Intramyocardial Lipid Quantification by MRS: In Vivo Validation in Human Subjects

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INTRODUCTION

The accumulation and abnormal metabolism of intramyocellular lipid (IMCL) has been associated with several cardiovascular disease processes including insulin resistance, diabetes, and apoptosis. Thus, understanding the correlations between cardiovascular disease and myocardial IMCL is paramount for disease prevention and management. Currently, the only non-invasive, in vivo method to access myocardial IMCL levels in humans is 1H magnetic resonance spectroscopy (MRS). This technique is challenged by nearby epicardial fat in combination with localization errors that result from cardiac and respiratory motion. Typical reported coefficients of variation (CV) range from 5 to 17%, however the specificity and accuracy of the method has not been determined in human heart. Accordingly, the primary purpose of this study is to cross-validate an in vivo 1H MRS measurement of human myocardial IMCL. To this end, the assay was first characterized with repeated intra- and interday measurements. Then, the MRS assay was cross-validated with endomyocardial biopsy samples.

METHODS

Study Subjects. 8 normal volunteers underwent multiple MRS assays to define the reproducibility of the measurement. 9 heart transplant patients also underwent the MRS immediately prior to their routine endomyocardial biopsy.
In vivo MRS. The MRS protocol is based on a free-breathing, PRESS sequence with both ECG and 2D-PACE respiratory gating, alternating gradient polarity every average, optimized crushers with 40 and 100 π phase dispersion before the first and second refocusing pulses, respectively, COG5(2,3,2:0) phase cycling, and an SLR excite and MAO refocusing pulses with BWTPs of 13.1 and 6.0, respectively. The imaging system was a Siemens 1.5T Sonata with the body coil used as the transmitter and an 8-element chest array coil used for reception. The analysis was via jMRUI/AMARES and results are reported as the ratio of the area of the IMCL resonance to that of the H2O resonance.
Ex vivo analysis. A right ventricular septal endocardial biopsy (~2 mg) was obtained percutanaeously using standard clinical procedures and immediately frozen in liquid nitrogen and stored at -80°C until it underwent analysis using a Varian Unity Inova-600 with a 5 mm, 3 axis gradients, triple resonance probe and a Mettler Toledo (Columbia, MA, USA) 50T/A851e TGA.

RESULTS

Based on 59 repeat measurements with IMCL levels ranging from 0.1 to 2% with an average of 1.1 ±0.5%, the CV for the MRS myocardial IMCL assay is 8.4%. In vivo and ex vivo measurements had an R^2 of 0.97.

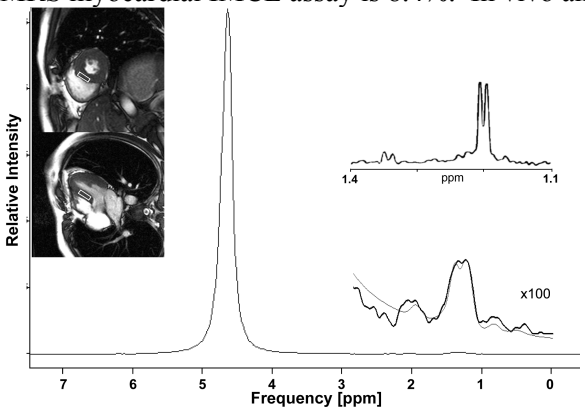

Figure 1. [1]H-MRS spectrum from the interventricular septum of a biopsy subject with Te = 24 ms and 120 averages. The lower inset on the right IMCL resonances (~0.4%) and the smooth, lighter line in the inset is from the AMARES fit. The upper inset is an expansion of the methylene region from the 600 MHz high resolution spectrum of the corresponding biopsy sample.

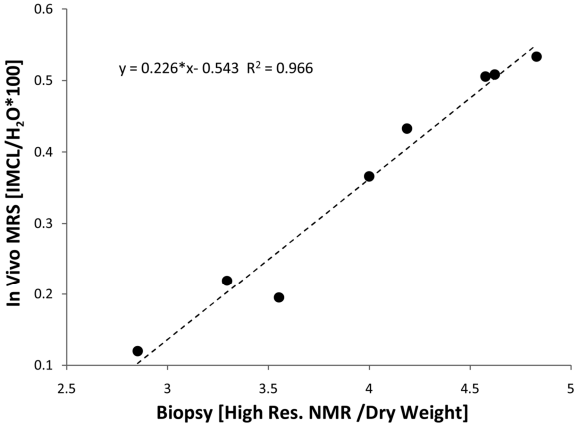

Figure 2. High resolution NMR analysis of the endomyocardial biopsy samples versus the corresponding *in vivo* MRS measurement. The line results from the regression analysis.

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