

# Time-domain calibration of fat signal dephasing from multi-echo STEAM spectroscopy for multi-gradient-echo imaging based fat quantification

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**TARGET AUDIENCE:** Researchers in quantitative fat signal fraction estimation.

**PURPOSE:** Advanced imaging reconstruction methods based on multi-gradient-echo acquisitions allow quantitative estimation of proton density fat signal fraction (PDFF) with relatively high spatio-temporal resolution<sup>1</sup>. The dephasing of fat signal relative to the water signal as a function of echo time is an essential part of the signal models used for this purpose. Several pre-calibrated multi-peak fat spectral models have been published, e.g.<sup>2-4</sup>, which lead to similar but not identical results<sup>5</sup>. Self-calibration of the fat spectrum is possible, but requires a-priori knowledge about the relative frequencies of different fat peaks<sup>6</sup>.

On the other hand, spectroscopy is considered the gold standard for PDFF quantification, provided that confounding factors such as relaxation effects are properly addressed<sup>7</sup>. Individual calibration of the fat spectrum from spectroscopy is possible, but may be difficult to perform automatically.

We show here that the direct use of complex-valued time-domain fat signal dephasing factors is an alternative to fat spectrum calibration. We also illustrate that these dephasing factors can be extracted directly from single-breath-hold multi-echo STEAM single-voxel spectroscopy (SVS) measurements in a simple fashion. This allows calibrating the fat signal dephasing, in particular for PDFF estimation from multi-gradient-echo imaging, for individual measurements and applications.

**THEORY:** The signal model used for advanced Dixon methods is given (for each pixel) by  $S(t) = (W + c(t)F) e^{-R_2^*t + i\varphi(t)}$  (equation 1),  $S(t)$  is the signal measured at different (echo) times  $t$ ,  $c(t)$  the fat dephasing,  $R_2^*$  the transverse relaxation rate (assumed to be equal for water and fat),  $\varphi(t)$  the phase evolution,  $W$  the water signal, and  $F$  the fat signal. Many advanced reconstruction methods use  $c(t)$  as fixed input values, and determine the remaining signal model parameters by a nonlinear fit to the acquired data. Determining the phase evolution may be avoided by magnitude fitting.

**METHODS:** Volunteer scanning of a single subject with elevated liver fat signal fraction was performed on a clinical 1.5T whole-body scanner (MAGNETOM Aera, Siemens Healthcare, Erlangen, Germany). For fat signal dephasing calibration, multi-echo STEAM SVS of the liver was performed as described in ref.<sup>7</sup> using a prototype sequence. For testing the calibration, 3D multi-gradient-echo imaging of the liver was performed using a prototype version of the volumetric interpolated breath-hold examination (VIBE) sequence.

For each SVS echo time, the calculation of the free induction decay (FID), including channel combination, was performed using a prototype version of the scanner spectroscopy reconstruction software. Magnitude images of the individual echoes of the VIBE acquisitions were reconstructed using the scanner image reconstruction software. All further processing was performed offline using custom software written in C++ and/or Matlab (The MathWorks, Natick, MA, USA).

For each FID of the multi-echo SVS measurement, the water contribution was determined by fitting a Lorentzian function in the time domain. This water model was then subtracted, and the frequency of the FID adjusted. Due to remaining water signal, the signals were further processed by zero-padding contributions outside a spectral interval [-4.9ppm, -1.9ppm] relative to the determined water peak. An extrapolated FID at zero echo time was then derived from a monoexponential decay model, which was fitted to the first 100ms of all obtained FIDs. Finally, this FID was normalized to a reference value of 1 at  $t = 0$ . The fat dephasing value  $c(t)$  is then given by the FID value at time  $t$ .

The magnitude intensities of individual gradient echo images were used in a pixel-wise nonlinear least-squares fit of the signal model parameters from the magnitude version of equation 1; several solutions were calculated using different values of  $c(t)$ , derived from the pre-processed spectroscopy FID, from the 7-peak fat spectral model of ref.<sup>2</sup>, and from the 9-peak model of ref.<sup>4</sup>. Fat signal fraction values  $FF$  were calculated as  $FF = F/(W + F)$ . Mean values from a ROI in the right liver hemisphere were recorded for  $FF$ ,  $R_2^*$ , and mean fit error as defined in ref.<sup>5</sup>.

**RESULTS:** Figure 1 shows a comparison between the dephasing factors  $c(t)$  from the fat spectral model of ref.<sup>4</sup> and the time-domain based fat calibration given by the pre-processed FID. The FID-based factors have a magnitude which is slightly higher initially, and slightly lower after approx. 10ms. Table 1 summarizes mean ROI values from the multi-echo VIBE data analysis. The  $FF$  values based on the fat spectral models are approx. 8% higher than the one based on the FID fat dephasing factors; the  $R_2^*$  values vary, having a mean of  $36.1s^{-1}$  and a standard deviation of  $1.5s^{-1}$ . The fit error values are comparable.

**DISCUSSION:** The dephasing factors of the two approaches match very well. Applied to  $FF$  estimation from multi-gradient-echo imaging, the FID-based fat signal fraction values are slightly lower than those based on the fat spectral models. Since the FID-based dephasing factors do not consider the fat signal contributions coinciding spectrally with the water signal, this is at least plausible; these regions account for approx. 4% of the total fat signal in the model from ref.<sup>2</sup>, and approx. 9% for the model from ref.<sup>4</sup>.

The proposed FID-based calibration is free of assumptions about the nature of the fat spectrum other than that there is no overlap between the water and fat contributions. The processing steps involved are fewer than those for the full analysis of a multi-peak fat line spectrum, and have the potential to be automatized. Hence, this procedure is applicable for individual calibration, e.g. in phantoms or different body parts. Fat signal contributions overlapping spectrally with water are small and constitute a relatively well-known fraction of the total fat signal; a correction by a simple factor after the multi-gradient-echo analysis appears feasible. However, investigation of more cases with varying conditions, including field strength, is necessary to gain more experience with the new approach. Other applications of the FID-based dephasing factors are possible, e.g. for improved Dixon water/fat separation in dual-echo acquisitions<sup>8</sup>.

**CONCLUSION:** Time-domain fat signal dephasing factors can be extracted from multi-echo STEAM single-voxel spectroscopy in a straightforward fashion, and can be used for fat signal fraction estimation from multi-gradient-echo acquisitions. Compared with calibration approaches involving multi-peak line spectra of the fat signal, the new approach is procedurally simpler, allowing individual calibration, appears to match the acquired signals at least as well, and leads to very similar results.

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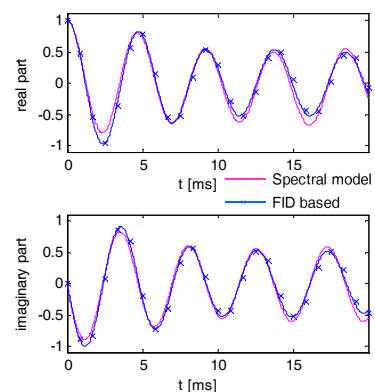


Figure 1: Fat dephasing factors  $c(t)$  from the spectral model of ref.<sup>4</sup> (magenta) and FID (blue).

dephasing factors	FF	$R_2^*$	fit error
from ref. <sup>2</sup>	11.3%	$36.2s^{-1}$	1.8%
from ref. <sup>4</sup>	11.4%	$34.6s^{-1}$	2.0%
from FID	10.5%	$37.5s^{-1}$	1.8%

Table 1: Mean ROI values of quantification results from the multi-echo VIBE imaging data based on different  $c(t)$ .