Robust phase correction for 1D NMR spectra: application to fully automated quantitation of whole-body adiposity in less than 5 seconds

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Introduction

Phase correction is important for proper display and integration of NMR spectra. The dispersive component of a spectral line is much broader than the absorptive component, particularly towards the baseline, so the overlap among spectral lines is substantially increased unless the spectrum is properly phased. Over the years, many metrics have been proposed for phase correction (e.g. see [1] to [3] and references therein), and their performance varies considerably depending on situations. In this work, we discovered a remarkably simple yet robust metric and applied it to 1D proton spectra in mice for quantitative assessment of whole-body adiposity. Even without paying specific attention to shimming, the phase correction allows sufficient separation of the water and fat spectral lines to allow accurate and fully automated quantitation. Combined with a non-localized single spin-echo sequence, this allows the whole body composition to be assessed in less than 5 seconds. The fast speed (even compared to relaxometry methods [4-5]) allows the measurement to be incorporated easily within a longer MR session for evaluating metabolic and muscular disorders such as obesity, type 2 diabetic mellitus, cachexia, among others.

Methods

Acquisition: Whole-body spectra were acquired in a Bruker PharmaScan 4.7T scanner (Bruker BioSpin, Ettlingen, Germany) with a 6-cm inner-diameter birdcage coil. Shimming was performed automatically using the system-default method based on the FID envelope. A non-localized spin-echo sequence was used with a 200us 90-deg excitation rectangular pulse, a 200us 180-deg refocusing rectangular pulse flanked by crusher gradients, an echo time of 3.5ms, a spectral bandwidth of 37.5ppm, and a spectral resolution of 0.0183ppm. With a single average, the data were acquired in less than a second.

Phase correction: The spin-echo signal was inverse Fourier transformed to yield a spectrum. Automatic phase correction was performed by searching for the zeroth- (θ_0) and first- (θ_1) order phase to minimize the following metric that penalizes the distance from the baseline, while minimizing the contribution (through log transformation) from high-signal regions such as spectral peaks:

$$\min_{\theta_0,\theta_1} \sum_f \log\left(\left|s'(f)\right|+1\right) \qquad (1)$$

$s'(f)$ indicates the real part of the phase-corrected spectrum, normalized by its root-mean square value ($s'(f) = real\{s(f)\cdot\exp(i(\theta_0+\theta_1 f))\}/rms\{s(f)\}$). To avoid local minima, the search is performed from multiple starting values for θ_0, spanning the entire 360-degree range in steps of 10 degrees, and from multiple values for θ_1 that align the highest echo magnitudes with the center point of the inverse Fourier transform. It should be noted that Eq. [1] does not distinguish between positive and negative peaks. Also, minimizing Eq. [1] for a half echo yields the real component, whereas for a full echo, it yields the imaginary component, due to its flatness. Therefore, the final step after the iterative search is to compare the real and imaginary components. The one with the highest magnitude is considered the correct real component. Then, the sum of the real component is evaluated. If it is negative, the spectrum is negated. The entire phasing procedure takes <2 seconds in Matlab (Mathworks, Natick, MA, USA) on a 1GHz Intel Core Duo computer.

Spectral quantitation: Separation of water and lipid (CH_2 from aliphatic chain) signals is performed by following the water peak (around 4.7ppm) and the methylene peak (around 1.3ppm) down to the baseline to divide the spectrum into two halves, and integrating the respective signals. According to [5], body weight (BW) can be estimated as a sum of the fat and lean mass components as follows:

$$BW = \alpha(\text{ Fat} + \beta \text{ Water}) \qquad (2)$$

where α denotes a set-up-specific conversion factor (e.g. sensitivity, instrument gains, etc.) between the signal integral and weight in grams. β denotes the ratio between lean mass and water, and should be applicable across experiments.

Animal study: This method was applied to quantifying the whole-body adiposity in a mouse model of diet-induced obesity (DIO). Mice aged 12-16wks were placed on a high fat diet (# D12492i from Research Diets, Inc.) for 6 – 10 wks.

Results

Figure 1 shows a representative spectrum for automatic phasing and quantification. The line shape is typical of what is usually achieved from a whole-body spectrum. Figure 2 shows the results from 165 independent measurements of mice between 28 and 44g. Fitting a subset of the data (N=100) to Eq. [2] yields a lean-mass-to-water ratio β of 1.3 (vs. 1.35 in [2]). It can be seen that in the DIO mouse model, the increase in body weight was primarily contributed by an increase in fat mass (green triangles) (slope of body weight vs. fat mass: 0.619 ± 0.050, p<0.001), while the lean mass (red crosses) remained essentially unchanged within the current range (slope of body weight vs. lean mass: -0.0921 ± 0.100, p=0.360)

Conclusion

This work shows a remarkably simple yet robust metric that can be used to achieve automatic phase correction. Combined with a non-localized spin-echo sequence and automatic quantitation, this allows body composition measurement in less than 5 seconds, allowing it to be easily incorporated with other MR measurements.

References [1] Craig EC et al. Rapid Comm Mass Spect (1987) 1:33-7. [2] Guentert P et al. J Biomol NMR (1992) 619-29. [3] Chen L et al. JMR (2002) 158:164-8. [4] Tinsley FC et al. Obesity Res (2004) 12, 150–160; [5] Kuennecke B et al. Obesity Res (2004) 12, 1604-1615.

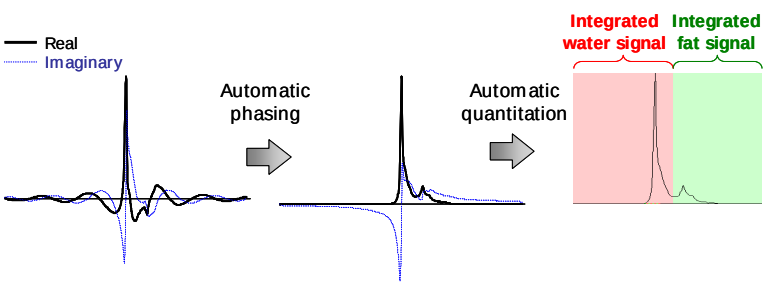

Fig. 1. Automatic phasing & quantitation.

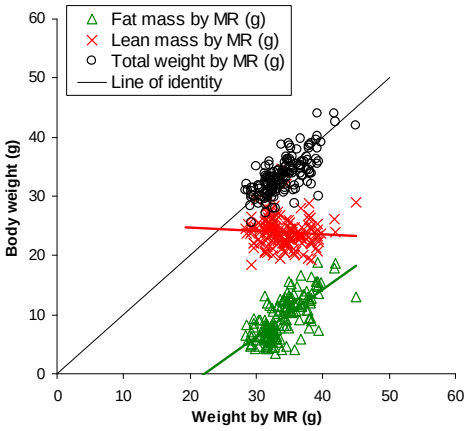

Fig. 2. MR-derived weight compared to body weight.