Potential effects of superficial fat on metabolite concentrations determined by water referencing studied with various acquisition settings

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Purpose: To corroborate or dispute the recently reported influence of superficial fat layers on metabolite quantification

Introduction: Water content is tightly regulated in the brain and therefore the unsuppressed water signal measured from the same region of interest (ROI) as the metabolite signals has long been used a quantification reference [1]. However, a recent ^{1}H MRS study [2] reported that the metabolite-to-water ratios were strongly reduced in the presence of superficial fat layers (10-35% in phantoms, 16-24% in vivo), thus questioning the clinical use of water as a reference for quantification. Also, given the suspected frequency dependence of the effect (NAA reduced most, Cho least), it would even question any simple means of absolute and relative quantification for MRS. However, this study had limitations such as a small number of phantom and in vivo experiments, and in addition, it was not performed using different acquisition settings (like different sequences, RF coils, field strengths, or MR scanners) to generalize the reported findings. Hence, in this study, we acquired single voxel spectroscopy (SVS) data using various localization and water suppression sequences, head coils, MR scanners, and two different field strengths to assess the conditions under which metabolite / water signal ratios are reduced in the presence of fat layers.

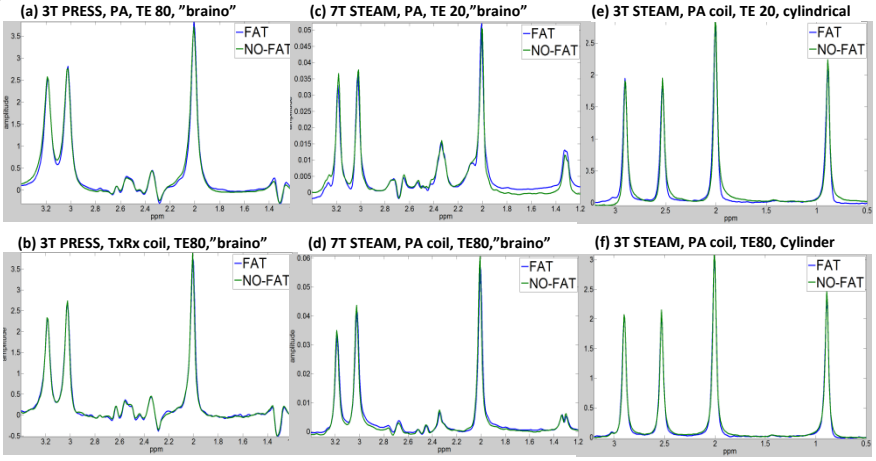

***Figure 1**: Linewidth-matched spectra (scaled by unsuppressed water) acquired using different acquisition conditions in the presence of superficial fat (blue) and without (green)*

Methods: Spherical ("braino" with 16.9 cm diameter: NAA, glutamate, creatine, choline, myo-inositol, lactate) and cylindrical (11.5 cm diameter; 20 cm length, 100 mM acetate, glycine, creatine) phantoms were measured using SVS with TEs of 20 ms and 80 ms on 3-T (Siemens) and 7-T (Philips) whole-body MR scanners, equipped with transmit-receive (Tx-Rx) and phased array (PA) receive head coils. Each session consisted of acquiring water-suppressed (WS) and unsuppressed (nWS) spectra, first with fat (two slabs of 135 x 95 x 8 mm^3) placed on the phantom and then without fat, using various sequences. An ROI of 25 × 25 × 20 mm^3 was placed ~ 15 mm away from the fat layer in all experiments, similar to the setup in [2]. Prescan parameters, in particular shim and B_1, were independently optimized for the ROIs in each setting. Several combinations (see Tables) of localization and WS sequences (PRESS and STEAM; standard WS, metabolite-cycling (MC) for WS, MC plus standard WS (MC+WS) were combined with other acquisition settings (TE 20 or 80 ms; TxRx or PA coil, 3T or 7T) and scans were repeated 3-5 times for each setting. The spectra from all the sessions were apodized to match the linewidths independent of shim (Figure 1). jMRUI QUEST [3] with basis sets created in VESPA [4] was used to quantify and obtain metabolite / water ratios. Percent differences were calculated as (results with fat) minus (results without fat) relative to (results without fat).

***Table 1:** Acquisition settings and quantification results for the cylindrical phantom*

B_0	coil	Seq.	# spectra	TE ms	% difference (Absolute values)				% difference (ratios)		
					Ace	Gly	Cr	H_2O	Ace	Gly	Cr
3 T	Tx-Rx	STEAM	6	20	2.06	2.12	3.92	3.78	-1.58	-1.51	0.11
3 T	Tx-Rx	STEAM	6	80	2.45	2.30	4.07	1.98	-0.09	-0.13	1.39
3 T	Tx-Rx	PRESS	6	80	3.08	2.49	4.23	2.03	1.06	0.48	2.19

***Table 2:** Acquisition settings and quantification results for the spherical phantom.*

B_0	coil	Seq.	# spectra	TE ms	% difference (Absolute values)				% difference (ratios)		
					NAA	Cho	Cr	H_2O	NAA	Cho	Cr
3 T	Tx-Rx	STEAM	5	20	2.86	7.02	2.39	2.30	0.51	4.51	0.07
3 T	Tx-Rx	STEAM	5	80	1.34	2.32	1.19	2.07	-0.71	0.18	-0.87
3 T	Tx-Rx	PRESS	5	80	4.53	2.38	4.16	2.31	2.16	-0.03	1.72
3 T	PA	PRESS	5	80	4.36	2.64	4.98	1.90	2.4	0.7	3.01
3 T	PA	MC+WS	5	80	3.31	-0.69	1.77	1.05	2.23	-1.73	0.71
3 T	PA	MC	5	80	4.94	0.50	0.90	1.43	3.45	-0.92	-0.52
7 T	PA	STEAM	3	20	1.66	7.01	0.94	5.13	-3.26	1.74	-3.98
7 T	PA	STEAM	3	80	6.31	9.45	6.29	8.18	-1.71	1.19	-1.72

Results: Line broadening in the presence of fat was observed across all experiments. Figure 1 shows some of the preprocessed spectra for different conditions. It can be appreciated that the spectra from both phantoms are very similar in the presence and absence of fat. The quantification results are listed in the Tables. While the absolute signal areas ranged slightly, but consistently, higher for both water and metabolites with the superficial fat layer, the percentage differences of metabolite to water ratios were all very small and did not show a consistent trend for the different acquisition settings, phantoms and field strengths.

Conclusions: The in vitro and in vivo reduction in metabolite / water signals reported in Ref [2] for 4T could not be reproduced in vitro at 3T and 7T with any of the different sequences and coils tested. From this, it appears that water referencing is still a valid option under common acquisition conditions, but that it remains to be evaluated what special factors lead to the observations reported in Ref [2].

References: [1] Christiansen et al. Magn Reson Imaging 11:1(1993); [2] Mon et al. NMR Biomed 26:1768 (2013); [3] Ratiney et al. MAGMA 16:284 (2004); [4] https://scion.duhs.duke.edu/vespa/

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