Supplementary information

1

Simulate 6 metabolite peaks :
- CrCH2
- Cho
- CrCH3
- Fat peak 1
- Fat peak 2
- Fat peak 3

- Lorentzian line shape
- Linewidth and amplitude randomly selected from normal distributions defined by means and standard deviations obtained from healthy volunteers.
- Gaussian noise added to obtain similar SNR as in vivo data
- Fitted to give 'true' value

2

Simulate 'normal' spectrum (S_{odd}) with 1 water peak:
- sum of 4 Lorentzians
- water-suppression factor set to 95 ± 3 %.

3

Simulate 13 'inverted' spectra ($S_{even,\,w}$) with different w factors, ranging from 0.1 to 10.

5

Simulate reference spectrum (S_{ref}) which will have different randomly generated Gaussian noise as Step 1.

4

Post-process S_{odd} with each $S_{even,\,w}$ as described in the paper to give 13 S_w spectra.

6

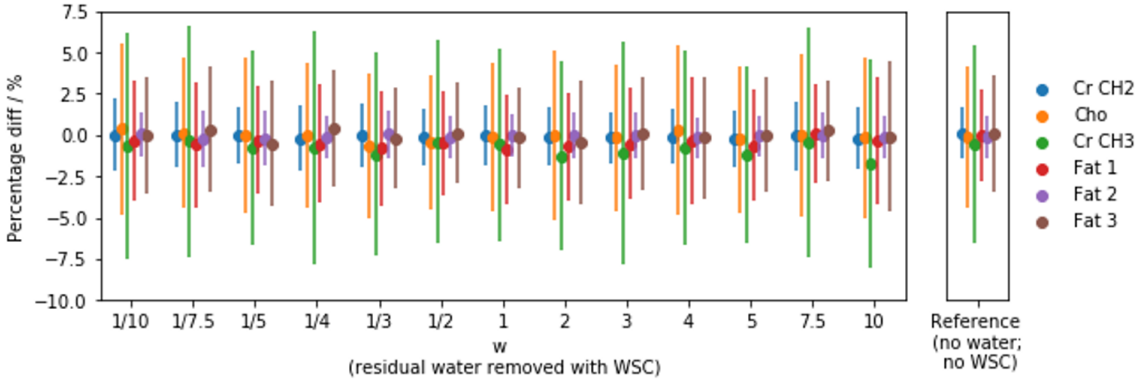
Fit all 13 S_w spectra and S_{ref} spectrum in OXSA tool box. Deviations from the 'true values' are expressed as an absolute percentage difference (δA_X):

$$\delta A_x = \frac{|A_{x,w} - A_{x,true}|}{A_{x,true}} \times 100\%$$

where $A_{x,w}$ refers to the peak amplitude of metabolite A in the fit of S_w or S_{ref}, and $A_{x,true}$ refers to the 'true' peak amplitude.

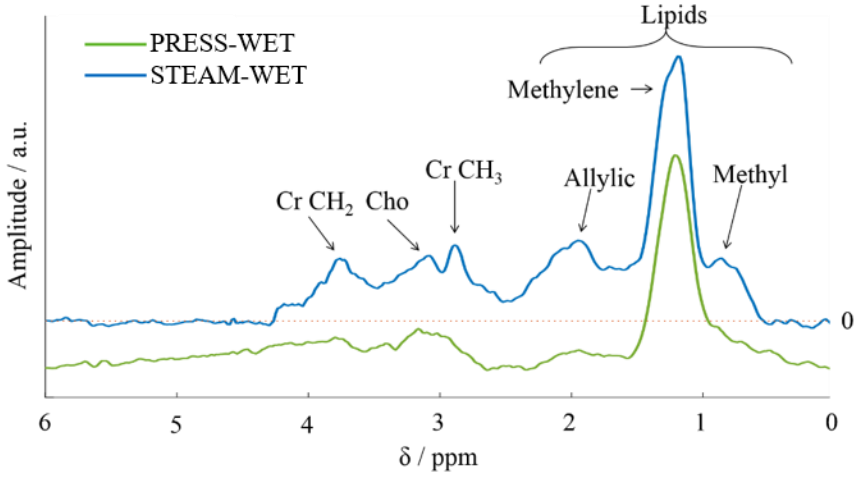
7

Repeat steps 1-6 200 times and average δA_x was across all 200 sets for each S_w/S_{ref} and metabolite.

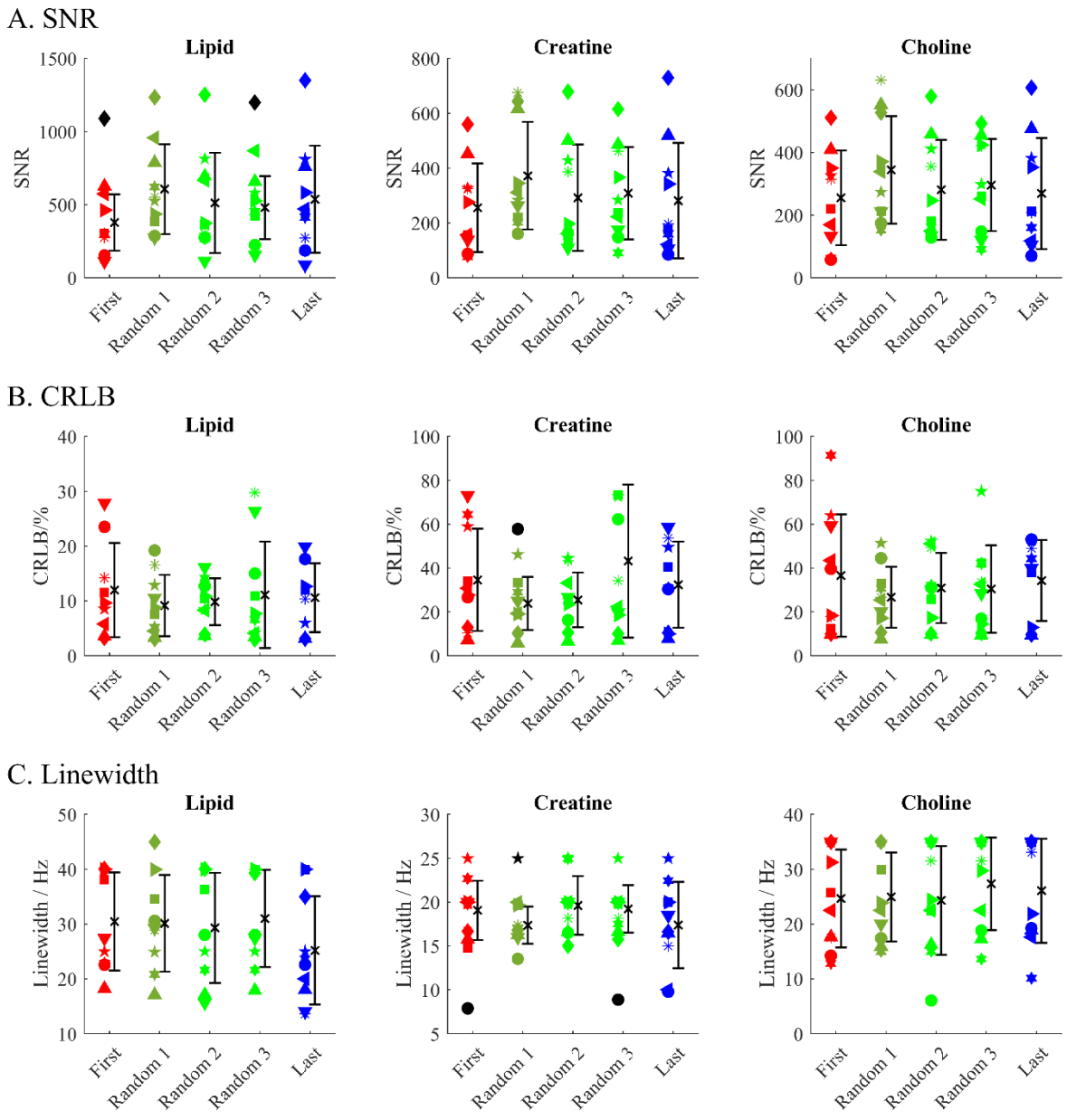


SI Figure 1: Simulation workflow and results showing that amplitudes of metabolite peaks remain unchanged by the weighting factor. The scatter plot at the bottom shows the mean and standard deviation in percentage difference across all 200 sets for each metabolite and each w factor and a reference set (where only the noise varied).

SI Figure 2: Six compartment phantom in silicone ice cube tray with six different concentrations of creatine (0, 5, 10, 20, 40, and 80 mmol/L). Each compartment is roughly 4.8 × 4.8 × 4.8 cm^3.



SI Figure 3: Cardiac spectra of a healthy volunteer obtained by PRESS-WET (green) and STEAM-WET (blue) showing the various metabolite peaks: CH_2 of total creatine (Cr CH_2), choline (Cho), CH_3 of total creatine (Cr CH_3) and lipid peaks. On average across six healthy volunteers, PRESS-WET had 23% smaller SNR and 88% larger CRLB value for the Cr CH_3 peak compared to STEAM-WET.



SI Figure 4: SNR (A), CRLB (B) and linewidths (C) for the first (red), last (blue) and 3 random sets (green) of 12 breathholds obtained from the STEAM-WET (150 meas.) acquisition in healthy volunteers. The random set corresponding to the data set used in the paper is labelled as 'Random 1' and plotted in a darker shade of green. Each volunteer is represented by a different symbol and data points more than 1.5 interquartile ranges above the upper quartile or below the lower quartile are treated as outliers (coloured black). The black cross and corresponding whiskers show the mean and standard deviation for each data set. No significant difference was found between any of the parameters in the various sets of 12 breathholds.

SI Table 1: Median and IQR of (A) SNR, (B) CRLB and (C) linewidths of fitted peaks in the STEAM-WET vs PRESS-WET pre-study pilot experiment involving 6 healthy volunteers.

A) Median (IQR) of SNR					
Group	Sequence	Meas.	Lipid	Creatine	Choline
Healthy n = 6	STEAM-WET	150	953 (611 – 1574)	511 (275 – 625)	520 (283 – 584)
	PRESS-WET	150	744 (180 – 1240)	356 (157 – 390)	297 (223 – 386)
B) Median (IQR) of CRLB / %					
Group	Sequence	Meas.	Lipid	Creatine	Choline
Healthy n = 6	STEAM-WET	150	10.5 (4.1 – 20.9)	14.7 (11.4 – 25.9)	18.2 (9.4 – 36.9)
	PRESS-WET	150	55.6 (34.0 – 79.4)	18.8 (13.5 – 57.2)	19.6 (17.7 – 88.6)
C) Median (IQR) of linewidth / Hz					
Group	Sequence	Meas.	Lipid	Creatine	Choline
Healthy n = 6	STEAM-WET	150	28.7 (23.8 – 38.1)	14.4 (11.9 – 19.0)	19.2 (16.2 – 19.5)
	PRESS-WET	150	47.1 (37.3 – 117.4)	41.8 (21.2 – 47.3)	41.2 (26.3 – 53.1)

SI Table 2: Table summarising patient demographics. Values are given as number(%), mean (SD) or median (quartile 1 – quartile 3).

n	13
Male	10 (77%)
Age	76 (7)
NYHA class	1.9 (0.4)
Body mass index (kg/m^2)	27 (4)
Body surface area (m^2)	1.95 (0.22)
Heart rate (/min)	66 (61 – 76)
Systolic blood pressure (mmHg)	140 (27)
Diastolic blood pressure (mmHg)	73 (9)
Mean arterial pressure (mmHg)	96 (12)
LV end-diastolic volume index (ml/m^2)	79 (15)
LV ejection fraction (%)	60 (10)
LV mass index (g/m^2)	83 (27)
Biopsy creatine (nmol/mg protein)	53 (18)
Time between MRI /MRS scan and biopsy (days)	7 (1 – 12)

SI Table 3: SNR and CRLB of each metabolite peak in the phantom. The measurements were obtained from the compartment containing 80 mmol/L of Cr. All acquisition parameters were as described in the Methods section of the paper, except a TE of 40 ms was used for all protocols to ensure a fairer comparison of SNR.

Mean SNR (CRLB / %)					
Sequence	Measurements	Creatine CH_2 (3.7 ppm)	Creatine CH_3 (3.0 ppm)	Lipid peak 1 (1.28 ppm)	Lipid peak 2 (0.84 ppm)
PRESS-WET	30	6068 (1.3 %)	10937 (0.7 %)	9986 (0.9 %)	4071 (19.8 %)
STEAM-WET	30	3267 (1.2 %)	5999 (0.6 %)	6100 (0.6 %)	1626 (3.8 %)
PRESS-WSC	30	5463 (1.2 %)	10171 (0.6 %)	9397 (0.8 %)	3572 (13.3 %)
STEAM-WSC	30	2674 (1.4 %)	5192 (0.7 %)	5607 (0.6 %)	1474 (5.2 %)

SI Table 4: Medians along with interquartile ranges (IQR) of SNR, CRLB and linewidths over all n subjects are shown in (A), (B) and (C) respectively.

A) Median (IQR) of SNR

Group	Sequence	Meas.	Lipid	Creatine	Choline
Healthy n = 10	STEAM-WET-150	150	801 (602 – 1093)	410 (293 – 600)	423 (294 – 533)
	STEAM-WET-60	60	539 (398 – 747)	298 (232 – 548)	306 (212 – 488)
	STEAM-WSC	60	389 (322 – 858)	214 (155 – 456)	222 (151 – 439)
	PRESS-WSC	60	812 (580 – 1025)	449 (328 – 556)	426 (329 – 514)
Patients n = 8	STEAM-WET-150	150	1878 (1088 – 2301)	461 (325 – 508)	440 (357 – 524)
	STEAM-WET-60	60	1054 (644 – 1536)	296 (222 – 373)	296 (224 – 356)
	PRESS-WSC	60	1078 (945 – 1415)	268 (247 – 478)	305 (252 – 463)

B) Median (IQR) of CRLB / %

Group	Sequence	Meas.	Lipid	Creatine	Choline
Healthy n = 10	STEAM-WET-150	150	8.4 (4.5 – 16.4)	18.9 (12.7 – 37.2)	20.1 (11.9 – 39.7)
	STEAM-WET-60	60	8.2 (4.7 – 12.3)	25.8 (19.1 – 32.3)	26.0 (17.9 – 32.3)
	STEAM-WSC	60	7.1 (3.6 – 12.2)	18.8 (11.2 – 29.7)	20.6 (12.4 – 25.8)
	PRESS-WSC	60	6.2 (3.4 – 8.2)	13.2 (9.0 – 16.8)	13.7 (7.4 – 17.8)
Patients n = 8	STEAM-WET-150	150	31.3 (12.3 – 41.1)	12.9 (7.2 – 15.9)	21.5 (9.3 – 39.6)
	STEAM-WET-60	60	36.3 (26.1 – 51.8)	17.3 (14.5 – 47.0)	40.1 (25.2 – 97.7)
	PRESS-WSC	60	27.4 (10.0 – 80.3)	14.4 (13.2 – 65.6)	23.1 (15.0 – 73.1)

C) Median (IQR) of linewidth / Hz

Group	Sequence	Meas.	Lipid	Creatine	Choline
Healthy n = 10	STEAM-WET-150	150	36.8 (31.4 – 39.4)	18.9 (15.6 – 21.1)	20.0 (17.3 – 20.0)
	STEAM-WET-60	60	29.9 (25.9 – 38.6)	17.2 (16.4 – 19.7)	23.2 (18.1 – 33.7)
	STEAM-WSC	60	13.7 (10.1 – 19.0)	5.3 (4.9 – 7.7)	13.1 (7.5 – 17.5)
	PRESS-WSC	60	24.5 (20.6 – 28.8)	11.9 (10.0 – 15.4)	17.4 (10.0 – 19.4)
Patients n = 8	STEAM-WET-150	150	32.9 (29.1 – 40.0)	12.6 (10.7 – 17.5)	27.4 (18.1 – 31.1)
	STEAM-WET-60	60	33.2 (23.3 – 39.3)	17.3 (9.8 – 20.0)	30.1 (23.9 – 35.0)
	PRESS-WSC	60	27.7 (16.6 – 34.0)	15.9 (10.6 – 19.1)	21.1 (18.7 – 25.4)