Resolving Glycerol-CH_2 Signal from Water in *In Vivo* ^{1}H Magnetic Resonance Spectroscopy at 9.4 T

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ABSTRACT

Purpose: To resolve the glycerol-CH_2 resonance (≈4–4.4 ppm) from that of water (≈ 4.7 ppm) in ^{1}H magnetic resonance spectroscopy (MRS) at 9.4 T.

Methods: A long echo time (TE) approach was used to exploit the shorter T_2 relaxation time of water. The glycerol-CH_2 signal is J-modulated; therefore, TE values were optimized to retain an in-phase positive or negative glycerol-CH_2 signal. A Point RESolved Spectroscopy (PRESS) sequence (TE_1=15ms) was employed at 9.4 T to acquire safflower oil spectra with a short TE of 25 ms and with long TE values ranging from 60-200 ms in 10 ms increments. The optimal TE values, together with a TE of 25 ms, were applied in vivo to a high-fat diet (60% kcal% fat) fed CD1 mouse. Spectra were acquired from visceral adipose tissue and liver to assess the feasibility of the method in different tissues. Liver spectra were also acquired with a CHEmical Shift Selective (CHESS) water suppression module (300 Hz pulse bandwidth) and were quantified using LCModel.

Results: Long TE values of 70 ms and 170 ms were selected, yielding glycerol-CH_2 areas of 41.0% and 7.2% of that of the short TE, respectively. The TE values resolved glycerol-CH_2 signal from water in adipose tissue but yielded negligible signal in liver, likely due to shorter hepatic T_2 times. However, the relatively narrower water peak in liver rendered water suppression feasible. Short-TE PRESS with water suppression yielded a well-resolved glycerol-CH_2 signal. LCModel analysis of the water-suppressed spectrum resulted in a glycerol-CH_2 area ≈0.6 times that of the non-suppressed spectrum. The lower signal may be due to less water contamination and due to some suppression of glycerol signal by the water suppression module.

Conclusions: Long-TE PRESS resolves the glycerol-CH_2 resonance in adipose tissue but is unsuitable in liver due to shorter T_2 times. Short-TE acquisition with water suppression is more appropriate for its quantification in liver.

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INTRODUCTION

- Quantification of the glycerol-CH_2 (≈ 4.0-4.4 ppm) protons using proton magnetic resonance spectroscopy (MRS) enables measuring free fats versus fats stored as triglycerides[1]. The measure can serve as a biomarker in NAFLD[2], leukemia[3], and diabetes[4].
- Its *in vivo* measurement is challenging because the dominant water resonance obscures that of the glycerol protons, impairing accurate quantification[5].
- Short echo time (TE), water suppressed (WS) spectra have been employed at 9.4 T for liver measurements *in vivo*, where the T_2 times are relatively short[6].
- In adipose tissue, where T_2 times are longer, a long-TE approach can be used to separate the glycerol and water peaks by exploiting the shorter T_2 of water relative to fats, as previously demonstrated at 3 T[5].
- The purpose of this work is to optimize a Point RESolved Spectroscopy (PRESS) MRS sequence for resolving glycerol signal at 9.4 T *in vivo*, using a short TE in liver and a long TE in adipose tissue.

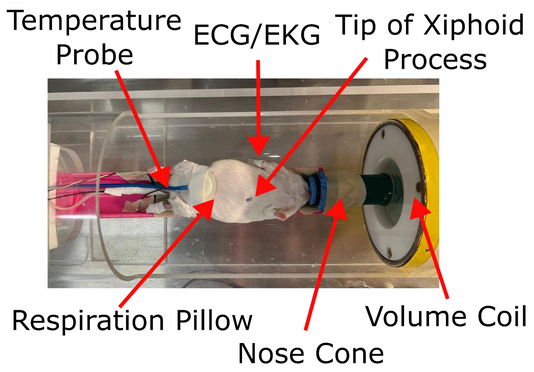

Figure 1. Experimental setup for *in vivo* mouse scans.

METHODS AND MATERIALS

Phantom Experiments

- PRESS spectra were acquired from a 5x5x5 mm^3 voxel in a safflower oil phantom.
- TE value varied from 60-200 ms in 10 ms increments.
- Optimal long TE was selected by visual inspection.

In Vivo Experiments

- PRESS spectra acquired from a high fat diet (HFD; 60% kcal% fat) fed mouse (22 weeks old; 11 weeks on HFD).
- Animal was maintained under isoflurane sedation with physiological monitoring (see Figure 1).
- Respiratory and ECG gating were used for liver acquisitions, whereas adipose tissue acquisitions used respiratory gating only.

Short-TE Method (*In Vivo*)

- Liver voxel was positioned to avoid major blood vessels (Figure 2).
- Spectra acquired at a TE=25 ms, with and without WS.
- A narrow-bandwidth CHEmical Shift Selective (CHESS) WS module was used to suppress water while preserving most of the glycerol-CH_2 signal.

Long-TE Method (*In Vivo*)

- Liver voxel was positioned as shown in Figure 2, and the visceral adipose tissue voxel was positioned as shown in Figure 3.
- Spectra were acquired with the optimal TE determined from phantom experiments for liver and visceral adipose tissue.

Spectral Analysis

- Phantom glycerol-CH_2 signal area was obtained by direct integration of the spectra.
- *In vivo* short-TE spectra were fit with LCModel to obtain glycerol-CH_2 areas. Fit was accepted given a Cramér-Rao Lower Bound (CRLB) estimate ≤ 20.

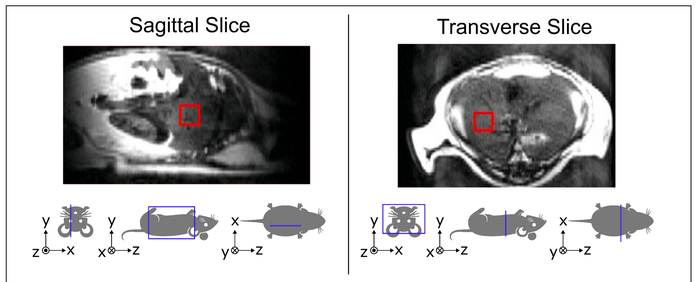

Figure 2. Voxel (4x4x4 mm^3) placement for *in vivo* liver measurements.

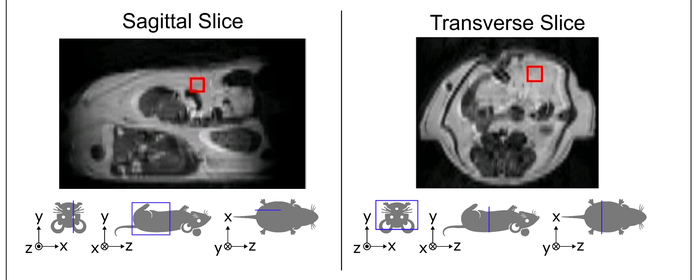

Figure 3. Voxel (3x3x3 mm^3) placement for *in vivo* adipose tissue measurements.

RESULTS

Short-TE Method (*In Vivo*)

- Liver glycerol-CH_2 and water resonances were resolved, as shown in Figure 4.
- WS and non-WS glycerol-CH_2 areas were 0.94 and 0.53, (other resonance areas were similar for both).

Long-TE Optimization (In Phantom)

- The glycerol-CH_2 signal in safflower oil was negatively in phase using TE values of 70 ms and 170 ms (Figure 5), retaining 41% and 7.2% of the short-TE signal, respectively.

Long-TE Method (*In Vivo*)

- Glycerol-CH_2 was detected and resolved in visceral adipose tissue but not in liver tissue (Figure 6).

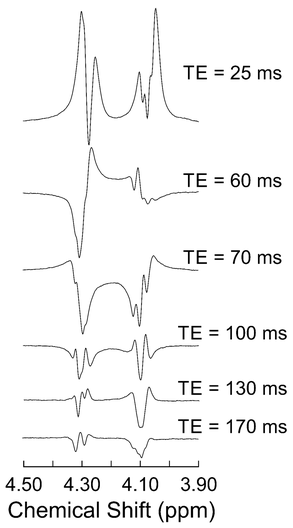

Figure 5. PRESS Safflower Oil Spectra.

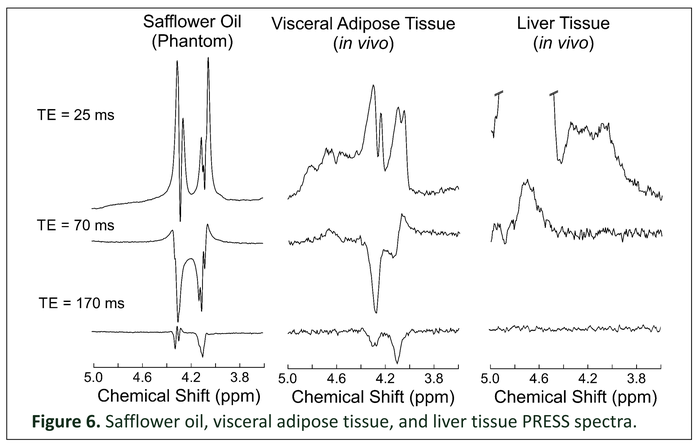

Figure 6. Safflower oil, visceral adipose tissue, and liver tissue PRESS spectra.

DISCUSSION

- In liver, WS short-TE resolved glycerol-CH_2 from water. However, WS may suppress some glycerol-CH_2 signal.
  - ≈0.6x lower WS compared to non-WS.
- Long TE not applicable in liver due to short T_2 values[6].
- In adipose tissue, while a TE of 70 ms effectively suppressed the water signal, a TE of 170 ms achieved complete water suppression, with both TE values retaining sufficient glycerol signal for quantification.

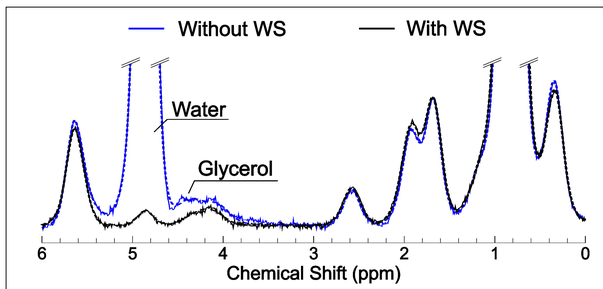

Figure 4. PRESS spectra (TE = 25 ms) from liver with and without water suppression. Dashed lines represents LCModel fits.

CONCLUSIONS

- In tissues such as liver, where T_2 times are relatively short, a short-TE PRESS approach with WS is effective for resolving the glycerol-CH_2 signal.
- In adipose tissue, longer TE values of 70 ms and 170 ms effectively suppresses water signal and can be used as an alternative to the short-TE WS approach.

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