Diffusion-weighted STEAM MRS to measure fat unsaturation in regions with low fat content

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Target audience: Basic scientists working in MRS of adipose tissue and clinical researchers interested in biomarkers of metabolic disorders

Purpose: The degree of fat unsaturation, reflecting the average number of double bonds in the triglycerides' fatty acids, is considered a useful biomarker in studies of obesity, diabetes and osteoporosis [1-3]. The degree of fat unsaturation can be non-invasively measured using magnetic resonance spectroscopy (MRS), relying on the quantification of the area ratio of the olefinic fat peak to the methyl fat peak [4]. However, in tissues with a low fat content, the water peak (at 4.7 ppm) is likely to dominate the olefinic fat peak (at 5.3 ppm), complicating the quantification of the area ratio. Long TE PRESS sequences [4, 5] have been previously proposed, taking advantage of the considerably faster T_2 relaxation of the water peak compared to the olefinic peak. However, a long TE (of the order of 200 ms at 3 T) should be employed in order to minimize J-coupling effects in the estimation of the olefinic to methyl peak area ratio [4, 5], resulting in a low signal-to-noise ratio (SNR) of the measured spectrum. Exploiting the much faster diffusion of the water peak relative to the fat peaks [6, 7] in a diffusion-weighted (DW) experiment provides an alternative approach to reduce the area of the strong water peak overlapping the olefinic fat peak. In parallel, STEAM MRS has been shown to have less sensitivity to J-coupling effects at moderate TEs than PRESS MRS [8]. Therefore, the purpose of the present work is to develop a DW-STEAM MRS sequence and examine its performance on the estimation of the olefinic fat peak area in presence of a broad water peak at a moderate TE.

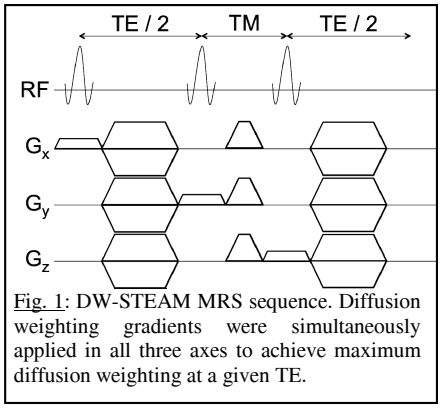

Fig. 1: DW-STEAM MRS sequence. Diffusion weighting gradients were simultaneously applied in all three axes to achieve maximum diffusion weighting at a given TE.

Methods: DW-STEAM sequence: The DW-STEAM MRS sequence (Fig. 1) was based on a standard STEAM MRS sequence with additional paired gradients after the first and third RF pulse to induce diffusion weighting. While diffusion gradient areas were maximized to achieve a reasonable b-value at short TE and short mixing time (TM), eddy current effects were visible in the acquired spectra. For compensation, the paired diffusion gradients were switched to opposite polarity for half of the acquired averages to cancel out eddy current distortion effects. A previously proposed signal combination routine [9] was adopted.

Phantom measurements: Four vegetable oils (coconut, rapeseed, sunflower, walnut) were scanned using a standard STEAM sequence (TE=40 ms, TR=3000 ms, TM=16 ms, BW=3000 Hz, 4096 samples, 16 averages, VOI=12x12x12 mm) and standard long TE PRESS sequence (TE=200 ms, TR=3000, BW=3000 Hz, 4096 samples, 16 averages, VOI=12x12x12 mm). Furthermore, data using the described DW-STEAM sequence (TR=3000 ms, TE=40 ms, TM=16 ms, BW=3000 Hz, 4096 samples, 32 averages, b-value=~2200 s/mm^2, VOI= 12x12x12 mm) was acquired.

In vivo measurements: Using the PRESS, STEAM and DW-STEAM sequence already described for the phantom measurements, the calf muscle of a healthy volunteer was scanned using 8 averages by placing the voxel (VOI= 12x12x14 mm) in a region with intramuscular fat visible on a T_1-weighted image.

All measurements were performed on a 3T Philips Ingenia scanner using an 8-channel extremity coil.

Post-processing: Preprocessing of the spectra included standard zero order phasing and apodization routines. Peak area quantification was then performed considering eight triglyceride peaks, while some peaks were fitted using multiple peaks if needed (methyl at 0.9 ppm, methylene at 1.30 ppm, β-carboxyl at 1.60 ppm, α-olefinic at 2.02 ppm, α-carboxyl at 2.24 ppm, diacyl at 2.75 ppm, glycerol at 4.20 and 5.19 ppm and olefinic at 5.29 ppm), and one water peak (at ~4.70 ppm) using a non-linear least square optimization, varying peak area, line width and peak profile. In the *in vivo* measurements, the olefinic peak at 5.29 ppm was considered to also include a small glycerol peak at 5.19 ppm.

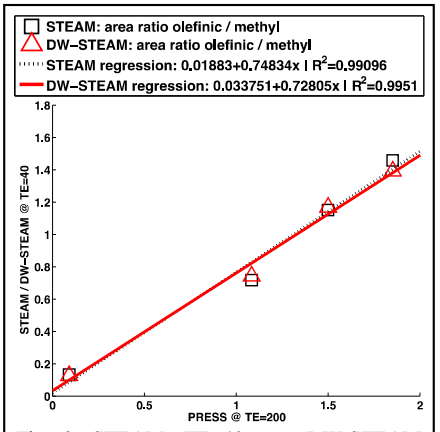

Fig. 2: STEAM (TE=40 ms), DW-STEAM (TE=40 ms) and PRESS (TE=200 ms) showed good correlation for the measurement of the area ratio of the olefinic to the methyl peak.

Results: The phantom measurements showed good correlation (Fig. 2) of the STEAM (TE=40 ms) and DW-STEAM (TE=40 ms, b-value=~2200 s/mm^2) with the long TE PRESS (TE=200 ms) on estimating the area ratio of the olefinic to the methyl peak in the vegetable oils without considering differences in T_2 relaxation and diffusion. The spectra acquired *in vivo* in the calf muscle (Fig. 3) at a region with a fat fraction of 10% using DW-STEAM (Fig. 3b) showed a strongly decreased water peak in comparison to STEAM (Fig. 3c) and therefore enabled the quantification of the olefinic fat peak area. Higher SNR (Fig. 3) for both, the olefinic and methyl peak, were obtained with DW-STEAM (Fig. 3a) compared to PRESS (Fig. 3b). In general more peaks of the triglyceride spectrum were visible with DW-STEAM.

Discussion & Conclusion: The present results show that, with moderate b-values (b-value=~2200 s/mm^2) diffusion of the triglyceride peaks seemed to be negligible, while the water peak decreased very fast. Therefore, DW-STEAM MRS enabled the estimation of fat unsaturation in tissues characterized by a dominating broad water peak with a higher SNR in comparison to long TE PRESS MRS. Doing not only a T_2 correction, but also a compensation for the apparent diffusion coefficients could further improve the estimation of the degree of unsaturation. Finally, DW-STEAM could also minimize the J-coupling effects for all fat peaks and improve the detection of fat peaks with very small areas and short T_2 (that would be not observable in a long TE PRESS due to the lower SNR), enabling in future further characterization of the fatty acid composition in tissues with low fat content [10].

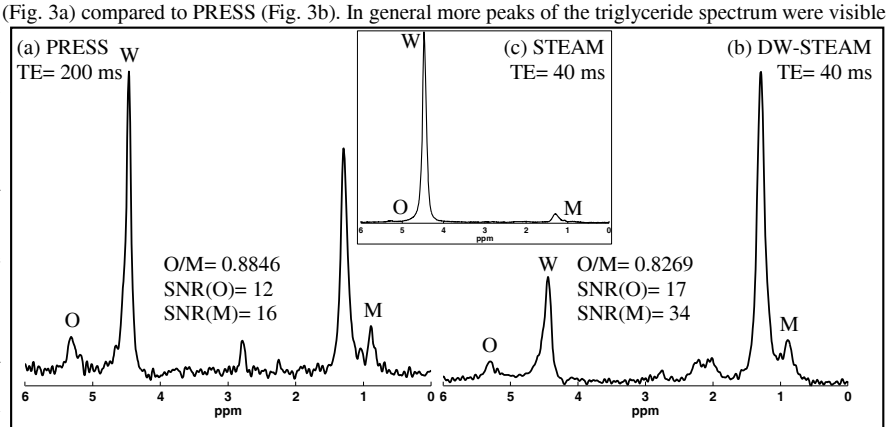

Fig. 3: *In vivo* spectra of calf muscle (10% fat fraction). 8 averages were acquired using a long TE PRESS MRS (a) and DW-STEAM MRS (b) sequence (b-value=~2200 s/mm^2). Standard STEAM MRS (c) is shown for comparison. Olefinic, methyl and water peak are marked with O, M and W, respectively. Area ratios of olefinic to methyl peak (O/M) and SNRs for both peaks are given for PRESS and DW-STEAM.

References: [1] Velan et al., Am J Physiol Regul Integr Comp Physiol. 2008 Oct;295(4):R1060-5. [2] Machann et al., NMR Biomed. 2013 Feb;26(2):232-6. [3] Yeung et al., J Magn Reson Imaging. 2005 Aug;22(2):279-85. [4] Lundbom et al., NMR Biomed. 2010 Jun;23(5):466-72. [5] Troitskaia et al., J Magn Reson Imaging. 2013 Apr;37(4):944-9. [6] Lehnert et al., J Magn Reson Imaging. 2004 Jan;22(1):39-46. [7] Taviani, Proc Intl Soc Mag Reson Med 21, 2013. [8] Hamilton et al., J Magn Reson Imaging. 2009 Jul;30(1):145-52. [9] Lin et al., J Magn Reson Imaging. 1994 Nov-Dec;4(6):823-7. [10] Hamilton et al., NMR Biomed. 2011 Aug;24(7):784-90.

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