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Pattern recognition for rapid T₂ mapping with Stimulate Echo Compensation

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Abstract

Indirect echoes (such as stimulated echoes) are a source of signal contamination in a multi-echo spin-echo T₂ quantification, and can lead to T₂ overestimation if a conventional exponential T₂ decay model is assumed. Recently, nonlinear least square fitting of a slice-resolve extended phase graph (SEPG) signal model has been shown to provide accurate T₂ estimates with indirect echo compensation. However, the iterative nonlinear least square fitting is computationally expensive and the T₂ map generation time is long. In this work, we present a pattern recognition T₂ mapping technique based on the SEPG model that can be performed with a single pre-computed dictionary for any arbitrary echo spacing. Almost identical T₂ and B₁ maps were obtained from in vivo data using the proposed technique compared to conventional iterative nonlinear least square fitting, while the computation time was reduced by more than 14 fold.

Keywords

Quantitative MRI; T₂ mapping; MR parameter; Stimulated echoes; Indirect echoes; Slice imperfection

Introduction

In recent years, there is an increasing interest in T₂ quantification due to its important role in tissue characterization and disease detection [1–5]. T₂ maps can be obtained from images acquired using a single-echo spin-echo (SESE) sequence with varying echo time (TE) but the acquisition of data is time consuming and impractical in clinical setting. Thus a multi-echo spin-echo (MESE) [6] type of acquisition is typically used for T₂ quantification. MESE

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sequences use multiple 180° refocusing radio-frequency (RF) pulses after a 90° RF excitation to generate a train of spin echoes whose amplitudes follow T_2 decay. However, due to RF pulse imperfections the ideal 180° refocusing flip angle (RFA) is not always achieved throughout the imaging volume. Non- 180° flip angles lead to the generation of indirect echoes which are echoes formed after more than one refocusing pulse (such as stimulated echoes). Indirect echoes lead to signal modulations that contaminate the T_2 decay curves [7] resulting in over-estimated T_2 values if the conventional single exponential decay model is used to fit the data.

Recently, Lebel and Wilman [7] proposed a slice-resolved extended phase graph (SEPG) algorithm to model the signal amplitude of MESE T_2 curves which takes into consideration the signal contribution from indirect echoes. The SEPG model, which is based on the extended phase graph (EPG) model proposed by Hennig [8], takes into account the spin evolutions throughout the echo train and the slice profile variation associated with the refocussing pulses. The latter requires dividing the slice profile into segments with each experiencing the same RFA and integrating the EPG model over the slice volume. Significant improvements on the accuracy of T_2 estimates have been shown from data acquired with MESE sequences using the SEPG model. In their work, a nonlinear least-square fitting of the SEPG model was used. The drawback is that iterative nonlinear least square fitting (iNLLS) is computationally expensive due to the continuous evaluation of the SEPG model function with different parameter sets including T_2 , T_1 and strength of the local B_1 field. Moreover, the finer the slice profile segmentation, the longer the computation time. For instance, the fitting of 25,000 pixels with 16 TE points and 85 discrete points along the slice profile takes 29 minutes using the StimFit toolbox [9] which is a state-of-art iNLLS fitting code. Thus, it will take several hours to process a multi-slice data set.

To accelerate the fitting, it is natural to consider pattern recognition techniques. In this type of approach, a dictionary of normalized T_2 decay curves with various T_2 , T_1 , and B_1 values is first generated. Pattern recognition is then performed for each voxel in the image using some norm of the differences between the normalized decay curve and the atoms in the dictionary. When obtaining a match between the acquired curve and an atom in the dictionary, the T_2 value associated with the atom is assigned to the acquired curve. Since the pattern recognition approach is non-iterative and only linear operations are involved, the mapping speed is significantly faster than an iNLLS approach. Pattern recognition techniques allow fitting of measured data with complex signal models. Recently, Ma et al and Ben-Eliezer et al presented parametric mapping techniques using dictionaries generated from the Bloch equation [10, 11].

One main limitation of the pattern recognition approach is the long time needed for the generation of the dictionary, particularly for complex signal models. As a result, it is time consuming to generate the dictionary after each data acquisition. When the acquisition parameters are known, it is possible to pre-generate the dictionary [10]. In the case of T_2 mapping based on MESE acquisitions, a different dictionary is needed for different echo spacings (i.e., the time two consecutive spin echoes). In practice, the echo spacing depends on many parameters including: number of sampling points per readout, readout bandwidth, field of view, slew rate of the scanner gradient system, length of the RF pulse, as well as the

user's choice of echo times. Thus, the range of echo spacings can be rather large and make it impractical to pre-compute the dictionary for every possible echo spacing. Although the dictionary is only computed once for each echo spacing, storing the entire dictionary for all possible echo spacings is tedious and will impose a memory/storage burden.

In this work, we prove that pattern recognition T_2 mapping with indirect echo compensation based on the SEPG model can be performed for any echo spacing and echo train length (ETL) with the same pre-computed dictionary which is independent of the echo spacing. By making the dictionary independent of echo spacing, its generation is largely simplified and the storage/memory burden is significantly reduced.

Theory

In Hennig's EPG signal model [8], under the assumption that the profile of the excitation pulse and refocusing pulse are perfectly rectangular, the signal intensity S_n of a voxel at the n^{th} spin-echo after a train of refocusing RF pulses with the identical RFA, α , experienced by the spins can be obtained by:

$$S_n = I_0 \sin(\alpha_0) \cdot EPG(T_1, T_2, \alpha, n, esp). \quad (1)$$

In Eq. (1) α_0 is the flip angle of the excitation RF pulse, I_0 , T_1 and T_2 and esp are, respectively, the longitudinal magnetization at excitation, the spin-lattice relaxation time, the spin-spin relaxation time, and the echo spacing. There is no explicit formula for the function $EPG(\bullet)$, however, it can be numerically calculated as follows:

The magnetization M at any time of a MESE sequence can be written as a vector with countable entries: $M = (M_x, M_y, M_z, F_1, F_1^*, Z_1, Z_1^*, F_2, F_2^*, Z_2, Z_2^*, \dots)$, where M_x and M_y are the transverse magnetizations, M_z is the longitudinal magnetization, the sub-state F_n is the state of the complex magnetizations at the point of the n^{th} refocusing pulse if no refocusing pulse was applied, F_n^* denotes the complex conjugate of F_n , whereas Z_n, Z_n^* are the sub-states generated by the refocusing pulses which stores the information about the phase of the spin system corresponding to F_n and F_n^* , respectively (details of the formulation can be found in Ref. 8). The initial magnetization before the excitation pulse can be written as $M = (0, 0, 1, 0, 0, 0, 0, 0, 0, 0, \dots)$. With this terminology, the signal can be calculated using the following 3 rules:

- 1. Transition rule of the refocusing pulses.** The complex magnetization M_n^+ immediately after a refocusing pulse can be calculated from the magnetization M_n immediately before the refocusing pulse with RFA= α :

$$M_n^+ = \mathbf{T}_p \times M_n, \quad (2)$$

where $\mathbf{T}_p$ is a block matrix given by

$$\mathbf{T}_p = \text{diag}(\mathbf{T}_0, \mathbf{T}_1, \mathbf{T}_1, \dots). \quad (3)$$

$\mathbf{T}_0$ and $\mathbf{T}_1$ are given by:

$$\mathbf{T}_0 = \begin{bmatrix} 1 & 0 & 0 \\ 0 & \cos\alpha & -\sin\alpha \\ 0 & \sin\alpha & \cos\alpha \end{bmatrix}, \quad (4)$$

and

$$\mathbf{T}_1 = \begin{bmatrix} \cos^2\alpha/2 & \sin^2\alpha/2 & \sin\alpha & 0 \\ \sin^2\alpha/2 & \cos^2\alpha/2 & 0 & \sin\alpha \\ \sin\alpha/2 & -\sin\alpha/2 & \cos\alpha & 0 \\ -\sin\alpha/2 & \sin\alpha/2 & 0 & \cos\alpha \end{bmatrix}. \quad (5)$$

- 2. Transition rule of the time evolution.** The time evolutions between the $(n-1)^{\text{th}}$ and n^{th} refocusing pulses are:

$$\begin{cases} F_n \rightarrow F_{n+1}; \\ F_n^* \begin{cases} \rightarrow F_{n-1}^* \text{ for } n > 1; \\ \rightarrow F_1 \text{ for } n = 1; \end{cases} \\ Z_n \rightarrow Z_n; \\ Z_n^* \rightarrow Z_n^*. \end{cases} \quad (6)$$

- 3. Relaxation rule.** To account for relaxation, after the performance of each time evolution transition rule, a multiplicative longitudinal relaxation factor $\exp(-\text{esp}/T_1)$ is applied to Z_n, Z_n^* and a similar multiplicative transverse relaxation factor $\exp(-\text{esp}/T_2)$ is applied to F_n, F_n^* . The observed signal at the n^{th} echo is only generated by sub-state F_1^* immediately before that echo:

$$S_n = F_1^* \exp\left(\frac{-\text{esp}}{2T_2}\right). \quad (7)$$

One observation can be made here is that the two transition rules (Eqs. (2) and (6)) only depend on the RFA α . As a result, the signal variation predicted by the SEPG model among spins experiencing the same train of RFA in a MESE sequence is only due to the relaxation rule. Since according to this rule the relaxation depends on esp/T_1 and esp/T_2 we can define the normalized longitudinal and transverse relaxation parameters $NR_1 = \text{esp}/T_1$ and $NR_2 = \text{esp}/T_2$. Note that these normalized relaxation parameters are ratios between T_1, T_2 and esp . Thus Eq. (1) can be reformulated as:

$$S_n = I_0 \sin(\alpha_0) \cdot \text{EPG}(NR_1, NR_2, \alpha, n). \quad (8)$$

In the case of the SEPG model, the variation of the RF flip angles along the slice direction is included into the model. The α_0 and α in Eq. (1) are replaced by $B_1 \alpha_0(z)$ and $B_1 \alpha(z)$ where $\alpha_0(z)$ and $\alpha(z)$ are functions of the nominal flip angles of the excitation and refocusing RF pulses along the slice profile, while B_1 is a spatially varying unit-less RF transmit factor.

Note that in this formulation, $\alpha_0(z)$ and $\alpha(z)$ are known functions which can be derived from the refocusing RF pulse waveforms as shown in Ref. 7. The SEPG model is formulated as:

$$S_n = \int_z I_0(z) \sin(B_1 \alpha_0(z)) \cdot EPG(T_1, T_2, esp, B_1 \alpha(z), n) dz. \quad (9)$$

Similar to Eq. (8), Eq. (9) can be rewritten as a normalized SEPG model (nSEPG):

$$S_n = \int_z I_0(z) \sin(B_1 \alpha_0(z)) \cdot EPG(NR_1, NR_2, B_1 \alpha(z), n) dz. \quad (10)$$

From the nSEPG model, it can be seen that since the slice profiles are known, the signal S_n only depends on NR_1 , NR_2 and B_1 . For curves with the same NR_1 , NR_2 and B_1 , the T_2 decay curve will have the exactly same pattern regardless of the *esp* value. This enables the performance of pattern recognition on T_2 curves using the same dictionary for data acquired with any *esp*. As a result, only one dictionary needs to be pre-computed and stored on the reconstruction computer. Note that a dictionary generated for a larger ETL (e.g., ETL=64) can be truncated and used for data acquired with smaller ETLs. This enables the same dictionary to be applied to data acquired with any $ETL < ETL$ of the dictionary.

Methods

Proof-of-principle

To illustrate that curves generated with the nSEPG model are the same regardless of the echo spacing, T_2 decay curves were simulated for sets of NR_1 , NR_2 B_1 using Eq. (10) and different *esp* values. The slice profiles $\alpha_0(z)$ and $\alpha(z)$ were generated by taking the Fourier transform of the RF waveforms as indicated in Ref. 11. To match the pulse sequence provided by the vendor, the refocusing slice, $\alpha(z)$, was simulated to be 1.6 times as thick as the excitation slice, $\alpha_0(z)$. The slice was divided into 101 segments to account for flip angle variation along the slice direction.

Dictionary generation

For a given range of NR_1 , NR_2 and B_1 , the dictionary was generated using Eq. (9) and the corresponding NR_1 , NR_2 and B_1 were stored together with the atoms of the dictionary. The computation of Eq. (9) was carried out using 101 segments of the slice profile. The B_1 range was selected to be 0.2–1 with a step size of 0.01 according to previous work on SEPG [7]. The B_1 values can also be extended to cover a larger range of B_1 values when necessary [12]. To discretize the continuous range of the T_2 values we derived the following formula:

$$T_2^j = esp \cdot (1 + 2 \cdot tol)^{j-1}, j=1, 2, \dots, J \quad (11)$$

which is equivalent to:

$$NR_2 = 1 / (1 + 2 \cdot tol)^{j-1}, j=1, 2, \dots, J, \quad (12)$$

where tol is the tolerance of the discretization accuracy of T_2 values, and

$J = \left\lceil \frac{\log 1000}{\log(1+2 \cdot tol)} \right\rceil$. The motivation of this formulation is that for any T_2 between esp and $1000 \cdot esp$, there exists a discrete T_2^j given by Eq. (11) such that this T_2 value can be approximated by T_2^j with relative error less than tol . In this work, tol was set to 0.5%, thus $J = 694$. The lower bound for T_2 was set to esp because it is not accurate to use an MESE sequence with echo spacing = esp to estimate a $T_2 < esp$. The upper bound was set to $1000 \cdot esp$ to ensure a proper representation of the T_2 of species with long T_2 s (e.g. CSF), even for esp values as short as 2 ms. All atoms in the dictionary were normalized such that the 2-norms were 1.

It was suggested in the original work on SEPG fitting that $T_1 = \infty$ can be a good approximation for fitting the T_2 decay when $T_1 \gg T_2$ [7]. The proposed technique can also be used with T_1/T_2 ratios different from ∞ when necessary [7, 13]. To demonstrate this, two NR_2 / NR_1 ratios (equivalent to T_1/T_2 ratios), ∞ and 10, were used in this work to demonstrate the capability of fitting with non-infinity T_1 values.

Pattern recognition

Pattern recognition was used to match the acquired decay curve to an atom in the dictionary. The pattern recognition was performed for each voxel using the following steps:

1. Normalized the decay curve by the 2-norm, such that the 2-norm of the decay is 1;
2. Calculate the 2-norms of the differences between the normalized decay curve and all the atoms in the dictionary;
3. Identify the atom in the dictionary with the smallest 2-norm difference, this atom will be considered as the match to the fitted decay;
4. Assign the corresponding T_2 and B_1 values of the matched atom to the voxel being fitted.

Note that the pattern recognition approach is independent for each voxel. Only linear operations are involved and no iteration is needed.

Iterative nonlinear least square fitting (iNLLS)

For comparison, conventional iNLLS was also performed (StimFit toolbox is one realization of the iNLLS algorithm which can be downloaded from <http://mrel.usc.edu> [9]). In the iNLLS fitting, the slice profile was divided into 85 segments according to Ref. 7.

In vivo data

In vivo brain data were acquired under the approval of the University of Arizona Institutional Review Board with a radial fast spin-echo (FSE) pulse sequence [14] on a GE 1.5T Signa HDxt (General Electric Healthcare, Milwaukee, WI) MR scanner using an 8-channel (receive only) head coil. The acquisition was performed with ETL=16, $esp = 12.93$ ms, thickness of the excitation slice = 8 mm, receiver bandwidth = ± 15.63 kHz, TR = 4 s. The acquisition matrix was 256×4096 so that there were 256 radial lines for each TE. Data

with two RFA (180° and 120°) were acquired. Filtered back-projection was used to reconstruct 16 TE images with dimensions of 256×256 per image.

Results

To validate that the T_2 decay curves based on the SEPG model are indeed identical for curves acquired using different esp as long as the NR_1 , NR_2 and B_1 are the same, curves were simulated using the SEPG model with the 3 sets of parameters shown in Table 1. The decay curves generated are shown in Figure 1 as a proof-of-principle. While each set of curves was generated for two different esp values, the decay curves are the same as long as NR_1 , NR_2 and B_1 are the same. This confirms that under the nSEPG model, the same dictionary can be used for any esp value.

T_2 and B_1 maps obtained from the nSEPG pattern technique from in vivo brain data acquired using two RFA are shown in Figure 2. As shown here, except for slight difference due to inter-scan motion, the two T_2 maps agree with each other despite the different RFAs and concomitantly, their different levels of indirect echo effect. This shows that the nSEPG model represents the signal decay accurately. Figure 2 also shows the corresponding difference maps between the T_2 and B_1 maps obtained with the proposed technique and iNLLS. Note that except for slight differences in the CSF region, the differences of the T_2 maps between the two techniques are mostly <1% for both RFAs. Specifically, the differences (mean $\pm$ standard deviation) of the T_2 maps are $-0.13\% \pm 0.35\%$ for RFA=180° and $-0.01\% \pm 0.67\%$ for RFA=120°. The corresponding differences (mean $\pm$ standard deviation) of the B_1 maps are $-0.01\% \pm 0.81\%$ and $0.06\% \pm 0.49\%$, respectively. The slightly larger variation in the B_1 difference maps for RFA=180° compared to RFA=120° is due to the fact that the SEPG model is less sensitive to B_1 changes for B_1 values close to 1 (RFA=180°) [7]. In other words, there is a wider range of B_1 values for a given T_2 that can fit the decay curves under noise when RFA=180°. This higher fluctuation of B_1 values translates to a larger variation of the B_1 difference maps at RFA=180° compared to 120°.

In Figure 2, the T_1/T_2 was fixed to ∞ following the initial work on SEPG fitting [7]. The dictionary used in this work can also be generated using other fixed T_1/T_2 ratios (equivalent to NR_2/NR_1 ratio). As shown in Figure 3 T_2 maps were also obtained using the proposed technique with $NR_2/NR_1 = 10$ for the same in vivo data used in Figure 2. The differences (mean $\pm$ standard deviation) of the T_2 maps obtained using pattern recognition and iNLLS are $0.12\% \pm 0.41\%$ for RFA=180° and $0.11\% \pm 0.63\%$ for RFA=120°.

Discussion

We have shown that T_2 maps compensated for the effects of indirect echoes can be obtained from the nSEPG pattern recognition approach in a computationally efficient manner. For the maps shown in Figure 2, there are 25887 fitted pixels excluding the region outside of brain. The T_2 and B_1 maps were generated using the proposed pattern recognition technique in less than 2 minutes on a desktop PC with Intel Core i5–2500 CPU and 4 GB memory running Matlab R2011a; it took approximately 29 minutes to process the same data set with iNLLS on the same computer system. Another advantage of the pattern recognition technique is that

because the approach only involves linear operations, it could be easily implemented on GPUs which should enable near real-time mapping generation capability.

Assuming that the dictionary is stored as single precision float point (4byte per entry), the 56214 ($694 T_2 \times 81 B_1$) atoms with ETL=64 in the dictionary used in this work occupies 13.7 Mbyte of memory or disk space. However, if we were going to generate and store the dictionaries for each possible *esp* without taking advantage of the nSEPG model, the memory/storage requirements would be much larger and depend on the *esp* range and step size. For instance, the memory/storage requirements for *esp* spanning from 3 ms to 20 ms with step sizes of 0.01 ms or 0.1 ms would be 23 Gbyte or 2.3 Gbyte, respectively. Note that these numbers will increase geometrically if T_1 variation is included in the dictionary. Also, since only one universal dictionary is needed for any *esp*, the construction of the dictionary only needs to be performed once. As a result, a good slice profile resolution can be chosen to minimize any error arising from the slice profile resolution.

In this work, fittings were performed with NR_2 / NR_1 equal to ∞ or 10. Besides fixing NR_2 / NR_1 ratios to a constant, the NR_2 / NR_1 ratio can also be considered as a fitting parameter and the atoms generated with various NR_2 / NR_1 can be included in the dictionary. This will increase the size of the dictionary, but because the insensitivity of the SEPG model to T_1 values [7] (similarly, the insensitivity of the nSEPG model to NR_2 / NR_1 values), not many NR_2 / NR_1 values need to be used. The selection of NR_2 / NR_1 can be conducted similarly to the T_2 selection in Eq. (11).

In this work, the proposed nSEPG pattern recognition technique was demonstrated in nearly fully sampled (63% sampled, 256 radial lines out of 408 radial lines according to Nyquist condition) radial FSE in vivo data. The technique can also be combined with a recently published method (CURLIE-SEPG [15]) which is an SEPG model-based algorithm designed to recover TE images from highly undersampled (~ 4% sampled) MESE data while preserving the signal from indirect echoes. The CURLIE-SEPG method yields accurate T_2 maps with high spatial resolution from rapidly acquired data (i.e., a breath hold). The framework requires two iterative processes: the reconstruction of the TE images (CURLIE) and the iNLLS SEPG fitting. The use of the proposed fast nSEPG pattern recognition approach in lieu of the SEPG fitting will speed up the latter process.

Conclusions

In this work, we demonstrated that the SEPG model can be used efficiently for T_2 mapping with indirect echo compensation using pattern recognition with a dictionary that is independent of echo spacing. Almost identical T_2 and B_1 maps were obtained from in vivo MESE data using the proposed nSEPG pattern recognition technique and the conventional iNLLS technique, while the computation time was reduced by more than 14 fold. The independence of the dictionary on echo spacing, a parameter that can vary widely and affect the number of atoms that need to be included in the dictionary, reduces considerably the memory/storage requirements for dictionary.

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Figure 1.

The normalized T_2 decay curves generated using the SEPG model for two different esp values. The parameters used for the curve generation are provided in Table 1.

Figure 2.

In vivo brain T_2 , B_1 maps obtained from radial FSE data acquired with 180° and 120° RFA and the pattern recognition technique based on the nSEPG model. The corresponding difference with respect to T_2 and B_1 maps obtained using the iNLLS technique are also shown.

Figure 3. (left) T₂ maps obtained using the pattern recognition technique based on the nSEPG model with $NR_2/NR_1 = 10$. (right) The corresponding difference with respect to the T₂ maps obtained using the iNLLS technique.

Table 1

Parameters for T2 decay curve simulation using the SEPG model.

	<i>esp</i> = 10 ms			<i>esp</i> = 20 ms		
	T ₂	T ₁	B ₁	T ₂	T ₁	B ₁
Decay curve 1	100 ms	∞	1	200 ms	∞	1
Decay curve 2	100 ms	200 ms	0.5	200 ms	400 ms	0.5
Decay curve 3	100 ms	∞	0.5	200 ms	∞	0.5

Decay curve 1

Decay curve 2

Decay curve 3