Frame-by-Frame 1H MRS for In Vivo Pancreatic Fat Quantification

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TARGET AUDIENCE: Investigators interested in pancreatic fat quantification and MR spectroscopy acquisitions in the body

PURPOSE: Human pancreatic fat content estimated from *in vivo* ^{1}H magnetic resonance spectroscopy (MRS) has been associated with body mass index (BMI) and β-cell function[1,2]. Accurate pancreatic fat quantification using ^{1}H MRS is challenging due to the facts that: (1) pancreas cross-section varies along the body of the pancreas and can be generally rather small, (2) pancreas is surrounded by visceral fat, and (3) pancreas moves with respiration. As a result, less reliable fat quantification of pancreas has been reported compared to liver fat measurements when same ^{1}H MRS technique was used[1,3]. Even though careful MRS voxel planning and respiratory compensation can potentially mitigate the contamination of proton spectroscopy data, inspection of individual spectrum may be necessary when such efforts fail in patients with inconsistent breathing patterns[1]. In a previous study, frame-by-frame acquisition of PRESS spectroscopy showed negligible effects of physiological motion on *in vivo* brain ^{1}H MRS[4]. In this study, we applied the same approach in a comparison study using different ^{1}H MRS techniques with different respiratory compensation methodology to assess the reliability of the different methods for pancreatic fat quantification *in vivo*.

METHODS: This was a prospective, IRB-approved, HIPAA-compliant study. After signing an informed consent, patients with known diabetes (BMI: 37.9±6.09) were examined on a 3T dual-transmit MRI scanner with either a body coil or a 16-channel SENSE-XL-Torso coil (Achieva, Philips Medical Systems, Cleveland, OH). T2-weighted single-shot fast spin-echo anatomical images of pancreas were acquired during expiration breath-hold in three orthogonal planes to aid single-voxel placement (7x7x20 mm^3). Using the chemical shift displacement tool provided on Philips MRI scanner, specific effort was made to position both water and lipid acquisition voxels within pancreas and to exclude surrounding visceral fat (Figure 1). Three single-voxel ^{1}H MRS acquisition methods were tested in each patient: (1) Cardiac- and respiratory-triggered PRESS (PRESS-TRIG) with TE/TR=31/6000 ms, Frames=16; (2) Cardiac- and respiratory-triggered STEAM (STEAM-TRIG) with TE/TM/TR=25/22/6000 ms, Frames=16; and (3) Breath-hold STEAM (STEAM-BH) with TE/TM/TR=25/22/3500 ms, Frames=4, Scan time=14 sec. All three sequences sampled 2048 points with spectral bandwidth of 2 kHz. LCModel[5] was used to quantify water and lipid peaks for individual frames as well as for the summed spectrum. Resonance areas were measured for water peak @ 4.7 ppm, and 4 groups of lipid peaks @ 0.9, 1.3, and 1.6 ppm; @ 2.1, 2.3, and 2.8 ppm; @ 4.1 and 4.3 ppm; @ 5.2 and 5.3 ppm. Total fat signal was defined as the sum of all lipid peaks. Fat fraction (FF) was then calculated as: FF=Fat/(Fat+Water). Generalized linear models were used to investigate the effects of three methods on FF (SAS 9.3). The first model used FF from all frames and compares the difference in mean FF among the three methods. The second model used only the minimum FF of each patient, assuming this value was close to the "true" FF value, and compared the difference among the three methods. The third model used the FF calculated from summed spectrum for each patient and compared the difference among the three methods.

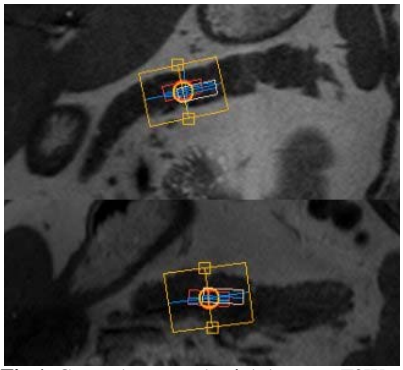
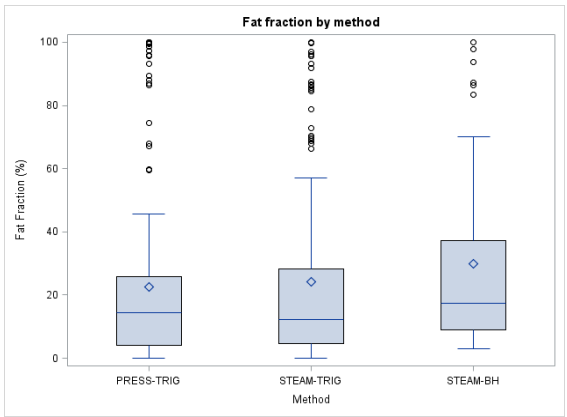


Fig.1. Coronal (top) and axial (bottom) T2W anatomic images. A single-voxel was carefully placed to ensure both water (red) and lipid (white) acquisition voxels were within pancreas, which is surrounded by visceral fat. Yellow box was the shimming volume.

RESULTS: Variation of the largest methylene peak @ 1.3 ppm was easily visualized among individual frames for all three acquisition methods within the same patient. Compared to STEAM, PRESS spectra showed better signal-to-noise ratio. The distributions of fat fractions of all frames acquired from a total of ten patients are shown in the box-plot. Two patients were excluded from the analysis since LCModel fitted only a couple of frames acquired due to poor quality of the spectra. All three methods demonstrated large right skewness (mean>median) and large outliers. No significant difference was found when mean FF or FF of the summed spectrum was compared among three methods. However, significant difference among three methods was found when the minimum FF was compared (Table).

DISCUSSION: Pancreatic fat quantification in human using ^{1}H MRS is challenging and time consuming in practice. Anatomic images are often acquired in different orientations to ensure the voxel for spectroscopy is planned within the pancreatic tissue, excluding visceral fat. Respiratory compensation methods such as respiratory-trigger or breath-hold are required to minimize the fat contamination from outside of the voxel due to breathing motion. However, respiratory-triggered acquisitions increase the scan time, and are prone to error due to variable breathing pattern during long acquisitions. Breath-hold acquisitions are fast and can eliminate motion of the pancreas compared to respiratory-triggered acquisitions. However, some patients may have difficulty to hold their breath. Moreover, inconsistent breath-holds may lead to variability in the position of the voxel both during voxel planning and actual data acquisition resulting in large errors in fat quantification. For example, in one of our patients, the breath-hold STEAM acquisition was repeated. The range of fat fraction from all frames was 3.04 -13.47% for 1st scan, and 56.13 – 66.54% for 2nd scan, clearly indicating the vulnerability of this method to fat fraction quantification.



Distribution of fat fraction demonstrates the mean (diamond), median (mid-line), and 25% and 75% (border of the box) of all frame-by-frame measurements from 10 patients.

CONCLUSION: Our study has demonstrated considerable variation of pancreatic fat quantification by *in vivo* ^{1}H MRS, despite of careful voxel planning and different motion compensation methods applied. Summed spectrum acquired in routine clinical study is not reliable due to the possible fat contamination in each spectrum frame. Our results indicate that frame-by-frame acquisition is crucial for ^{1}H MRS of pancreas *in vivo*. We propose using the minimum fat fraction of all frames to estimate pancreatic fat content. Future studies comparing this approach with Dixon-based imaging methods are currently underway.

REFERENCES: 1. Tushuizen ME. Diabetes Care 2007; 2. Lingvay I. J Clin Endocrinol Metab 2009; 3. Livingstone R. ISMRM 2012; 4. Katz-Brull R and Lenkinski RE. MRM 2004; 5. Provencher SW. MRM 1993.

Comparison of Fat Fraction (FF) using different MRS methods

FF (%)	PRESS-TRIG	STEAM-TRIG	STEAM-BH	P value
Mean	10.1716	11.1775	18.7952	0.0544
Minimum	1.2839	0.63737	7.70138	0.0058
Summed	11.4238	10.9135	18.752	0.4368