Fast $T_2$ Mapping with Multiple Echo, Caesar Cipher Acquisition and Model-Based Reconstruction

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**Purpose:** Fast, quantitative $T_2$ mapping is of value to both clinical and research environments. However, many protocols utilizing fast spin echo (FSE) pulse sequences contain acceleration-induced artifacts that are compounded when fitting parameter maps, especially in the presence of imperfect refocusing. This work presents a $B_1$-corrected, model-based reconstruction and associated Cartesian FSE phase-encode ordering that provides enhanced accuracy in $T_2$ estimates compared with other common accelerated protocols.

**Theory and Methods:** The method, known as multiple echo, Caesar cipher acquisition and model-based reconstruction (ME-CAMBREC), directly fitted $T_2$, flip angle, and proton density maps on a row-by-row basis to k-space data using the extended phase graph model. Regularization was enforced in order to minimize noise amplification effects. ME-CAMBREC was evaluated in computational and physical phantoms, as well as human brain, and compared with other FSE-based $T_2$ mapping protocols, DESPOT2, and parallel imaging acceleration.

**Results:** In computational, phantom, and human experiments, ME-CAMBREC provided $T_2$ maps with fewer artifacts and less or similar error compared with other methods tested at moderate-to-high acceleration factors. In vivo, ME-CAMBREC provided error rates approximately one-half those of other methods.

**Conclusion:** Directly fitting multi-echo data to k-space using the extended phase graph can increase fidelity of $T_2$ maps significantly, especially when using an appropriate phase-encode ordering. *Magn Reson Med 000:000–000, 2014. © 2014 Wiley Periodicals, Inc.*

**Key words:** $T_2$; fast imaging; extended phase graph; model-based reconstruction; nonlinear reconstruction

**INTRODUCTION**

The fast spin echo (FSE, also TSE, RARE) pulse sequence is widely used in magnetic resonance imaging (MRI) due to its ability to quickly acquire high-resolution $T_2$-weighted images, which are relatively insensitive to spatial magnetic field variations (1). However, when FSE is used for quantitative $T_2$ mapping, image artifacts caused by amplitude modulation in the phase-encoded direction of k-space, particularly in the presence of $B_1$ field variations, can induce significant errors in estimated relaxation time values. The sensitivity to $B_1$ field variation can be addressed through use of the extended phase graph (EPG) algorithm (2), and model-based reconstruction of parametric images such as $T_2$ maps from k-space data can inherently eliminate acceleration-induced artifacts in FSE images (3,4). This work integrates these ideas into a fast and $B_1$-insensitive method for $T_2$ and proton density mapping.

The EPG algorithm for calculating echo amplitudes (2) has received attention recently for its ability to compensate for indirect- or stimulated-echo pathways in multiple spin-echo acquisitions, such as those used for FSE (5–7), $T_2$ mapping (8,9), or multiexponential $T_2$ analysis (10,11). These coherence pathways occur as a result of refocusing flip angles that deviate from $180^\circ$, which may be by design (5–7) or due to in-plane field variations or slice profile effects. Prasloski et al. (12) also used the EPG algorithm for analysis of combined gradient and spin-echo imaging, which provided accelerated $T_2$ mapping at a predictable signal-to-noise ratio cost (13), but the EPG analysis remained decoupled from the reconstruction problem.

In most Fourier-reconstructed fast $T_2$ mapping methods, two general approaches are used to provide both acceleration and sensitivity to $T_2$. In the first, multiple acquisitions are made using a single (usually center-out) k-space trajectory prepared by a spin echo period to provide $T_2$ image contrast. In the second method, the k-space trajectory is altered (14) [or data is reordered, such as in view-shared protocols (15,16)] from one image to the next in order to weight the center of k-space differently without extending the echo train. Here, the former is referred to as an echo-prepared (EP) acquisition and the latter as a variable trajectory (VT) acquisition. Whereas EP techniques waste information before or after the echo trains, each VT image will have a unique set of artifacts that will be compounded when fitting $T_2$ maps. Because both of these acquisition strategies are tailored to the requirements of Fourier-reconstructed images, a novel “Caesar cipher” acquisition strategy—named after the famed emperor’s method of encoding text by wrapping the alphabet modulo its length—which is more...
suited to the proposed model-based reconstruction algorithm was developed. The proposed method is referred as multiple echo, Caesar cipher acquisition and model-based reconstruction (ME-CAMBREC).

THEORY

ME-CAMBREC simultaneously fits three parameters on a voxel-wise basis—the relaxation time constant $T_2$, refocusing pulse flip angle $\theta$, and the complex transverse magnetization immediately after excitation, $M_\perp$. First, $N_Q$ FSE k-space pseudo images $Q_j (k_{ro}, k_{pe})$ (with unique effective echo time indexed by $j$, $j = 1$ to $N_Q$) are acquired in a number of echo trains, $N_T$, less than the number of phase-encoded lines in $Q$, depending on the desired acceleration. (Note that when $N_T = N_{pe}$, the number of points in the phase encoded direction, the acquisition requires the same scan time as a nonaccelerated multiple spin-echo pulse sequence.) Since all points along the readout direction of a given line occur in the same echo and are therefore assumed to have the same $T_2$ weighting, $Q$ can be Fourier transformed in one dimension to create hybrid-space images $H_j (x, k_{pe})$. The ensemble of points corresponding to a certain spatial position, $x_0$, in the read direction (i.e., all phase encoded points $k_{pe}$ across all $N_Q$ pseudo images for a given $x = x_0$) are collected in a vector $S_{x_0}$ (indexed by $n$) and paired with vectors $t$ and $k_{pe}$, the echo times and phase encode $k$-values at which $S_{x_0}$ were collected, respectively. Figure 1 demonstrates this data transformation in graphical form.

Additionally, a reference image, $I$, is generated by inverse two-dimensional (2D) Fourier transform of the $Q_1$ image, i.e. the k-space image with the shortest effective echo time, $I = F^{-1}_{2D}[Q_1] = F^{-1}_{pe}[H_j]$. This reference image is used in the model-based reconstruction as an initial guess, as part of a regularization penalty, and to threshold the parameter maps a priori. For each row of data (i.e., each value of $x_0$), voxels with magnitude $< z \%$ of the maximum of $|I(x_0, y)|$ are not fitted and constrained to zero.

Once the vector $S_{x_0}$ has been constructed for a given image row, $M_\perp$, $T_2$, and $\theta$ are fitted simultaneously using the following cost function

$$
cost = \sum_{n=1}^{N_Q} \sum_{l=1}^{N_T} \left| \sum_{j=1}^{L} C_{c,l} M_{i,l} EPG(t_n, T_1 = 1, T_2 = 1, \theta = 1) \right|^2 \times \exp \left( -\frac{i2\pi l k_{pe,n}}{L} - \frac{S_{n,c}}{L} \right)^2 + \lambda \cdot \rho(M_\perp, I)
$$

[1]

where $EPG(\cdot)$ represents the extended phase graph calculation, $l$ is an index corresponding to $y$ position ($l=1$ to $L$), and $\rho$ is the regularization function, defined below, which is weighted in the cost by $\lambda$. The parameter $C_{c,l}$ is the complex coil sensitivity at position $l$ of the $c$th receive coil element of an $N_C$ coil array.

The regularization is a fractional variation constraint designed to penalize added sharpness in the fitted $M_\perp$ over the reference image $I$:

$$
\rho = \sum_I \left( \frac{\text{Re} \left[ M_{i,l+1} - M_{i,l} \right]}{\text{Re} \left[ M_{i,l+1} + M_{i,l} \right]} - \frac{\text{Re} \left[ I_{i,l+1} - I_{i,l} \right]}{\text{Re} \left[ I_{i,l+1} + I_{i,l} \right]} \right)^2
$$

$$+
\sum_I \left( \frac{\text{Im} \left[ M_{i,l+1} - M_{i,l} \right]}{\text{Im} \left[ M_{i,l+1} + M_{i,l} \right]} - \frac{\text{Im} \left[ I_{i,l+1} - I_{i,l} \right]}{\text{Im} \left[ I_{i,l+1} + I_{i,l} \right]} \right)^2
$$

[2]

The spatial difference taken in the penalty function makes this regularization similar in spirit to total variation constraint, but with the following important distinctions: 1) the use of a blurred reference image, $I$, which will reduce the penalty burden in regions of genuine spatial variation of $M_\perp$, 2) the normalization by the sum of the values of $M_\perp$ or $I$, which is required due to the different scaling of the reference image caused by signal decay before the first echo, and 3) the usage of a 2-norm rather than a 1-norm, for ease of computation. The behavior of this regularization is intuitively straightforward. When the penalty weighting factor $\lambda$ is close to zero, noise amplification from phase encoded lines acquired near the end of the echo train causes significant image degradation. As the weighting factor increases, the $M_\perp$ image becomes increasingly similar to a scaled version of $I$. The regularization used here is not intended to be optimal, but rather as an intuitive use of a priori knowledge regarding the $M_\perp$ map. Further study may find alternate regularization strategies that provide better
FIG. 2. Artifact and k-space trajectory. The upper portion of the figure represents the acquired echo train from shot to shot as effective echo time increases; the solid line is a center-out acquisition common to most FSE schemes, while the dashed line demonstrates a later TEeff using the given acquisition strategy. In the echo-prepared image, blurring (but not ghosting) is present. Both types of artifact exist in other sampling schemes, with the proposed Caesar cipher acquisition clearly being unsuited to Fourier-based reconstruction.

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performance, such as a sparsity constraint over some transform of the data.

Optimal tuning of \( \lambda \) is a nontrivial process. Here, a non-linear L-curve approach was used (17), where the optimal \( \lambda \) is selected as the point where a marginal increase in penalty weighting begins to induce a notable increase in solution residuals. Mathematically speaking, the value of \( \lambda \) chosen is the value that maximizes the curvature, \( \kappa \), of a log-residual versus log-penalty graph parameterized by \( \lambda \):

\[
\kappa = \frac{\frac{r}{\lambda^2} \left( 1 + \frac{r^2}{\kappa^2} \right)^{1/2} \left( 1 + \frac{r^2}{\kappa^2} \right)^{1/2} \left( \frac{r}{\lambda^2} \left( \frac{r}{\kappa^2} \right)^{1/2} \left( 1 + \frac{r^2}{\kappa^2} \right)^{1/2} \right)}{1 + \frac{r^2}{\kappa^2}} - \left( \frac{r}{\lambda^2} \left( \frac{r}{\kappa^2} \right)^{1/2} \left( 1 + \frac{r^2}{\kappa^2} \right)^{1/2} \right)}
\]

This equation was adapted from Gulliksson and Wedin (18), correcting for typographical errors. Here, \( r \) is the sum-squared residual term, and \( p \) is the scalar penalty term from Eqs. 1 and 2. The gradient vector with respect to model parameters \( \beta \) is defined as \( \nabla \beta p \), and \( H \) is the Hessian (second derivative) matrix of the entire cost function. By plotting \( \kappa \) against \( \lambda \), an optimal value for \( \lambda \) can be estimated; in the following, a single value of \( \lambda \) was selected for each image using a small sample of the image rows.

ME-CAMBREC also uses a novel acquisition scheme to further reduce noise amplification. Unlike Fourier reconstruction, which introduces artifacts related to the properties of a k-space amplitude modulation function, image noise in model-based reconstructions will be amplified at any spatial frequencies not sampled at early echo times. It is, therefore, disadvantageous to acquire the high spatial frequency lines of Cartesian k-space at the end of every echo train. Instead of using either the EP or VT methods to provide \( \text{T}_2 \) contrast, ME-CAMBREC provides \( \text{T}_2 \) contrast by sampling phase encoded lines in a Caesar cipher-like (CC) pattern. This trajectory can be considered an application of the rotated rapid acquisition relaxation enhanced (19) methodology to a center-out framework. In this acquisition strategy, the first echo train(s) acquire a center-out image \( (Q_1) \). The next pseudo images \( (Q_j, j = 2, 3, \ldots) \) are acquired by pushing the entire trajectory down the echo train and moving the last phase encode lines—those which would require the echo train to be extended if they were acquired in center-out order—to the beginning of the echo train. For example, given the first trajectory \( k_{pe} = 0, 1, 2, 0 \), the second trajectory is \( k_{pe} = 2, 0, 1, 2, 0 \), and so on, as shown in Fig. 2. Acquiring fewer pseudo-images than the echo train length provides accelerated acquisition compared to conventional multiple spin echo imaging.

METHODS

Computational Studies

The ME-CAMBREC method was compared with analysis of Fourier-reconstructed images using previously established trajectories, namely the EP and VT methods. The computational phantom used for each experiment was as follows: a 128 \((N_x) \times 128 (N_y)\) Shepp-Logan phantom with intensity values ranging from 0.8 to 1 was used as a proton density map; each compartment of that map had its own uniform \( \text{T}_2 \), ranging from 60 to 500 ms. A flip angle map varying smoothly across the image over 110°–130° was used for all EPG-based analysis, and a similar map varying from 170°–190° was used for exponential model fitting. A four-shot \((N_T = 4N_Q)\) mock acquisition using each trajectory was performed with the following parameters: echo spacing (ESP) = 10 ms, echo train length (ETL) = 32 echoes, effective echo time (TEeff) = 10, 90, 170, 240 ms for CC and EP, TEeff = 10, 40, 90, 160 ms for VT. (The VT acquisition scheme used lower effective echo times because it is not suited to acquiring the \( k_{pe} = 0 \) line after the halfway point of the echo train; doing so would require an outside-in type trajectory.) Since \( N_T = 4N_Q = 16 = N_{pe}/8 \), the acceleration rate, \( R \), for all mock acquisitions was equal to 8. Noise was added to the data at a magnitude image SNR of 15 for the median intensity voxels of the Shepp-Logan phantom, which.
represents about the lowest SNR permissible for quantitative imaging. The ME-CAMBREC reconstructions were regularized using optimal weighting levels (see the “Fitting Algorithm” section later in this paper). The resultant parameter maps were compared with the actual underlying parameters, as were reconstructed maps using data with a median SNR of 30, 60, and 120. Additionally, parameter maps from Fourier-reconstructed voxel-wise fitting to the extended phase graph and exponential models were created for comparison using both EP and VT trajectories. Error metrics were calculated using root-mean-square (RMS) errors relative to known values, reflecting parameter estimate variance more than bias error at low SNR and the opposite at high SNR.

In order to compare the proposed method with a more disparate fast T2 mapping protocol, DESPOT2 (20), the Cramer-Rao lower bound of the variance of T2, was calculated for both ME-CAMBREC and a sample implementation of DESPOT2 (21) using the same Shepp-Logan phantom. The mean coefficient of variation of T2 estimates (defined as the Cramer-Rao bound divided by the true value) across an image row was calculated. Additionally, since each method will have unique noise characteristics and scan times, these were accommodated in an overall calculation of SNR efficiency (i.e., T2 SNR per unit root scan time). The DESPOT2 acquisitions simulated the following parameters: for spoiled gradient-recalled echo, repetition time (TR) = 11.7 ms, flip angles = 4° and 15°, receiver bandwidth = 15.6 kHz; for steady-state free precession, TR = 3.7 ms, flip angles = 15° and 55°, receiver bandwidth = 62.5 kHz. Both methods assumed a 256 × 256 in-plane matrix, with DESPOT2 acquiring 128 points in the third dimension and ME-CAMBREC acquiring this many 2D slices. Scan parameters for ME-CAMBREC were adapted from the human imaging protocol (see the “Human Experiments” section later in this paper), with the receiver bandwidth adjusted to 36.6 kHz to acquire the new matrix size in the same echo spacing. Simplifying assumptions for DESPOT2 included instantaneous approach to steady state, no compressed sensing/partial Fourier acceleration, and a priori knowledge of confounding factors such as off-resonance/flip angle maps, which are often measured in practice.

Phantom Studies
An eight-tube phantom containing copper sulfate and manganese chloride solutions (T2 range: ~15–150 ms) was imaged on a 4.7 T/31 cm Agilent/Varian (Santa Clara, California, USA) DirectDrive MRI system equipped with single element volume coil (NC = 1, Eq. 1) using CC, EP, and VT k-space sampling methods. A multiple spin echo pulse sequence with constant gradient dephasing in every interecho period was used with the following parameters: matrix size = 64 (NQ × Np); ETL = 16 echoes; TEoff = 5, 25, 45, and 60 ms for CC and EP and 5, 15, 25, and 30 ms for VT; refocusing flip angle = 120°; NQ = 4; NV = 16; ESP/TR = 5/2500 ms; slice thickness = 2 mm; refocusing pulse width = 5 mm. It should be noted that this wide refocusing pulse width would require a 1.5-mm gap between slices if the acquisition were performed in multislice mode, although only one slice was acquired here. These data were subjected to ME-CAMBREC (CC) and Fourier-reconstructed EPG analysis (EP, VT). The T2 maps resulting from these protocols were compared with EPG analysis of a fully sampled multiple spin echo dataset acquired using the same scan parameters and double the echo train length. The errors were calculated as relative errors of the mean of each sample tube, reflecting systematic bias and artifact more than noise characteristics.

Human Studies
The brain of a healthy volunteer was imaged on a 3.0-T Philips (Best, The Netherlands) Achieva MRI system using an eight-element head coil (NC = 8, Eq. 1) and a multiple spin echo pulse sequence with uniform echo spacing and constant gradient dephasing in every interecho period. The following sequence parameters were used: TEoff = 32; ESP/TR = 10/2500 ms; slice thickness = 5 mm (excitation)/15 mm (refocusing); in-plane resolution = 2 × 2 mm2; number of averaged acquisitions = 1; sensitivity encoding (SENSE) acceleration factor = 1; and image matrix = 105 (NQ × Np). This resulted in a scan time of 4 min, 23 s. (The slice gap required if a user wished to perform this scan in multislice mode would be 5 mm.) Coil sensitivity maps (CC, estimated from the first echo image using a cubic polynomial basis. Two fully sampled multiecho image sets were acquired, one using refocusing pulse flip angles prescribed at 120° and the other at 180°, in order to compare EPG methods with exponential decay fitting. These data were subsampled into datasets emulating CC, EP, and VT acquisition schemes, each with NQ = 4, NV = 16 (Np/6.6), and ETL = 26 (to roughly match the matrix size of 105). The CC ordered subsample used TEoff = 10, 80, 150, and 210 ms; for VT, the subsample used TEoff = 10, 40, 60, and 110 ms; and for EP, the subsample used TEoff = 10, 20, 30, and 50. The EP TEoff times were low in order to prevent extending the echo train and substantially changing the total scan time between protocols. These subsampled data represented an R = 6.6 acceleration compared with the fully sampled data. These data were analyzed in a similar manner to the phantom studies, specifically focusing on a heterogeneous rectangular region of interest containing both white matter and deep gray matter, but excluding cerebrospinal fluid due to its long T2. For all accelerated methods, error was defined as the difference between estimated T2 values and those estimated from fully sampled data. Error metrics were tabulated as RMS errors over a heterogeneous region, reflecting both noise and artifact. For comparison, previously published (22) T2 values of the dominant signal component of various brain regions have also been presented.

ME-CAMBREC was also compared with the SENSE method of parallel imaging acceleration (23). The same coil sensitivity maps were used for ME-CAMBREC and SENSE. ME-CAMBREC was performed using fully sampled data reduced by a factor of R = 2 (NQ = 13, NV = 52 ≈ Np/2). The ME-CAMBREC T2 map was compared with one resulting from voxel-wise EPG fitting of
Table 1

<table>
<thead>
<tr>
<th>Reconstruction + Acquisition</th>
<th>( r_{\text{rms}, M+} ) (a.u.)</th>
<th>( r_{\text{rms}, T2} ) (ms)</th>
<th>( r_{\text{rms}, \theta} ) (°)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Model-Based + CC (ME-CAMBREC)</td>
<td>0.21</td>
<td>8.3</td>
<td>22.0</td>
</tr>
<tr>
<td>Fourier-EPG + EP</td>
<td>0.15</td>
<td>15.7</td>
<td>21.7</td>
</tr>
<tr>
<td>Fourier-EPG + VT</td>
<td>0.16</td>
<td>14.0</td>
<td>17.4</td>
</tr>
<tr>
<td>Fourier-EXP + EP</td>
<td>0.05</td>
<td>7.6</td>
<td>—</td>
</tr>
<tr>
<td>Fourier-EXP + VT</td>
<td>0.05</td>
<td>10.8</td>
<td>—</td>
</tr>
</tbody>
</table>

Results are from the computational study utilizing four FSE images (at SNR = 60) for each method. The labels, such as Fourier-EPG + EP, denote the method of reconstruction (Fourier transform or model-based fitting), the decay model used in the fit (EPG or exponential [EXP]), and the k-space view ordering (CC, EP, or VT). ME-CAMBREC provided lower RMS errors in T2 estimates than any other method except echo-prepared FSE fit to an exponential decay curve. a.u., arbitrary units.

32 SENSE-reconstructed images with an acceleration factor of \( R = 2 \). In turn, ME-CAMBREC was performed on a data subset that was both undersampled in k-space (\( R = 2 \) [i.e., all odd \( k_p \) lines were excluded]) and undersampled in the echo dimension (\( N_Q = 13 \), \( N_T = 26 \)) for a total acceleration factor of roughly \( R = 4 \). This “sub-Nyquist” ME-CAMBREC reconstruction was compared with purely accelerating in the k-spatial dimension (SENSE, \( R = 4 \)) and purely accelerating in the echo dimension with \( R \approx 4 \) (ME-CAMBREC, \( N_Q = 7 \), \( N_T = 28 \approx N_p / 4 \)).

Fitting Algorithm

For fitted voxels, initial guesses for \( M_a \) (real and imaginary values) were taken from the image \( I \). \( T_2 \) was initialized to a linearized least-square estimate for all points in \( S \) where \( k_p = 0 \), and \( \theta \) was initialized to the prescribed value. For all cases, \( T_1 \) was constrained to 1 s, and the intensity threshold, \( z \), was set to 5 %.

The iterative nonlinear least-squares solver \( \text{lsqnonlin} \) in MATLAB (MathWorks, Natick, Massachusetts, USA) was used to minimize the cost function. In order to accelerate the computation of each iteration, the gradient of the cost function with respect to model parameters was calculated using a direct analytical formulation of the penalty gradient and a computational shortcut for the gradient of the sum-squared residual:

\[
\frac{\partial \text{cost}}{\partial \beta} = 2 \text{Re} \left[ \sum_i \frac{\partial M_{a, \text{EPG}}(t_i, T_1 = 1 \text{s}, T_2, \theta)}{\partial \beta} \right] \times \exp \left( \frac{-2\pi i a k_p a}{M} \right) r_n^* \right] + \lambda \frac{\partial p}{\partial \beta}
\]

where \( r_n^* \) is the complex conjugate of the residual at index \( n \), and \( \beta \) represents any of the fitted parameters. This shortcut is enabled through the knowledge that each reconstruction parameter \( \beta \) only appears in the equations of a single spatial point \( a \). An extension of this equation into a second differential order can be used to expedite calculation of the cost function’s Hessian matrix as well, for use in determining the optimal regularization level. The entire algorithm allows for fitting one image row in 15–30 s on standard personal computer hardware, but this should not be considered an optimized reconstruction time.

RESULTS

Computational Experiments

Table 1 summarizes the RMS error \( (r_{\text{rms}}) \) of all three reconstructed parameter maps from simulated data, excluding cerebrospinal fluid-like regions with very long \( T_2 \) (500 ms) that would otherwise dominate error calculations. The errors presented were for data with a median SNR of 60. Propagation of error laws dictate that parameter estimate variance should decrease at least linearly with the standard deviation of the image noise, but Fig. 3 shows a diminishing return in total RMS error due to inherent bias in the estimators. Model-based reconstruction of CC k-space encoded data (i.e., ME-CAMBREC) performed well relative to Fourier-reconstructed protocols. Perhaps unsurprisingly, the simple echo-prepared, exponential fit FSE protocol demonstrated high sensitivity to \( T_2 \) and the lowest error when near-perfect refocusing was simulated.

ME-CAMBREC was discovered to have an SNR efficiency (i.e., \( T_2 \) SNR per unit root scan time) 2.4 times higher than that of a previously published four-angle implementation of DESPOT2. This was primarily due to the sensitivity of multiple spin echo sequences compared with steady-state sequences.

Phantom Experiments

Figure 4 shows \( T_2 \) maps (top) and relative errors (bottom) from the phantom experiments for different acquisition and analysis protocols. The ME-CAMBREC method performed well across the range of \( T_2 \) times, with relative

![Image](https://via.placeholder.com/150)
errors of <5%. Although any EPG analysis of the CuSO4 solutions \( (T_1 \approx T_2) \) in the presence of imperfect refocusing will result in a small bias in the \( T_2 \) estimates (8), Fig. 4 shows that the unknown \( T_1 \) does not result in additional error or artifact in ME-CAMBREC maps. As was the case in the computational study, accelerated Fourier-reconstructed EPG analysis performed poorly for certain \( T_2 \) times, especially short ones such as those of tubes 4 and 7. \( T_2 \) was underestimated by both Fourier FSE methods, in some cases by more than 30%. Severe artifact was also present in both Fourier-based \( T_2 \) maps.

Human Experiments

Figure 5 shows \( T_2 \) maps from the in vivo human brain imaging. The upper left frame shows a \( T_2 \) map generated from the fully sampled 120° refocused multiple spin echo sequence. Each of the other frames shows a \( T_2 \) map derived from a subset of the data which could be acquired in less than one-sixth the time; the images in Fig. 5b–5d were taken from the 120° refocused scan and the images in Fig. 5e and 5f used data refocused by 180° pulses. As in the phantom experiments, ME-CAMBREC generated a \( T_2 \) map most closely resembling that of the fully sampled dataset. The middle and lower panels of Fig. 5, those corresponding to Fourier-reconstructed images, show enhanced artifact such as blurring and asymmetry compared with the maps from fully sampled data and ME-CAMBREC. Unlike in the computational experiment (Table 1), fitting in vivo high-refocusing flip angle data to the exponential model (Fig. 5e, 5f) did not provide better error rates than the proposed method; these error rates were similar to those of maps fitted to the EPG model.

Table 2 quantitatively compares the \( T_2 \) estimates of various cerebral structures made using accelerated Fourier-based \( T_2 \) mapping methods, ME-CAMBREC, fully sampled data, and values from the literature. Fully
sampled data from the present study agreed well with literature values, showing no systematic bias. ME-CAMBREC accelerated at $R = 6.6$ underestimated $T_2$ relative to the fully sampled data, but differences were comparable in absolute value to those between the fully sampled data and literature. Similar absolute differences in estimated $T_2$ resulted from Fourier reconstruction of $R = 6.6$ EP trajectory data. The $R = 6.6$ VT trajectory data underestimated $T_2$ with somewhat greater absolute differences to fully sampled data. In all cases, voxel-wise paired $t$ tests indicated that differences between fully sampled data from the present study and all accelerated acquisitions were statistically significant.

The comparison between ME-CAMBREC and SENSE acceleration/EPG fitting is presented in Fig. 6. At acceleration factor $R = 2$, the methods are comparable, with SENSE performing better in regions with little aliasing and worse in regions with more intense aliasing. At
higher acceleration rates \((R = 4)\), ME-CAMBREC outperformed SENSE as visible in the left halves of Fig. 6e and 6f. Fig. 6d shows the reaching of an \(R = 4\) acceleration by combining subsampling in k-space, and the echo dimension by a factor of 2 each provided a poorer result than ME-CAMBREC with \(R = 4\). That is, one can in principle combine traditional parallel acceleration with ME-CAMBREC, but for this case at least, acceleration by ME-CAMBREC alone was superior.

**DISCUSSION**

In experimental environments designed to test noise propagation (computational), artifact and systemic error (phantom), and a combination of the two (human), ME-CAMBREC performed at least comparably to the best conventional FSE methods tested. Noise propagation was kept similar to Fourier-reconstructed exponential fitting (Table 1 and Fig. 3), despite significant artifact reduction (Fig. 4). The in vivo implementation, in which both noise and artifact can contribute to significant errors, yielded the greatest advantage over the other accelerated \(T_2\) mapping methods tested. Visually, all ME-CAMBREC images presented here contain smearing artifacts in the phase encode direction that are not smooth in the readout direction, apparently caused by the row-by-row nature of the reconstruction. It is possible that extending the algorithm to jointly fit multiple rows with 2D regularization could alleviate this shortcoming at the cost of computational complexity. There is also an apparent underestimation of \(T_2\) when averaged across regions of interest (Table 2) that can be seen in VT Fourier reconstruction fitted to the EPG model as well. This may imply that the artifact is caused by noise amplification at moderate spatial frequencies interacting with the EPG fitting. However, the quantitative errors of these artifacts and underestimation remain lower than those of Fourier-reconstructed fitted \(T_2\) values. Whereas ME-CAMBREC bias, like that of Fourier-based accelerated methods, limits accuracy at high SNR (Fig. 3), deeper control over regularization-induced bias as compared with image artifact permits \(T_2\) bias to be somewhat tunable parameter, able to be traded off for estimate precision.

For high acceleration factors, each of the studies presented demonstrated that Fourier-reconstructed EPG fitting induces high errors in \(T_2\) maps. This is not surprising, since the EPG model is a three-parameter model involving oscillating signal behavior: when fitting to a small subset of effective echo times, sensitivity to oscillations \((\theta)\) and decay \((T_2)\) must be traded off through the selection of a proximate or disparate set of time points. However, the disagreement between the computational and human studies regarding the expected error of EP-FSE when fit to the exponential model is less parsimonious. The computational study suggests that EP-FSE may be a better option than model-based reconstruction when near ideal refocusing pulses are realized. As this is a Fourier-reconstructed approach, though, the results of EP-FSE will be heavily dependent on the imaging subject’s sensitivity to artifact, which has been shown to rely on many additional factors, such as feature size and echo train length (24). The large feature size of elements of the Shepp-Logan phantom, combined with the slowly varying underlying \(T_2\) distribution, likely contributed in large part to the apparent superiority of the EP-FSE protocol.

In all experiments, ME-CAMBREC performed at or above the standards of conventional FSE \(T_2\) mapping at a given acceleration factor (from 4 in the phantom experiments to 8 in the computational experiments). However, a wide variety of other fast \(T_2\) mapping methods exist. The proposed method was compared directly with DESPOT2 by way of SNR efficiency, but no experiments were performed to test other aspects of the method, which may or may not be limiting factors. For example, DESPOT2 can provide single-slice parameter maps at a slightly faster rate than ME-CAMBREC, although at lower precision due to differences in sensitivity. It should also be noted that DESPOT2 is typically run as a three-dimensional protocol, whereas extending ME-CAMBREC to three dimensions would be nontrivial. The model-based reconstruction would have to be applied simultaneously in multiple dimensions, both enabling acceleration in a second spatial dimension and creating new challenges in computational stability.

Accelerating using parallel imaging provided excellent results in the case of small acceleration factors \((R = 2)\), as Fig. 6c shows, but at higher acceleration factors \((R = 4)\) generally provided poor results compared with ME-CAMBREC. Using ME-CAMBREC itself as a parallel imaging reconstruction method by sampling k-space in the same sub-Nyquist pattern across all pseudo-images provided lower quality results than purely undersampling in the echo dimension (Fig. 6d, 6e). This is somewhat intuitive, since the number of echoes acquired is typically many times larger than the number of elements in a receive array, allowing more degrees of freedom in that dimension. Readers should note that undersampling k-space in a unique sub-Nyquist pattern between pseudo images (e.g., all even k-space lines for one image and all odd lines the next) is essentially equivalent to Nyquist-sampled ME-CAMBREC, since all data are fitted simultaneously.

Another accelerated \(T_2\) mapping method that should be considered is view-shared projection-reconstruction (15,16), such as k-space weighted image contrast (KWIC). One primary advantage KWIC maintains over ME-CAMBREC is motion insensitivity due to the repeated sampling of the center of k-space. Otherwise, KWIC is still somewhat vulnerable to high-spatial frequency image artifact and requires more scan time: the typical KWIC scan requires 32 echo trains, while the highest-accelerated method proposed here used only 16 excitations. Variations on PR-FSE have included a model-based reconstruction (3), which shares certain benefits of ME-CAMBREC with the motion insensitivity and data redundancy of KWIC. While this is certainly advantageous from a problem conditioning perspective, the Cartesian approach used by ME-CAMBREC and at least one other model-based \(T_2\) mapping method (25) can be used to separate reconstruction into \(N_e\) independent inverse problems, simplifying the computation considerably. Ultimately, this trade-off allows ME-
CAMBREC easier implementation and quicker reconstruction at the cost of parameter SNR relative to radial methods.

One other fast T2 mapping protocol, curve reconstruction via principal component-based linearization with indirect echo compensation (CURLIE), uses PR-FSE, a model-based reconstruction, and the extended phase graph model (4). Although appearing at first glance to be very similar to ME-CAMBREC, CURLIE uses training data to effectively remove artifact from images using linear decompositions, then performs a voxel-wise fitting to the EPG model. Thus, compared to the proposed method, CURLIE has major computational advantages, but applies an intermediate principal component-space rather than attempt to directly fit k-space signal to an underlying model. In the same vein, compressed sensing-based protocols which utilize sparse spaces in the parametric (T2* or T2) dimension (26) or a similar “model dictionary” dimension (27) can theoretically be used with the EPG model for accelerated T2 mapping, especially when combined with a pseudo-random acquisition scheme.

Implementing ME-CAMBREC for volumetric coverage will present challenges for two reasons. As presented here, ME-CAMBREC used wider refocusing pulses compared with the excitation pulse, thereby requiring a slice gap if one wanted to implement a multislice acquisition. In principle, this limitation can be overcome by incorporating the known radiofrequency profiles into the reconstruction model, similarly to prior work (8). Also, under certain circumstances, multislice multiple spin echo acquisitions may be limited by specific absorption rate. However, ME-CAMBREC does offer the ability to use low-angle refocusing pulses without sacrificing image quality or quantitative accuracy, and this feature may be exploited to reduce the stringency of specific absorption rate limits or accelerate further by extending echo trains at the cost of added T2 bias.

Finally, it should be noted that ME-CAMBREC does not accommodate or account for non-monoexponential transverse relaxation, as is known to occur in cerebral white matter due to the presence of myelin (28) and will occur whenever individual voxels include partial volume averages of two or more tissues with widely different T2. One would expect this to be a particular problem in brain regions neighboring cerebral spinal fluid, although Figs. 5 and 6 and a cursory analysis of data therein did not indicate any widespread problem. Extension of ME-CAMBREC to account for multicomponent transverse relaxation would likely be SNR-limited and thus a nontrivial research effort. ME-CAMBREC will face similar challenges/limitations when motion or physiological noise sources significantly alter the signal from the model, although further study is necessary to assess such challenges.

CONCLUSIONS

The work presented here demonstrates a novel regularized model-based reconstruction algorithm for generating T2 maps from undersampled multiecho data, such as those acquired via FSE sequences. A Cartesian acquisition scheme that is better tailored to its advantages than previously established k-space trajectories was also proposed and evaluated. The proposed method, ME-CAMBREC, generated T2 maps with low error in computational, phantom, and human studies, and was demonstrated to be more efficient than the comparably accelerated non-FSE relaxometry protocol DESPOT2. While other accelerated methods may have particular advantages, such as motion insensitivity, the ease of implementation of ME-CAMBREC, combined with its demonstrated accuracy and precision, make it a potentially valuable tool in both research and clinical environments.

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REFERENCES


