans were constructively averaged. Spectra were quantified using the AMARES algorithm (7). Five peaks (TMA, creatine, EMCL, IMCL and CH3 lipids at 3.2, 3.0, 1.5, 1.3 and 0.9 ppm respectively) were analyzed and prior knowledge was used for all peak locations by using soft constraints. All peaks were fitted using Lorentzian lineshapes. Results from $^1$H MR spectra were compared to previous data from five healthy volunteers (age = 33±14 yrs; BMI= 21.4±1.8 kg/m$^2$). Spectra were quantified using the same model functions and prior knowledge as for patient data values are mean±SD.

Results

Figure 2A shows a spectrum from a 12.7 ml volume in the septum of a muscular dystrophy patient. The two peaks corresponding to the EMCL and IMCL could be distinguished and were quantified in all five patients. Conversely, only IMCL resonances were reliably quantifiable in the myocardial spectra of normal subjects (Figure. 2B). The mean chemical shift difference between EMCL and IMCL in the five patients was 0.16±0.01 ppm. Additionally, IMCL normalized to water content was significantly higher in patients than in normal volunteers, (9.2±0.59)% vs (0.27±0.10)%, p<0.05. Patients showed EMCL ranging from 0.26 % to 4.25 %, while a small (0.09%) EMCL content was found in only one normal volunteer (Figure 3). Water linewidths were 13.6±3.0 Hz in normal volunteers and 15.5±4.3 Hz in patients (p=0.4)

Discussion

To our knowledge, this is the first study demonstrating the feasibility of proton $^1$H MRS at 3 T to differentiate between IMCL and EMCL resonances in the inter-ventricular septum of patients with suspected high lipid myocardial content. Particularly, in the group of muscular dystrophy patients investigated here, the identification of fat infiltration to areas between the muscle fibres (EMCL) and also high fat content within the cytoplasm of cardiac myocytes suggests impaired fat utilization and suggests lipotoxicity as a potential disease mechanism.


Grant support: This study was financially supported by the British Heart Foundation grant PG/05/115

Figure 1 Cine short-axis (A) and long-axis (B) frames at mid-diastole used for positioning the STEAM voxel (yellow box) in the septum.

Figure 2 Proton spectra from septal myocardium of a muscular dystrophy (A) and a normal (B) subject. Both spectra are quantified using the same model functions and prior knowledge as for patient data. Values are mean±SD.

Figure 3 IMCL content was increased in patients. A wide range of EMCL values was found in patients, whereas an EMCL peak was detected and fitted in only one normal volunteer. N: normal, MD: muscular dystrophy, *p<0.05.