NOTE

Multi-parametric liver tissue characterization using MR fingerprinting: Simultaneous $T_1$, $T_2$, $T_2^*$, and fat fraction mapping

Olivier Jaubert$^1$ | Cristobal Arrieta$^2$ | Gastão Cruz$^1$ | Aurélien Bustin$^1$
Torben Schneider$^3$ | Georgios Georgiopoulos$^1$ | Pier-Giorgio Masci$^1$
Carlos Sing-Long$^{2,4}$ | Rene M. Botnar$^{1,5}$ | Claudia Prieto$^{1,5}$

$^1$School of Biomedical Engineering and Imaging Sciences, King’s College London, London, United Kingdom
$^2$Biomedical Imaging Center and Millennium Nucleus for Cardiovascular Magnetic Resonance, Pontificia Universidad Católica de Chile, Santiago, Chile
$^3$Philips Healthcare, Guilford, United Kingdom
$^4$Instituto de Ingeniería Matemática y Computacional and Millennium Nucleus for the Discovery of Structures in Complex Data, Pontificia Universidad Católica de Chile, Santiago, Chile
$^5$Escuela de Ingeniería, Pontificia Universidad Católica de Chile, Santiago, Chile

Correspondence
Olivier Jaubert, Department School of Biomedical Engineering and Imaging Sciences, Institute King’s College London, 3rd Floor, Lambeth Wing, St Thomas’ Hospital, London SE1 7EH, United Kingdom.
Email: jaubert.oli@gmail.com

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Purpose: Quantitative $T_1$, $T_2$, $T_2^*$, and fat fraction (FF) maps are promising imaging biomarkers for the assessment of liver disease, however these are usually acquired in sequential scans. Here we propose an extended MR fingerprinting (MRF) framework enabling simultaneous liver $T_1$, $T_2$, $T_2^*$, and FF mapping from a single ~14 s breath-hold scan.

Methods: A gradient echo (GRE) liver MRF sequence with nine readouts per TR, low flip angles (5-15°), varying magnetisation preparation and golden angle radial trajectory is acquired at 1.5T to encode $T_1$, $T_2$, $T_2^*$, and FF simultaneously. The nine-echo time-series are reconstructed using a low-rank tensor constrained reconstruction and used to fit $T_2^*$, $B_0$ and to separate the water and fat signals. Water- and fat-specific $T_1$, $T_2$, and $M_0$ are obtained through dictionary matching, whereas FF estimation is extracted from the $M_0$ maps. The framework was evaluated in a standardized $T_1$/$T_2$ phantom, a water-fat phantom, and 12 subjects in comparison to reference methods. Preliminary clinical feasibility is shown in four patients.

Results: The proposed water $T_1$, water $T_2$, $T_2^*$, and FF maps in phantoms showed high coefficients of determination ($r^2 > 0.97$) relative to reference methods. Measured liver MRF values in vivo (mean ± SD) for $T_1$, $T_2$, $T_2^*$, and FF were 671 ± 60 ms, 43.2 ± 6.8 ms, 29 ± 6.6 ms, and 3.2 ± 2.6% with biases of 92 ms, −7.1 ms, −1.4 ms, and 0.63% when compared to conventional methods.

Conclusion: A nine-echo liver MRF sequence allows for quantitative multi-parametric liver tissue characterization in a single breath-hold scan of ~14 s. Future work will aim to validate the proposed approach in patients with liver disease.
1 | INTRODUCTION

Non-alcoholic fatty liver disease (NAFLD) is highly prevalent worldwide (25%) and is associated with many hepatic and extra-hepatic diseases creating an increasingly large clinical and economic burden.1 In the Western and industrialized countries, NAFLD is one of the main causes of cirrhosis and highly prevalent in patients with hepatocellular carcinoma the main causes of liver-related deaths.2 Pathogenesis of NAFLD can be subdivided into four stages, which are progressively characterized by fat accumulation, inflammation (non-alcoholic steatohepatitis, or NASH), and potentially leading to irreversible fibrosis (cirrhosis), hepatocellular carcinoma, or other life-threatening complications.3 Liver biopsy remains the current reference standard for diagnosing and staging NAFLD; however, they are invasive, costly, and potentially hazardous. Liver biopsies are also prone to sampling errors and suffer from inter-rater variability (with agreement potentially during separate breath-holds,9 thus leading to long scan times, patient fatigue, and potentially mis-registered parameter maps. Joint parameter mapping has been proposed to map liver T2∗ and PDFF simultaneously11 and more recently to map liver T1, T2, and M0,12 with both methods accounting for inter-parametric dependencies. The first method fits multiple echo images to a multi-peak water-fat signal model with T2 decay13,14 while the latter uses MR fingerprinting (MRF)15 to generate multiple parametric maps from a highly undersampled acquisition with dynamically varying contrasts. Recent works combining water-fat imaging and MRF have been proposed to map water-specific T1 and T2 and fat fraction (FF)16,17 simultaneously to further reduce inter-parametric biases and overall scan time.

Here, we propose to jointly map T1, T2, T2∗, and FF for comprehensive liver tissue characterization. This is achieved by extending our previous work on 3-echo Dixon cardiac MRF17 to a 9-echo gradient rewound echo (GRE) acquisition and graphcut method18 for estimation of B0 and T2∗ and water-fat separation. To the best of our knowledge, this is the first time that liver T1, T2, T2∗, and FF are simultaneously quantified in a single acquisition. The proposed framework was evaluated in phantoms against spin echo T1 and T2 and 12-echo GRE (PDFF and T2∗) reference measurements, and in 12 subjects against MOLLI, T2-GRASE, and 12-echo GRE. Preliminary clinical feasibility is shown in four patients.

2 | METHODS

The proposed framework combines (1) a nine-echo GRE acquisition; (2) a B0 and B1 insensitive acquisition scheme using fixed repetition time (TR), gradient spoiling, low flip angles (FA), and magnetization preparations; (3) an undersampled reconstruction with temporal compression and patch-based low-rank tensor regularization; (4) a graphcut based method for estimation of B0, T2 and water-FFs; (5) a dot-product matching step; and (6) an FF estimation step from the relative proton density (M0) images. Details of the framework are described below.

2.1 | Acquisition

The proposed liver MRF acquisition (Figure 1) consists of a nine-echo, golden angle radial (~111°) GRE acquisition with bipolar readouts and varying inversion recovery (IR) and T2 preparation (T2prep) pulses.17 The acquisition scheme includes T2 preps with four adiabatic refoocusing pulses19 and varying durations, noted as T2prepX and hyperbolic hypersecant IR pulses with varying inversion delays, noted as T2prepY, where X and Y are durations in ms. A total of 12 magnetization preparations followed by data acquisition are applied during a single breath-hold scan of 13.9 s with the following pattern: T112, no preparation (noPrep), T2prep40, T2prep80, T2prep160, T2prep300, noPrep, T2prep40, T2prep80, T2prep160, T112, noPrep. The data acquisition block consists of varying low FAs (9 linear ramp-up radiofrequency [RF] pulses from 5° to 15° followed by 26 fixed 15° RF pulses20), 35 TRs, bandwidth 746 Hz/pixel, nine echoes per TR, TR/echo time 1 [TE1]/ΔTE = 20/1.5/2 ms leading to 700 ms data acquisition blocks. Acquisition blocks are spaced regularly every 1.2 s allowing for recovery (varying between ~200–500 ms) before the next magnetization preparation module. A fixed TR, low FAs, and 4π gradient spoiling along slice selection were used to reduce the sensitivity to B0 and B1 inhomogeneities.20-22
2.2 | Image reconstruction

MRF time-series reconstruction was performed using a multi-contrast patch-based high-order low-rank reconstruction (HD-PROST)\(^23\) with temporal dictionary based compression. Temporally compressed singular images \(x_i = U_H R x\)\(^i\) approximating the MRF time-series \(x_i\)\(^\text{uni}2032\).\(^\text{var}\) are reconstructed for each echo \(i\) using HD-PROST, where \(U_R\) are the left singular vectors of the MRF dictionary matrix truncated to rank \(R\). Reconstruction parameters included a rank \(R = 6\) and a sparsity promoting parameter \(\lambda = 10^{-3}\)\(^{17,23}\).

2.3 | \(T_1^*, B_0\), and water-fat separation

Given a water \((W)\) and a set of fat \((F_k)\) compartments time-series,\(^{14,26,27}\) the reconstructed singular images at each echo \(i\), can be written as:

\[
x_i = U_R H x_i = U_R H \left( W + \sum_j F'_j e^{i2\pi \Delta f_{ij}} \right) e^{-\frac{i}{2} + j2\pi \Delta f_{iw} t_i} = (W + F) e^{-\frac{i}{2} + j2\pi \Delta f_{iw} t_i}
\]

where \(W\) and \(F = U_R H \sum_j F'_j e^{i2\pi \Delta f_{ij}}\) are the water and fat (or combined fat compartments) singular images, \(\Delta f_i\) is the known difference in precession frequency between water and fat compartment \(i\), \(\Delta f_{w0}\) is the precession frequency difference induced by \(B_0\) field inhomogeneities and \(t_i\) is the echo time \(i\). A graphcut scheme\(^18\) is used to solve for \(B_0\), \(T_1^*\) and water-fat separation using a pre-defined six-peak fat model.\(^28\) First singular images of all echo times are used for \(B_0\) and \(T_1^*\) estimation. The resulting maps are subsequently used to separate the other singular images by pseudo inverse\(^29\) into water and fat. This model ignores the different \(T_1\) and \(T_2\) values\(^28\) of the fat peaks which can lead to varying signal peak weights during the MRF acquisition. The impact of this simplified model was investigated in simulations.

2.4 | \(T_1\), \(T_2\), and FF maps

The water and fat singular images are then matched (using dot-product) to a previously generated MRF dictionary (with fixed \(TE = 0^+\) ms) to obtain the water- and fat-specific \(T_1\), \(T_2\), and \(M_0\) maps. The dictionary was generated using the extended phase graph formalism,\(^30\) including slice profile\(^31\)
(51 points along the slice profile) and inversion efficiency corrections. The dictionary contained signal evolutions corresponding to combinations of $T_1$ and $T_2$ of interest (ie, [50:10:1400, 1430:30:1600, 1700:100:2200, 2400:200:3000] ms for $T_1$ and [5:2:80, 85:5:150, 160:10:300, 330:30:600] ms for $T_2$ as well as the standardized $T_1/T_2$ phantom reference values. The FF map is estimated from the water and fat $M_0$ and phase images (for noise bias correction).}

### 2.5 Experiments

Experiments were performed on phantoms and 2 cohorts of subjects. Cohort 1 (12 subjects, 7 females; age: 31 ± 4 years; body mass index (BMI): 23.9 ± 3.5 kg/m$^2$) underwent the proposed liver MRF and conventional techniques. Cohort 2 (four subjects, one female; age: 56 ± 13 years; BMI: 27.9 ± 4.0 kg/m$^2$) underwent only the proposed liver MRF during a clinically referred scan. Cohort 2 had large BMI > 25 kg/m$^2$ or previously diagnosed liver iron overload. All experiments were approved by the Institutional Review Board and written informed consent was given by all participants before scanning. Acquisitions were performed on a 1.5T Ingenia MR scanner (Philips Healthcare, The Netherlands).

Preliminary experiments investigated the number of echoes necessary for $T_2^*$ mapping in phantom (Supporting Information Text S1, which is available online) and the performance of the framework in numerical simulations (Supporting Information Text S2 and Figure S1).

### 2.6 Phantom study

Acquisitions were performed on a standardized $T_1/T_2$ phantom (TIMES) with 0% fat and on a water-fat phantom built in-house. The standardized $T_1/T_2$ phantom was used to validate the water $T_1$ and $T_2$ measurements against $T_1$ inversion recovery spin echo (IRSE) and $T_2$ multi-echo spin echo (MESE). The reference $T_1$ and $T_2$ methods do not consider fat suppression/separation thus only the phantom with 0% fat was used to validate the $T_1$ and $T_2$ measurements avoiding biases due to incomplete fat suppression. FF and $T_2^*$ measurements were performed in the standardized phantom and water-fat phantom and validated against a reference 12-echo GRE. The reference PDFF and $T_2^*$ maps were obtained using the same graph cut method, fat model, and noise bias correction as described for the proposed nine-echo liver MRF. Acquisition and mapping parameters for all reference sequences are included in Supporting Information Table S1.

Scan parameters for the proposed liver MRF were described in the Acquisition section, remaining parameters were: field of view (FOV) = 496 × 496 mm$^2$, 2 × 2 mm$^2$ resolution, 8 mm slice thickness.

### 2.7 In vivo study

The proposed liver MRF $T_1$, $T_2$, and $T_2^*$ maps were validated against reference $T_1$ MOLLI (5(3)3), $T_2$-GRASE, and 12-echo GRE ($T_2^*$ and PDFF), respectively, in cohort 1. Acquisition parameters for all conventional sequences are included in Supporting Information Table S1. All acquisitions were performed in transversal orientation under breath-hold at end-expiration.

The same liver MRF acquisition was performed on cohort 2 to show preliminary feasibility of the approach in a clinical setting.

### 2.8 Analysis

Regions of interest (ROIs) were manually drawn in each vial of the phantoms. Coefficients of determination, lines of best fit and biases are reported for each parameter map in comparison to their corresponding reference measurements.

For each subject, CX.Y (cohort X, subject number Y), ROIs were manually drawn in the liver (in four different areas of the liver avoiding blood vessels, the median value is reported), posterior muscle, subcutaneous fat, and the spleen. Mean measurements and range in 11 subjects with no history of liver disease (C1.1-10) or benign hemangioma (C1.11) are reported for all parameters for the proposed liver MRF and the corresponding conventional maps. C1.12 has been previously diagnosed with mild liver steatosis. Mean values, range, mean bias, 95% (±1.96 SD) confidence intervals (CI), and coefficients of determination are used to compare the measurement methods for cohort 1. A paired t-test was performed to test for statistically significant differences ($P < .05$) between the proposed liver MRF and conventional measurements.

### 3 RESULTS

#### 3.1 Preliminary studies

$T_2^*$ maps of the preliminary phantom acquisition (standardized $T_1/T_2$ and water/fat phantoms) obtained using the first 3, 6, 9, or 12 echoes for map estimation are shown in Supporting Information Figure S2A. Bland Altman plots (Supporting Information Figure S2B) and maps show large bias of $T_2^*$ estimation when using only the first 3 echoes, and small bias but noisy measurements when using 6 echoes. Maps obtained using the first 9 echoes compare qualitatively and quantitatively well with the ones obtained using all 12 echoes, albeit enabling shorter TR and thus scan time. The $T_2^*$ map obtained using the first 9 echoes of the 12-echo MRF
acquisition presented a mean bias of 1.4 ms when compared to the reference $T_2^*$ map obtained from a conventional 12-echo GRE scan.

Numerical simulations of the proposed framework led to accurate (<1%) liver $T_2^*$ and $B_0$ estimation and ensuing water $T_1$, water $T_2$, and FF estimation despite the simplified model used for water-fat separation (Supporting Information Figure S3), although overestimation of subcutaneous fat $T_2^*$ was observed. Simulated errors in the estimation of $B_0$ before water-fat separation caused significant errors in FF maps (>9%) and low errors in water $T_1$ or $T_2$ maps (<20 ms and <1 ms respectively) (Supporting Information Figures S4 and S5). Errors in $T_2^*$ did not show an effect in the subsequent $T_1$, $T_2$, and FF estimation.

### 3.2 Phantom study

Water $T_1$, water $T_2$, FF, and $T_2^*$ maps for the proposed MRF approach (Supporting Information Figure S6) are quantitatively compared to $T_1$ IRSE, $T_2$ MESE, and $T_2$ and FF (12-echo GRE) reference maps (Figure 2A). Correlation plots with lines of best fit show high coefficients of determination for water $T_1$ and water $T_2$ (standardized phantom only, 0% fat) ($r^2 > 0.99$) and for FF and $T_2^*$ (standardized and water-fat phantoms) ($r^2 > 0.97$). Biases were measured at $-15$ ms, $-4.7$ ms, 1.9 ms, and $0.5$ ms for $T_1$, $T_2$, $T_2^*$, and FF respectively. The bias for short $T_2$ s (0.73 ms) was smaller than for $T_2$ s outside the range of interest ($T_2 > 80$ ms).

### 3.3 In vivo study

Water $T_1$, water $T_2$, FF, and $T_2^*$ ROI measurements for the proposed liver MRF in subjects C1.1-12 are compared to conventional techniques (Figure 2B) showing high coefficients of determination ($r^2 > 0.93$) for all parameters. Water $T_1$ and $T_2$ measurements were not performed in the subcutaneous fat ROI due to its low water content.

Liver values (mean [min, max]) measured in subjects C1.1-11 with the proposed approach were 676 ms [607, 803] ms for water $T_1$, 43.6 ms [35.9, 57.8] ms for water $T_2$, 30.1 ms [17.9, 39] ms for $T_2^*$, and 2.56% [1.2, 5.3]% for FF. Corresponding mean values and range for muscle, spleen,
and subcutaneous fat are reported in Supporting Information Table S2 in comparison to the conventional methods and literature values when available. Fat-specific T1 and T2 are reported for the subcutaneous fat ROI. Boxplots showing T1, T2, FF, and T2* mean, median, interquartile, SD and outliers obtained with the proposed liver MRF and conventional sequences are included in Figure 3 for subjects C1.1-12. Biases and CI (bias [CI]) observed with the proposed liver MRF in comparison to conventional methods for all ROIs combined (excluding subcutaneous fat for water T1 and T2 measurements due to its low water content) were 110 ms [23; 200] ms for water T1, −9.1 ms [−18; −0.19] ms for water T2, 2.1 ms [−8.6; 13] ms for T2*, and 0.32% [−4.4; 5.0]% for FF. For liver measurements alone slightly lower biases and tighter CIs were observed (ie, 92 ms [18; 170] ms, −7.1 ms [−12; −2.2] ms, −1.4 ms [−4.4; 1.5] ms, and 0.63% [−1.4; 2.7]% for T1, T2, T2* and FF respectively) with statistically significant differences for T1, T2, and T2*.

Water T1, water T2, FF, T2*, and B0 maps for the proposed liver MRF are shown for two subjects in comparison to the corresponding conventional mapping techniques (Figure 4). An elevated liver FF was measured in subject C1.12 at 10.3% with the proposed approach and 9.2% with conventional PDFF (Figure 4A). Subject C1.11, with a previously diagnosed benign hemangioma (ie, abnormal mass of small blood vessels), is shown in Figure 4B. Water T1, water T2, T2*, and FF in the hemangioma were measured at 1603 ms, 112 ms, 80 ms, and 1.2% with the proposed liver MRF and 1469 ms, 163 ms, 71 ms, and −0.2% with conventional methods respectively.

Water T1, water T2, FF, T2*, and B0 maps for the proposed liver MRF are shown in Figure 5 for all cohort 2. C2.2-4 presented elevated liver FF (15.25%, 12.45%, and 18%, respectively) with water T1, water T2, and T2 values within the range obtained in cohort 1.1-11 (Supporting Information Table S2) for C2.2 and C2.3 and abnormally low for C2.4 (520 ms, 20.9 ms, 1.95 ms, respectively) consistent with previously diagnosed elevated hepatic iron concentration.

4 DISCUSSION

A nine-echo MRF approach is proposed for multi-parametric and simultaneous T1, T2, T2*, and FF liver tissue characterization in a single 14 s acquisition. The proposed approach relies on the reconstruction of a transient signal sampled for different echo times. The echo sampling allows for T2* and B0 estimation and separation of the transient signal into a water and fat fingerprints. The fingerprints can then be used for MRF dictionary matching to obtain water and fat T1, T2, and relative M0 maps, whereas FF can be estimated from the water and fat M0 maps. Compared to previous water-fat MRF

FIGURE 3 Boxplots showing T1, T2, T2* and FF measurements mean (+), median (−), interquartile range (IQR) (box), Tukey whiskers and remaining outliers (●) obtained in cohort 1 (12 subjects, C1.1-12) for liver, muscle, spleen, and subcutaneous fat for proposed 9-echo liver MRF and conventional (Conv) methods (ie, MOLLI, T2-GRASE, and 12-echo GRE T2* and PDFF). Statistically significant differences (paired t-test) in mean measurements are indicated with * (P < .05) and are shown for each body organ. Please note that water T1 and water T2 are reported for the liver, muscle and spleen ROIs with the proposed MRF approach, whereas fat T1 and fat T2 are reported for subcutaneous fat. Numerical mean and full range values for C1.1-11 (with no history of liver disease) are reported in Supporting Information Table S2.
works using multi-peak fat models.\textsuperscript{16,17,37} In this work, $T_2^*$ decay is included in the signal model (Equation 1) to improve water and fat separation and additionally map $T_2^*$ for liver iron content assessment. Dictionary-based methods\textsuperscript{37,38} could be investigated for single step FF, water and fat $T_1$, $T_2$, $T_2^*$, and $B_0$ estimation; however, this may lead to challenging dictionary sizes while relying on single voxel information. Chemical shift based approaches\textsuperscript{18,39} usually enforce $B_0$ field smoothness for robust estimation and water-fat separation. Previously proposed water-fat MRF works have used these approaches\textsuperscript{16,40,41} but mapped less parameters and required an additional (separately acquired) $B_1$ map.

Phantom experiments show high coefficients of determination between the proposed approach and reference measurements for the $T_1$, $T_2$, $T_2^*$, and FF ranges of interest. Good agreement of the $B_0$ maps (Figure 4) and low FF errors compared to those observed in simulations suggest accurate $B_0$ estimation. Sequence modifications might be necessary if the tissue of interest has long $T_2$ and $T_2^*$. Biases with respect to conventional and literature values were observed in vivo. These are expected for a few reasons: (1) Magnetization transfer effects in biological tissues and flow are expected to bias MRF\textsuperscript{42-44} as well as conventional\textsuperscript{45} measurements. (2) In vivo conventional mapping present their own biases and are suboptimal references (e.g., MOLLI has a tendency to underestimate $T_1$\textsuperscript{46,47} and T2-GRASE to overestimate $T_2$ compared to T2-prep bSSFP\textsuperscript{48}). Moreover, previously proposed MRF approaches\textsuperscript{17,20,49} have shown overestimation of $T_1$ when compared to MOLLI and underestimation of $T_2$ compared to conventional scans in vivo. (3) Acquisitions were performed sequentially during separate breath-holds leading to potentially mis-registered MRF and conventional measurements. (4) Fat model simplifications led to overestimation of $T_2^*$ in subcutaneous fat in simulations and in vivo. Despite these biases, good correlations were obtained in vivo between the proposed approach and conventional techniques. The proposed approach requires shorter scan time and fewer breath-holds while keeping similar resolutions as those proposed in recent multi-parametric\textsuperscript{50} and NAFLD clinical studies.\textsuperscript{51-53} Additionally, it provides inherently
co-registered maps ensuring mapping of the same slice of the liver for all parameters and enabling pixel-wise multi-parametric measurements.

Water-fat separation and $T_2^*$ corrections do not correct for the effect of iron content on $T_1$ and $T_2$ measurements directly as seen in subject C2.4 (Figure 5); however, additional corrections could be incorporated to better correlate results with biopsy fibrosis scores in the presence of iron overload. This would require simulating multiple compartments and magnetization transfer effects while making strong model assumptions. Further investigation of the precision (reproducibility) and accuracy of this framework in clinical settings is still needed.

5 | CONCLUSION

A multi-echo MRF framework is proposed for fast and simultaneous quantitative multi-parametric liver tissue characterization. Co-registered parametric maps ($T_1$, water $T_2$, $T_2^*$, and FF) are acquired in a single breath-hold (13.9 s). The proposed approach was validated in phantoms showing good correlation with reference measurements. The feasibility of the proposed approach was evaluated in vivo in 16 subjects. Future investigation in patients with liver disease is now warranted.

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CONFLICT OF INTEREST
Torben Schneider is employed by Philips Healthcare.

ORCID
Olivier Jaubert https://orcid.org/0000-0002-7854-4150
Gastão Cruz https://orcid.org/0000-0002-7397-9104
Aurélien Bustin https://orcid.org/0000-0002-2845-8617
Claudia Prieto https://orcid.org/0000-0003-4602-2523

TWITTER
Olivier Jaubert @olivier_jaubert

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**SUPPORTING INFORMATION**

Additional Supporting Information may be found online in the Supporting Information section.

**FIGURE S1** A, T1, T2, chemical shift (ppm) and peak weight (for each of the 6 peaks considered for fat. B, The six peak and combined fat signal evolutions are simulated using the EPG framework and model parameters provided in (A). C, Example of a simulated signal evolution for a 50-50% mix of liver (water T1 = 650ms, water T2 = 50ms) and fat. D, Within TR signal evolution for pure liver, pure fat and 50-50% mix for the first MRF timepoint

**FIGURE S2** A, T2 maps obtained using the proposed MRF framework and the first 3, 6, 9 and 12 echoes of a 12-echo MRF acquisition. B, Corresponding Bland-Altman plots comparing 3, 6, 9 and 12 echoes MRF T2 maps with the reference measurement (12-echo GRE). Please note that the vertical scales change between the plots

**FIGURE S3** Numerical simulations from realistic water T1, water T2, FF, T2* and B0 maps (Ground Truth, top row) and resulting maps obtained using the proposed framework (second row). Absolute error in the liver was <1% for all parameters (third row). T2* estimation errors in the subcutaneous fat in simulations suggests that the fixed peak weight model induces T2* overestimation in fat. T2* overestimation in fat was also observed in vivo experiments

**FIGURE S4** Numerical simulations with fixed water T1 (650 ms), water T2 (50 ms), FF (20%), B0 (0 Hz) and T2* (30 ms). Errors were introduced to the B0 field (left-right gradient) and T2* (top-down gradient) estimations (Top row) and used instead of the estimated maps before water-fat separation. The resulting absolute errors for water T1, water T2 and FF estimation (second row) and zoom in ([−4:4] for T2* errors and [−20:20 Hz] errors) on the absolute error maps (third row) are shown. The third row exhibited maximum errors of 20 ms, 1 ms and 9.36% errors for water T1, water T2 and FF estimation respectively

**FIGURE S5** Numerical simulations from realistic water T1, water T2 and FF maps. Errors were introduced to the B0 field
(left-right gradient) and $T_2^*$ (top-down gradient) estimations and used instead of the normally estimated maps before water-fat separation to generate the resulting water $T_1$, water $T_2$ and FF maps (second row) with the proposed MRF approach. Corresponding absolute error maps and reported liver error (white ROI) are shown in the third row

**FIGURE S6** Proposed 9-echo MRF phantom $T_1$, $T_2$, $T_2^*$ and FF maps acquired in a 13.9s scan

**TABLE S1** Acquisition and reconstruction parameters for reference phantom mapping sequences (IRSE, MESE and 12-echo GRE) and conventional in vivo sequences (MOLLI, T2-GRASE, 12-echo GRE)

**TABLE S2** Reported average and range of values ([min, max]) observed in 11 subjects (C1.1-11) with no history of liver disease using the proposed 9-echo liver MRF and conventional MOLLI, T2-GRASE and 12-echo GRE ($T_2^*/FF$) for the liver, muscle, spleen and subcutaneous fat. Literature values when available were reported for $T_1$, $T_2$, $T_2^*$ and FF. Please note that MRF water $T_1$ and MRF water $T_2$ values are reported for the liver, muscle and spleen and MRF fat $T_1$ and MRF fat $T_2$ values for subcutaneous fat

**TEXT S1** Number of echoes required for liver MRF $T_2^*$ estimation

**TEXT S2** Liver MRF simulations

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