Assessment of Ex-Vivo Livers for Steatosis Using MRI: Feasibility in Cadaveric Livers

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Introduction: The most common contraindication for transplantation of a human liver is the presence of fatty infiltration. Hepatic steatosis is an increasingly common condition, affecting up to 30% of all Americans[1] and is commonly seen in donor livers. Transplantation of steatotic human livers may result in poor liver function or even primary dysfunction of the allograft[2] . Current techniques of assessment of livers for transplant involve biopsy of the tissue, which damages the liver, can introduce infection, and is prone to high sampling variability. MRI is a potential tool for detection and assessment of tissue fat content. IDEAL (Iterative Decomposition with Echo Asymmetry and Least-Squares Estimation)[3,4] is a chemical shift-based water separation imaging method and PRESS (Point Resolved Spectral Selection) is a spectroscopic method capable quantifying fatty infiltration in vivo. The purpose of this work was to compare estimates of hepatic fat-fraction using IDEAL and PRESS with histological findings in human livers rejected for transplantation.

Methods: Three explanted human livers rejected for transplantation were scanned using a 3D spoiled gradient echo IDEAL sequence[3,4] that provides separated water and fat images, which were used to calculate fat-fraction images. Two of the three livers were rejected due to excessive steatosis, and the third for congestion. A modified IDEAL water/fat decomposition that uses a pre-calibrated fat signal model that takes all spectral peaks of fat into account (details submitted separately) and subsequent calculation of fat-fraction images were performed online. This algorithm also uses a magnitude discrimination method to calculate fat-fraction, free from noise bias[5]. Echo times for the IDEAL-SPGR sequence were 2.0, 3.6, and 5.2ms; these times are chosen to maximize SNR performance[7,8]. A 5^o flip angle was used to minimize bias in fat measurements caused by differences in T_1 between fat and water[5].

Additionally, a PRESS sequence was acquired without water suppression using a voxel size of 8.0 cm^3, 4 averages, TE/TR = 25 / 2500ms, BW = ± 2500 or 5000Hz, and 2048 readout points. Percent fat was measured from calculated fat-fraction images from IDEAL, and raw spectroscopy data were post-processed using Matlab (Mathworks, Natick, MA) to integrate water and total area under the fat peaks to obtain PRESS fat-fraction.

Since the rejected livers were prepared on ice, the chemical shift between fat and water was altered, thus changing the resonant frequency between the water and fat peaks. This frequency was measured to be approximately -238Hz at 1.5T and -476Hz at 3T using the acquired PRESS spectrum. The IDEAL reconstruction, which assumes the resonant frequency between water and fat is known, was adjusted accordingly.

H&E slides of the rejected livers were also prepared, and estimates of the percentage of cells affected by steatosis were assessed by a pathologist blinded to imaging results. Finally, a sample two of the three livers was analyzed for fat quantification from two of the livers using a modified Folch lipid extraction[6]. Percent fat was expressed as the mass of total lipids recovered from the sample.

Results: The results of IDEAL, PRESS, lipid extraction, and Pathology are summarized in Table 1 below. Fig. 1 shows a calculated fat-fraction image acquired using IDEAL in a rejected steatotic liver. Fig. 2 is the corresponding PRESS spectra obtained from the same liver, and Fig. 3 displays the corresponding H&E, where the presence of white indicates fat vacuoles. Fig. 4 shows correlation between IDEAL, PRESS, lipid extraction and the percent of cells affected, where blue denotes IDEAL, red denotes PRESS, and green denotes lipid extraction fat-fractions.

Discussion and Conclusion: IDEAL, PRESS and Pathology results displayed good correlation; primary causes of disagreements could result from using a limited number of livers studied, as well as lack of T_2* correction since diseased livers often have elevated iron levels. Alternatively, the cold temperature may have affected relaxation parameters for both IDEAL and PRESS, changing signal behavior. Due ease of imaging the livers in a cooler or attached coil, imaging can be performed easily to assess pre-transplant livers. This work demonstrates the feasibility of assessing steatotic livers with MRI. Future work will involve additional comparisons of IDEAL, PRESS, histology and lipid extraction.

Liver	IDEAL Fat Fraction (%)	Lipid Extraction Fat Fraction (%)	PRESS Fat Fraction (%)	Cells Affected (%)
1	11.5 ± 1.5	Not Obtained	13.7	70
2	5.6 ± 2.3	6.6	2.2	0
3	40.0 ± 2.1	31.3	23.2	90

Table 1: IDEAL, Lipid Extraction, PRESS, and Pathology Results show good correlation of imaging, spectroscopy, histology and total lipid extraction.

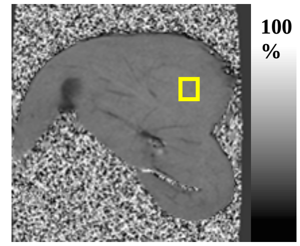

Figure 1: Representative fat fraction image of a human liver rejected for transplant due to the presence of steatosis. Square indicates voxel placement for PRESS. 42.3 ± 2.3% fat according to IDEAL.

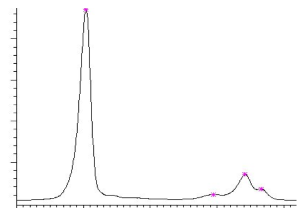

Figure 2: PRESS spectrum of rejected liver shown in Figure 1 estimated 23.2% fat. Stars denote water and three visible fat peaks.

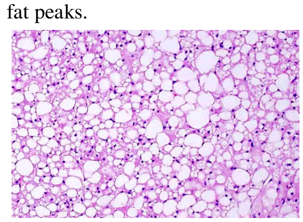

Figure 3: H&E slide (100x) of liver in Figure 1. Subjective grading estimated 90% of cells affected.

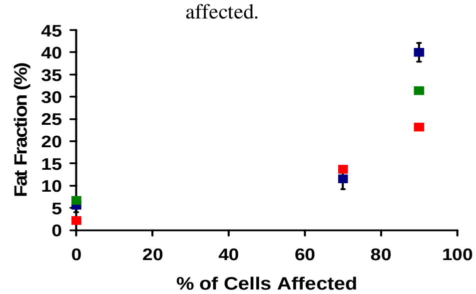

Figure 4: Fat-fraction measured from IDEAL (blue), lipid extraction (green) and PRESS (red) correlates with qualitative histological estimates of the percentage of cells affected with steatosis.

References:

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