Novel strategy to differentiate water and lipid composition

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Introduction: The prevalence of obesity and diabetes is an increasing world-wide problem. Not only the lipid content but also the distribution of lipid composition is of special importance in the pathogenesis of these diseases (1). A detailed analysis of lipid content and distribution of lipid composition appears indispensable for a better understanding of lipid metabolism and its regulation. Proton magnetic resonance spectroscopy has evolved to be a reliable method for measuring both fat content and composition non-invasively. Adipose tissues and liver are critical for lipid regulation. Typically, this method measures one region of interest and the refocusing pulses required in the PRESS sequence involve high RF power deposition. The objective of this study was to demonstrate the feasibility of a magnetic resonance imaging based method to assess the lipid distribution in neck fat pad.

Materials and methods: *Phantom*: 2 standard NMR tubes were used, filled with 100% alcohol and intralipid (<20%) separately. *Animals*: One ob/+ mouse 38 weeks of age was used. The mouse was anesthetized using isoflurane (1.5%-2.25%) in an oxygen-air mixture (150/400) throughout the experiments with intubation. The body temperature and respiration were monitored. The respiration signal was used for respiration gating during MR acquisition. All animal experiments were performed in strict adherence to the Swiss Law for Animal Protection. *MRI experiment:* All MRI measurements were performed on a Bruker BioSpec 94/30 (Bruker BioSpin MRI, Ettlingen, Germany) system using a volume resonator for excitation and a surface coil for signal detection. Gradient Echo sequence was applied with the following parameters: VOI 1.6*2.2 cm^2 (phantom), 2.5*2.5 cm^2 (neck), slice thickness = 1.0 mm; number of slice = 1, matrix size = 128*128, flip angle = 52°, TR = 600.0 ms, TE = 3.0 to 28.4 ms with $\Delta TE = 0.2\ ms$ (phantom), and TE=3.0 to 4.5 ms $\Delta TE = 0.1\ ms$ (neck), band width=8000.00Hz, number of sampling points = 256, acquisition time = 2.56 ms, number of averages NA = 1 (phantom) and NA = 2 (Neck) for sufficient SNR. Single-voxel localized ^{1}H MR spectra were acquired using the PRESS sequence with additional outer volume suppression with the following parameters: VOI 1.5*1.5*1.5 mm^3, TR = 6s, T_E = 12ms, band width = 4006.41 Hz, number of sampling points = 6009, acquisition time = 1499.85 ms, number of averages (NA) = 20. *Analysis of MRS data:* All MRI data were processed using Matlab *(*2007*)*(MathWorks, Inc.Natick, MA, US.). All spectroscopy data were processed using jMRUI 4.0. The intensity S of an on-resonance signal at echo time TE_k is given as*(2)*

$$S(TE_k) = \frac{M(1-e^{-TR/T_1})e^{-TE_k/T2^*}sin\alpha}{(1-e^{-TR/T_1}cos\alpha)} = M\eta e^{-TE_k/T2^*} \text{ where } \eta = \frac{(1-e^{-TR/T_1})sin\alpha}{(1-e^{-TR/T_1}cos\alpha)}.$$

Correspondingly the signal arising from the contribution of N spectral components characterized by frequency offset Δf_i becomes

$$S(TE_k) = \sum_{j=1}^{N} M_j \eta_j e^{-TE_k/T2_j^*} e^{2\pi i \Delta f_j TE_k}$$

And it depends on proton density M_j, repetition delay TR, echo delay TE_k, relaxation times T_{1j} and $T2_j^*$, flip angle α and the offset frequency Δf_j relative to water. Fourier Transform of $S(TE_K)$ data were used to differentiate individual resonances Δf_i.

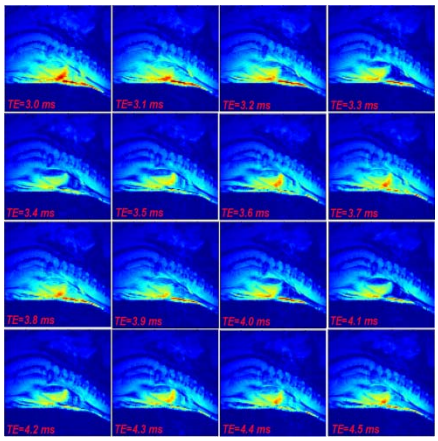

Fig 2. MR images from neck of ob/+ mouse for a TE series (TE=3 to 4.5ms).

Results: Anatomical MR images displaying phantom at TE=3.0, 3.2, 3.4 3.6 ms are shown in Fig.1A (from left to right) with single voxel spectra of alcohol and intralipid at TE/TR=12/6000ms (Fig.1B). Typical results processed from MRI TE series reveal the spectra of alcohol (Fig.1C) and intralipid (Fig1D). A typical image series with 16 different TE values is displayed in Fig.2 and reveals periodicity in the intensity patterns. FT of the modulation patterns yields the regional distribution of individual frequency components (Fig.3). Furthermore, Fourier Transformed data from two typical regions are plotted in the same figure.

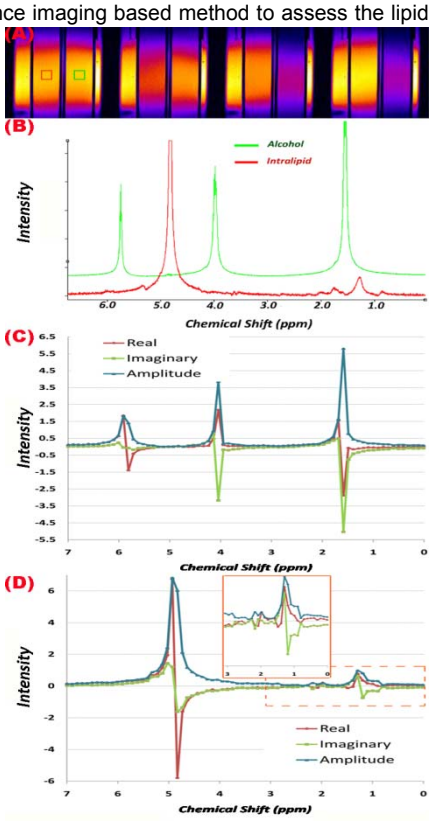

Fig1. (A) MR images from phantom, (B) single voxel spectrum from one voxel in alcohol and intralipid respectively as indicated in (A), typical MRI derived results from alcohol (C) and intralipid (D).

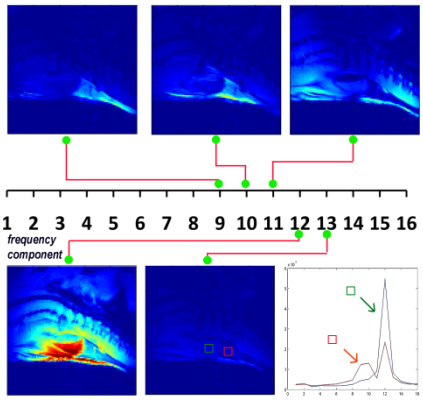

Fig 3. Chemical shift specific MR images obtained following FT of image series shown in Fig.2. Spectra of two voxels are plotted.

Discussion and conclusion:
The present study demonstrates that in vivo ^{1}H MRI TE series can reveal the distribution of individual frequency components at high spatial resolution compare to single voxel spectroscopy or chemical shift imaging (CSI). This method is attractive under conditions when few resonances have to be resolved, i.e. the spectral resolution requirement is relatively low. In such case the available measurement time can be invested to increase spatial resolution. Moreover, the method uses relatively low flip angle, hence reducing power deposition. Accurate spectral quantification requires T1 and T2* maps for individual resonances. Also the spectral resolution has to be high enough to accurately reproduce lineshapes. An attractive application of this method is the analysis/monitoring of the distribution of lipid content and composition within various tissue compartments yielding insights into normal and disordered lipid metabolites.

References:

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2. Liu CY, et al. 2007. Fat quantification with IDEAL gradient echo imaging: correction of bias from T(1) and noise. *Magn Reson Med*. **58**: 354