^{1}H-MRS in the *in vivo* mouse heart: a comparison between PRESS and STEAM

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Target audience - This work is relevant to the field of myocardial metabolism in general, and to those interested in strategies for (mouse) cardiac MR spectroscopy in particular.

Purpose - Cardiac lipid metabolism has become an important area of research, particularly due to the increasing prevalence of cardiovascular diseases associated with obesity and diabetes. Proton MR spectroscopy (^{1}H-MRS) allows for the noninvasive detection of myocardial metabolites such as myocardial triglyceride (TG). So far, its application in preclinical rodent studies has been limited [1]. For ^{1}H-MRS of brain, liver, and skeletal muscle, two different single-voxel single-shot localization techniques are commonly used: STEAM (stimulated echo acquisition mode) and PRESS (point resolved spectroscopy). While STEAM may benefit from a reduced minimal echo time (TE) and the absence of refocusing pulses, it suffers from 50% signal reduction and is more susceptible to motion artifacts compared to PRESS. The small (~100 mg), fast-beating (400-600 min^{-1}) mouse heart imposes challenges regarding optimization of sensitivity and minimization of motion artifacts. The aim of this work is to compare the suitability of PRESS and STEAM for ^{1}H-MRS of the *in vivo* mouse heart. Also, mouse myocardial water and TG T_1 relaxation times at 9.4 T were determined.

Methods - We implemented ECG-triggered, respiratory-gated PRESS and STEAM sequences on a horizontal-bore 9.4 T MR system (Bruker BioSpin) equipped with a quadrature-driven birdcage coil (Ø 35 mm) for RF transmission and signal reception. PRESS parameters were TE = 9.1 ms; 0.4 ms Hermite-shaped 90° excitation pulse (bandwidth 33 ppm); 0.9 ms Mao-type 180° refocusing pulses (bandwidth 15.5 ppm). STEAM parameters were TE = 3.6 ms; TM = 3.8 ms; 0.4 ms Hermite-shaped 90° pulses (bandwidth 33 ppm). To maintain steady state of magnetization, which is required for quantitative assessment of metabolite levels, dummy pulses were performed during respiratory gates [2]. Water suppression was performed with a CHESS module prior to the localization sequence. In anesthetized male C57BL/6 mice (n = 12), cardiac ^{1}H MR spectra (NA = 256) were obtained from a 4 µL voxel positioned in the end-diastolic interventricular septum using PRESS and STEAM at TR = 2 seconds. Series of 32 water spectra were acquired in the same voxel, and quantified using jMRUI to assess signal stability via the standard deviations (SD) of the signal amplitude and zero-order phase. Finally, in a subset of mice (n = 6), saturation recovery experiments were performed using PRESS to determine *in vivo* myocardial water and TG methylene T_1 values.

Results - Water signal amplitude stability was comparable for PRESS and STEAM (SD 9.3 ± 6.4 % vs. 7.8 ± 7.2 %, respectively). Zero-order phase was slightly more stable for PRESS than for STEAM (SD 13.4 ± 6.3 ° vs. 20.2 ± 9.8 °; $P < 0.05$). Water line width was smaller for PRESS than for STEAM (28.8 ± 4.3 Hz vs. 38.0 ± 6.8 Hz; $P < 0.001$), and SNR of the water signal was almost two-fold higher for PRESS than for STEAM (99.7 ± 13.7 vs. 51.1 ± 12.1; $P < 0.0001$). In water-suppressed spectra, peaks from several metabolites could be distinguished, although small peaks such as for creatine methyl protons (Cr-CH_3; 2.99 ppm) were obscured by noise in STEAM spectra (Figure 1). The amplitudes of the dominant TG methylene (TG -CH_2-; 1.28 ppm) signals, determined from PRESS and STEAM spectra, showed a good correlation (r = 0.92; $P < 0.001$, Figure 2). T_1 relaxation times were 1.69 ± 0.24 s for mouse myocardial water and 0.62 ± 0.19 s for TG -CH_2- (Figure 3).

Discussion - Here, we demonstrated the feasibility to acquire ^{1}H MR spectra in the *in vivo* mouse heart using both PRESS and STEAM. Water signal stability was slightly better for PRESS than for STEAM. Evidenced by a good correlation between PRESS and STEAM measurements, both methods can be used to quantify mouse myocardial TG content. However, the two-fold higher SNR for PRESS compared to STEAM with the current parameter settings makes PRESS superior to STEAM for *in vivo* detection of myocardial metabolites, particularly for low-concentration metabolites such as creatine. The T_1 value for mouse myocardial water at 9.4 T is in agreement with a previous report using MRI to determine myocardial water T_1 [3], demonstrating the effective maintenance of steady state of magnetization with dummy pulses during respiratory gates. Importantly, with this approach, we were able to estimate the T_1 for mouse myocardial TG at 9.4 T. In future research, these T_1 values can be used to convert semi-quantitative measures of myocardial TG content to absolute values of myocardial TG levels.

References - [1] Faller, K.M.E. *et al*. 2012, *Heart Fail Rev*, in press. [2] Schneider, J.E. *et al*. 2004, *Magn Reson Med*, 52:1029-35. [3] Coolen, B.F. *et al*. 2011, *NMR Biomed*, 24:154-62.

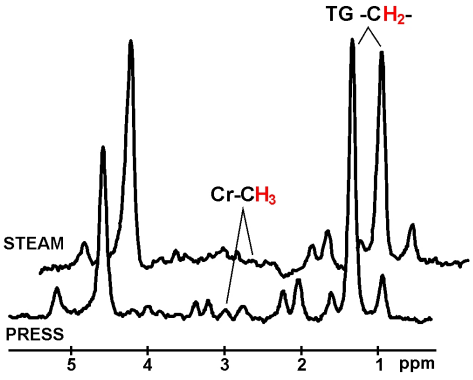

Figure 1. Water-suppressed STEAM (top) and PRESS (bottom) ^{1}H MR spectra from the *in vivo* mouse heart.

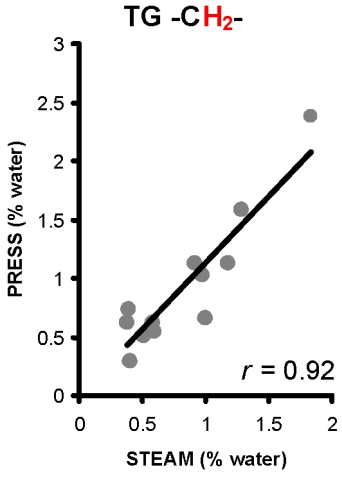

Figure 2. Correlation between PRESS and STEAM for myocardial TG methylene signal amplitude.

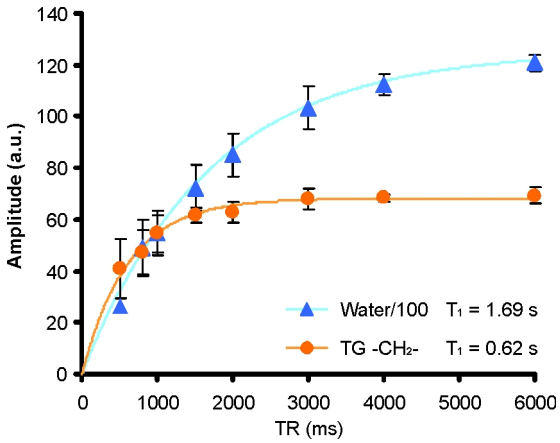

Figure 3. Saturation recovery curves for *in vivo* mouse myocardial water and triglyceride TG obtained with PRESS-localized acquisitions.