Bone Marrow 1D and 2D Correlation MR Spectroscopy at 7T

S. Ramadan[1], E. M. Ratai[2], L. L. Wald[2], G. C. Wiggins[2], and C. E. Mountford[3]

[1]Department of Radiology, Brigham and Women's Hospital, Boston, MA, United States, [2]Department of Radiology, Massachusetts General Hospital, Boston, MA, United States, [3]Radiology, Brigham and Womens Hospital, Boston, MA, United States

INTRODUCTION

The altered chemistry of bone marrow has been shown to be indicative of disease. One-dimensional (1D) proton magnetic resonance spectroscopy (MRS) at 1.5T has previously been used to non-invasively investigate a range of diseases including musculoskeletal tumors[1], anorexia nervosa[2], multiple myeloma[3] and osteoporosis[4]. The ratio of saturated to unsaturated lipids was indicative of diagnostic markers for osteoporosis. Two-dimensional (2D) MRS has been shown to be particularly amenable to monitoring lipid alterations with disease[5]. In an attempt to unambiguously assign and monitor resonances, localized 2D correlation spectroscopy[6] (L-COSY) of bone marrow at 1.5T was used to study acute leukemia patients[7]. The results were ambiguous due to crosspeak overlap. The goal of the present study is to develop the L-COSY method to study bone marrow at the higher field strength of 7T and separate those lipid resonances that were composites at 1.5T.

MATERIALS AND METHODS

The technique was developed on apparently healthy volunteers with institutional review board approval. MR data was obtained using a 7T MR scanner (Siemens Medical Solutions, Erlangen, Germany), a 28 cm diameter de-tunable birdcage coil for excitation and an 8.5 cm diameter surface coil for signal reception. Localizer images were obtained using a gradient-echo imaging sequence. The voxel was placed in the tibial bone marrow. For a 1D spectrum the spectral width was 4000 Hz, vector size 2048 points, voxel size of 6x6x35 mm^3, 8 averages and a repetition time of 2000 ms. The "WET" water suppression method[8] was applied before the acquisition sequence. The 1D spectra were processed using the MestReNova program[9]. The L-COSY sequence was applied with a TE (initial) of 30ms, TR of 2000ms, 8 averages, a voxel size of 6x6x35 mm^3, t1 increment size of 0.4 ms. The indirect spectral width used was 2500 Hz and the number of increments was 64. The total acquisition time was 17 min. The processing parameters used were: F2 domain (skewed sine-squared window, 2048 points, magnitude), F1 domain (sine-squared window, linear prediction to 128 points, zero-filling to 256 points, magnitude)[10]. The (C**H**2)n resonance at 1.30 ppm was used as an internal reference[11].

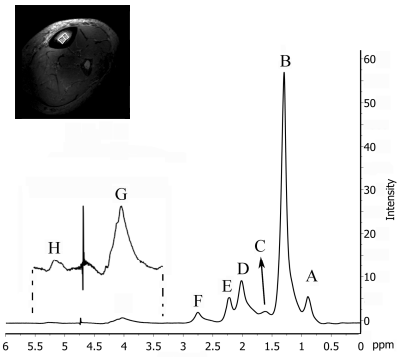

Figure 1. Axial image of voxel. 7T MR ^{1}H 1D spectrum of tibial bone marrow (38 yo volunteer). High frequency spectral region amplified vertically to show detail.

	Frequency (ppm)	Assignment
A	0.90	C**H3**
B	1.30*	(C**H2**)n
C	1.62	–O–(C=O)–CH2–C**H2**–
D	2.02	–C**H2**–CH=CH–
E	2.23	–C**H2**–(C=O)–OR
F	2.76	–CH=CH–C**H2**–CH=CH–
G	4.04	–(C=O)–O–C**H2**–
H	5.28	–**H**C=C**H**–, –(C=O)–O–C**H**R–

RESULTS AND DISCUSSION

Typical 7T 1D proton MR spectrum of tibial bone marrow from a healthy volunteer is shown in Figure 1. The resonances are assigned and listed in the legend. This 1D spectrum is superior in resolution to published 1.5T literature[4] as the 2–3 ppm spectral region is now resolved into three resonances (resonances D, E and F in Figure 1). The methylene and methine resonances (denoted 'G' in Figure 1) of triglyceride are seen in the 1D spectrum. These resonances are usually encompassed by the water resonance or lost when water suppression is enabled at lower field strength. The composite and broad nature of resonances in 1D spectra, even at 7T, highlights the advantages provided by the L-COSY method shown in Figure 2, where the data is collected from the same volunteer and voxel as in Figure 1. Each of the olefinic cross peaks (K and J) (Figure 2, inset) has two different F2 frequencies. Thus, the broad resonance denoted 'H' (Figure 1) is a composite resonance. Apart from the contribution of the glyceride CH group to this resonance, two different types of olefinic species are seen to be contributing to this resonance. In addition, the contribution of the high frequency component seems to be larger than the low frequency component. The identity of these two species is currently unknown. This is suggestive of the presence of different compartments or environments, reported for muscle[12], but not before bone marrow. A close inspection of the F2 region, 4.0 - 4.5 ppm, of the 2D spectrum, reveals that this is also composed of a minimum of 3 resonances of which two are J-coupled at 4.07 ppm and 4.29 ppm (achiral CH2 of triglyceride) and an additional singlet at 4.44 ppm. Cross peaks U and V reveal a complex relationship between the allylic/diallylic protons and alpha-carbonyl protons. The unsaturation index can be calculated by summing up the peaks K and J and dividing the result by the volume of (CH2)n diagonal peak. This improved spectral resolution at 7T offers a new opportunity for inspection of lipid alterations in bone marrow associated with a range of diseases.

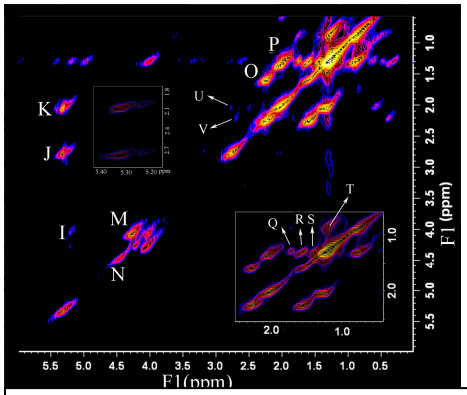

Figure 2. 7T 2D localized ^{1}H L-COSY of tibial bone marrow (from voxel in Figure 1). Following cross peaks (F2, F1) were identified:

Crosspeak (F2,F1)	Assignment
I (5.19,4.02)	Glyceride (CH2)-Glyceride (CH)
J (5.23, 2.76), (5.32,2.76)	Olefinic-diallylic
K (5.23,2.02), (5.32,2.02)	Olefinic-allylic
M (4.29,4.07)	Glyceride geminal coupling (CH2)
N (4.44,4.44)	Singlet
O (2.25,1.6)	α-carbonyl–β-carbonyl
P (2.03,1.36)	Allylic-(CH2)n
Q (1.75,1.29)	β-carbonyl–(CH2)n (Sat.)
R (1.59,1.29)	β-carbonyl–(CH2)n (Unsat.)
S (1.45,1.30)	β-carbonyl–(CH2)n (doubly Unsat.)
T (1.27,0.86)	(CH2)n-CH3
U (2.78,2.05)	diallylic-allylic (long range)
V (2.69,2.20)	diallylic-α-carbonyl (long range)

CONCLUSION The 2D L-COSY spectrum obtained at 7T from bone marrow provides a wealth of information on lipid content and chemical structure not available at the lower field strength of 1.5T. This offers an opportunity to understand the molecular structure of bone marrow lipid and its unique chemical characteristics associated with disease.

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