Variable Performance of Chemical Shift-Based Multipoint Water-Fat Separation MRI and Its Impact on the Diagnosis of Fatty Liver

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INTRODUCTION

Chemical shift-based multipoint water-fat separation MRI methods (multipoint water-fat separation MRI) have been widely used as a means of estimating fat content in the liver. However, the sensitivity and dynamic range of the methods can be strongly influenced by many factors such as sampling strategies and post-data processing algorithms [1-3]. In this report we address such variability in the performance of multipoint water-fat separation MRI and its influence on the diagnosis of fatty liver. Hepatic fat fractions (HFFs) are estimated in humans by using ^{1}H-MRS as a reference [4], the 2-point Dixon in conjunction with a spoiled gradient echo sequence (SPGR) and the magnitude-based post-data processing (2PD) [5] and a 3-point IDEAL method (3PI) [2, 6].

METHODS

Human Subjects: A total of 28 subjects entered the study. Five were lean (2M/3F; body mass index (BMI) = 20.0–23.1 (21.6±1.4) kg/m^2)) and 22 were obese (9M/13F; BMI = 25.8–46.0 (34.6±4.9)). One male subject was lean with an abnormal liver and was therefore included only in the total subject group.

^{1}H-MRS: ^{1}H-MRS was performed on a whole body 4.0T Medspec (Bruker Instruments Inc., Billerica, MA) system using in-house designed and built MRS probes. Hepatic fat content was measured by ^{1}H respiratory-gated STEAM spectroscopy [7]: TE/TM = 20/15 ms, 16 averages, 2048 points over 2500 Hz, voxel size = 15x15x15 mm^3. To prevent voxel mis-registration due to chemical shift effects, hepatic fat content was estimated from the comparison of 2 spectra: a water-suppressed lipid spectrum (TR= 3000 ms) and a lipid-suppressed water spectrum (TR = 5000 ms), with the appropriate peak for each spectrum on-resonance. This sequence was carried out in different locations of the liver to account for liver inhomogeneity. A minimum of 8 spectra were acquired for each subject and the total lipid content was averaged. Hepatic fat content was expressed as HFF (= lipid peak area/(water peak area+lipid peak area)x100).

MRI: All MRI studies were conducted on a 1.5T Siemens Sonata scanner with a single channel body coil and a phased-array torso coil (USA Instruments, Inc., Aurora, USA) for the 2PD and 3PI data collection, respectively.

Two-point Dixon (2PD): The 2-point measurement of HFF was performed using an SPGR sequence as modified by Fishbein et al [5]: matrix size = 128x256, flip angle (α) = 30^o, TR = 18 ms, TEs = 2.38/4.76 ms (out-of-phase (OP) and in-phase (IP), respectively), bandwidth = 420 Hz/pixel, 6 averages, slice thickness = 10 mm, 1 slice, scan time = 14 sec on a single breath-hold. Five regions of interest (ROIs) were drawn on each magnitude image, and the mean pixel signal intensity level was recorded. The 2PD HFF was calculated as $[(S_{in}-S_{out})/(2xS_{in})]x100$ [5], where S_{in} and S_{out} are signal intensity of IP and OP images, respectively.

Three-point IDEAL (3PI): All 3PI data were collected using trueFISP: matrix size = 144x256, α = 55^o, TR = 5.38 ms, TEs = 1.49/2.69/3.89 ms, bandwidth = 1028 Hz/pixel, 1 average, slice thickness = 10 mm, number of slices = 8–14 (mean number of slices ~ 11), scan time = 18-32 sec on a single breath-hold. All 3PI images were reconstructed according to the original IDEAL algorithm [6] written in MATLAB^{TM} (MathWorks Inc., Natick, USA). ROIs were defined in the source images. From the calculated water-only and fat-only images HFF images were obtained (HFF = fat/(water+fat)x100) and mean HFF was calculated over the predefined ROIs. The standard deviation (SD) of HFF across the slices was calculated for each subject and its correlation with the mean HFF was examined.

Combined Data Analysis: The correlations between HFFs measured by ^{1}H-MRS, 2PD and 3PI were examined. The performance of the 2PD and 3PI as a means of diagnosing fatty liver was evaluated by differentiating between normal and fatty livers. Firstly, a HFF of 2.9% (= fat to water ratio of 3.0%) was used for the MRS data as a cutoff for normal livers according to our previous finding using ^{1}H-MRS [4]. Secondly, the upper limit for normal liver was defined for each of the MRI methods as m x SD above the mean HFF of lean subjects where SD is the standard deviation of the HFFs of lean subjects and m varies from 0 to 4 with a step size of 0.1. Finally, for the varying upper limits of HFF for normal liver, the percentages of correctly diagnosed cases were examined based on the diagnosis made by ^{1}H-MRS.

RESULTS

^{1}H-MRS: For the lean and obese groups, the range of HFF as measured by ^{1}H-MRS was 0.3–3.5% (1.1±1.4%) and 0.3–41.5% (11.7±12.1), respectively. When an HFF of 2.9% was used for the MRS data as a cutoff for normal [4], there were 8 normal and 20 fatty livers in the MRS data.

MRI: ***Two-point Dixon (2PD):*** For the lean and obese group, the range of HFF as measured by the 2PD was -6.3–2.2% (-2.0±3.7%) and -2.4–42.9%, respectively.

Three-point IDEAL (3PI): For the lean and obese group, the range of HFF as measured by 3PI was 7.9–12.8% (10.1±2.0%) and 11.1–49.3% (22.0±12.2%), respectively. The SD of HFF across the slices measured by 3PI was 0.6–6.1% and is only moderately correlated with the mean HFF (r = 0.503, p = 0.006).

Combined Data Analysis: The HFF measured by 2PD is strongly correlated with that measured by MRS (r = 0.954, p < 0.001; Fig. 1a). The HFF measured by 3PI is also strongly correlated with that measured by MRS (r = 0.973, p < 0.001; Fig. 1b). The HFFs measured by both MRI methods are also strongly correlated with each other (r = 0.978, p < 0.001; Fig. 1c). The HFFs measured by 3PI are relatively higher than those by 2PD (Fig. 1c). With the diagnostic findings from the MRS data as a reference, Fig. 2 illustrates the percentages (y-axis) of correctly diagnosed cases with 2PD and 3PI when the HFF cutoff for normal is set to m x SD above the mean HFF of lean subjects for each MRI method. For 0 ≤ m ≤ 2.5, the HFF cutoff for normal liver for 2PD ranged from -2.0–6.3%, and 21–26 of 28 subjects were correctly diagnosed (75–93%). In the same range of m, the HFF cutoff for normal liver for 3PI ranged from 10.1–15.1%, and 22–25 of 28 subjects were correctly diagnosed (79–89%).

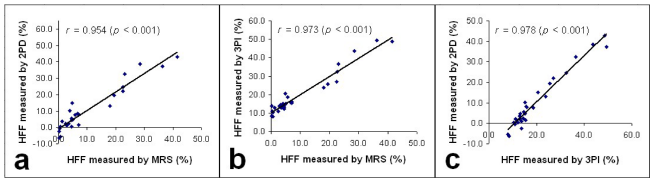

Fig.1 *Correlations between (a) MRS and 2PD, (b) MRS and 3PI, (c) 2PD and 3PI.*

DISCUSSION

The negative HFFs obtained by 2PD from some of the normal livers and the tendency of overestimation of HFF by 3PI can be attributed to the limited sensitivity of multipoint water-fat separation MRI in general. As a result, the mean HFFs of the lean group obtained by using these two MRI methods significantly differ from each other. In addition to the limited sensitivity, several sequence-specific factors should be considered in association with the tendency of overestimation of HFF by 3PI. That is, it may arise from the T2/T1-weighting nature of bSSFP as well, which is known to give rise to the "brighter fat signal" in comparison to T1-weighting SPGR. It may also be due to the J-(de)coupling effect of fat spins as seen in fast spin echo sequences, which also results in "brighter fat signal" [8]. Thus, together with the variable performance of multipoint water-fat separation MRI for *a given sequence* depending on sampling strategies and post-data processing [1-3], these potential *sequence-dependent* sources of variability in apparent fat content can limit the clinical application of the MRI methods, particularly when a diagnosis of early fatty liver needs to be performed. To this end, it may be necessary to establish an HFF cutoff for normal liver specific to each imaging protocol's sequences and sequence parameters in order to minimize errors in the diagnosis of fatty liver. For instance, if HFF cutoffs for normal liver of 1.3% and 12.1% are chosen for the 2PD and 3PI, respectively (m = 1 for both), the resulting diagnostic precision can be comparable to that of MRS (~ 90% precision for both), although the HFF cutoffs for the two MRI methods are quite dissimilar.

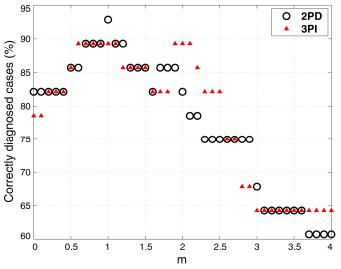

Fig.2 *The percentages (y-axis) of correctly diagnosed cases using 2PD and 3PI with the upper limit of HFF for normal given as m x SD above the mean HFF of lean subjects for each of the MRI methods where m (x-axis) varies from 0 to 4.*

REFERENCES: [1] Glover, JMRI, 1, 521, 1991. [2] Reeder et al, MRM, 54, 636, 2005. [3] Lodes et al, J Comput Assist Tomogr, 13, 855, 1989. [4] Petersen et al, PNAS, 103, 18273, 2006. [5] Fishbein et al, MRI, 15, 287, 1997. [6] Reeder et al, MRM, 51, 35, 2004. [7] Frahm et al, MRM, 9, 79, 1989. [8] Henkelman, JMRI, 2, 533, 1992.

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