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Robustness of Fat Quantification using Chemical Shift Imaging

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Abstract

This purpose of this study was to investigate the effect of parameter changes that can potentially lead to unreliable measurements in fat quantification. Chemical shift imaging was performed using spoiled gradient echo sequences with systematic variations in the following: 2D/3D sequence, number of echoes, delta echo time, fractional echo factor, slice thickness, repetition time, flip angle, bandwidth, matrix size, flow compensation and field strength. Results indicated no significant (or significant but small) changes in fat fraction with parameter. The significant changes can be attributed to known effects of T1 bias and the two forms of noise bias.

Keywords

Water-Fat Separation; IDEAL; Chemical Shift; Robustness

Introduction

A continuing topic of interest in magnetic resonance (MR) imaging is the reliable and accurate separation of fat and water using chemical shift imaging. Many methods have been proposed based on specific echo times and careful approximations, however more recent approaches have taken advantage of computational brute-force to try to accurately model the MR signal [^{1,2,3}]. Real world complexities, such as the multi-peak spectrum of fat, J-coupling, exponential (or other types of) decay and physical constraints upon the field inhomogeneity and initial phase, can be incorporated relatively easily into numerical models.

Different groups have converged on similar models of the fat-water system and there is agreement reported with independent references (e.g. spectroscopy) when the experiments and analysis methods are well matched [^{4,5,6,7,8}]. It should also be noted that other studies have shown less good agreement between different methods [^{9,10}], which may be due to the different assumptions made regarding T1/T2* relaxation and the fat spectrum.

The robustness of fat quantification to perturbation of T1 and T2* has been investigated previously using injected contrast agents [^{11,12}]. It may also be expected that quantification would be robust to perturbation of imaging parameters that relate to T1 and T2*, e.g. flip angle, bandwidth, voxel size. However, many published studies have tended to focus on only one or two key parameters, e.g. echo time choices (and/or number of echoes) [¹³] and

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type of analysis [Error: Reference source not found,^{14,15}]. Robustness is an important consideration in clinical practice where scanner hardware differences, scheduling demands and the radiologist preferences can contribute to variations in imaging protocols.

Thus, the primary purpose of this study is to prospectively assess the robustness of fat quantification techniques to changes in imaging parameters over a clinically relevant range. Protocol variants included 2D/3D acquisition, number of echoes, delta echo time, fractional echo factor, slice thickness, repetition time, flip angle, bandwidth, matrix size, flow compensation and field strength.

Methodology

Subjects including normal controls and adults with known or suspected fatty liver disease were prospectively recruited. Informed consent was obtained prior to scanning; all activities were compliant with the Health Insurance Portability and Accountability Act and were approved by the local Institutional Review Board. A total of 24 subjects were scheduled between June and September 2009, of which 4 did not complete the study and 4 received only a partial exam at 1.5 T due to technical problems.

Imaging and MR spectroscopy (MRS) were performed as breath-hold sequences of approximately 20 seconds duration on two MR scanners: 1.5 T and 3.0 T Signa HDx version 14M5 (GE Healthcare, Milwaukee, WI) using 8-channel torso array coils. Approximately 42 separate breath-holds were performed over a 2 hour period. Imaging experiments were conducted around “core” 2D and 3D spoiled gradient recalled echo (SPGR) sequences. The core sequences were performed multiple times with a change in a single parameter at a time to assess the effect of that parameter on the estimated fat fraction. All protocol variants were run on all subjects. Also, to compare accuracy and repeatability of the fat fraction measurements, each sequence (2D, 3D imaging and MRS) was repeated three times at 1.5 T and 3.0 T. The mean and 95 % confidence interval were recorded. The reference for accuracy was defined as the average of the spectroscopy measurements at both field strengths.

The core 2D sequence used flip angle 10, repetition time (TR) of 130 – 170 ms and first echo time (TE) of 2.3 ms at 1.5 T (1.1 ms at 3.0 T). The Δ TE was chosen to give consecutive in-phase (IP) and out-of-phase (OP) images, which were acquired with a bipolar echo train (8 echoes total). A fractional echo factor of 0.6 – 0.8 was required to achieve the TE and Δ TE spacing at 3.0 T; for consistency the same factor was used at 1.5 T although is not essential with the wider echo spacing. Eight slices were acquired. Magnitude images (sum-of-squares from all coils) were collected and modeling was performed on magnitude data. Protocols are given Tables I.

The core 3D sequence used Array Spatial Sensitivity Encoding Technique (ASSET) parallel imaging factor 2 with TR / first TE / Δ TE of approximately 10.8 / 1.2 / 1.0 ms at 1.5 T and 8.3 / 0.9 / 0.7 ms at 3.0 T. A fly-back echo train was used and 2 interleaves of 4 echoes were acquired (note reported Δ TE is the effective echo spacing). Twelve slices were acquired and ASSET-combined complex images were collected. Modeling was performed on both complex and magnitude data using a hybrid method [Error: Reference source not found]. Protocols are given Tables II.

The precise TR / first TE / Δ TE for the 3D sequence varied slightly, since the scanner automatically chose the minimum values dictated by the hardware, matrix size and bandwidth. This meant some parameters could not be changed independently, however this reflects a real-world usage of this sequence. In most cases the changes were small; two exceptions were flow compensation, where the TEs and TR were shifted by +0.5 ms, and

number of echoes, which caused TR to lengthen substantially. To ensure constant TR, an 8 echo protocol was used and different numbers of echoes (4, 6 or 8) were analyzed in reconstruction.

Analysis involved modeling the (magnitude and/or complex) signal variation with echo time using nonlinear least squares curve-fitting. The fat spectrum employed six fat peaks at defined frequencies and in fixed proportions taken from Ref [16] and a common exponential T2* decay for water and all fat peaks, as in previous studies [Error: Reference source not found, Error: Reference source not found]. Regions of interest (ROIs) containing 60 – 100 pixels (3 – 5 cm²) were drawn on the fat fraction maps in the right lobe of the liver, co-localized to a MRS voxel and avoiding major vessels and artefacts. The mean and variance were recorded.

Stimulated echo acquisition mode MRS was performed to provide the reference for fat fraction accuracy in 20×20×20 mm³ voxels with TR 3500 ms, mixing time 5 ms and TE 10, 15, 20, 25, 30 ms to allow correction for T2 decay. One dummy excitation was applied to establish longitudinal equilibrium and all saturation pulses (water, fat, spatial) were disabled. The acquisition and analysis follows the method described in Ref [Error: Reference source not found]

Statistical calculations were performed in MATLAB R2010b (The Mathworks, Natick MA) using the functions *regress*, *ttest* (two tailed), *var* (sample variance) and *mean*. Statistical significance was reported in terms of the p-value.

Results

Parameter Variations

Figure 1 shows typical plots of the fat fraction versus parameter value for representative cases. The mean change in fat fraction (over subjects) between the minimum and maximum parameter value is given in the title. These plots indicate, for example, that changing TR between 130 and 170 ms for the 2D sequence results in a negligible change in the fat fraction whereas changing the flip angle from 3 to 9 degrees for the 3D sequence causes a large increase in the fat fraction. In the case of matrix size, both 2D and 3D sequences show a slight decrease.

To determine statistically whether these changes were distinguishable from 0 (which would indicate no relationship between fat fraction and parameter) paired t-tests were performed. Results for all parameters are given in Table III – IV and indicate several significant changes in the 2D and 3D sequences. Other than flip angle, the magnitudes of these changes are <1% for all parameters over the ranges tested. The flip angle effect is consistent with the known amplification of fat fraction due to T1 bias.

A point to note is that all of the highly significant fat fraction changes in Tables III – IV follow the expected change in signal to noise ratio (SNR). For the 2D sequence these are slice thickness (increase), bandwidth (decrease) and fractional echo (increase) and for the 3D sequence these are matrix (decrease), flip angle (increase) and field strength (increase). While the latter two parameters include an increase due to T1 bias, it would appear that the SNR is associated with many of the observed changes with imaging parameter. The effect of noise bias on different types of reconstruction is reviewed at the end of Results.

Figure 2 shows example plots of the variance within the ROI versus parameter value; results of the change in variance are given in Tables III – IV. The variance inside the ROI is the sum of two contributions: measurement noise and spatial variation of the fat fraction. The

latter can be assumed to be approximately constant due to co-localization of the ROIs, therefore changes in variance were attributed solely to changes in parameter. Significant effects were observed for several parameters, largely consistent with basic SNR considerations, e.g. slice thickness, matrix, bandwidth, field strength, flip angle. Non-significant effects were observed in some cases where a significant effect would be expected, e.g. increasing the bandwidth in the 3D sequence did not lead to a significant increase in variance. As noted in Methods, it was difficult to isolate parameter changes due to the automatic use of minimum TR, first TE and ΔTE . The latter are important variables in the noise performance of the fat fraction calculation [Error: Reference source not found,¹⁷]. Clearly the concomitant changes in TE (from 1.3π to 1.2π) and ΔTE (from 1.05π to 0.96π) were sufficiently favorable to overcome the decrease in SNR with bandwidth.

Accuracy and Repeatability

Figure 3 compares the accuracy of fat fractions against the reference (note that the dashed line on each scatterplot is the identity line, not a regression line). Data were strongly correlated in all cases ($r > 0.99$). Intercepts and slopes were close to zero and unity, respectively, although at the $p < 0.05$ significance level, there were deviations from identity: the 2D sequence at 1.5 T (slopes 0.81 ± 0.11 and 0.90 ± 0.10) and the 3D sequence at 3.0 T (intercept 2.0 ± 2.0) (note: errors represent the 95% confidence intervals). Qualitatively, from the scatterplots it was apparent that the 2D sequence tended to underestimate (slopes less than unity) and the 3D sequence tended to overestimate (intercepts greater than zero). Paired t-tests between the reference and imaging methods, given in Table V, confirmed these differences were significant. Clearly the differences between 2D and 3D imaging methods were also significant.

Also shown in Table V is the average (over subjects) variance for the three repeats for each method. These yield 95 % confidence intervals of between 0.60 and 0.76 % for fat fractions measured consecutively. The variances were consistently lower at 3.0 T for all sequences, which may be expected due to the higher SNR at 3.0 T. The difference in variance between field strengths should be related to $\Delta \text{Variance}$ given in Tables III – IV (bottom row). The former represents the change in variance of the mean (over pixels in the ROI) while the latter represents the change in variance; thus the proportionality factor should be equal to the number of pixels (i.e. 60 – 100). For the 2D sequence this factor was $8.77 / (0.284 - 0.129) \approx 57$ and for the 3D sequence it was $3.82 / (0.470 - 0.413) \approx 67$.

Figure 4 shows plots of $T2^*$ versus field strength and Tables III – IV give results for all parameters. Other than field strength, the effects on $T2^*$ were mostly small and not significant. There was a tendency for $T2^*$ to decrease with voxel size (e.g. slice thickness and matrix), which would be expected theoretically. The means and 95 % confidence intervals for three repeated measurements of $T2^*$ were: 30.3 ± 3.1 (1.5 T) and 18.0 ± 1.9 ms (3.0 T) for the 2D sequence, and 30.1 ± 4.4 (1.5 T) and 21.0 ± 4.2 ms (3.0 T) for the 3D sequence. Differences between field strengths were significant but differences between sequences were not significant ($p = 0.586$ at 1.5 T and $p = 0.059$ at 3.0 T).

Noise Bias

As noted above, the SNR may have an influence on the estimated fat fraction. There are two forms of bias associated with noise that lead to either overestimation [Error: Reference source not found] or underestimation [Error: Reference source not found]. The first applies to estimation from complex data and comes about when fat and water are modeled as independent variables. This results in over-fitting of noise (or other types of error) and causes overestimation of the fat fraction at the low range [Error: Reference source not found]. This can be avoided by constraining the phases of water and fat to be equal at zero

echo time [Error: Reference source not found] or using a hybrid complex/magnitude reconstruction that downweights errors in the phase [Error: Reference source not found].

The second effect of noise bias applies to magnitude estimation and occurs when noise rectification reduces signal cancellation between fat and water. This causes underestimation of the fat fraction in the mid-range [Error: Reference source not found]. Figure 5 shows ROIs drawn on magnitude images and the results of curve-fitting with and without

quadrature subtraction of background noise, i.e. $\sqrt{\text{signal}^2 - \text{background}^2}$. The difference in fat fraction (0.05 at a fat fraction of 0.29) is of sufficient magnitude to explain the observed underestimation in Figure 3. A second observation from Figure 5 is that the background signal differs on forward and reverse echoes of the bipolar readout and is highest on the first echo. Such effects may be attributed to asymmetric response of the receiver coils and eddy currents [18], and likely cause further underestimation of the fat fraction since the changes reduce signal cancellation.

Discussion

The main purpose of this study was to evaluate the effect of imaging parameters on clinical methods of fat quantification in the liver. Two imaging methods were evaluated and a third method (spectroscopy) used as a reference for accuracy. The primary findings, summarized in Table III – IV, are that most imaging parameters have little effect on the fat fraction over a useful range.

For several parameters, the change in fat fraction between minimum to maximum parameter value was statistically significant but small (<1%). For flip angle, however, a large and significant change was observed in the 3D sequence. Flip angle is known to induce T1 bias that elevates the fat fraction [19,20]. Figure 1 suggests the use of a 6° flip angle accounts for 1–2% overestimation (on average) compared to a 3° acquisition. Due to the longer T1 of water at 3.0 T, fat fractions would also be expected to be higher than at 1.5 T and this was in fact observed. The shorter TR at 3.0 T (8.3 ms versus 10.8 ms at 1.5T), necessitated by hardware and bandwidth differences, likely also contributed to this effect.

The core 2D protocol used a fixed flip angle of 10° and varied TR from 130 to 170 ms to probe T1 bias. These were sufficient to avoid an significant effect, whereas the 3D protocol should be run with a lower flip angle. Recent studies using 3D sequences with lower flip angle and/or longer TR do not exhibit T1 bias [6, Error: Reference source not found]. Numerical calculations (taking T1s for water and fat to be 690 and 260 ms) indicate the T1 bias in the core 3D sequence (6° and TR 10.8 ms) would be the equivalent of running the 2D sequence with flip angle 22° and TR 150 ms.

Accuracy experiments, shown in Figure 3, indicate reasonable agreement between imaging and spectroscopy, although the 2D technique tended to underestimate fat fractions (slope less than unity) and the 3D technique tended to overestimate (intercept greater than zero). Mean differences of around –1% and +2% for 2D and 3D sequences, respectively, were statistically significant. The source of the 3D overestimation can be understood to be a consequence of T1 bias while the source of 2D underestimation can be attributed primarily to noise bias. Quadrature correction for noise bias is appropriate, although the correct scaling of the background term depends on many factors [21,22]. Noise bias can be largely avoided by using specialized methods of coil combination [23,24]. A further source of 2D underestimation is the asymmetric response of receiver coils and eddy currents, although the effect is much smaller than noise bias and is also likely to be spatially non-uniform and specific to individual MR systems.

In summary, the present study has investigated the robustness of MR fat quantification methods appropriate to a clinical setting. The fat fraction was found to be robust to parameter changes, with exceptions that can be explained by known sources of bias: T1 and noise bias (two types). Practical implications are that changing the number of echoes, delta echo time, fractional echo factor, slice thickness, bandwidth, matrix size and flow compensation are benign whereas changing the TR, flip angle and field strength require caution.

Acknowledgments

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References

1. Reeder SB, Wen Z, Yu H, Pineda AR, Gold GE, Markl M, Pelc NJ. Multicoil Dixon chemical species separation with an iterative least squares estimation method. *Magn Reson Med*. 2004; 51:35. [PubMed: 14705043]
2. Hernando D, Haldar JP, Sutton BP, Ma J, Kellman P, Liang ZP. Joint estimation of water/fat images and field inhomogeneity map. *Magn Reson Med*. 2008; 59:571. [PubMed: 18306409]
3. Bydder M, Yokoo T, Yu H, Carl M, Reeder SB, Sirlin CB. Constraining the initial phase in water-fat separation. *Magn Reson Imaging*. 2011; 29:216. [PubMed: 21159457]
4. Yokoo T, Bydder M, Hamilton G, Middleton MS, Gamst AC, Wolfson T, Hassanein T, Patton HM, Lavine JE, Schwimmer JB, Sirlin CB. Nonalcoholic Fatty Liver Disease: Diagnostic and Fat-Grading Accuracy of Low-Flip-Angle Multiecho Gradient-Recalled-Echo MR Imaging at 1.5 T. *Radiology*. 2009; 251:67. [PubMed: 19221054]
5. Hines CDG, Yu H, Shimakawa A, McKenzie CA, Warner TF, Brittain JH, Reeder SB. Quantification of Hepatic Steatosis with 3-T MR Imaging: Validation in ob/ob Mice. *Radiology*. 2010; 254:119. [PubMed: 20032146]
6. Yu H, Shimakawa A, McKenzie CA, Brodsky E, Brittain JH, Reeder SB. Multiecho water-fat separation and simultaneous R2* estimation with multifrequency fat spectrum modeling. *Magn Reson Med*. 2008; 60:1122. [PubMed: 18956464]
7. Meisamy S, Hines CDG, Sirlin CB, McKenzie CA, Yu H, Brittain JH, Reeder SB. Quantification of hepatic steatosis with T1-independent, T2*-corrected MR imaging with spectral modeling of fat: a blinded comparison with MR spectroscopy. *Radiology*. 2011 available online.
8. Hines CDG, Frydrychowicz A, Hamilton G, Tudorascu DL, Vigen KK, Yu H, McKenzie CA, Sirlin CB, Brittain JH, Reeder SB. T1 Independent, T2* Corrected Chemical Shift Based Fat-Water Separation With Multi-peak Fat Spectral Modeling Is an Accurate and Precise Measure of Hepatic Steatosis. *J Magn Reson Imag*. 2011; 33:873.
9. Kim H, Taksali SE, Dufour S, Befroy D, Goodman TR, Petersen KF, Shulman GI, Caprio S, Constable RT. A Comparative MR Study of Hepatic Fat Quantification Using Single-voxel Proton Spectroscopy, Two-point Dixon and Three-point IDEAL. *Magn Reson Med*. 2008; 59:521. [PubMed: 18306404]
10. Hu HH, Kim HW, Nayak KS, Goran MI. Comparison of Fat-Water MRI and Single-voxel MRS in the Assessment of Hepatic and Pancreatic Fat Fractions in Humans. *Obesity*. 2010; 18:841. [PubMed: 19834463]
11. Yokoo T, Collins JM, Hanna RF, Bydder M, Middleton MS, Sirlin CB. Effects of Intravenous Gadolinium Administration and Flip Angle on the Assessment of Liver Fat Fraction with Two-point Dixon Technique. *J Magn Reson Imaging*. 2008; 28:246. [PubMed: 18581393]
12. Bydder M, Shiehorteza M, Yokoo T, Sugay S, Middleton MS, Girard O, Schroeder ME, Wolfson T, Gamst AM, Sirlin C. Assessment of liver fat quantification in the presence of iron. *Magn Reson Imaging*. 2010; 28:767. [PubMed: 20409663]
13. Pineda AR, Reeder SB, Wen Z, Pelc NJ. Cramér-Rao bounds for three-point decomposition of water and fat. *Magn Reson Med*. 2005; 54:625. [PubMed: 16092102]

14. Yu H, Shimakawa A, Hines CDG, McKenzie CA, Hamilton G, Sirlin CB, Brittain JH, Reeder SB. Combination of complex-based and magnitude-based multiecho water-fat separation for accurate quantification of fat-fraction. *Magn Reson Med*. Feb 24.2011 published online.
15. Hernando D, Liang ZP, Kellman P. Chemical shift-based water/fat separation: a comparison of signal models. *Magn Reson Med*. 2010; 64:811. [PubMed: 20593375]
16. Hamilton G, Yokoo T, Bydder M, Cruite I, Schroeder ME, Sirlin CB, Middleton MS. In-Vivo Characterization of the Liver Fat 1H Magnetic Resonance Spectrum. *NMR Biomed*. Dec 12.2010 published online.
17. Yu H, McKenzie CA, Shimakawa A, Vu AT, Brau ACS, Beatty PJ, Pineda AR, Brittain JH, Reeder SB. Multiecho Reconstruction for Simultaneous Water-Fat Decomposition and T2* Estimation. *J Magn Reson Imaging*. 2007; 26:1153. [PubMed: 17896369]
18. Yu H, Shimakawa A, McKenzie CA, Lu W, Reeder SB, Hinks RS, Brittain JH. Phase and Amplitude Correction for Multi-Echo Water-Fat Separation With Bipolar Acquisitions. *J Magn Reson Imaging*. 2010; 31:1264. [PubMed: 20432366]
19. Hussain HK, Chenevert TL, Londy FJ, Gulani V, Swanson SD, McKenna BJ, Appelman HD, Adusumilli S, Greenson JK, Conjeevaram HS. Hepatic Fat Fraction: MR Imaging for Quantitative Measurement and Display—Early Experience. *Radiology*. 2005; 237:1048. [PubMed: 16237138]
20. Liu CY, McKenzie CA, Yu H, Brittain JH, Reeder SB. Fat quantification with IDEAL gradient echo imaging: correction of bias from T1 and noise. *Magn Reson Med*. 2007; 58:354. [PubMed: 17654578]
21. Gudbjartsson H, Patz S. The Rician Distribution of Noisy MRI Data. *Magn Reson Med*. 1995; 34:910. [PubMed: 8598820]
22. Dietrich O, Raya JG, Reeder SB, Ingrisch M, Reiser MF, Schoenberg SO. Influence of multichannel combination, parallel imaging and other reconstruction techniques on MRI noise characteristics. *Magn Reson Imaging*. 2008; 26:754. [PubMed: 18440746]
23. Walsh DO, Gmitro AF, Marcellin MW. Adaptive Reconstruction of Phased Array MR Imagery. *Magn Reson Med*. 2000; 43:682. [PubMed: 10800033]
24. Bydder M, Larkman DJ, Hajnal JV. Combination of signals from array coils using image-based estimation of coil sensitivity profiles. *Magn Reson Med*. 2002; 47:539. [PubMed: 11870841]

Figure 1.

Raw plots are shown for each patient's fat fraction versus representative parameter variations. The abscissa gives the parameter values and the mantissa gives the fat fraction. The mean change (over subjects) and the 95% confidence interval are reported.

Figure 2.

Raw plots are shown for the variance of each patient's fat fraction versus representative parameter variations. The abscissa gives the parameter values and the mantissa gives the variance. The mean change (over subjects) and the 95% confidence interval are reported.

Figure 3.

Plots of fat fraction by the three different methods (MRS, 2D and 3D) at 1.5T and 3.0T versus the gold standard, which was defined as the average of the MRS data. The dashed line shows the 1:1 line of identity. Text gives the results of a linear regression with 95% confidence intervals and the correlation coefficient.

Figure 4.

Raw plots are shown for each patient's T2* versus field strength. The abscissa gives the parameter values and the mantissa gives the T2* value. The mean change (over subjects) and the 95% confidence interval are reported.

Figure 5.

Magnitude images from the 2D sequence at 3.0 T at two echo times (out of eight total) with ROIs drawn in the right lobe of the liver and in the background noise. The resultant fat fraction map is shown. The mean signal in the ROIs is plotted versus echo time (circle and diamond markers) and also the signal corrected for background noise (square marker). Best fit values of fat fraction and T2* are displayed in the textbox along with r-squared (quality of fit). Note the non-negligible influence of background noise on the fitted values.

Table I

Matrix of the 2D imaging protocols used: the core protocol was performed multiple times with changes in one parameter at a time. The core 2D sequence used flip angle 10 and consecutive in- and out-of-phase echo times (bipolar gradient). Values in parentheses indicate the 3.0T protocol, when different from 1.5T.

Parameter		Core Protocol	
ΔTE	2.2 (1.1) ms	2.3 (1.2) ms	2.4 (1.3) ms
No. Echoes	4	8	6
Slice Thickness	6 mm	8 mm	10 mm
TR	130 ms	150 ms	170 ms
Matrix	160	192	224
Bandwidth	62 (125) kHz	83 (166) kHz	100 (200) kHz
Fractional Echo	0.6	0.8	-
Field Strength	1.5 T	3.0 T	-

Table II

Matrix of the 3D imaging protocols used: the core protocol was performed multiple times with changes in one parameter at a time. The core 3D sequence used flyback gradients with two interleaves to give TR / first TE / Δ TE of 10.8 / 1.2 / 1.0 ms at 1.5T (or 8.3 / 0.9 / 0.7 ms at 3.0T). Values in parentheses indicate the 3.0T protocol, when different from 1.5T.

Parameter		Core Protocol	
No. Echoes	4	8	6
Slice Thickness	6 mm	8 mm	10 mm
Matrix	160	192	224
Bandwidth	62 (125) kHz	83 (166) kHz	100 (200) kHz
Flow Comp.	On	Off	-
Flip Angle	3	6	9
Field Strength	1.5 T	3.0 T	-

Difference and statistical significance of changes in fat fraction (in absolute %), variance and T2* with imaging parameters for the 2D sequence. The average changes over subjects between minimum and maximum parameter values are given. Errors represent the 95% confidence intervals.

Table III

Parameter	ΔFF (%)	p-value	Δ Variance	p-value	$\Delta T2^*$ (ms)	p-value
ΔTE	0.449 ± 0.401	0.040	1.14 ± 1.75	0.216	0.056 ± 0.720	0.881
No. Echoes	0.123 ± 0.133	0.086	-5.17 ± 1.87	<0.001	-0.501 ± 0.627	0.135
Slice Thickness	0.749 ± 0.308	<0.001	-12.2 ± 3.0	<0.001	-3.42 ± 1.22	<0.001
TR	-0.063 ± 0.254	0.634	0.645 ± 1.25	0.325	-1.29 ± 1.96	0.211
Matrix	-0.322 ± 0.317	0.061	8.05 ± 2.10	<0.001	1.10 ± 1.02	0.049
Bandwidth	-0.988 ± 0.282	<0.001	4.34 ± 1.11	<0.001	0.361 ± 0.592	0.247
Fractional Echo	0.579 ± 0.396	0.010	-1.70 ± 1.79	0.080	-1.12 ± 1.12	0.066
Field Strength	0.135 ± 0.469	0.579	-8.77 ± 4.17	<0.001	-12.2 ± 1.6	<0.001

The same analysis as in Table III but for the 3D sequence. * This result was strongly affected by a single data point, for which the change in variance between 1.5T and 3T was +40.0 compared to the average change of -0.451 ± 6.57 ($p = 0.895$). Excluding this data point as an outlier yields an average change of -3.82 ± 1.84 ($p = 0.002$).

Table IV

Parameter	ΔFF (%)	p-value	Δ Variance	p-value	$\Delta T2^*$ (ms)	p-value
No. Echoes	-0.161 ± 0.349	0.378	-2.47 ± 2.99	0.122	-0.393 ± 2.94	0.796
Slice Thickness	-0.340 ± 0.377	0.093	-4.96 ± 1.83	<0.001	0.35 ± 1.42	0.636
Matrix	-0.672 ± 0.483	0.013	3.26 ± 2.54	0.021	4.66 ± 6.15	0.154
Bandwidth	-0.229 ± 0.540	0.417	-5.29 ± 7.18	0.165	-0.53 ± 4.05	0.800
Flow Comp.	-0.082 ± 0.306	0.607	-0.476 ± 0.994	0.360	-1.22 ± 2.46	0.342
Flip Angle	2.380 ± 0.962	<0.001	-7.15 ± 2.67	<0.001	0.64 ± 2.62	0.635
Field Strength	0.582 ± 0.427	0.018	-0.451 ± 6.57 *	0.895 *	-7.5 ± 2.3	<0.001

Table V

Mean difference (with statistical significance) in the fat fraction for each method versus the reference. The reference was the average of the spectroscopy measurements, which explains the high accuracy for MRS. Also shown is the average (over subjects) variance for three repeated measurements, which is consistently lower at 3.0 T for each of the sequences. Comparison of the variance between sequences is not meaningful due to differences in the experimental parameters.

Method	ΔFF (%)	p-value	Variance
MRS 1.5T	0.076 ± 0.165	0.393	0.368
MRS 3.0T	-0.076 ± 0.165	0.393	0.308
2D 1.5T	-1.141 ± 0.773	0.011	0.284
2D 3.0T	-1.006 ± 0.504	<0.001	0.129
3D 1.5T	1.453 ± 0.420	<0.001	0.470
3D 3.0T	2.155 ± 0.507	<0.001	0.413