Published in final edited form as:

Magn Reson Med. 2020 December ; 84(6): 3409–3422. doi:10.1002/mrm.28381.

Slice-selective extended phase graphs in gradient-crushed, transient-state free precession sequences: an application to magnetic resonance fingerprinting

Jason Ostenson^{1,2,3}, David S. Smith^{1,3}, Mark D. Does^{1,3,4,6}, Bruce M. Damon^{1,2,3,4,5,†}

¹Vanderbilt University Institute of Imaging Science, Nashville, TN 37232

²Chemical and Physical Biology Program, Vanderbilt University

³Dept. of Radiology and Radiological Sciences, Vanderbilt University Medical Center

⁴Dept. of Biomedical Engineering, Vanderbilt University

⁵Dept. of Molecular Physiology and Biophysics, Vanderbilt University

⁶Dept. of Electrical Engineering, Vanderbilt University

Abstract

Purpose: Slice-selective, gradient-crushed, transient-state sequences such as those used in magnetic resonance fingerprinting (MRF) relaxometry are sensitive to slice profile effects. While balanced steady-state free precession MRF profile effects have been studied, less attention has been given to gradient-crushed MRF forms. Extensions of the extended phase graph (EPG) formalism are proposed, called slice-selective EPG (ssEPG), that model slice profile effects.

Theory and Methods: The hard-pulse approximation to slice-selective excitation in the spatial domain is reformulated in k-space. Excitation is modeled by standard EPG shift and transition operators. This ssEPG modeling is validated against Bloch simulations and phantom slice profile measurements. ssEPG relaxometry accuracy and variability are compared with other EPG methods in phantoms and human leg in vivo. The role of B_0 interactions with slice profile and gradient crushers are investigated.

Results: Simulations and slice profile measurements show that ssEPG can model highly dynamic slice profile effects of gradient-crushed sequences. The MRF ssEPG T_2 estimates over $0 < T_2 < 100$ ms improve accuracy by > 10 ms at some values, relative to other modeling approaches. Small deviations in B_0 can produce substantial bias in T_2 estimations from a range of MRF sequence types, and these effects can be modeled and understood by ssEPG.

Conclusion: Transient-state, gradient-crushed sequences such as those used in MRF are sensitive to slice profile effects, and these effects depend on RF pulse choice, gradient crusher strength, and B_0 . It was found ssEPG was the most accurate EPG-based means to model these effects.

[†]Address for correspondence: Bruce M. Damon, PhD, AA1105 Medical Center North, 1161 21st Ave S, Nashville TN USA, bruce.damon@vanderbilt.edu, Phone: 615 322-8355, FAX: 615 322-0734.

Keywords

extended phase graph; slice profile; magnetic resonance fingerprinting; relaxometry; off-resonance

Introduction

Gradient-crushed, transient-state free precession sequences, such as those used in unbalanced “steady-state” free precession (uSSFP) MR fingerprinting (MRF),¹ have states of partial or fully defocused magnetization that may interact with slice selection, biasing parameter estimates. These sequences can be modeled with Bloch simulations or extended phase graphs (EPG) using idealized slice profiles. The repeated dephasing of the crusher gradients motivates the use of EPG modeling, but current EPG methods idealize the slice profile or the crusher gradient in ways that may bias these models.

The EPG formalism is a method for modeling signals from pulsed MRI experiments.² EPG is particularly useful for calculating the effects of coherence pathways, states of dephased magnetization that may later be refocused and manifest as spin-echoes or stimulated echoes. These echoes may contribute substantially to the observed signal in a given gradient-crushed sequence. The equivalence of EPG to a conventional Bloch simulation has been shown.³ EPG was employed for signal modeling in the original uSSFP MRF work¹ using idealized slice profiles.

EPG has been used to improve signal modeling accuracy of slice-selective sequences with inhomogeneous slice profiles⁴ as well spatially non-uniform radiofrequency effects⁵. The approach taken by Lebel and Wilman^{4,6} for slice-selective multiple spin-echo (MSE) T_2 estimation is to discretely partition the slice profile based on precomputed excitation and refocusing profiles. The partitioned components are each fed through an EPG algorithm, then summed to determine the cumulative effect of the non-uniform excitation/refocusing profile. A similar approach has been apparently adopted in slice-selective uSSFP MRF,^{7–9} but the EPG implementations used in these works are not detailed. It is known that slice-selective balanced SSFP MRF relaxometry estimates improve with slice profile modeling using Bloch simulations.^{10,11} With a sufficient number of isochromats, a Bloch simulation can successfully model multiple coherence pathways, but uSSFP MRF is often modeled with EPG because of EPG’s greater efficiency in dealing with multiple signal pathways. This complex signal evolution suggests the partitioned EPG (pEPG) approach used in MSE for modeling uSSFP MRF. However, pEPG idealizes gradient crushing action and has not been closely studied in the context of MRF.

Gradient crushers of insufficient strength and non-uniform slice profiles may lead to inaccurate pEPG signal models. As an example, consider a pulse profile that is a scaled delta function and a finite strength crusher. After a single pulse and crusher, the crusher will have caused an offset of phase of the transverse magnetization but no dephasing: ignoring relaxation effects, the signal magnitude is unchanged. On the other hand, pEPG predicts complete annihilation of the signal by the crusher. While this example is extreme, it illustrates how the pEPG method may fail to accurately model the signal due to slice profile inhomogeneity if the slice is partitioned so finely that crushing is not complete over

the partition. Furthermore, pEPG models the crusher gradients as completing prior to an instantaneous RF excitation, which also may lead to bias. In summary, it is unclear how to use the pEPG method accurately when there are only a few cycles of dephasing per nominal slice thickness, a situation often encountered in uSSFP MRF,¹ and to what extent gradient idealization biases relaxometry estimates.

Parameter estimates in uSSFP may also be complicated by static field heterogeneity. Recent preliminary work has shown that off-resonance effects may bias T_2 estimates made with uSSFP MRF.^{12,13} This effect was attributed to insufficient dephasing prior to radiofrequency (RF) excitation. Since the dephasing gradient strength and slice-selective gradient are coupled, this off-resonance effect may need to be modeled to obtain accurate parameter estimates.

In this work, we propose slice-selective EPG (ssEPG) to study transient-state, gradient-crushed (along the slice selection direction) sequences with an application to spiral encoded uSSFP MRF. Unlike previous EPG slice profile methods, the ssEPG model operates entirely in k-space. It uses a hard-pulse approximation method to closely approximate soft RF signal responses, integrated with the conventional EPG method. The ssEPG method accurately accounts for crusher/slice profile interactions, works in EPG state-space using familiar transition and shift operators, and accurately models intra-slice signal evolution in the transient state. We use ssEPG to examine relaxometry bias in uSSFP MRF due to slice profile effects as well as interactions with static field heterogeneity.

Theory

In this section we introduce the mathematical framework for ssEPG. Using a spatial-frequency representation of the Bloch equations, as well as a hard-pulse approximation, we show that we may write the effect of an RF pulse in terms of shift and transition operators familiar to conventional EPG. These operations apply to the normal EPG state matrix using conventional notation².

The Bloch equations in the Fourier domain for an applied radiofrequency pulse

The magnetization $\mathbf{M}=[M_x, M_y, M_z]^T$ in the RF rotating frame under the influence of an applied RF field in a slice-selective pulsed MRI sequence, neglecting relaxation, at time t is related to its time derivative as

$$\frac{d\mathbf{M}}{dt} = \begin{pmatrix} 0 & \omega & -\omega_1 \sin(\phi) \\ -\omega & 0 & \omega_1 \cos(\phi) \\ \omega_1 \sin(\phi) & -\omega_1 \cos(\phi) & 0 \end{pmatrix} \mathbf{M}(t). \quad [1]$$

Here $\omega=\gamma Gz$, with gyromagnetic ratio γ , gradient amplitude G , and slice position z , $\omega_1=\gamma B_1(t)$ where $B_1(t)$ is the amplitude of the applied radiofrequency and ϕ is its phase. By expressing this form of the Bloch equations in complex magnetization (i.e. $M_+=M_x+iM_y$ and $M_-=M_x-iM_y$) and taking the Fourier transform in z , it can be shown (Supporting Information Note 1) that Eq. (1) is equivalent to

$$\frac{\partial \mathbf{F}(k_z, t)}{\partial t} = \begin{pmatrix} \frac{\gamma}{2\pi} G \frac{\partial}{\partial k_z} & 0 & i\omega_1 e^{i\phi} \\ 0 & -\frac{\gamma}{2\pi} G \frac{\partial}{\partial k_z} & -i\omega_1 e^{-i\phi} \\ \frac{i\omega_1}{2} e^{-i\phi} & -\frac{i\omega_1}{2} e^{i\phi} & 0 \end{pmatrix} \mathbf{F}(k_z, t). \quad [2]$$

Here $\mathbf{F}(k_z, t) = \mathcal{F}_z \{ [M_+, M_-, M_z]^T \}$ is the Fourier transform of the complex magnetization, and $\partial / \partial k_z$ represents the partial derivative operator with respect to the spatial-frequency in the z dimension.

Solution of the k-space representation of the Bloch equations by the hard-pulse approximation

Splitting the matrix in Eq. (2) we can write

$$\frac{\partial \mathbf{F}(k_z, t)}{\partial t} = (\mathbf{A} + \mathbf{B}) \mathbf{F}(k_z, t), \quad [3]$$

where

$$\mathbf{A} = \begin{pmatrix} 0 & 0 & i\omega_1(t) e^{i\phi} \\ 0 & 0 & -i\omega_1(t) e^{-i\phi} \\ \frac{i\omega_1(t)}{2} e^{-i\phi} & -\frac{i\omega_1(t)}{2} e^{i\phi} & 0 \end{pmatrix}, \quad [4]$$

and

$$\mathbf{B} = \begin{pmatrix} \frac{\gamma}{2\pi} G \frac{\partial}{\partial k_z} & 0 & 0 \\ 0 & -\frac{\gamma}{2\pi} G \frac{\partial}{\partial k_z} & 0 \\ 0 & 0 & 0 \end{pmatrix}, \quad [5]$$

where $\omega_1(t)$ is the applied RF over the time t to $t + \Delta t$, which the RF is considered constant in a hard-pulse approximation. The matrix operators $\mathbf{A}$ and $\mathbf{B}$ do not commute. By splitting the matrices as we have done, we may use an approximation accurate to the second-order¹⁴ for a bounded magnetization over a finite region of support

$$\mathbf{F}(k_z, t + \Delta t) \approx e^{\mathbf{A} \Delta t / 2} e^{\mathbf{B} \Delta t} e^{\mathbf{A} \Delta t / 2} \mathbf{F}(k_z, t). \quad [6]$$

Eq. (6) is a convenient expression if we use the conventions of Ref². The matrix exponential $\exp(\mathbf{A}_t \Delta t / 2)$ is the normal EPG transition matrix for half of the flip-angle $\omega_1(t) \Delta t$, which we denote as $\mathbf{T}_n$ for n^{th} time interval in the RF pulse. The matrix exponential of diagonal matrix $\mathbf{B}$ is given by the exponentiation of the diagonal elements

$$e^{\mathbf{B}\Delta t} = \text{diag} \left\{ e^{\frac{\gamma}{2\pi}\Delta t G \frac{\partial}{\partial k_z}}, e^{-\frac{\gamma}{2\pi}\Delta t G \frac{\partial}{\partial k_z}}, 1 \right\} \quad [7]$$

and

$$e^{\pm \frac{\gamma}{2\pi}\Delta t G \frac{\partial}{\partial k_z}} F_{\pm}(k_z, t) = F_{\pm}\left(k_z \pm \frac{\gamma}{2\pi}\Delta t G, t\right). \quad [8]$$

Eq. (8) describes the conventional EPG gradient shift operator denoted as $\mathcal{S}$. The accuracy of Eq. (6) is limited by the discretization in t .

The effect of the entire RF pulse of length τ , discretized into N_{RF} components, can then be given as $\mathbf{F}(k_z, \tau) = \mathbf{T}_{N_{\text{RF}}} \mathcal{S} \mathbf{T}_{N_{\text{RF}}} \mathbf{T}_{N_{\text{RF}}-1} \mathcal{S} \mathbf{T}_{N_{\text{RF}}-1} \cdots \mathbf{T}_1 \mathcal{S} \mathbf{T}_1 \mathbf{F}(k_z, 0)$. Discretizing k -space into units of $\Delta k_z = tG\gamma/2\pi$, we can solve for the EPG state matrix $\mathbf{\Omega}(t) = [\mathbf{F}(0, t), \mathbf{F}(\Delta k_z, t), \mathbf{F}(2\Delta k_z, t), \dots] \in \mathbb{C}^{3 \times Q}$ as

$$\mathbf{\Omega}(\tau) = \mathbf{T}_{N_{\text{RF}}} \mathcal{S} \mathbf{T}_{N_{\text{RF}}} \mathbf{T}_{N_{\text{RF}}-1} \mathcal{S} \mathbf{T}_{N_{\text{RF}}-1} \cdots \mathbf{T}_1 \mathcal{S} \mathbf{T}_1 \mathbf{\Omega}(0). \quad [9]$$

The hard-pulse and matrix splitting approximations give the response of a soft RF pulse in terms of the native EPG representation of the magnetization using shift and transition operations. The standard EPG framework for interpulse relaxation and gradient dephasing is used to model the remainder of the pulse sequence. The signal magnitude at each echo time T_E is the first entry of $\mathbf{\Omega}(T_E)$ (i.e. the DC component of k -space). If desired, the slice profile can be calculated from the Fourier transform of the $F_+(k_x; t)$ (see the Appendix).

The spacing between EPG states in ssEPG is coupled to the product of the slice-select gradient strength G and hard-pulse time interval t (Eq. 8). As a result, coupled relationships between the RF pulse profile characteristics and the uSSFP gradient crusher emerge. These are detailed in the Appendix.

Methods

Numerical and experimental validation of ssEPG

To validate the proposed method of slice profile computation in a transient-state sequence, we calculated slice profiles from a soft RF pulse in a 10 excitation uSSFP sequence (i.e. it has 10 repetitions) using a linear ordinary differential equation (ODE) solver of the Bloch equations and using the proposed ssEPG method. For reference, the sequence was also modeled with EPG using an idealized slice profile. All computations were performed in MATLAB (v. 2018a; MathWorks). A Hanning-windowed sinc excitation pulse with time-bandwidth product (TBW) of four and a nominal flip angle of 90° was used. Slice thickness was 8 mm; the gradient crushing introduced four cycles of phase across the nominal slice thickness; T_1 and T_2 were 1000 and 100 ms, respectively; and the T_E/T_R were 3/15 ms. We used a nonstiff ODE solver based on the Runge-Kutta method (MATLAB function ode45) with 5000 isochromats over four times the nominal slice thickness. The number of states

Q (the number of columns in Ω) used for the ssEPG method was defined to match the resolution of the Bloch simulation.

The measured transient slice profiles were compared to modeled slice profiles and signals from ssEPG and pEPG. A 50 mL conical centrifuge tube was filled with 3% aqueous agar (w/w) and doped with 1.0 mM gadolinium-based contrast agent. The tube was imaged with an uSSFP sequence with crusher strengths of one and four cycles per nominal slice thickness of 6 mm. All imaging measurements in this work were done with a Philips Ingenia 3 T (Philips Healthcare). The sequences were 10 excitations in length and used Hanning-widowed sinc pulses with TBWs of two, four, and eight for excitation. Different TBWs were used to explore the effect of signal model accuracy relative to slice profile shapes and parsing of the uSSFP gradient crushing between crusher gradient and slice-selective gradient, which are coupled (further detailed in the Appendix). Three nominal flip angles of 30°, 60°, and 90° were used. The readout gradient was along the through-slice direction with an FOV of 32 mm and a resolution of 125 μ m. The body coil was used for signal reception to minimize coil sensitivity changes over the slice. Thirty-two averages were used with a time delay of 5.5 s between averages to permit full recovery of magnetization between averages. The T_1 and T_2 of the agar phantom were estimated using single voxel MR spectroscopy. ssEPG slice profiling modeling matched the resolution of the measurement. The pEPG method used 256 partitions to match the resolution of the measurement. The slice profile partitions were calculated by ssEPG from equilibrium using the respective RF pulse type and flip angle. Signal magnitude root-mean-square-errors (RMSE) were calculated for the normalized EPG signal models using the normalized signal measurement as a reference. To compare the behavior of ssEPG and pEPG in the steady state, these models were used to calculate the slice profile and signal magnitudes after 100 excitations.

ssEPG applied to MRF in phantom

To assess EPG's effect on parameter estimation accuracy using uSSFP MRF, we estimated T_1 and T_2 in an MRI system phantom with ssEPG and pEPG slice profile modeling, as well as EPG without slice profile modeling. The same RF pulses used in the agar slice profile experiment (TBWs four and eight) were used to image the system phantom¹⁵ (High Precision Devices) composed of MnCl₂-doped calibrated contrast spheres whose relaxometry specifications were temperature corrected with conventional measurements. The MRF acquisition used the first 1250 excitations (i.e. "repetitions" with varying flip angle) of a previously reported flip-angle pattern¹⁶, fixed $T_R = 16$ ms, a T_E ramped linearly through the sequence from 3 to 7 ms, and a crusher strength of one or four cycles per nominal slice thickness. The readout used 32 spiral interleaves rotated 11.25° between excitations, with an in-plane resolution of 1 mm x 1 mm and 8 mm slice thickness. The pEPG dictionary used 50 partitions for four times the nominal slice thickness. All dictionaries used the same T_1 s and T_2 s ranging from 10 to 3000 ms and 2 to 1500 ms, respectively. The B_{1+} ranged from 1.0 to 1.35 (relative to the nominal B_{1+}), which matched the range of a separately acquired B_{1+} map¹⁷ over the contrast spheres. Comparison of relaxometry estimates between MRF and the reference were made using the concordance correlation coefficient (CCC)¹⁸.

To accelerate ssEPG and pEPG dictionary modeling, the code was parallelized for use with MRF. GPU functionality within MATLAB as well as a modified CUDA kernel from an EPG-based fast dictionary modeling approach¹⁹ were employed. Dictionaries were generated using an NVIDIA TITAN RTX (NVIDIA Corp.). Conventional EPG MRF dictionaries were generated on an Intel Xeon 12-core 3.0 GHz CPU (Intel Corp.). The number of time steps used in the ssEPG hard pulse approximation was 128 and 256 for TBW of four and eight, respectively. Errors in ssEPG modeling will come from truncation of the state matrix: if Q is too small relative to the number of states spanned by repeated gradient crushing (each of number N), information can be lost. Using the relationships in the Appendix, we optimized Q for each TBW and crusher strength used in the MRF sequence. Over a physiological range of T_1 (300 to 1500 ms) and T_2 (5 to 150 ms) we selected 10 log-spaced values for both T_1 and T_2 , and used all 100 pairings from all combinations of each metric's 10 values. We generated high resolution signal models using ssEPG for all these T_1 and T_2 pairings for each RF pulse and crusher strength. For each set of signals, we sequentially incremented the value of Q/N , which defined Q for the given pulse and crusher strength, and then modeled all T_1 and T_2 combinations and 2% above and below the query values (i.e. the dictionary had 9 closely spaced atoms $\times$ 100 log-spaced atoms = 900 atoms). The unbiased ssEPG high resolution signals were then matched against the truncated dictionary and Q/N was increased until the maximum absolute error in the estimated T_1 and T_2 for all 100 signals was zero.

MRF B_0 effects and in vivo application

To model slice profile effects in vivo, we must consider the interaction of static field heterogeneity with slice profile effects. It is difficult to achieve the same homogeneity of the static field in vivo as in a phantom, so we model B_0 deviations under free precession within the EPG model using the relation in the Appendix.

The ssEPG slice profiles for several off-resonance frequencies were calculated for the second excitation of the MRF sequence described above using a T_1 and T_2 of 1320 and 30 ms, respectively. The B_0 s were defined in relation to the fundamental frequency of repetition time of the MRF sequence at the following factors of $1/T_R$: 0, 1/4, 1/2, 5/4, and 3/2. We also modeled the magnitude and phase of the MRF signals for the given T_1 and T_2 at the same frequencies. We investigated the off-resonance frequency periodicity of the slice profile, signal magnitude and signal phase modulations.

We evaluated the bias of MRF T_1 and T_2 estimates when fitting with B_0 modeling against dictionaries with slice profile effects without B_0 effects for TBWs of four and eight at crusher cycles (phase dispersions by 2°) per nominal slice thickness of one and four. The bias calculations were done for the following T_1/T_2 combinations (in ms) as rough estimates of mono-exponential relaxation times of skeletal muscle, liver, gray matter, and white matter²⁰ at 3 T: 1320/30, 800/30, 1400/85, and 800/65, respectively. These evaluations of bias were tested with the following sequences: the MRF sequence described above (variable T_E /fixed T_R), the MRF sequence described above without variations in echo time (fixed T_E /fixed T_R), and an MRF sequence with variable T_R (fixed T_E /variable T_R). To reduce discretization effects in fitting, all three dictionaries were generated over a finely

spaced domain of 35 T_1 s and 165 T_2 s log-spaced over the ranges of 100 to 3000 ms and 2 to 300 ms, respectively. The variable T_R sequence is similar to the first reported uSSFP MRF sequence¹, using the same T_R extension with a minimum T_R of 16 ms, as well as the same flip angle modulation pattern with a maximum flip angle of 60°, and 1000 excitations. The mean relative bias and standard deviation of the T_1 and T_2 estimates were calculated for each TBW, crusher strength, dictionary/modeling type, and B_0 across the four physiological T_1 and T_2 combinations.

A spherical NiCl₂-doped agar phantom was imaged, as well as a single volunteer in the calf after informed consent and with approval from the local institutional review board. The (variable T_E /fixed T_R) MRF sequence in the MRI system phantom experiment was used for acquisition. The geometry and the coil for the phantom experiment matched that of the MRI system phantom experiment. A B_0 gradient was introduced across the phantom to study B_0 effects on parameter estimates in a homogeneous phantom. For the calf acquisition an FOV of 320 mm × 320 mm, and in-plane and through-plane resolution of 1.25 mm × 1.25 mm and 5 mm, respectively, were used. A 16-channel transmit-receive knee coil was used for image acquisition. Images were reconstructed using the Berkley Advanced Reconstruction Toolbox²¹ with numerically calculated sample density compensation²². Dictionaries with EPG, pEPG, ssEPG, and ssEPG with B_0 effects were used to fit the T_1 and T_2 from the phantom and calf data. For the phantom and the calf, B_{1+} modeling ranged from 0.7 to 1.15, which matched the range of a separately acquired B_{1+} map¹⁷. The dictionary parameters for the EPG, pEPG (including number of partitions), and ssEPG models were otherwise the same as those for the MRI system phantom.

Results

Numerical and experimental validation of ssEPG

The ssEPG slice profile model closely matches the ODE Bloch solution (Fig. 1; detail provided in Supporting Information Figure S1). The relatively long T_2 (100 ms) relative to the T_R (15 ms) permits the development of multiple coherence pathways that modulate the slice profile, manifesting as oscillations in the profile magnitude. These oscillations in the pulse profile are in close agreement between the two models. The normalized signal from the ssEPG simulation has an RMSE of 0.002 relative to the signal from the Bloch simulation. The normalized signal from the standard EPG model without slice profile modeling has an RMSE of 0.115. The times for the Bloch simulation and ssEPG simulation were 707.8 s and 9.2 s, respectively.

ssEPG applied to MRF in phantom

The ssEPG model of the pulse profile in agar closely matches that of the measurement, and the ssEPG signal model error is lower than that of the pEPG method. An example plot of the measured and modeled slice profiles, scaled by their root-mean-square values of the first profile, shows general agreement between the slice shapes (Fig. 2; detail provided in Supporting Information Figure S2). The oscillations in the measured profile are generally matched in the ssEPG model. High frequency components visible in ssEPG appear slightly attenuated in the 1D projection measurement. pEPG does not model these oscillations.

Fig. 3 shows that the signal RMSEs of the various EPG modeling methods. The RMSE is lowest in ssEPG relative to the other methods. The RMSE generally increases with increasing flip angle, and RMSE increases and decreases with TBW for pEPG and EPG, respectively. In the steady state, Supporting Information Figure S3 and Table S1 show that pEPG and ssEPG slice profiles and signal magnitudes are different. Steady state signal magnitude ratios ranged from 0.84 to 1.23. The TBW of two and four with four crusher cycles pEPG-to-ssEPG signal ratios were closest to unity, ranging from 1.00 to 1.04.

The T_2 estimates of the MRI system phantom from ssEPG modeling more closely match the ground truth than those from other EPG methods. The plots of T_2 estimates over a physiological range of T_2 (0 to 100 ms) are shown in Fig. 4a–c. The CCCs in this T_2 range are shown in Fig. 4d. Over the full dynamic range, the mean CCCs over all RF pulses and crusher strengths for T_1 are 0.994, 0.999, and 0.999 for EPG, pEPG, and ssEPG, respectively; and over the full range of T_2 s they are 0.919, 0.975, 0.996 for EPG, pEPG, and ssEPG, respectively. As measured by an independent B_0 mapping, the B_0 of the MRI system phantom contrast inserts did not deviate more than 6.6 Hz, using the mean B_0 for each insert.

To further compare pEPG and ssEPG T_2 estimation under the closest to ideal crushing conditions used in the MR system phantom experiment, the relative difference in T_2 when fitting with pEPG using the ssEPG model as signal reference was modeled for a broad range of T_1 and T_2 combinations for the TBW of four with four crusher cycles, and then compared with the MR system phantom experimental results. Supporting Information Figure S4 shows that differences in T_2 when fit by pEPG using the ssEPG signals as reference range from 0 to ~20% and the experimental results roughly match this modeling.

MRF B_0 effects and in vivo application

The simulation of B_0 effects in the variable T_E /fixed T_R MRF sequence modeled with ssEPG are shown in Fig. 5. For a fixed T_R sequence such as this, there are modulations in the slice profile magnitude and these modulations are periodic in B_0 by frequencies of $1/T_R$. Fig. 5a shows that the slice profile magnitudes of $B_0 = 1/4 T_R$ and $1/2 T_R$ are equal to $5/(4 T_R)$ and $3/(2 T_R)$, respectively. The MRF signal magnitudes at these off-resonant frequencies are also modulated (Fig. 5b). These modulations in magnitude also follow the periodicity of the slice profiles. The phase modulations (Fig. 5c) of the MRF signals show monotonic as well as oscillatory behavior. Again assuming the fixed T_R MRF sequence, we find that the phase modulations for $|B_0| \approx 1/T_R$, for MRF signal s at excitation n (parameterized by a given T_1 , T_2 and B_{1+}), can be modeled by multiplying the signal with modulo $1/T_R$ frequency by the added complex phase,

$$s_n(\Delta B_0) = e^{i2\pi \frac{m}{T_R} T_E s_n \left(\Delta B_0 \bmod \frac{1}{T_R} \right)}, \quad [10]$$

where $m = T_R \{ B_0 - [B_0 \bmod (1/T_R)] \}$, so m is an integer. Two examples of using Eq. (10) to construct higher order frequencies can be seen in Fig. 5c, denoted by asterisks. Using Eq. (10), B_0 effects for a given T_1 , T_2 , and B_{1+} can be modeled if the signal is known for $B_0 < 1/T_R$.

The modeled T_1 biases from B_0 effects were generally small for the fixed T_E sequences, but the relative bias increased with B_0 values from the variable T_E sequence. The maximum magnitude of relative T_1 bias for the fixed T_E sequences was $< 1\%$ for all TBW and crusher strength combinations. For the variable T_E sequence, the T_1 bias increased steadily with B_0 . The maximum magnitude of relative T_1 bias for the variable T_E sequence for all TBW and crusher strength combinations was $< 1\%$, $< 1\%$, 10% , 22% , and 35% for B_0 values (in units of $1/T_R$) of 0, $1/4$, $1/2$, $5/4$, $3/2$, respectively.

Substantial T_2 bias can be observed at low B_0 values for several sequences. The relative bias in T_2 from signals with B_0 effects fit against ssEPG dictionaries without B_0 effects are shown in Fig. 6. The T_2 bias for sequences with $TBW/2 < N_{crush}$ increases from B_0 of $1/(4T_R)$ to $1/(2T_R)$ and decreases from $1/(2T_R)$ to $5/(4T_R)$. Relative to this, the T_2 bias is reduced for sequences with $TBW/2 < N_{crush}$, where N_{crush} is given as C in Fig. 6 for readability. The T_2 bias from the fixed T_E /fixed T_R sequence is equal between steps in B_0 of $1/T_R$. The bias of the variable T_E /fixed T_R sequence for the three lowest B_0 values is generally equal to or less than that from the other sequences. The contributions to the total crusher strength from the slice-selective gradient before the isodelay and added dephasing gradient (calculated using relations given in the Appendix) for each TBW and crusher combination relative to T_2 bias are given in Table 1.

The parameter maps from the $NiCl_2$ -doped phantom and calf using EPG fitting can be seen in Supporting Information Figure S5 and main text Fig. 7, respectively. The T_1 maps (Supporting Information Figure S5a, Fig. 7a) of the three different crusher strengths and four different EPG fitting models yield similar results. The EPG T_1 estimates without profile effects in the calf muscles appear slightly lower than those from the other EPG modeling. The T_2 estimates (Supporting Information Figure S5b, Fig. 7b) are substantially biased using EPG without slice profile effects. The pEPG and ssEPG show drops or abrupt increases in the T_2 estimates in the phantom along the B_0 gradient, and in the lateral aspects of the calf parameter maps. These deviations are reduced in the maps fit using ssEPG with B_0 effects. The mean T_1 for the entire non-zero calf parameter maps for EPG, pEPG, ssEPG, and ssEPG with B_0 modeling are 1231, 1289, 1290, and 1282 ms, respectively; for T_2 they are 63, 22, 24, and 23 ms, respectively. The dictionary generation times for the EPG, pEPG, ssEPG, and ssEPG with B_0 modeling are, approximately: 6 min, 58 min, 62 to 316 min (depending on TBW), and 17.4 to 69.1 h (depending on TBW), respectively. Once these dictionaries were computed they could be stored and used repeatedly.

Further analysis of the phantom and calf data can be seen in Supporting Information Figure S6 and main text Fig. 8, respectively. The coefficient of variation (COV) of estimated T_2 across the different crushers for the different EPG fitting methods (Supporting Information Figure S6a, Fig. 8a) show that ssEPG with B_0 modeling has the lowest COV across the different measurements. Regions that are within 30% of the an off-resonance magnitude of $1/(2T_R)$ (Supporting Information Figure S6c, Fig. 8c) correspond to regions of highest COV in ssEPG without B_0 modeling. These regions have reduced COV after B_0 is considered.

Discussion

Slice profile effects can substantially bias relaxometry estimates in gradient-crushed, free precession sequences. The ssEPG method proposed here accounts for soft RF pulse effects. It also improves on other EPG methods, by accounting for the non-idealized gradient crushing interaction.

The simulation, phantom, and in vivo results demonstrate that ssEPG accurately models slice profiles and associated effects on signal. The simulations with ssEPG indicate that it accurately captures the highly variable magnitudes of slice-selective profiles that result from unbalanced gradients. Such slice profile modulations may be relevant in the context of partial volume effects, and possibly in multicompartment MRF parameter estimation,^{23,24} depending on the length scale of the heterogeneity of the tissue. The ssEPG model has the lowest RMSE (Fig. 3) and highest CCC (Fig. 4) compared to other EPG methods. The MRI system phantom and in vivo results show that the ssEPG modeling translates to more accurate relaxometry estimates using uSSFP MRF in regions of the $|B_0| < 7$ Hz relative to other EPG-based methods.

The pEPG method markedly reduces RMSE and T_2 estimation bias relative to EPG without slice profile considerations, but it is not as accurate as ssEPG over a physiological range of T_2 . The pEPG RMSE (Fig. 3) and relaxometry estimates (Fig. 4) from the phantom measurements are better than those from EPG without profile modeling. In the steady state (Supporting Information Table S1), pEPG signal is closest to that of ssEPG when two cycles or more of crushing have been completed prior to the commencement of the RF pulse, yet there is still divergence between the pEPG and ssEPG signal models at higher flip angles. The pEPG model in MRF apparently exhibits variable relaxometry bias depending on crusher strength and TBW (Fig. 4). The pEPG model has more variability in T_2 across crusher strengths for the given TBW in vivo. Even with the closest to optimal crushing for the MR system phantom experiment, Supporting Information Figure S4 indicates significant differences in T_2 estimation between pEPG and ssEPG, suggesting that pEPG T_2 estimation bias may be unavoidable in some circumstances.

The effect of B_0 on MRF uSSFP T_2 relaxometry is substantial and pertains to both fixed and variable T_R MRF sequences, whereas the T_1 estimates were relatively unbiased by B_0 effects. Matching what has been previously reported,^{12,13} we observe periodicity in the T_2 bias at a period of frequency $1/T_R$, which parallels the modulation of the slice profile over B_0 . Fig. 6 shows that the T_2 bias from the fixed and variable T_E MRF sequence are similar at $B_0 1/(2T_R)$, indicating it is not the phase dispersion of the variable T_E causing the bias seen in vivo variable T_E /fixed T_R MRF T_2 maps in Figs. 7–8. Table 1 implies that the source of the T_2 bias is insufficient crushing before the slice-select gradient: off-resonance signal components are being transferred by RF action to refocusing and longitudinal states prior to their complete dephasing, later contributing to the net signal. A higher TBW does not reduce this bias, but Table 1 indicates the majority of the T_2 bias is eliminated if the transverse magnetization has been dephased more than one cycle per nominal slice thickness prior to the beginning of the next RF pulse. The Appendix details a simple relationship between TBW and crusher strength to ensure sufficient dephasing. Fig. 8 demonstrates that

incorporation of B_0 into ssEPG reduces the variability of in vivo T_2 estimates, particularly in regions of B_0 near integer multiples of $1/T_R$ from $1/(T_R)$.

Depending on the crusher strength and TBW, the B_0 effects and the MRF contrast effects in a fixed T_R MRF sequence are not separable as they are with idealized crushing^{16,25}. However, B_0 effects are still separable for higher order frequencies as shown in Eq. (10) and Fig. 5. This separability should be restored for higher crusher strengths and most 3D acquisitions. Yet, in cases where rapid acquisition is required, 3D may not be an option, and diffusion effects²⁶ may limit the use of high crusher strengths.

Limitations of this study are the uncertainty of all sources of influence on in vivo T_2 estimates and code optimization. Slice profile effects are only one component that contribute to relaxometry errors. Undersampling effects in MRF have shown to limit the accuracy of MRF.²⁷ Multi-compartment effects, with or without exchange, may bias parameter estimates.²⁸ Notably, a 3D MRF uSSFP study of the brain showed T_2 values much lower than those from conventional estimates.²⁹ The skeletal muscle T_1 and T_2 values in this study are, respectively, consistent with and lower than conventional estimates²⁰. Conversely, the ssEPG T_2 estimates in phantom (Fig. 4) are entirely consistent with conventional measurements. Depending on TBW and inclusion of B_0 effects, the ssEPG dictionary calculation can be substantially slower than other EPG-based calculation methods. Optimization of the CPU and GPU code is the subject of future work. For example, the number of discrete time steps, N_{RF} , in the ssEPG hard pulse approximation was not optimized in this work. Since the number of ssEPG states scales with N_{RF} (see Appendix), the computation time should scale as N_{RF}^2 , and memory requirements may be decreased by reducing N_{RF} . Reducing N_{RF} may decrease modeling accuracy, but the optimal setting of N_{RF} for a given sequence and desired accuracy is not explored here. Despite these limitations, we have shown: ssEPG provides accurate signal and slice profile calculations, MRF T_2 estimation can be improved using ssEPG, gradient crusher interactions with slice-selective excitation may lead to bias that can be corrected with ssEPG modeling, and a simple relationship between TBW and crusher strength can be applied to ameliorate T_2 bias in uSSFP MRF without explicit modeling.

While the focus of this work was to apply ssEPG to transient state uSSFP slice profiles, such as those in MRF, this modeling technique could be applied to slice-selective MSE measurements, as well. In situations of low gradient crusher strength or inhomogeneous pulse profiles, ssEPG may yield improvements in T_2 estimation. However, further investigation is required to determine ssEPG's utility in MSE.

In support of reproducible research, the source code along with figure reproduction scripts and data are freely available for download at https://github.com/jostenson/mrm_ssepg (SHA-1: ac87d44).

Conclusions

Transient gradient-crushed sequences such as uSSFP MRF are sensitive to slice profile effects. These profile effects are dependent on RF pulse, crusher strength, and B_0 . All these

effects can be modeled with ssEPG to improve MRF relaxometry estimates as well as to provide insights into the source and relationship of different modes of bias.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

The authors would like to thank: the Vanderbilt University Institute of Imaging Science Human Imaging Core, including Ms. Clair Kurtenbach, Ms. Leslie McIntosh, and Mr. Christopher Thompson for expert technical assistance; Prof. Will Grissom and Prof. Doug Hardin for useful discussions; and Prof. Bennett Landman and Dr. Melissa Hooijmans for assistance in phantom and in vivo measurements.

Funding Sources

NIH R01 DK105371, NIH R01 AR073831, NIH K25 CA176219, NIH R01 EB017230

Appendix

The following is a description of relationships between RF model properties, crusher gradient, and spatial/frequency resolution in ssEPG. The action of off-resonance frequency under free precession in EPG is also noted.

If we define the constant slice-selective gradient strength G , in terms of time-bandwidth product κ , RF pulse approximated in N_{RF} discrete steps of duration $\tau = N_{\text{RF}}^{-1} t$, and slice thickness Δ_{sl} as

$$G = \frac{2\pi\kappa}{\gamma\tau\Delta_{\text{sl}}} \quad [\text{A.1}]$$

and insert this into the definition of k_z from Eq. (8), we can see that spatial-frequency discretization can also be given as

$$\Delta k_z = \frac{\kappa}{N_{\text{RF}}\Delta_{\text{sl}}} . \quad [\text{A.2}]$$

The EPG state matrix is $\Omega \in \mathbb{C}^{3 \times Q}$, with Q states, has the effective field-of-view equal to the reciprocal of Eq. (A.2). The discrete spatial-frequency representation of the complex magnetization

$$F_+[n; t] = \begin{cases} \Omega^*[2, n; t], & 1 \leq -n \leq Q-1 \\ \Omega[1, n; t], & 0 \leq n \leq Q-2 \end{cases}, \quad [\text{A.3}]$$

where $F_+ \in \mathbb{C}^{2Q-2}$, with spacing between states of k_z and Ω^* is the complex conjugate of Ω . For a given resolution in the spatial domain Δ_z , using Eq. (A.2), Q can be given as

$$Q = \frac{\Delta_{\text{sl}} N_{\text{RF}}}{2\Delta_z \kappa} + 1 . \quad [\text{A.4}]$$

A gradient crusher may be applied to $\mathbf{Q}$, shifting its transverse states by multiples of k_z . If N_{crush} is the number of crusher cycles per nominal slice thickness, and f_r is the fraction of the RF duration before the isodelay, then the number of discrete steps applied by the gradient crusher N_{cycle} is

$$-N_{\text{cycle}} = f_r N_{\text{RF}} - \frac{N_{\text{crush}}/\Delta_{\text{sl}}}{\Delta k_z}. \quad [\text{A.5}]$$

Combining Eqs. (A.2) and (A.5) we can write

$$N_{\text{cycle}} = N_{\text{RF}} \left(\frac{N_{\text{crush}}}{\kappa} - f_r \right). \quad [\text{A.6}]$$

The net number of discrete steps, N , taken in a time T_R from the gradient crusher and the portion of slice-select gradient before the isodelay is given by

$$\Delta N = f_r N_{\text{RF}} + N_{\text{cycle}} = \frac{N_{\text{crush}} N_{\text{RF}}}{\kappa}. \quad [\text{A.7}]$$

From this expression and Eq. (A.4) we can write the number of ssEPG states relative to the net shift in state-space over each T_R as

$$\frac{Q}{\Delta N} = \frac{1}{N_{\text{crush}}} \left(\frac{\Delta_{\text{sl}}}{2\Delta_z} + \frac{\kappa}{N_{\text{RF}}} \right). \quad [\text{A.8}]$$

From Eqs. (A.5–A.7), N_{cycle} comes from the slice-select and separate dephasing gradient contributions. The number of cycles per nominal slice thickness advanced by the slice-select gradient, $N_{\text{crush,ss}}$, is $f_r \kappa$. The remainder from the dephasing gradient is $N_{\text{crush,g}} = N_{\text{crush}} - N_{\text{crush,ss}}$. So, for $f_r = 1/2$, there will be at least one cycle of dephasing prior to RF excitation for

$$N_{\text{crush}} \geq \frac{\kappa}{2} + 1. \quad [\text{A.9}]$$

Under free precession, complex transverse magnetization $M_{\pm}$ at position z experiencing an off-resonance of frequency B_0 for a time τ can be written as

$$M_{\pm}(\tau + t; z) = e^{\pm i 2\pi \Delta B_0 \tau} M_{\pm}(t; z). \quad [\text{A.10}]$$

By taking the Fourier transform of Eq (A.9) and assuming that B_0 is independent of z , we can write

$$F_{\pm}(\tau + t; k_z) = e^{\pm i 2\pi \Delta B_0 \tau} F_{\pm}(t; k_z). \quad [\text{A.11}]$$

References

1. Jiang Y, Ma D, Seiberlich N, Gulani V, Griswold MA. MR fingerprinting using fast imaging with steady state precession (FISP) with spiral readout. *Magn Reson Med*. 2015;74(6):1621–1631. doi:10.1002/mrm.25559 [PubMed: 25491018]
2. Weigel M Extended phase graphs: Dephasing, RF pulses, and echoes - Pure and simple. *J Magn Reson Imaging*. 2015;41(2):266–295. doi:10.1002/jmri.24619 [PubMed: 24737382]
3. Malik SJ, Sbrizzi A, Hoogduin JM, Hajnal JV. Equivalence of EPG and Isochromat-Based Simulation of MR Signals. In: *Proc Intl Soc Mag Reson Med*; 2016:3196.
4. Lebel RM, Wilman AH. Transverse relaxometry with stimulated echo compensation. *Magn Reson Med*. 2010;64(4):1005–1014. doi:10.1002/mrm.22487 [PubMed: 20564587]
5. Malik SJ, Padormo F, Price AN, Hajnal JV. Spatially resolved extended phase graphs: Modeling and design of multipulse sequences with parallel transmission. *Magn Reson Med*. 2012;68(5):1481–1494. doi:10.1002/mrm.24153 [PubMed: 22246975]
6. McPhee KC, Wilman AH. Transverse relaxation and flip angle mapping: Evaluation of simultaneous and independent methods using multiple spin echoes. *Magn Reson Med*. 2017;77(5):2057–2065. doi:10.1002/mrm.26285 [PubMed: 27367906]
7. Buonincontri G, Sawiak SJ. MR fingerprinting with simultaneous B1 estimation. *Magn Reson Med*. 2015;00:1–9. doi:10.1002/mrm.26009
8. Cloos MA, Knoll F, Zhao T, et al. Multiparametric imaging with heterogeneous radiofrequency fields. *Nat Commun*. 2016;7:12445. doi:10.1038/ncomms12445 [PubMed: 27526996]
9. Jaubert O, Cruz G, Bustin A, et al. Water–fat Dixon cardiac magnetic resonance fingerprinting. *Magn Reson Med*. 2020;83(6):2107–2123. doi:10.1002/mrm.28070 [PubMed: 31736146]
10. Hong T, Han D, Kim MO, Kim DH. RF slice profile effects in magnetic resonance fingerprinting. *Magn Reson Imaging*. 2016;41:73–79. doi:10.1016/j.mri.2017.04.001
11. Ma D, Coppo S, Chen Y, et al. Slice profile and B1 corrections in 2D magnetic resonance fingerprinting. *Magn Reson Med*. 2017;78(5):1781–1789. doi:10.1002/mrm.26580 [PubMed: 28074530]
12. Guzek B, Körzdörfer G, Mathias N, Pfeuffer J. Influence of Off-Resonance on FISP Magnetic Resonance Fingerprinting (FISP-MRF). In: *Proceedings of the Joint Annual Meeting ISMRM-ESMRMB, Paris, France*; 2018:4264.
13. Körzdörfer G, Guzek B, Jiang Y, et al. Description of the off-resonance dependency in slice-selective FISP MRF. In: *Proceedings of the Joint Annual Meeting ISMRM-ESMRMB, Paris, France*; 2018:4232. <http://indexsmart.mirasmart.com/ISMRM2018/PDFfiles/4232.html>.
14. Bain AD, Anand CK, Nie Z. Exact solution to the Bloch equations and application to the Hahn echo. *J Magn Reson*. 2010;206(2):227–240. doi:10.1016/j.jmr.2010.07.012 [PubMed: 20692859]
15. Keenan KE, Stupic KF, Boss MA, et al. Multi-site, multi-vendor comparison of T1 measurement using ISMRM/NIST system phantom. In: *Proc Intl Soc Mag Reson Med*; 2016:3290.
16. Ostenson J, Damon BM, Welch EB. MR fingerprinting with simultaneous T1, T2, and fat signal fraction estimation with integrated B0 correction reduces bias in water T1 and T2 estimates. *Magn Reson Imaging*. 2019;60:7–19. doi:10.1016/j.mri.2019.03.017 [PubMed: 30910696]
17. Jankiewicz M, Gore JC, Grissom WA. Improved encoding pulses for Bloch-Siegert B1 + mapping. *J Magn Reson*. 2013;226:79–87. doi:10.1016/j.jmr.2012.11.004 [PubMed: 23220183]
18. Crawford SB, Kosinski AS, Lin HM, Williamson JM, Barnhart HX. Computer programs for the concordance correlation coefficient. *Comput Methods Programs Biomed*. 2007;88(1):62–74. doi:10.1016/j.cmpb.2007.07.003 [PubMed: 17709153]
19. Wang D, Ostenson J, Smith DS. snapMRF: GPU-accelerated magnetic resonance fingerprinting dictionary generation and matching using extended phase graphs. *Magn Reson Imaging*. 112019. doi:10.1016/j.mri.2019.11.015
20. Bojorquez JZ, Bricq S, Acquitier C, Brunotte F, Walker PM, Lalande A. What are normal relaxation times of tissues at 3 T? *Magn Reson Imaging*. 2017;35:69–80. doi:10.1016/j.mri.2016.08.021 [PubMed: 27594531]
21. Uecker M, Tamir JI. BART: version 0.4.02 (Version v0.4.02). 2017. doi:10.5281/zenodo.1066014

22. Zwart NR, Johnson KO, Pipe JG. Efficient sample density estimation by combining gridding and an optimized kernel. *Magn Reson Med*. 2012;67(3):701–710. doi:10.1002/mrm.23041 [PubMed: 21688320]
23. McGivney D, Deshmane A, Jiang Y, et al. Bayesian Estimation of Multicomponent Relaxation Parameters in Magnetic Resonance Fingerprinting. 2018;170:159–170. doi:10.1002/mrm.27017
24. Nagtegaal M, Koken P, Amthor T, Doneva M. Fast multi-component analysis using a joint sparsity constraint for MR fingerprinting. *Magn Reson Med*. 2019;(July):mrm.27947. doi:10.1002/mrm.27947
25. Flassbeck S, Schmidt S, Breithaupt M, Bachert P, Ladd ME, Schmitter S. On the Influence of Intra-Voxel Dephasing in FISP-MRF with Variable Repetition Time. *Proc Intl Soc Mag Reson Med*. 2017:1492.
26. Kobayashi Y, Terada Y. Diffusion-weighting Caused by Spoiler Gradients in the Fast Imaging with Steady-state Precession Sequence May Lead to Inaccurate T_2 Measurements in MR Fingerprinting. *Magn Reson Med Sci*. 2018:1–9. doi:10.2463/mrms.tn.2018-0027
27. Stolk CC, Sbrizzi A. Understanding the Combined Effect of k-Space Undersampling and Transient States Excitation in MR Fingerprinting Reconstructions. *IEEE Trans Med Imaging*. 2019;38(10):2445–2455. doi:10.1109/TMI.2019.2900585 [PubMed: 30802852]
28. Does MD. Inferring brain tissue composition and microstructure via MR relaxometry. *Neuroimage*. 2018;182(December 2017):136–148. doi:10.1016/j.neuroimage.2017.12.087 [PubMed: 29305163]
29. Ma D, Jiang Y, Chen Y, et al. Fast 3D magnetic resonance fingerprinting for a whole-brain coverage. *Magn Reson Med*. 2018;79(4):2190–2197. doi:10.1002/mrm.26886 [PubMed: 28833436]

Fig. 1.

The magnitudes of the simulated, transient slice-profile shapes calculated by numerical solution to the Bloch equations and the slice-selective extended phase graph (ssEPG) techniques. The unbalanced SSFP sequence uses an Hanning-windowed sinc pulse with a time-bandwidth factor of four, a nominal flip angle of 90° , and four crusher cycles per nominal slice thickness, which produces large dynamic oscillations in the profiles.

Fig. 2.

The measured and simulated magnitudes of the slice profiles from the agar phantom. The measured, slice-selective EPG (ssEPG), and partitioned EPG (pEPG) profiles were scaled by the root-mean-square of their respective first profiles.

Fig. 3.

The root-mean-square error (RMSE) of the normalized signals magnitudes modeled by slice-selective (ssEPG), partitioned (pEPG), and conventional EPG without slice profile modeling, relative to the measured signal from the agar phantom over 10 excitations for a crusher strength of one cycle per nominal slice thickness and for four cycles. The time-bandwidth product (TBW) of the Hanning-windowed sinc pulses and the nominal flip angles (FA) in degrees are listed.

Fig. 4.

The MRF T_2 estimates over a physiological range in the MRI system phantom and concordance correlation coefficients (CCC) from different slice profile modeling techniques for different RF time- bandwidth products (TBW) and crusher cycles per nominal slice thickness (C). The EPG without slice profile corrections are shown in (a), the partitioned EPG (pEPG) results in (b), and the slice-selective EPG (ssEPG) estimates in (c). The dotted line is that of perfect concordance. The CCCs are in panel (d) with error bars indicating 95% confidence intervals.

Fig. 5.

The magnitude of the slice profiles from the second excitation of the MRF sequences for a TBW of four RF pulse and one cycle per nominal slice thickness gradient crusher at the listed B_0 s (a). The magnitude of the of MRF signals modeled at the listed B_0 s (b). The slice profiles and signal magnitudes of $B_0 = 1/4$ and $1/2$ overlap with $5/4$ and $3/2$, respectively, in (a) and (b). The phase of the MRF signals are shown in (c). The $5/4^*$ and $3/2^*$ B_0 signals were reconstructed from the $1/4$ and $1/2$ B_0 signals, respectively, using

Eq. (10). These reconstructed signals overlap with the explicitly calculated $5/4$ and $3/2$ B_0 signals.

Fig. 6.

The mean relative T_2 bias from MRF signals modeled with B_0 effects, fitted against models without B_0 effects for three different MRF sequences and six different time-bandwidth (TBW) and crusher cycles per nominal slice thickness (C) combinations. The mean is across four physiological T_1/T_2 combinations noted in the text. Error bars represent the standard deviation of the relative bias.

Fig. 7.

The MRF T_1 (a) and T_2 (b) maps of the calf from three different crusher strengths fit by four different EPG models for a TBW of four RF excitation pulse. The “EPG” fits do not consider slice profile effects. The “pEPG” method accounts for slice profile effects from the RF pulse but idealizes crusher action. The “ssEPG” method accounts for RF pulse and the differences in crusher strength. The T_2 of the “EPG” method exceeds the dynamic range of the color mapping, which is reduced to better capture variations in the other fitting models.

Fig. 8. The coefficient of variation (COV) of estimated T_2 across the different crusher strengths in the calf for the four different fitting methods (a). The mean B_0 map in (b) is estimated from the slice-selective EPG (ssEPG) with B_0 modeling. An overlay shows regions of B_0 that are within 30% of an integer multiple of $1/(T_R)$ from $1/(2T_R)$ (c).

Table 1.Modeled T_2 bias with RF time-bandwidth product and crusher strength

TBW^a	N_{crush}^b	$N_{\text{crush,ss}}^c$	$N_{\text{crush,g}}^d$	Max. Rel. T_2 bias ^e
4	1	2	-1	0.933
4	4	2	2	0.057
4	8	2	6	0.011
8	1	4	-3	0.543
8	4	4	0	0.504
8	8	4	4	0.028

^a TBW – time-bandwidth product^b N_{crush} – number of crusher cycles per nominal slice thickness^c $N_{\text{crush,ss}}$ – number of crusher cycles from slice-select gradient before isodelay^d $N_{\text{crush,g}}$ – number of crusher cycles from dephasing gradient^eMaximum relative T_2 bias from fixed T_R /fixed T_E MRF sequence from the data used in Fig. 6