RESEARCH ARTICLE

Single-voxel short-TR multi-TI multi-TE STEAM MRS for water–fat relaxometry

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Purpose: To propose a short-TR multi-TI multi-TE (SHORTIE, [ˈʃɔːr-ɪ]) STEAM single-voxel MRS acquisition scheme for the simultaneous assessment of T₁ relaxation, T₂ relaxation, and the proton density fat fraction at reduced scan times when compared with conventional long-TR multi-TI STEAM and long-TR multi-TE STEAM single-voxel MRS.

Methods: Theoretical analysis for multi-TI (TI = 10, 100, 500, 1500 ms; scan time = 2:43 minutes), multi-TE (TE = 12, 15, 20, 25 ms; scan time = 2:24 minutes), and SHORTIE STEAM (all TI and TE combinations; scan time = 2:52 minutes) was carried out including Cramér-Rao lower bound and parameter estimation efficiency analysis for T₁ (150–2000 ms) and T₂ (5–150 ms) relaxation. The SHORTIE STEAM acquisition was compared with multi-TI STEAM and multi-TE STEAM in water–fat phantoms and in a human in vivo study of the adipose tissue depot in the supraclavicular fossa in 7 volunteers at 3 T.

Results: Cramér-Rao lower bound analysis revealed similar to increased variances for T₁ and T₂ estimators for SHORTIE STEAM. Parameter efficiency analysis demonstrated superior performance of SHORTIE, particularly for shorter T₁ and T₂ when compared with multi-TI STEAM and multi-TE STEAM. For the phantom data, linear regression and Bland-Altman analysis yielded a slope/intercept/mean difference of 1.07/−15.40/−17.18 for T₁ (in ms; r = 0.999), 0.93/+1.32/+1.09 for T₂ (in ms; r = 0.995), and 0.98/−0.04/+0.78 for the fat fraction (in percent; r = 0.999); and for the in vivo data 1.08/+1.77/−62.2 for T₁ (r = 0.994), 0.88/+6.69/−1.55 for T₂ (r = 0.884), and 0.56/+34.40/−0.46 for the fat fraction (r = 0.673), respectively.

Conclusion: The SHORTIE STEAM acquisition allows shorter scan times for the simultaneous probing of relaxation properties and spectral content in the water–fat environment when compared with combined long-TR multi-TI, and long-TR multi-TE STEAM.
1 | INTRODUCTION

The probing of the water–fat environment using single-voxel MRS allows the spectrally resolved characterization of tissue-specific MR properties including applications in the liver, bone marrow, white adipose tissue, and brown adipose tissue. Traditionally, fat-containing tissues are characterized by their proton density fat fraction (PDFF) and relaxation properties, including T1 relaxation and T2 relaxation of the water and fat component, respectively. Specifically, one recent application in which tissue differentiation based on differences in the PDFF and relaxation properties gained interest is the detection of brown adipose tissue in humans. Because the differentiation between white and brown adipose tissue solely based on the PDFF is problematic, additional probing of complementary properties is needed, including, for example, T2*(as an estimate of the abundance of iron-rich mitochondria) or T1 of fat (as an estimate of tissue oxygenation).

Magnetic resonance spectroscopy is particularly suited for the extraction of spectrally resolved MR properties in the water–fat environment, because the nontrivial signal behavior does not require exact a priori knowledge of the spectral content, which is required in model-based imaging approaches. Previously, the probing of spectrally resolved proton densities including the PDFF was achieved using multi-TE STEAM or PRESS single-voxel MRS acquisition schemes with long TRs to minimize T1 bias and multiple TEs to corrected for T2 weighting. Furthermore, long-TR multi-TE STEAM MRS is also suitable for the characterization of T2 relaxation, while inversion-recovery acquisition schemes such as multi-TI STEAM MRS are used for the probing of T1 relaxation. However, conventional study protocols often perform two independent measurements for the assessment of the T1 and T2 relaxation parameters, which can be inefficient and hence time-consuming. Thus, a STEAM MRS acquisition scheme that allows the assessment of the PDFF simultaneously with both T1 and T2 relaxation is desirable to reduce the overall required scan time for probing the water–fat tissue environment.

The purpose of the current study is (1) to propose a single-voxel short-TR multi-TI multi-TE (SHORTIE, [ˈʃɔrt-ɪ]) STEAM MRS acquisition scheme for the simultaneous spectrally resolved parameter assessment of T1 relaxation, T2 relaxation, and PDFF; (2) to compare its performance and efficiency with traditionally used long-TR multi-TI and long-TR multi-TE STEAM MRS, respectively; and (3) to evaluate the measurement agreement between the aforementioned methods in a phantom experiment and in vivo in the fat depot within the supraventricular fossa in human volunteers at 3 T.

2 | THEORY

Throughout the present study, single-voxel long-TR multi-TI STEAM MRS and single-voxel long-TR, multi-TE STEAM MRS are compared against single-voxel SHORTIE STEAM MRS for the assessment of T1 relaxation, and T2 relaxation and fat fraction, respectively. In the following, a brief theoretical description of the signal contrast is given for these three sequences together with two measures used for comparing these sequences in terms of the minimum variance of estimators (Cramér–Rao lower bound [CRLB]) and parameter estimation efficiency.

2.1 | Signal models

The signal model for the classical STEAM experiment can be described as

\[
S(TE, TM) = \rho e^{-\frac{TM}{T_1}} e^{-\frac{TE}{T_2}} \left(1 - e^{-\frac{TR-TE/2-TM}{T_1}} \right),
\]

where \(\rho\) is the proton density, and TM is the mixing time. Diffusion effects and constant factors are neglected for simplicity.

To increase sensitivity to T1, an inversion pulse followed by an inversion delay time (TI) can be added to the beginning of the pulse sequence. Adjusting Equation 1 accordingly for a multi-TI STEAM measurement then yields

\[
S(TI, TE, TM) = \rho \left(1 - 2e^{-\frac{TI}{T_1}} e^{-\frac{TM}{T_1}} e^{-\frac{TE}{T_2}} \left(1 - e^{-\frac{TR-TE/2-TM}{T_1}} \right) \right).
\]

In the case of long-TR experiments, when the TR is assumed to be much longer than T1, \(\{TR > 5 \times T1_{max}\}\), the TR-related terms \(1 - e^{-\frac{TR-TE/2-TM}{T_1}}\) and \(1 - e^{-\frac{TR-TE/2-TM}{T_1}}\) are usually dropped in Equations 1 and 2, respectively.
Weakening the requirement for long TRs and assuming shorter TRs in the order of $T_1$, the signal equation for a SHORTIE STEAM acquisition\(^{20}\) (Figure 1) can be approximated by

$$S(TI, TE, TM, \tau) = \rho \left(1 - 2e^{-\frac{TI}{T_1}} + e^{-\frac{TM}{T_1}} + e^{-\frac{TE}{T_1}}\right) e^{-\frac{TM}{T_1}} e^{-\frac{TE}{T_1}},$$  \hspace{1cm} (3)

where $\tau$ is in this case the constant recovery delay between the third 90° RF pulse and the 180° pulse of the subsequent TR. In addition, Equation 3 requires $\tau > 5 * T_{2\max}$. The derivation of Equation 3 is described in the Supporting Information.

### 2.2 | Cramér-Rao lower bound analysis

The CRLB provides a theoretical lower bound on the variance of an unbiased estimator of a parameter by the inverse of the Fisher information.\(^{21-25}\) The simplified Fisher information matrix\(^{26}\) can be written as

$$I(\Theta) = J^T J / \sigma^2,$$  \hspace{1cm} (4)

where $J$ is the Jacobian matrix for the signal model $S$ with respect to the parameter set $\Theta$, and $\sigma^2$ is the variance in the presence of Gaussian noise.

The CRLB of the (co)variances of the estimators can then be computed by

$$CRLB = I^{-1} \leq \text{var}(\Theta).$$  \hspace{1cm} (5)

### 2.3 | Efficiency analysis

To compare the parameter estimation efficiency for a given parameter $\theta$ for different acquisition schemes, a parameter efficiency measure $\eta_\theta$ was defined as the parameter-to-noise ratio (PNR) per scan time $T_{\text{seq}}$\(^{27}\) in this case for the parameters $T_1$ and $T_2$, as follows:

$$\eta_{T1,2} = \frac{\text{PNR}}{\sqrt{T_{\text{seq}}}} = \frac{T_{1,2}}{\sigma(T_{1,2}) \cdot \sqrt{T_{\text{seq}}}} = \frac{T_{1,2}}{\sqrt{\text{CRLB}(T_{1,2}) \cdot T_{\text{seq}}}}$$  \hspace{1cm} (6)

where $\sigma(T_{1,2})$ is the SD of the estimates $\hat{T}_1$ and $\hat{T}_2$ of the true $T_1$ and $T_2$, respectively.

The total parameter estimation efficiency $\eta$ for the set of parameters $\Theta$ can then be calculated as the square root of the sum of squares as follows:

$$\eta = \sqrt{\sum_{\theta} \frac{\text{PNR}_\theta^2}{T_{\text{seq}}}}.$$  \hspace{1cm} (7)

![Figure 1](https://example.com/figure1.png)

**Figure 1** Short-TR multi-TI multi-TE (SHORTIE) STEAM MRS sequence diagram: an adiabatic hyperbolic secant inversion pulse is followed by a conventional single-voxel STEAM MRS sequence pattern including three slice-selective 90° pulses along the three axes $m$, $p$, and $s$. The constant delay time $\tau$ is defined as the duration between the third slice-selective 90° pulse and the subsequent inversion pulse of the next TR. AQ, acquisition; TM, mixing time.
3 | METHODS

3.1 | Cramér-Rao lower bound and efficiency analysis

The CRLB analysis was performed by deriving analytical CRLB expressions using MATLAB’s symbolic toolbox (MATLAB R2021a; The MathWorks, Natick, MA) for $T_1$ in long-TR multi-TI STEAM (Equation 2), for $T_2$ in long-TR multi-TE STEAM (Equation 1), and for $T_1$, $T_2$, and $\rho$ in SHORTIE STEAM (Equation 3), respectively.

All CRLBs were examined for the sequence parameters used in the in vivo study (see Table 2) and $T_1$ ranging from 150 ms to 2000 ms, and for $T_2$ ranging from 5 ms to 150 ms.

The parameter-estimation efficiencies $\eta_{T_1}$, $\eta_{T_2}$, and $\eta(\Theta = [T_1, T_2])$ were calculated using the aforementioned CRLB analysis with matching sequence parameters and relaxation properties.

3.2 | Magnetic resonance spectroscopy measurements

All measurements (phantom and in vivo) were performed on a clinical whole-body 3T scanner (Ingenia Elition X; Philips Healthcare, The Netherlands) in an air-conditioning-controlled scanner room (at approximately 21°C) after some acclimatization time.

3.2.1 | Phantom experiment

For the phantom measurements, agar-based water–fat phantoms were manufactured with nominal fat fractions of 0%, 5%, 10%, 15%, and 100% (100% fat fraction phantom contained pure oil) according to the recipe by Hines et al.\textsuperscript{28} (batch A) and with nominal fat fractions of 0%, 25%, and 50% according to the recipe by Bush et al.\textsuperscript{29} without and with 0.05 mM MnCl$_2$ for varying relaxation properties (batch B). The two batches were scanned in two separate sessions using (1) a long-TR multi-TI STEAM, (2) a long-TR multi-TE STEAM, and (3) SHORTIE STEAM MRS with the parameters given in Table 1. All phantoms were scanned using the standard built-in 12-channel posterior coil array and 16-channel anterior torso coil array.

3.2.2 | In vivo measurements

The (1) long-TR multi-TI STEAM, (2) long-TR multi-TE STEAM, and (3) SHORTIE STEAM MRS were adapted for in vivo measurements and applied without respiratory/electrocardiogram triggering in the fat region within the supraclavicular fossa of 7 volunteers (5 males, 2 females, age: 27.2–30.8 years) based on a water–fat imaging scout. The voxel location is illustrated in Figure 5E. All measurements were performed using the standard 16-channel head coil plus built-in 12-channel posterior coil array and 16-channel anterior torso coil array. Sequence parameter details are found in Table 2.

3.2.3 | Ethics statement

The study was approved by the local institutional review board in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Informed consent was obtained from all volunteers included in the studies.

| TABLE 1 | Sequence parameters used in the phantom experiment |
|----------|----------------------------------|----------------|----------------------------------|----------------|
| TI (ms)  | 10/100/500/1500 | 10/100/500/1500 | — | 10/100/500/1500 |
| TE (ms)  | 10               | 10/15/20/25      | 10/15/20/25       | 10/15/20/25   |
| TM (ms)  | 17               | 17               | 17               | 17               |
| TR (ms)  | 4000             | 5000             | 4000             | 5000           |
| $\tau$ (ms) | —              | —                | —                | 710              |
| Number of samples | 4096 | 4096 | 2048 |
| Bandwidth (Hz) | 3000   | 3000 | 3000 |
| Number of averages | 4   | 4   | 4   |
| Number of phase cycles | 4    | 2   | 4   |
| Voxel size (mm$^3$) | $12 \times 12 \times 24$ | $10 \times 15 \times 10$ | $12 \times 12 \times 24$ | $10 \times 15 \times 10$ |
| Scan time (minutes) | 01:31 | 02:28 | 01:20 | 01:15 | 01:41 | 01:01 |
3.3 Magnetic resonance spectroscopy data processing

The MRS data-processing pipeline consisted of the following main steps: singular value decomposition–based coil combination,30 signal averaging, zero-order phase correction, frequency offset correction, methylene signal–based frequency referencing, and signal model fitting. For the signal model fitting, a joint-series time domain–based model fitting was performed using the nonlinear least-squares solver NL2SOL.31 The signal models for the multi-TI STEAM (Equation 2), multi-TE STEAM (Equation 1), and SHORTIE STEAM (Equation 3) were mapped to the following time discrete signal model functions, respectively:

\[ S_{\text{multi-TI}}(t) = \sum_i \rho_i e^{i \phi_i} e^{i \omega_i d_i - g_i t} e^{\frac{-TM}{T_1,i}} e^{-\frac{TM}{T_2,i}} \left(1 - 2e^{-\frac{TM}{T_1,i}}\right) e^{-\frac{TM}{T_1,i}} \]  
\[ S_{\text{multi-TE}}(t) = \sum_i \rho_i e^{i \phi_i} e^{i \omega_i d_i - g_i t} e^{-\frac{TM}{T_2,i}} \]  
\[ S_{\text{SHORTIE}}(t) = \sum \rho_i e^{i \phi_i} e^{i \omega_i d_i - g_i t} \left(1 - 2e^{-\frac{TM}{T_1,i}} + e^{-\frac{TM}{T_1,i}} + e^{-\frac{TM}{T_2,i}}\right) \]

where \( \rho_i \) is the proton density; \( d_i \) and \( g_i \) are the Lorentzian and Gaussian damping factors, respectively; \( \omega_i \) is the precession frequency; and \( \phi_i \) represents an additional phase term of the \( i \)th frequency component. The used fitting strategy was comprised of a relaxation-constrained 10-peak-triglyceride model. Briefly, the model constrained all proton densities of the triglyceride peaks to a theoretical triglyceride model, and all triglyceride peaks were constrained to a common \( T_1 \) and \( T_2 \) relaxation time, respectively, with the exception of the methyl peak, which was fitted with an individual \( T_1 \). The fitting strategy is summarized in Table 3. All acquired data were processed with an equivalent relaxation-constrained 10-peak-triglyceride model, meaning that the full model was used for SHORTIE STEAM data, the \( T_2 \) dimension was not fitted for multi-TI STEAM data, and the \( T_1 \) dimension was not fitted for the multi-TE STEAM data, respectively. All data processing and signal model fitting was carried out using MATLAB (R2019b).

3.4 Magnetic resonance spectroscopy data analysis

Linear regression and Bland-Altman33 analysis was performed in both phantom and in vivo data for the following measures: \( T_1 \) of water and methylene, and \( T_2 \) of water and methylene and fat fraction.

The analysis was carried out using Python (V3.6.10) and the scipy package (V1.4.1).

4 RESULTS

4.1 Cramér-Rao lower bound and efficiency analysis

Results of the CRLB analysis depicted in Figure 2 showed similar estimation performance for \( T_1 \) and \( T_2 \) when comparing long-TR multi-TI STEAM (Figure 2A) with SHORTIE STEAM (Figure 2C) and long-TR multi-TE STEAM (Figure 2B) with SHORTIE STEAM (Figure 2D), respectively. Although both \( T_1 \) and \( T_2 \) estimator variances showed a slightly stronger increase with increasing \( T_1 \) for the comparison of SHORTIE STEAM with its respective conventional counterpart. Variance for the estimator

| TABLE 2 Sequence parameters used in the in vivo study |
|-----------------------------------------------|
|                                 | Multi-TI STEAM | Multi-TE STEAM | SHORTIE STEAM |
| TI (ms) 10/100/500/1500 — | 10/100/500/1500 | 10/100/500/1500 |
| TE (ms) 10 12/15/20/25 10/15/20/25 |
| TM (ms) 17 17 17 |
| TR (ms) 4000 4000 742 (min) – 2240 (max) |
| \( \tau \) (ms) - - 710 |
| Number of samples 4096 4096 2048 |
| Bandwidth (Hz) 3000 3000 3000 |
| Number of averages 8 8 8 |
| Number of phase cycles 4 4 4 |
| Default voxel size (mm\(^3\)) 9 × 9 × 9 9 × 9 × 9 9 × 9 × 9 |
| Scan time (minutes) 02:43 02:24 02:52 |
ρ (Figure 2E) was increasing with increasing $T_1$ and decreasing $T_2$, respectively.

An overview of the parameter-estimation efficiency is shown in Figure 3 for $\eta_{T_1}$ (Figure 3A–C), $\eta_{T_2}$ (Figure 3D–F), and $\varphi$ (Figure 3G,H). For $\eta_{T_1}$, a dependency was observed on $T_2$ for multi-TI STEAM (Figure 3A,B) and on both $T_1$ and $T_2$ for SHORTIE STEAM (Figure 3C). Similarly, $\eta_{T_2}$ showed a dependency on $T_2$ for multi-TE STEAM (Figure 3D,E) and on both $T_1$ and $T_2$ for SHORTIE STEAM (Figure 3F). The total parameter-estimation efficiency $\eta$ appeared to be higher for SHORTIE STEAM (Figure 3H) in comparison with combined multi-TI STEAM and multi-TE STEAM (Figure 3G). Moreover, $\varphi$ exhibited a similar pattern as $\eta_{T_1}$ for the same sequence.

### 4.2 Phantom experiments

Linear regression analysis (Figure 4A,C,E) revealed good correlation for all three investigated parameters between multi-TI STEAM and SHORTIE STEAM for $T_1$ with a slope of 1.07 and intercept of $-15.40$ for $T_1$ (in ms; $r = 0.999$); between multi-TE STEAM and SHORTIE STEAM for $T_2$ with a slope of 0.93 and intercept of $+1.32$ for $T_2$ (in ms; $r = 0.995$), and with a slope of 0.98 and intercept of $-0.04$ for fat fraction (in percent; $r = 0.999$), respectively. The Bland-Altman analysis (Figure 4B,D,F) showed for the same sequence comparisons as in the linear regression analysis mean differences of $-17.18$ ms for $T_1$, $+1.09$ ms for $T_2$, and 0.78% for fat fraction, respectively. Measurements ranged in the phantom experiment from approximately 130 ms to 1500 ms for $T_1$, 15 ms to 55 ms for $T_2$, and 0% to 100% for fat fraction.

### 4.3 In vivo measurements

Example spectra acquired in a single volunteer from the in vivo study are shown in Figure 5 to exhibit spectral content, achievable line widths, relaxation behavior, as well as fitted and residual signals. One of the multi-TE STEAM measurements was rejected due to severe motion artifacts.

The linear regression analysis (Figure 6A,C) showed good correlation for the investigated relaxation parameters between multi-TI STEAM and SHORTIE STEAM for $T_1$ with a slope of 1.08 and intercept of $+1.77$ for $T_1$ (in ms; $r = 0.994$); and between multi-TE STEAM and SHORTIE STEAM for $T_2$ with a slope of 0.88 and intercept of $+6.69$ for $T_2$ (in ms; $r = 0.884$), respectively.

The correlation for measuring the fat fraction between multi-TE STEAM and SHORTIE STEAM (Figure 6E) exhibited a weaker correlation with a slope of 0.56 and intercept of $+34.40$ (in percent; $r = 0.673$). The Bland-Altman analysis (Figure 6B,D,F) resulted in a mean differences of $-62.2$ ms for $T_1$, $-1.55$ ms for $T_2$, and $-0.46$% for fat fraction. Measurements ranged from approximately 325 ms to
1400 ms for $T_1$, 15 ms to 95 ms for $T_2$, and 60% to 90% for fat fraction.

5 | DISCUSSION

The current study proposes a SHORTIE single-voxel MRS acquisition scheme for the efficient and simultaneous assessment of $T_1$ and $T_2$ relaxation as well as PDFF in fat-containing tissues. The superior performance of the SHORTIE MRS acquisition scheme compared with long-TR multi-TI STEAM MRS and long-TR multi-TE STEAM MRS was theoretically confirmed by the conducted CRLB analysis and parameter-estimation efficiency analysis. The feasibility of SHORTIE MRS was demonstrated in a phantom experiment and in vivo in the supraclavicular fossa in comparison with conventional long-TR multi-TI STEAM MRS and long-TR multi-TE STEAM MRS.

The presented in vivo study, which aims to characterize tissue in the human supraclavicular fossa, is of high relevance in the context of brown adipose tissue detection.\textsuperscript{34–37} For example, SHORTIE STEAM allows the simultaneous probing of multiple MR properties, including $T_1$ and $T_2$ relaxation and PDFF, and may be a promising candidate
for the assessment of brown adipose tissue microstructure and quantification of brown adipose tissue, independent of its activation status. Additionally, the assessment of spectrally resolved relaxation properties in the (water-) fat environment is a well-studied topic with applications not only in the characterization of adipose tissue or the differentiation between white and brown adipose tissue, but also in other tissues including bone marrow, muscle, and liver.

There are only a limited number of previous studies investigating similar single-voxel spectroscopy-based methods for the efficient probing of multiple MR parameters including $T_1$, $T_2$, and PDFF. For example, Hamilton et al. and Simchick et al. proposed a multi-TR multi-TE STEAM acquisition scheme with a variable recovery delay for the simultaneous assessment of the PDFF and relaxation parameters in the liver. However, the proposed SHORTIE STEAM scheme has two favorable characteristics, when compared with multi-TR acquisition schemes. The first favorable characteristic is that the use of an inversion pulse allows the full dynamic range of $T_1$ relaxation to be sampled. The second favorable characteristic is that keeping the recovery delay constant allows the signal to be described with simple expressions independent of the signal evolution history. Recently, Kulpanovich and Tal proposed a MR fingerprinting-inspired approach in the context of multi-parametric single-voxel MRS, where they varied TE, TR, and flip angle in a PRESS sequence applied in the brain. One major difference between SHORTIE
and the approach by Kulpanovich and Tal is the less-complex signal modeling in SHORTIE STEAM.

The theoretical inspection of the three acquisition schemes using the CRLB analysis (Figure 2) indicated that the estimator variances for $T_1$ and $T_2$ are comparable between SHORTIE STEAM MRS and the corresponding conventional STEAM MRS sequence. Only for species with both long $T_1$ and long $T_2$, the variances appeared to increase faster for SHORTIE STEAM for the investigated sequence parameter set. Due to the dependence of all sequences on both $T_1$ and $T_2$, theoretical CRLB for spin density could only be calculated for SHORTIE STEAM, and a comparison with neither the multi-TI STEAM nor the multi-TE STEAM sequence alone was possible.

The parameter-efficiency analysis (Figure 3) then showed higher $\eta_{T_1}, \eta_{T_2},$ and $\eta(\Theta = [T_1, T_2])$ for SHORTIE STEAM when compared individually with multi-TI STEAM and multi-TE STEAM, but especially when compared with the combined experiment in which both multi-TI STEAM and multi-TE STEAM were acquired. In addition, in the parameter-estimation efficiency analysis, SHORTIE STEAM showed a higher dependence of all three $\eta_{T_1}, \eta_{T_2},$ and $\eta$ on $T_1$ and $T_2$, respectively. Moreover, the patterns of the parameter-estimation efficiency analysis resembled the results from the CRLB analysis for corresponding parameters, especially for SHORTIE STEAM. Yet, this behavior is not surprising, given that the parameter-estimation efficiency was calculated using the CRLB in combination with the required scan time.

It is worth noting that the results of both the CRLB analysis and the parameter-estimation efficiency analysis are dependent on the chosen set of sequence parameters. However, in the context of the present study, the set of sequence parameters was thoughtfully designed, and the parameters of the in vivo study were exactly matched to the theoretical analysis.

The measurement agreement between SHORTIE STEAM MRS and the corresponding conventional STEAM MRS was shown to be high and close to the identity line in the phantom experiment for the assessment of $T_1$ relaxation and $T_2$ relaxation of water and methylene as well as PDFF. The analogous comparison of methods in the in vivo study could not entirely reproduce the goodness-of-measurement agreement compared with the phantom experiments, given a slightly lower agreement for the $T_2$ relaxation and an even more reduced agreement for the fat fraction. The observed discrepancy in the measurement agreement may be attributed to the presence of signal fluctuations due to respiratory motion, cardiac motion, or pulsating vessels in the supraclavicular fossa.

The current study also has some limitations. First, measurements in the supraclavicular fossa are potentially prone to artifacts due to breathing motion or vessel pulsation. Therefore, the application of a motion-compensated MRS acquisition scheme would have been preferable to mitigate motion-induced signal fluctuations. However, the overall spectral quality appeared to be acceptable for the purpose of the present investigation, with the exception...
of a single measurement that retrospectively had to be discarded due to severe artifacts. Second, the used sampling scheme, or rather the set of sequence parameters, was not fully optimized for the purpose of probing $T_1$ and $T_2$ relaxation in the expected $T_1$ and $T_2$ parameter ranges and the assessment of the PDFF. Therefore, the optimal performance of the present approach may not be achieved yet and is left to future application-centered studies. However, even the ad-hoc set of sequence parameters demonstrated the superior performance of SHORTIE STEAM. Third, the used fitting strategy rigorously constrained the triglyceride relaxation properties, assuming a common $T_1$ relaxation (except for methyl) and $T_2$ relaxation for all triglyceride peaks. Although this crude assumption is known to be not...
entirely correct, it is considered a valid approximation for improving the robustness of the fitting process in the present context. Likewise, the considered relaxation properties in this study of the water peak and the triglyceride methylene peak should not be substantially affected by the used set of constraints. Fourth, the present theoretical advantage of SHORTIE STEAM shown in the CRLB and parameter-estimation efficiency analysis are strongly dependent on the set of sequence parameters and may not hold in all cases. Therefore, the utility of SHORTIE STEAM may have to be re-evaluated in scenarios with different requirements and sequence parameters. Furthermore, a Gaussian parameter distribution was assumed throughout the noise performance analysis. Fifth, J-modulations may affect the quantification but were not accounted for in the data-fitting routine. However, the investigated water peak is not subject to J-modulations, and the methylene peak may only be subject to small modulations for the used TE range of up to 25 ms.

In the future, the utility of the SHORTIE acquisition scheme can also be explored in other applications, as the technique is not limited to fat-containing tissue and is not organ-specific.

6 | CONCLUSIONS

Single-voxel SHORTIE STEAM MRS allows shorter scan times by enabling more efficient simultaneous probing of relaxation properties and spectral content in the water–fat environment when compared with combined long-TR multi-TI STEAM and long-TR multi-TE STEAM measurements.

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CONFLICT OF INTEREST

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**SUPPORTING INFORMATION**

Additional supporting information may be found in the online version of the article at the publisher’s website.

TEXT S1 Derivation of the SHORTIE STEAM signal equation

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