Localized Correlated Spectroscopy of Bone Marrow: Determination of Unsaturation and Apoptosis

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Introduction: Bone marrow consists of both hematopoietic (red) and fatty (yellow) components, the proportions of which are thought to be related to the remodeling capacity of bone. Further, the bone strength depends on both bone mineral density and also marrow quality (1). The apoptosis (programmed cell death) is important for the growth and maintenance of the skeleton and provides information on molecular regulation of apoptosis of bone cells (2). In this study we employed a localized 2D MRS (L-COSY) technique to separate the saturated and unsaturated components and also to determine the apoptosis within the bone-marrow lipids. Both the degree of unsaturation and apoptosis has implications in osteoporosis.

Methods: Eight subjects (age range 25 ± 5 years) with BMI (range 20 - 25 kg/m^2) participated in this study. All measurements were performed on a GE Excite HD 3.0 T whole-body clinical MRI/MRS scanner using an extremity coil. Fig. 1 shows a 3mm gradient echo image of the knee with the location of MRS voxel within the tibial bone marrow. All experiments were performed within a single voxel (2x2x2 cm^3), TR=2s, minimum TE=30ms, 50 t_1 increments with 8 averages, and a total acquisition time of ~ 13 minutes.

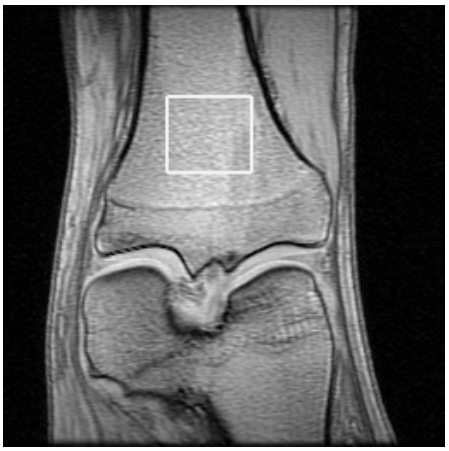

Fig. 1

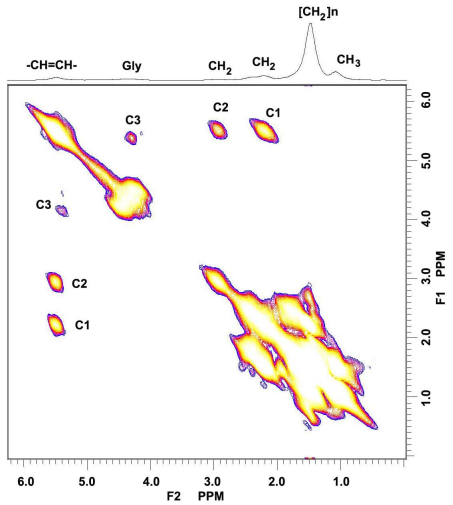

Fig. 2

Figure 2 shows a 2D L-COSY spectrum recorded in the bone marrow of a subject. We identified the various resonances from the bonemarrow lipids including methyl [1.0, 1.0 ppm], n-methylene [1.4, 1.4 ppm], allylic methylene [2.2, 2.2 ppm], diallylic methylene [2.9, 2.9 ppm], and the olefinic protons at [5.5, 5.5 ppm]. Cross peaks C1 [2.2, 5.5 ppm & 5.5, 2.2 ppm] are due to the scalar coupling between olefinic (-CH=CH-) and allylic methylene protons C*H*$_2$CH=CH, and thus appear if the methylene protons are adjacent to only one unsaturated site. Cross peaks C2 arise from the scalar coupling between the olefinic (-CH=CH-) and diallylic methylene protons (-CH=CH-C*H*$_2$-CH=CH-). They occur if there are at least two unsaturated sites between which the methylene protons are located. The degree of unsaturation was 0.9433 ± 0.13 from the eight subjects as determined using the cross peaks C2 and C1 using previously described procedure (3). Apoptosis was 6.54 ± 1.12 as determined from the ratio of n-methylene [CH_2]n resonating at [1.4, 1.4 ppm] and CH_3 resonating at [1.0, 1.0 ppm] using the procedure described in earlier work (4).

Discussion: The desaturation of fatty acids is an oxidative reaction catalyzed by desaturase enzymes that convert -CH_2-CH_2- to -CH=CH-. These enzymes function abnormally in diabetes mellitus, obesity, metabolic syndrome and other lipid disorders. Furthermore, mounting evidence indicates that systemic hormones, local growth factors, cytokines, and pharmacological agents, as well as mechanical forces regulate the rate of bone cell apoptosis (2).

Conclusions: We have demonstrated the feasibility of determination of degree of unsaturation and apoptosis in vivo using localized two-dimensional correlated spectroscopy. Measuring both these parameters may serve as a potential biomarker in diagnosis and treatment interventions of osteoporosis.

References:

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