SPIN ECHO SS-PARSE: A PARSE MRI METHOD TO ESTIMATE R2, R2’ AND FREQUENCY IN A SINGLE SHOT

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SPIN ECHO SS-PARSE: A PARSE MRI METHOD TO ESTIMATE R2, R2’ AND FREQUENCY IN A SINGLE SHOT

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BIOMEDICAL ENGINEERING

ABSTRACT

Rapid and accurate mapping of relaxation rates applies to a number of neuroimaging and functional magnetic resonance imaging (fMRI) studies. Previously developed relaxation rate mapping methods are based mostly on non-linear fitting of intensity images. For the first time, this study developed an ultrafast and direct transverse relaxation rate mapping technique, Spin Echo Single-Shot Parameter Assessment by Retrieval from Single Encoding (SE-SS-PARSE). Four useful imaging parameters, local transverse magnetization magnitude (M_{xy0}), frequency (f), reversible and irreversible transverse relaxation rate (R2’ and R2), can be estimated using an iterative searching algorithm simultaneously and quantitatively. In addition, the SE-SS-PARSE technique is free of geometric errors and blurring artifacts that commonly occur in the other SS techniques, such as echo planar imaging (EPI).

Specifically, this work developed the signal model of SE-SS-PARSE and tested this technique with computer simulations, experimental phantoms and biological samples. In simulations, even at a noise level with low signal-to-noise ratio (SNR) of 20dB, SE-SS-PARSE is able to generate accurate local magnetization parameter maps subject to statistical comparison with actual parameter values. After successful testing with a numerical phantom, the SE-SS-PARSE technique was performed on a realistic four-tube phantom, which was designed to produce in-vivo-like and different R2 and R2’ values in each tube. The estimated relaxation rates from SE-SS-PARSE were highly correlated with relaxa-
tion rates computed from slower “gold standard” conventional MRI methods (correlation coefficients r1=0.9636 for R2’, r2=0.9788 for R2). The ultrafast SE-SS-PARSE technique was also compared with a widely used T2-weighted imaging MRI technique, fast spin echo (FSE), in mapping R2 values. Four-tube phantom studies indicate that SE-SS-PARSE produces results with accuracy equivalent to FSE, but with a much shorter acquisition time. In addition, biological sample studies show that SE-SS-PARSE with fat saturation pulse produces more accurate R2 estimates than used without fat saturation when fat is present. In conclusion, SE-SS-PARSE is an ultrafast MRI method that can produce reliable R2 and R2’ mapping. It is expected that SE-SS-PARSE will find important applications in neuroimaging and fMRI studies, especially in recording rapidly changing physiological phenomena.

Keywords: Rapid relaxation rate mapping, PARSE MRI, Single-shot, Spin Echo.
DEDICATION

I would like to dedicate this dissertation to my dearest parents, Bingqi Rao and Yunti Li, and to my beloved husband, Ming Yan.
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<td>3D</td>
<td>3-Dimensional</td>
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<td>BOLD</td>
<td>Blood Oxygenation Level Dependent</td>
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<td>CPMG</td>
<td>Carr-Purcell Meiboom-Gill</td>
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<td>CT</td>
<td>Computed Tomography</td>
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<td>DESPOT</td>
<td>Driven Equilibrium Single Pulse Observation</td>
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<td>EPI</td>
<td>Echo Planar Imaging</td>
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<td>FARM</td>
<td>Fast Acquisition Relaxation Mapping</td>
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<td>FID</td>
<td>Free Induction Decay</td>
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<td>fMRI</td>
<td>functional MRI</td>
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<td>FSE</td>
<td>Fast Spin Echo</td>
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<td>FFT</td>
<td>Fast Fourier Transform</td>
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<td>FT</td>
<td>Fourier Transform</td>
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<td>Gradient Echo</td>
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<td>MRI</td>
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<tr>
<td>PLCG</td>
<td>Progressive Length Conjugate Gradient</td>
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<tr>
<td>RF</td>
<td>Radiofrequency</td>
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<td>SE</td>
<td>Spin Echo</td>
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<td>SNR</td>
<td>Signal to Noise Ratio</td>
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<td>SPGR</td>
<td>Spoiled Gradient Recalled-Echo (SPGR)</td>
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<td>SS-PARSE</td>
<td>Single-Shot Parameter Assessment by Retrieval from Signal Encoding</td>
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<td>TA</td>
<td>Acquisition Time</td>
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<td>TE</td>
<td>Echo Time</td>
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<td>TR</td>
<td>Repetition Time</td>
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<td>TSE</td>
<td>Turbo Spin Echo</td>
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INTRODUCTION

During the past few decades, magnetic resonance imaging (MRI) has evolved into a primary imaging modality in medical treatment, clinical diagnosis and scientific research. Today’s MRI provides superior *in-vivo* information and soft tissue contrast as compared to other established imaging technologies, such as computed tomography (CT). Novel and fast MRI sequences, improved image quality, 3-dimensional (3D) imaging and many other advanced MRI methods such as diffusion MRI, perfusion MRI and functional MRI (fMRI) are in constant development [1]. Current, MRI techniques are capable of obtaining high-quality 3D images and monitoring human brain functions.

This dissertation focuses on developing ultrafast quantitative MRI techniques with acceptable image qualities. The present MRI scan time has been dramatically reduced since the first imaging result published in the early 1970s [2]. Fast MRI methods are in demand to reduce cost for both patients and hospitals. Shorter scan time can potentially diminish image artifacts from random motions as well as minimize interference from subtle environmental or physiological changes. Furthermore, modern functional neuroimaging also requires rapid data acquisition to record dynamic functional
brain responses. Currently, enhanced MRI hardware performance has made very short
repetition time (TR) and echo time (TE) feasible, thus enabling complete image
acquisition at the sub-second level [3]. This has encouraged innovation in the design of
novel single-shot (SS) MRI sequences. However, such SS MRI usually suffers from
geometric distortions or blurring artifacts due to the off-resonance effect.

The recently developed SS-Parameter Assessment by Recovery from Signal
Encoding (SS-PARSE) [4] is an ultrafast and advanced parameter-based SS MRI
technique. The signal model of SS-PARSE considers both transverse magnetization
magnitude (M_{xy0}) decay and phase evolutions. Therefore, it is free of geometric errors
and blurring, which leads to more reliable and robust image measurements. By searching
the parameter space iteratively, the progressive length conjugate gradient (PLCG)
algorithm has been used to reconstruct parameter maps of local transverse magnetization
magnitudes (M_{xy0}), transverse relaxation rates (R2*) and frequencies (f). In this work, a
spin echo version of SS-PARSE technique (SE-SS-PARSE) has been developed to
produce information on two additional image parameters: the reversible transverse
relaxation rate (R2’) and irreversible transverse relaxation rate (R2). Rapid and accurate
mapping of R2 and R2’ applies to a number of neuroimaging studies and functional MRI
(fMRI) research. SE-SS-PARSE has been validated with computer simulations, phantom
studies and *in-vivo* subjects. The accuracy assessment was made by comparing results from the SE-SS-PARSE method and a “gold-standard” MRI method. To fully understand the SE-SS-PARSE technique, the following Section I includes theoretical background on k-space in conventional MRI, transverse relaxation rate mapping methods and theory of SS-PARSE. Section II provides detailed information on the SE-SS-PARSE technique and also discusses the potential applications of R2 and R2’ mapping. A brief overview of this dissertation research is included in Section III.

Section I: Background

*K-space in conventional MRI*

Unlike many other imaging techniques, MRI image data in the spatial domain are not directly obtained in experiments. Instead, MRI acquires raw data containing encoded spatial information of the target image. This encoded spatial information is stored as a matrix of spatial frequencies in the spatial frequency domain, which is often referred as k-space [5]. In k-space, each data point at \((k_{fe}, k_{pe})\) contains information from the entire image at that particular spatial frequency. Here subscript \(fe\) refers to frequency encoding, while \(pe\) represents phase encoding with magnetic gradients fields. The magnetic gradients usually vary in amplitude and duration time to perform frequency encoding and
phase encoding to fill each of the k-space grids. After the k-space array has been filled up, images will be reconstructed by taking the fast Fourier Transform (FFT) of the k-space data. Examples of k-space data and their associated FFT results are shown in Fig. 1. In general, data points around the center of k-space correspond to image contrast, while the peripheral data points determine the spatial resolution [6].

After introducing the k-space, now it is possible to see how the conventional MRI works. Generally speaking, conventional MRI methods collect all k-space data in a very regular order. For the standard SE or gradient echo (GE) MRI sequences, one line of k-space data is collected after a radiofrequency (RF) excitation, then the subsequent line of k-space data is collected following another RF excitation. This process is repeated until the entire k-space has been filled. The initial RF excitation brings down the proton magnetization to the transverse plane. The next RF excitation is applied after the magnetization has recovered to a steady-state longitudinal value, with zero transverse components. In this process, the time constant for the longitudinal magnetization recovery is called longitudinal relaxation time, or T1. The time constant for the transverse magnetization recovery is referred to as transverse relaxation time, or T2*. The different MRI time constants in different types of tissues form the contrast in an MRI image. The time interval between successive RF excitations is the repetition time (TR). TR varies
from a few hundred milliseconds to a few seconds depending on the experimental target.

The total acquisition time (TA) in the conventional MRI is thus expressed as: \( TA = N \times TR \), where \( N \) is the number of k-space lines or the number of RF excitations. If \( TR \) is 3 seconds, the TA for acquiring an image of 256x256 matrix size would be \( 256 \times 3 \) sec = 12.8 min. Such a long scan time may not be appropriate in practice for some human body or brain imaging applications. Respiratory motion, random motion, and physiological and environmental changes during longer imaging times can lead to numerous image artifacts and degrade image quality.

*Transverse Relaxation Rate Mapping Methods*

The normally observed transverse relaxation rate \( R_2^* (1/T_2^*) \) depends on both macroscopic magnetic field inhomogeneities and pure molecular effects. The magnetic field inhomogeneities lead to signal dephasing that is reversible and can be characterized by the reversible transverse relaxation rate \( R_2' (1/T_2') \). Spin-spin relaxation, on the other hand, leads to irreversible signal dephasing characterized by the irreversible relaxation rate \( R_2 (1/T_2) \). The mathematical relationship of the three types of relaxation rates is as:

\[
R_2^* = R_2 + R_2' \quad (1)
\]
A spin echo excitation sequence, including a 90-degree pulse followed by an 180 refocus pulse, can separately measure R2 and R2’, which are two useful parameters in diagnosis of neural-degenerative diseases and study of human brain functions.

To map both R2 and R2’ using conventional MRI, a multiple echo (ME) GE and an ME-SE sequence is used. The MR signal amplitude decays with a rate of R2* as the echo time (TE) increases in the ME-GE method. So an R2* map can be computed by fitting the non-linear exponential decay of the intensity map S_i pixel by pixel at each TE_i:

$$S_i = S_0 \cdot e^{-\frac{TE_i}{R2^*}} \quad (2)$$

where $S_0$ is the initial signal intensity. In the ME-SE sequence, the 180-degree pulse refocuses the inhomogeneity of the magnetic field; thus the signal decays at the rate of R2 as TE increases. Similarly, fitting the non-exponential signal decay along TE produces the R2 map:

$$S_i = S_0 \cdot e^{-\frac{TE_i}{R2}} \quad (3)$$

Subtracting the R2 map from the R2* map gives us the R2’ map:

$$R2’=R2*-R2 \quad (4)$$

As discussed in the last section, the typical TA for acquiring one image is a few minutes. At least 3 or more images are needed to generate R2* maps and R2 maps in order to fit the signal decay accurately in conventional MRI. The total TA in mapping transverse
relaxation rates would be too long for practical clinical scans. A second classical approach toward R2 mapping uses the Carr-Purcell [7] Meiboom-Gill [8] (CPMG) sequence and a spin-warp imaging sequence [9]. Although both of these techniques are straightforward and have been used as a standard R2 mapping method, the time they consume would still be a problem in practice for some applications.

Instead of multiple scans, a single-scan method, Gradient Echo Sampling of the Free Induction Decay and Echo (GESFIDE) was proposed by Ma and Wehrli [10] to reduce MRI scan time. The sequence map of GESFIDE is illustrated in Fig. 2. It contains two signal sections: one is descending immediately following the α excitation pulse and one is ascending following the refocus β pulse. The α and β pulses are usually set to 90-180 to optimize the signal strength. As shown in the sequence map, the signal in the first section decays exponentially with a constant rate of R2*, while the signal in the second section increases exponentially with a constant rate of R2’. Linear combinations of R2* and R2’ generate R2 and R2’ maps, as shown in Eq (5) and (6):

\[ R2 = 0.5 \times (R2^* + R2') \] (5)

\[ R2' = 0.5 \times (R2^* - R2') \] (6)

A big advantage of the GESFIDE method is that it is insensitive to the RF pulse imperfection. Although GESFIDE reduces scan durations by measuring two image
parameters at the same time, it may still be time-consuming with multiple-shot acquisitions.

Another method uses the Snapshot FLASH [11] technique to quantitatively map R2 values rapidly. In this method, TA is reduced by shortening the magnetization recovery time through a small flip angle RF excitation, typically 5 to 10 degrees. With a small flip angle it is possible to work with a TR that is around 2 to 3 milliseconds. Deichmann et al. [12] has shown that T2-mapping Snapshot FLASH imaging can be further accelerated by decreasing the time delay between successive acquired T2-weighted images. Furthermore, accurately and rapidly acquired T2 values can be determined with T1-measurement at the same time. Least-square fitting was used in their experiments to generate T1 and T2 maps acquired within 30 seconds.

Recently, a high-resolution, rapid, R2 and R1 combined mapping approach was proposed by Deoni et al. [13], referred as driven equilibrium single-pulse observation (DESPOT). In DESPOT1, T1 values are computed from a series of spoiled gradient recalled-echo (SPGR) images with varied RF flip angle and a constant TR. Similarly, R2 values can be computed from a series of steady-state free precession (SSFP) images with different RF flip angle and a constant TR. But T1 values are required in the calculations of R2. The linearity of the SPGR and SSFP signal requires acquisition of images with
only two flip angles to calculate R1 and R2 values. This property of the DESPOT method not only greatly reduces the data acquisition time but also leads to simple post-processing. Therefore, DESPOT is ideal for studying high-resolution relaxation maps.

There are two major ways to achieve faster scanning: one is to shorten TR, which has been discussed in the Snapshot FLASH technique above; the other one is to increase the areas covered in k-space following each RF excitation. One primary example of such a technique that applies to R2 mapping is fast spin echo (FSE) or turbo spin echo (TSE) imaging [14]. FSE dramatically reduces the MR scan time by collecting multiple k-lines following each RF excitation. An example of the FSE sequence and its corresponding k-space trajectory is shown in Fig. 3. Multiple 180 refocusing pulses following the 90-degree pulse provide multiple spin echo signals, from which multiple k-space lines can be collected. Each echo signal has its own phase encoding. If N_{fse} is the number of 180-degree pulses, then the TA is reduced by N_{fse} times. In other words, FSE is N_{fse} time faster than the conventional SE method. For this reason, FSE has replaced the conventional SE method to become the most commonly used clinical T2-weighted imaging tool. The scan time for FSE is acceptable in most cases except carotid artery imaging. To reduce motion artifacts due to respiration and blood pulsation in carotid
artery imaging, two breath-hold-based FSE methods have been proposed [15,16] for accurate R2 mapping.

To further reduce the MRI scan time, SS techniques have been widely developed which cover the whole k-space following only one set of RF excitations. Half-Fourier Single-Shot Turbo Spin Echo (HASTE) [17, 18] proposed by Kiefer et al. is a single-shot version of FSE. Followed by one 90-180-180... pulse, slightly more than half of the k-space data are acquired with a relatively long echo train. The other half of k-space is filled by the symmetry property of the k-space. However, low SNR and imaging blurring artifacts usually occur in HASTE due to the signal decay during acquisition of multiple echoes, and large RF deposition from multiple successive 180-degree pulses is a concern [19]. After the introduction of parallel imaging, a HASTE with parallel acquisition (PHASTE) [19] has been proposed to minimize effects of R2 decay during the data acquisition by parallel sampling.

Echo planar imaging (EPI) is the most widely and frequently used SS technique. Mansfield and Pykett [20] introduced EPI in 1978, for the first time allowing a whole image to be collected after a single RF pulse. Fig. 4 shows an example of a GE-EPI sequence diagram and the corresponding k-trajectory. At the beginning, a frequency encoding gradient pulse and a phase-encoding gradient put the spins at the corner of k-
space [5]. Then more phase and frequency-encoding directions are cycled to transverse the whole k-space. In the usual signal recording period, 64 or more phase and frequency encoding gradients are filled in. Whereas the conventional MRI method measures one line of k-space in a single repetition time (TR), EPI is capable of measuring the entire k-space in a single TR. ME-GE and ME-SE based EPI are usually used in producing R2*-weighted and R2-weighted images. R2*, R2 and maps are computed through a similar least square fitting process as in the conventional MRI. However, due to off-resonance effects, EPI often suffers from geometric distortion and blurring artifacts [21-25].

Combining the EPI and FSE techniques, Oshio and Feinberg proposed a rapid gradient and spin echo (GRASE) imaging technique [26, 27]. The GRASE pulse sequence is adapted from the FSE sequence, including multiple refocusing pulses to produce multiple spin echo signal and gradient recalled echoes for each spin echo. Due to the combination of multiple spin echo and short gradient echo trains, GRASE is relatively insensitive to magnetic field inhomogeneity effects and large chemical shift [27]. In addition, the data acquisition time in GRASE is greatly reduced by EPI factor and FSE turbo factor. The product of the EPI factor and turbo factor gives the factor by which acquisition time is reduced [3]. Therefore, a GRASE sequence with EPI factor of 3 and
turbo factor of 8 will decrease the TA by 1/24 (1/3 x 1/8). However, the trade-off for the short data acquisition is usually poorer image resolution and signal to noise ratio (SNR).

Combining the EPI technique, GESFIDE technique and parallel imaging, Jochimsen et al. introduced the ultrafast multi-gradient-echo single-shot sampling of spin-echo refocusing (MESSER) sequence based on parallel imaging to measure both R2* and R2 values at the same time [28]. The data acquisition in MESSER can be divided into 3 parts: the free induction decay (FID), the ascending part of the SE signal and the descending part of the SE signal. In each period of these signals, three consecutive EPI readouts producing three completed images are collected. For the normal multiple echo EPI (MEPI) method, the data acquisition time for a single frame typically lasts for more than 20ms. The signal usually dies away after two frames of EPI acquisitions. Using parallel imaging reduces the data collection time for each EPI frame, and thus enables three frames of EPI data acquisition in MESSER. Three intensity images are the minimum requirement for computing signal decaying rates, through the nonlinear fitting as in the GESFIDE method.

All the R2 or R2’ or R2* mapping methods introduced so far are indirectly calculated by the non-linear least square fitting of directly measured intensity maps. A rapid technique named T2 fast acquisition relaxation mapping (T2-FARM) [29] allows
direct mapping of T2 or R2 maps quantitatively within a few seconds. Although the previously described single-shot technique can acquire single intensity image within a short time, R2 calculation are often based a number of intensity images, which would slow down the whole R2 measuring process. On the other hand, T2-FARM reconstructs T2 maps directly from the raw k-space data. In a single scan, two k-space data sets with minimal T2 weighting independent of phase encoding position and strong T2 weighting with varying phase encoding position are obtained sequentially. Quantitative T2 maps are computed from k-space data through an iterative least square algorithm directly. However, imperfect refocusing pulses and eddy current effects can induce measurement errors arising in T2-FARM. A few seconds data scan time may still be too long for acquiring functional MRI data.

SS-PARSE

Conventional MRI works on the assumption that the local signal does not change during the data acquisition time. However, the local transverse magnetization decays in amplitude and evolves with phase angles simultaneously. The amount of signal change can be ignored in MRI sequences with many brief signals. However, SS MRI requires a relatively long data acquisition time in order to cover the whole k-space with a single
excitation. The considerable signal changes in SS MRI during this longer time often lead
to image artifacts such as geometric errors and blurring due to the accumulated phase
evolution of off-resonance components. Shimming can improve the field inhomogeneities
to some extent. However, it may not work effectively on large susceptibility gradients
existing in tissue near air spaces. In addition, the field inhomogeneity problem becomes
worse with the higher magnetic fields, which are increasingly popular in current MRI due
to their higher sensitivity and SNR.

The recently proposed SS-PARSE [4] technique uses a more accurate
interpretation of the local signal with consideration of temporal intra-signal magnitude
and phase evolution. SS-PARSE samples each raw data in k,t-space rather than k-space,
where t refers to the time. In principle, the SS-PARSE technique promises better and
more reliable measurements of image parameters. The parameterized signal models of
SS-PARSE are as follows:

\[ S_c(t_n) = \int\int M_{xy0}(x) \cdot e^{-[R^*_2(x)+2\pi f(x)]t} \cdot e^{-2\pi ik(t)x} \, dx \]  

(7)

where \( S_c(t) \) refers to the net MRI signal. \( M_{xy0}, f, \) and \( R^*_2 \) are the local transverse
magnetization, frequency offset and transverse relaxation rate, which is of great interest
to fMRI studies. Data sampling in SS-PARSE follows a rosette trajectory [30, 31] in k,t-
space. The rosette trajectory is a rapid sinusoidal oscillation that rotates in the k_x-k_y plane.
and evolves with time. It frequently passes through the k-origin (center of k-space) and thereby obtains low-spatial-frequency information that varies with time, corresponding to a better SNR.

The image reconstruction in SS-PARSE is achieved by solving the inverse problem of the nonlinear signal model. SS-PARSE currently employs the PLCG algorithm [32] to estimate magnitude, frequency and relaxation rate maps by iteratively searching the parameter space. At each iteration, image parameters in the signal model will be updated to reduce the difference between experimental signal and model signal. The iteration stops once a manually set tolerance has been reached and the latest updated parameters will be used as the final estimation. This process is computationally intensive but can provide quantitative and simultaneous parameter estimations.

Section II: Spin Echo SS-PARSE

The Fourier-based GE sequence is widely used in MRI for its easy implementation and high sensitivity. In the GE sequence, a 90 degree RF pulse comes first in conjunction with a slice selective gradient, followed by a phase and frequency encoding gradients. A strong gradient recalled echo signal could be recorded after the FID. However, the effects of magnetic field inhomogeneity degrade GE signals and thus
lead to artifacts in regions with varying susceptibility. In fMRI studies, GE sequence produces strong signals around large draining veins that could obscure responses from neural activities in the parenchyma [33-37]. Another easily implemented sequence, the SE sequence has an additional 180 degree RF pulse following the 90 degree RF pulse. The 180 degree RF pulse rephases the spins to regain coherence, leading to a spin echo signal. SE-based MRI is less sensitive to field inhomogeneity and thereby is more suitable for detecting and locating effects of neuronal activities than GE MRI [38]. Some non-neuronal contributions, such as movement-related effects, are also refocused when they are slower than TE. Although the SE signal is relatively smaller than the GE signal, the echo response is greatly increased at high magnetic field (> 3T), preferable for producing high-resolution images [39-42]. Furthermore, the relatively long TE in the SE method allows additional sequence encoding before data acquisition, such as encoding for diffusion, flow etc.

In this work, we proposed a spin echo version SS-PARSE method [43] to produce two additional image parameters: irreversible transverse relaxation rates R2 and reversible transverse relaxation rate R2’. Data acquisition in SE-SS-PARSE includes two parts: the FID followed 90 degree RF pulse and SE followed the 180 refocusing pulse.
The corresponding observed local signal $S_c$ at time $t_n$ thus can be modeled differently at different time period:

$$S_c(t_n) =$$

$$\int M_{x0}(x) \cdot e^{-(R'_2(x)+2\pi f(x)+R_2(x)) \cdot (t_n+\tau_0)} \cdot e^{-2\pi ik(t_n)x} dx, \quad 0 < t_n < \frac{TE}{2} - \tau_1$$

$$\int M_{x0}(x) \cdot e^{(R'_2(x)-2\pi f(x)-R_2(x)) \cdot (t_n+\tau_1+\tau_2)} \cdot e^{-2\pi ik(t_n)x} dx, \quad \frac{TE}{2} - \tau_1 < t_n < TE - (\tau_0+\tau_1+\tau_2)$$

$$\int M_{x0}(x) \cdot e^{-(R'_2(x)+2\pi f(x)+R_2(x)) \cdot (t_n+\tau_1+\tau_2)} \cdot e^{-2\pi ik(t_n)x} dx, \quad TE - (\tau_0+\tau_1+\tau_2) < t_n$$

(8)

The signal model is the integral of the individual pixel signal at location $x$ over space. The last part of the integral $e^{-2\pi ik(t_n)x}$ represents the spatial phase modulation imposed by the gradients [1] at time $t_n$. The first part of signal model corresponds to the FID, where $\tau_0$ refers to the time period between the effective center of the 90 degree pulse and the beginning of data acquisition. The second and third part of Eq. (8) represents the ascending and descending section of the echo signal, where $\tau_1$ and $\tau_2$ are delays before and after the middle of the 180 degree pulse, including the time duration of spoiler gradients. No data is sampled during $\tau_0$, $\tau_1$ and $\tau_2$ periods, so they should be excluded from the signal model. These short time periods can be recorded in the calibration. Due to the chemical shift effects in the in-vivo study, fat signal can interfere with the water signal, resulting in inaccurate signal measurements. So a fat suppression pulse, consisting of a 90 degree frequency-selective RF pulse with a spoiler gradient following it, can be
employed before excitations. The sequence diagram including fat saturation pulse is illustrated in Fig. 5, in which the magnetization parameter $M_{xy0}$ is estimated at $t=0$. The parameter estimation in SE-SS-PARSE employs the same PLCG algorithm to estimate four image parameters: $M_{xy0}$, $f$, and $R_2$ and $R_2'$ quantitatively and simultaneously. The PLCG algorithm searches FID and spin echo signal sequentially and reduces the least square difference between experimental and model signal to satisfy a manually set threshold. The trend of estimation history changes three times, corresponding to the FID, and the successive rephasing SE and dephasing SE signals.

Similar to SS-PARSE, SE-SS-PARSE is an ultrafast MRI method that is free of geometric and blurring errors and promises more reliable and robust image parameter estimations. For the first time, SE-SS-PARSE provides information on both $R_2$ and $R_2'$ with a sub-second time scale. $R_2$ and $R_2'$ are valuable in detecting functional brain activities and assessing neuro-degenerative brain diseases.

In fMRI research, the blood $R_2$ values can be useful to measure tissue oxygen extraction fractions. Also, separating $R_2$ and $R_2'$ can be useful to distinguish BOLD responses in parenchyma from responses in large draining veins. Knowledge of the blood $R_2$ and $R_2'$ values are important to quantify the BOLD signal changes from
intravascular contribution and extravascular contribution, which together make the total observed signal changes.

Clinically, the measure of R2, R2’ values are valuable in quantifying the iron deposition induced neurological disorders. Iron is usually highly concentrated in certain regions of human brain, including the basal ganglia associated structures (the globus pallidus, substantia nigra) and dentate nucleus of the cerebellum [44]. In MRI studies, small amounts of iron can result in only very small changes to the main field. However, within the highly concentrated iron areas in neuro-degenerative patients’ brains, the amount of iron is large enough to significantly affect the MR signal decay. After the RF pulse is turned off in a MRI study, the paramagnetic iron atoms tend to realign to the direction of the main magnetic field faster than the neighboring tissue. Field gradients occur can alter the homogeneity feature of the main field. The results of these gradients are shortening of the local T2 values and the signal loss in the T2-weighted images. Specifically, the high iron level region appears dark in the T2-weighted images. Griffiths et al. [45, 46] found that R2* and R2 values were higher and R2’ was lower in putamen in the substantia nigra of patients with Parkinson’s disease. Similarly, increased iron content has been reported in the globus pallidus, substantia nigra, thalamus and frontal white matter for patients with age-related neuro-degenerative disease such as
Huntington’s disease and Alzheimer’s disease [47, 48]. There are also suggestions in the literature that measurement of brain iron content be used to assess HIV-infected patients [49] and stage of strokes [50-54].

Section III: Overview of Dissertation Research

Much of current MRI method development is directed to decrease data acquisition time and improve image accuracy. This dissertation research focuses on developing a fast scan MRI method to estimate several important image parameters, including $M_{xy0}$, $f$, $R2$ and $R2'$. Transverse relaxation rate $R2$ and $R2'$ are of great interest to a number of medical and clinical applications. The previously introduced transverse relaxation rate mapping methods [8-29], however, require at least few seconds to obtain the raw data. Parameter maps may be degraded due to motions, physical movements and environmental alterations during acquisitions lasting only a few seconds. In fMRI studies, the situation becomes worse because the typical neural activity induced blood-oxygen level dependence (BOLD) responses change continuously. The SE-SS-PARSE method developed in this work aims to quantitatively map multiple image parameters ($M_{xy0}$, $f$, $R2$ and $R2'$) within a very short time, typically a few hundreds of milliseconds. In addition, SE-SS-PARSE offers better parameter estimation and more reliable undistorted results by
sampling data in k,t-space rather than k-space. This dissertation completes the signal model building, technique development, numerical and realistic phantom testing as part of the PARSE MRI project. The PARSE MRI provides a completely different story than conventional MRI in all aspects, including a different signal model, different data sampling strategies and different image reconstruction algorithm. Although the present reconstruction is computationally intensive, constant improvement has been made. It is hoped that in the long-term PARSE MRI can replace conventional MRI for rapid measurement of intensity maps, field maps and transverse relaxation rates maps.

This dissertation can be divided into two main parts. The first part of the dissertation research involves a complete design of the SE-SS-PARSE technique, including design of the pulse sequence, calibration of the rosette trajectories and generation of code for image reconstruction. The developed SE-SS-PARSE method was first performed in computer simulations and then experimentally with a realistic four-tube phantom. For the numerical phantom, various noise levels, different offset frequencies and magnitudes were simulated. In the experiments, different transverse relaxation rates were provided in different tubes. Under all these different circumstances, both simulation and experimental phantom results demonstrated relatively accurate parameter estimations compared to standard MRI. The results of this part are presented in the first article of this
dissertation, which has been accepted by *Magnetic Resonance Imaging* as a full-length original research paper.

The second part of the dissertation research deals with comparing SE-SS-PARSE with FSE on rapid R2 mapping. By shortening scan duration with a turbo-factor, FSE has replaced conventional SE method in R2-weighted imaging for most clinical applications. SE-SS-PARSE and FSE data were collected on both experimental phantoms and biological samples. Conventional SE data were also collected and reconstructed to provide the reference image information. It has been shown that SE-SS-PARSE provides relatively equal accurate estimations comparing to FSE, with a much shorter data acquisition. The results of this part are presented in the second article of this dissertation, which has been submitted to *Magnetic Resonance Imaging* as a full-length original research paper.
Fig. 1. Examples of k-space and their corresponding Fourier Transform (FT). B is the FT of k-space data in A. By randomly masking out the center of k-space data, as shown in C, corresponding FT in D has lost most of its contrast.
Fig. 2. Timing diagram of the GESFIDE pulse sequence. Dephasing and rephasing signals prior and after the β RF pulse are sampled. The gradient echo train followed the initial excitation samples the signal with a decaying rate of $R_2^*$. The second echo train after the β RF pulse samples the increasing signal with a rate constant of $R_2^-$. $R_2^*$ and $R_2^-$ can be computed from the linear combination of $R_2^*$ and $R_2^-$. The excitation pulses α-β are usually set to 90-180 to optimize signals.
Fig. 3. Timing diagram of the FSE pulse sequence. A is an example of the FSE or TSE sequence with a turbo factor of three. Three 180 RF pulses following the 90 RF pulse produce three sequentially decayed spin echo signals. B illustrates partial k-space covering order in the FSE method. In order to acquire the whole k-space, multiple shots are taken. The k-space data are covered interleaved with shot 1, 2 and 3. For each shot, multiple k-space lines are obtained after multiple 180 RF pulses. Lines covered by different shots are indicated by different colors.
Fig. 4. Timing diagram of the GE-EPI pulse sequence. A is an example of GE-EPI sequence diagram and B is the corresponding k-trajectory. In this sequence, the gradient echo train signal is generated by rapidly revising the readout or frequency encoding gradient. All the k-space lines are covered after one single RF excitation.
Fig. 5. Timing diagram of the SE-SS-PARSE pulse sequence. The fat-saturation pulse, indicated by Fatsat, is optional for different studies. The FID signal and SE signal are acquired after the 90 degree and 180 degree RF pulses, respectively. τ0, τ1 and τ2 are short time durations during which no data is sampled. Image parameter $M_{xy0}$ estimated in SE-SS-PARSE is at time $t=0$. It should be noted that the actual “phase” and “frequency” encoding readout gradients are sums of two sinusoids. Only zoomed in sections are illustrated in the figure for clarity.
SPIN ECHO SS-PARSE: A PARSE MRI METHOD TO ESTIMATE R2, R2’ AND FREQUENCY IN A SINGLE-SHOT

by

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ABSTRACT

Spin echo signals allow separate measurements of irreversible and reversible relaxation rates in MRI. A spin echo version of Single-shot Parameter Assessment by Retrieval from Signal Encoding (SE-SS-PARSE) method has been developed to quantitatively and accurately map transverse magnetization magnitude, frequency, irreversible and reversible relaxation rates in a single shot. These image parameters can be applied to fMRI research as well as a number of neuroimaging applications. Following a description of the signal model, this paper demonstrates the performance of SE-SS-PARSE in simulations with different noise levels and in phantom experiments. By solving an inverse problem, the estimated irreversible and reversible relaxation rates in SE-SS-PARSE are highly correlated with the reference relaxation rates from a standard technique (correlation coefficients $r_1=0.9636$ for reversible relaxation rate, $r_2=0.9788$ for irreversible relaxation rate). The rapid SE-SS-PARSE technique has the potential to monitor transient changes in $R_2$ and $R_2'$ while minimizing motion artifacts, and also is free of geometric and ghosting errors. It is expected that this fast scan technique will find applications in both scientific research and clinical diagnosis.

INTRODUCTION

Fast scan MRI techniques have been highly developed and widely applied in both scientific research and clinical diagnosis for their ability to obtain images within a short
time. Rapid data acquisition is in demand to minimize motion and undesirable flow artifacts as well as reduce the time and expense for both patients and hospitals. SS-PARSE (Single Shot-Parameter Assessment by Recovery from Signal Encoding) [1] is a novel quantitative parameter-based fast MRI technique. Using a continuous signal model, SS-PARSE promises improved accuracy and robustness in the estimation of local signal parameters (local transverse magnetization magnitudes $M_{xy0}$, transverse relaxation rates $R2^*$ ($1/T2^*$) and frequencies ($f$). The total observable transverse relaxation rate $R2^*$ depends on both macroscopic magnetic field inhomogeneities and pure spin-spin relaxation. The field inhomogeneities lead to the reversible signal dephasing characterized by the reversible relaxation rate, $R2'(1/T2')$, while the pure molecular effects cause the irreversible signal dephasing characterized by the irreversible relaxation rate, $R2 (1/T2)$.

A spin echo signal permits separate measurements of $R2$ and $R2'$. This combined measurement is significant for both neuroscience research and clinical studies. In functional MRI (fMRI), separate measurement of $R2$ and $R2'$ has been recognized as an approach to distinguish BOLD responses in parenchyma from responses in large draining veins [2]. Also, the blood $R2$ values can be useful to measure tissue oxygen extraction fractions while the changes in $R2'$ are approximately linearly related to the changes in blood oxygenation level [3]. Clinically, the measure of $R2$, $R2'$ values are valuable to quantify iron deposition in neurological disorders, such as Parkinson’s disease,
Huntington’s disease and Alzheimer’s disease [4-8]. The excess iron in certain areas of the human brain causes the MR signal decay, which leads to the signal loss in the T2-weighted images for such diseases. It has been demonstrated that brain iron measurement can also be used to assess the stage of stroke [9-11] and HIV-infected patients [12].

The conventional approach to separate R2 and R2’ values is to first measure R2* from multi-echo gradient echo images, and R2 from spin-echo data, then derive R2’ by subtracting R2 from R2*. Numbers of methods have been proposed for mapping R2 (T2) values. The commonly used multi-echo Carr-Purcell-Meiboom Gill (CPMG) method [13,14] is most accurate, but not suited for rapid monitoring of dynamic changes in relaxation rates. Recently, some fast scan MRI methods have been proposed to reduce the data acquisition time in mapping R2, R2’ and R2* values. A single scan method, Gradient Echo Sampling of the Free Induction Decay and Echo (GESFIDE) was proposed by Ma and Wehrli [15]. In this method, R2 and R2’ maps are obtained by finding the differential evolution of the transverse magnetization between the ascending side and the descending side of a Hahn echo. However, information on relaxation from the FID signal is neglected in this approach. Another R2 mapping technique, fast acquisition relaxation mapping (FARM), has been introduced by McKenzie et al. [16]. In this technique, quantitative R2 mapping can be reconstructed directly from k-space data obtained within 3 sec. However, both imperfect refocusing pulses and eddy currents can disturb the R2 decay, and maximum gradient amplitude and slew rates need to be
controlled to minimize the eddy current effects. The single shot Echo Planar Imaging (EPI) technique [17] has been widely used in modern functional studies. It is capable of producing a set of whole brain images at video rates, which is useful in functional neuroimaging. However, EPI based imaging is vulnerable to geometric distortion artifacts [18-22]. Chen et al. [23] have recently proposed a less field inhomogeneity sensitive method, Line-Scan Echo Planar Spectroscopic Imaging (LSEPSI). However, the 30 sec data acquisition time for a 2-dimensional slice image is too long to monitor rapidly changing signals, such as the BOLD fMRI responses.

Here we propose a fast scan MRI method that can measure \( R_2 \) and \( R_2' \) separately with a data acquisition time much less than a second. The spin echo SS-PARSE technique (SE-SS-PARSE) extends the FID-only SS-PARSE technique to provide estimation of four image parameters, \( M_{xy0} \), \( f \), \( R_2 \) and \( R_2' \). Through use of an iterative optimization algorithm [24], these image parameters can be estimated simultaneously and quantitatively. The SE-SS-PARSE method is based on the PARSE technique, and is free of geometric errors and \( N/2 \) ghosting artifacts that commonly occur in single-shot techniques, such as EPI [24]. Moreover, the rapid data acquisition of SE-SS-PARSE eliminates the motion artifacts effectively. In general, SE-SS-PARSE may be well suited for several types of MRI studies, especially for tracking dynamic changes such as BOLD responses in fMRI.
THEORY

The theory of using the SS-PARSE technique to estimate magnetization parameters from a FID signal has been previously described [1]. Each sample point in the PARSE acquisition is recognized as a point in the (k, t, b) space, where t refers to the time and b is an encoding parameter. The signal model of SS-PARSE considers both transverse magnetization decay and phase evolutions, and thus, in principle it can provide more robust and reliable image parameter estimates quantitatively. The parameter estimation in SS-PARSE employs a Progressive Length Conjugate Gradient (PLCG) algorithm, which works by iteratively searching the parameter space to minimize the sum square error between experimental signal and model signal [24].

In the SE-SS-PARSE method, a spin echo rf sequence is applied to produce both FID and echo signals. From these two signals, four image parameters, complex magnetization $M_{xy0}$, frequency f, and relaxation rates $R2$ and $R2'$ can be modeled and estimated. The observed local signal $S_c$ at time $t_n$ during the data acquisition time can be modeled as:

$$S_c(t_n) = \left\{ \begin{array}{ll}
\int_{\frac{-TE}{T_2}-\tau_1}^{\frac{-TE}{T_2}} M_{xy0}(x) \cdot e^{-(R_c(x)+2\pi f(x)+R_2(x))} \cdot e^{-2\pi ik(t_n)x} \, dx, & 0 < t_n < \frac{TE}{T_2} - \tau_1 \\
\int_{\frac{-TE}{T_2}-\tau_1}^{\frac{-TE}{T_2}} M_{xy0}(x) \cdot e^{(R_c(x)-2\pi f(x)-R_2(x))} \cdot e^{-2\pi ik(t_n)x} \, dx, & \frac{TE}{T_2} - \tau_1 < t_n < \frac{TE}{T_2} - (\tau_0 + \tau_1 + \tau_2) \\
\int_{\frac{-TE}{T_2}}^{\frac{-TE}{T_2}-\tau_1} M_{xy0}(x) \cdot e^{-(R_c(x)+2\pi f(x)+R_2(x))} \cdot e^{-2\pi ik(t_n)x} \, dx, & \frac{TE}{T_2} - (\tau_0 + \tau_1 + \tau_2) < t_n 
\end{array} \right. \quad (1)$$

which is the integral of the individual pixel signal at location x over the space. The last part of the integral $e^{-2\pi ik(t_n)x}$ represents the spatial phase modulation imposed by the
gradients [1] at time $t_n$. Here $\tau_0$ refers to the time between the effective center of the 90 degree pulse and the beginning of data acquisition. $\tau_1$ and $\tau_2$ are delays before and after the middle of the 180 degree pulse, respectively, during which the signal is not sampled.

The timing diagram of the SE-SS-PARSE sequence is shown in Fig. 1. The magnetization parameter $M_{xy0}$ is estimated at $t=0$. In Eq. (1), the first part corresponds to the FID signal while the second and third parts correspond to the ascending and descending section of the echo signal. The PLCG algorithm was employed to estimate image parameters as in the SS-PARSE technique.

METHODS

Simulations

SE-SS-PARSE was tested initially with a simulated numerical phantom. Both signal simulations and data reconstructions were implemented in Matlab (Version 7.5; The MathWorks, Inc., Natick, MA) running on a dedicated 8 AMD Opteron 880 dual-core processor computer with 64 GB of Random Access Memory (@Xi Computer Corp.). The simulated phantom (Fig. 2) was a clock shaped set of disks in a 12.8-cm field of view (FOV). The radius for the central disk and outside disks was 2.5 cm and 1 cm, respectively. The image resolution was 64 by 64. Magnitude of transverse magnetization, relaxation rates and frequency value were varied among disks, as indicated by Fig. 2. Random zero-mean Gaussian distributed noise was added to the simulated signal with
four different magnitudes to simulate the experimental situation. The corresponding signal to noise ratios (SNR) were $\infty$, 40 dB, 30 dB and 20 dB.

Phantom Study

The experimental acquisitions were performed with a four-tube phantom, consisting of four 1.6cm-diameter tubes in an 8cm-diameter beaker filled with water. Different concentrations of agarose were added to different tubes to provide \textit{in vivo} like R2 values [25]. Small quantities of FeSO$_4$ were added to two tubes to increase the R2’ values. The chemical concentration for individual tubes is indicated in Table 1.

The R2 modifier agarose was used as a gelling agent as well. The R2 values and the agarose concentration are: 1.3% to 4% of agarose solution corresponding to R2 value of 15 to 7 sec$^{-1}$. We were unable to achieve larger R2 values with agarose alone, because the agarose concentration less than 1.3% was so low that it is insufficient to solidify. FeSO$_4$ was used in our study as the R2’ modifier, which can effectively increase the R2’ values with low concentration. Another R2’ modifier used in our study was sephadex beads, however, the R2’ values were not increased to the extent we expected with sephadex beads alone.

The experimental phantom study was implemented on a 4.7T 60cm-vertical-bore Varian primate MRI system (Varian Inc., Palo Alto, CA), using a stripline resonator quadrature head coil (Insight Neuroimaging, Worcester, MA). Data were sampled along
the rosette k,t-trajectory [26, 27]. To establish reference values of R2 and R2’, standard
multi-echo gradient echo (ME-GE) and multi-echo spin echo (ME-SE) techniques were
used. In all cases, the FOV was 12.8cm, resolution was 64 by 64, and slice thickness was
2mm. For SE-SS-PARSE, six separate single shots were taken with the repetition time
(TR) of 6 sec, and echo time (TE) of 98 msec. TR for ME-GE and ME-SE techniques
were 300ms and 500ms, respectively. TE values for ME-GE and ME-SE method were (6,
7, 10, 15, 30) msec and (12, 14, 20, 30, 60) msec, respectively. The multiple-echo data
were used to compute relaxation rates from the magnitude images. Parameter maps of
M_{xy0}, f, R2 and R2’ were estimated by the PLCG algorithm from the SE-SS-PARSE data.
By fitting the magnitude decay along the echo time of each pixel in ME-GE/SE images,
reference R2* and R2 maps were computed. Decay rates were computed by exponential
fit to the decay of the magnitude image values through the series of echo times. Fitting
was performed by nonlinear least-squares using Matlab, and R2’ was then simply derived
by subtracting R2 from R2*. Statistical methods were used to assess the accuracy of the
SE-SS-PARSE results by comparing the R2 and R2’ maps to the values computed from
standard techniques.

RESULTS

Simulations
The simulation results of the clock phantom are shown in Fig. 3. Four local parameter images of $M_{xy0}$, $f$, $R2$ and $R2'$ were estimated with different noise levels. As the signal noise level increases, the final estimation parameter maps become noisier. To assess the accuracy of the estimates, four representative square areas were chosen from disk 1, disk 5, disk 9 and the central disk in the estimated $R2$ and $R2'$ maps, as indicated by the black squares in the upper-left corner magnitude image in Figure 3. Fig. 4 illustrates the comparison between the reference and estimated $R2$ and $R2'$ values from these selected areas. In each figure, the solid black line represents the reference $R2$ and $R2'$ values while the estimation results are represented by the mean and standard deviations, as indicated by the error bars. Even with the high noise level (SNR=20dB), the estimated mean values in both $R2$ and $R2'$ maps match the reference values well. As expected, larger estimate deviations were seen for higher signal noise levels.

Phantom Study

Fig. 5 demonstrates the estimation results for both SE-SS-PARSE technique and the standard ME-GE/SE technique. Note that the SE-SS-PARSE results were acquired with a single 148ms shot, in contrast to those requiring almost an hour with the ME-GE/SE technique. Also very different methods were employed to reconstruct final parameter maps for both techniques. The iterative PLCG algorithm was used in the SE-SS-PARSE technique to produce four parameter maps of $M_{xy0}$, $f$, $R2$ and $R2'$ at the same
time. For the standard technique, a Fourier transform (FT) was used to convert raw k-space data into magnitude maps, and exponential decay curves were fitted to the magnitudes at each echo time to compute relaxation rate maps. A side-by-side comparison of the reconstructed R2 and R2’ maps obtained using SE-SS-PARSE and the standard technique in Fig. 5 demonstrates that the SE-SS-PARSE results are highly consistent with the reference values.

To demonstrate convergence of the parameter search, four representative pixels were picked randomly from the inside area of four tubes, and their estimation histories during convergence were recorded, as shown in Fig. 6. For all four pixels, the estimation histories before 200 iterations were the same for R2 and R2’. In the PLCG searching process, the data length was progressively increased to avoid secondary minimum artifacts [24]. Before 200 iterations for this particular study, the data length was no more than the length of the FID signal, so the algorithm could not distinguish the difference between R2 and R2’. Estimates of R2 and R2’ from FID data only were approximately equal. The estimation history of R2 and R2’ began to differ as the echo signal was added to the PLCG search data length after 200 iterations. At the final PLCG stage, estimates from the whole data length converged to steady values, as seen in the flat portion at the end of the estimation history of Fig. 6.

To assess the accuracy of the estimation in SE-SS-PARSE, 100 3x3 pixel areas were picked in the R2 and R2’ maps for both techniques used in this study, avoiding
areas with pixels on the tube boundaries. Mean of the estimates from both techniques were calculated as $\bar{R}_2$ and $\bar{R'}_2$. Shown in Fig. 7 are the correlation results between $\bar{R}_2$ and $\bar{R'}_2$ values from the selected areas in the results from both SE-SS-PARSE and standard technique. Linear fits to the $\bar{R}_2$ and $\bar{R'}_2$ correlation data yield correlation coefficients of 0.9636 and 0.9788, respectively. The highly correlated results between the SE-SS-PARSE and the standard technique demonstrate the SE-SS-PARSE method is capable of accurate rapid R2 and R2’ mapping.

In addition to the results shown in Fig. 5, five more shots of SE-SS-PARSE data were obtained and analyzed. Fig. 8 depicts profiles across R2 and R2’ maps at row 46 from all six shots of SE-SS-PARSE and standard technique, which pass through both water and tube sections. The differences from shot to shot with the SE-SS-PARSE technique are expected due to signal noise. The mean and standard deviation of the profile at row 46 of R2 and R2’ values from all shots were calculated. Fig. 9 compares the mean (dashed line) and standard deviation (dotted line) of the same profile from all six shots with the reference value from standard technique (solid line). Because of the Gibbs ringing artifacts and possible phantom shaking during the data acquisition, reference R2 and R2’ values exhibited spatial variations, especially noticeable in R2’. The variations could be decreased by averaging R2 and R2’ values from neighborhood profiles. Here we did not average reference R2 or R2’ values, in order to make a pixel by pixel based comparison with SE-SS-PARSE. The mean difference may come from bias
errors arising from model discrepancies [24]. As noted above, the standard deviation in Fig. 9 reflects the random noise difference among different shots.

**DISCUSSION**

A fast single-shot MRI technique, SE-SS-PARSE, has been described in this paper. Although obtaining data within only 200msec, SE-SS-PARSE is able to produce quantitative multiple parameter estimate images at the same time. The signal model in SE-SS-PARSE models the decay and precession of the local transverse magnetization during the data acquisition time, which enables more precise and robust estimation for local image parameters. More importantly, by using the dynamic signal model, SE-SS-PARSE is free of geometric and blurring artifacts, and in principle is less sensitive to large susceptibility gradients in vivo [1]. Because a spin echo signal is used in SE-SS-PARSE, the two image parameters R2 and R2’ can be computed in addition to the $M_{xy0}$, f and $R2^*$ estimated using the SS-PARSE technique. Measurements of R2 and R2’ values in both simulations and experiments from the SE-SS-PARSE technique are in good agreement with those from standard techniques, suggesting the reliability of this method.

Accurate timing plays an important role in the SE-SS-PARSE technique. The previously developed SS-PARSE technique measures all the data points within an uninterrupted time period. The estimation algorithm for SS-PARSE simply models this single signal. In contrast, the SE-SS-PARSE measures data in two separate time periods
after the 90 and 180 degree rf-pulses. Spoiler gradients have been applied on both sides of 180 degree pulses to eliminate any FID signal from an imperfect refocusing pulse. The interval between the FID signal and the echo signal includes the time for the 180 degree pulse along with these spoiler gradients. The time durations of rf-pulses and spoiler gradients need to be noted precisely and represented in the signal model. These time durations can be measured once in the calibration process [28] and will only change if the rf-pulses or gradients change. Because the reconstruction in SE-SS-PARSE uses a signal that is a spliced combination of FID and echo signals, the difference between the two signals should be noted, such as the small net phase change in the echo induced by imperfect 180 degree pulse. In principle, and as verified in our results, this system-dependent difference in phase angle needs to be measured only once for a given refocusing pulse.

Although the SE-SS-PARSE results were highly correlated to the “gold standard” results, there are several aspects of the comparison that merit discussion. The difference between the estimated parameters and the actual parameters, here represented by the reference values, can be characterized as estimation errors. For the SE-SS-PARSE technique, estimation errors include both bias errors arising from signal model discrepancies and random errors caused by the measurement noise. Random errors in our phantom studies are characterized by the standard deviations in Fig. 9. Due to the space limit, only random errors in selected locations were presented. By implementing multiple
shots, averaged estimates of R2 and R2’ were obtained. The difference between the average and reference values can be characterized by bias errors coming from various sources [24], especially (1) The local signal model in SE-SS-PARSE did not measure the non-exponential effects of dephasing across the voxel that exist in the actual object (These effects may become worse with larger susceptibility variations increases in human tissue); and (2) The mismatch between evaluation k-band (square) and the acquisition k-band (disc) in the SE-SS-PARSE may lead to under- or over-estimates of high spatial frequencies from the gap between two k-bands. These sources of bias errors may be reduced and minimized by multiple solutions proposed in another report [24].

The reconstruction accuracy and efficiency in SE-SS-PARSE depends on the convergence behaviors of the PLCG algorithm. The typical convergence time for the spin echo four-tube phantom data on our computational platform is around 30min to an hour, which is very slow compared to the fast Fourier Transform (FFT). The algorithm may be optimized by (1) Reducing the progressive data lengths over which successive estimation are performed, which may speed the estimation (However, the number of lengths must be sufficient to prevent convergence to a secondary minimum), (2) Increasing the stopping tolerance for each PLCG data length (This can accelerate the searching process but can reduce estimation accuracy), (3) Adjusting weighting factors that scale the magnitude of the decay rate parameters relative to the other parameters. The weighting factors play an important role in the speed of convergence, especially when R2 and R2’ are significantly
different. Proper weighting factors can effectively balance the size of the search gradients for R2 and R2’, and thus accelerate the algorithm. Faster computing hardware (e.g., Graphical Processing Units) may offer substantial acceleration.

In comparison with many R2 (or T2) and R2’ measurement methods [13-23], SE-SS-PARSE has several potential basic advantages. In conventional methods, R2’ values are measured by subtracting R2 from R2* values. The precision of the R2’ measurements is then limited by the errors introduced by both R2 and R2* measurements. In contrast, the SE-SS-PARSE technique estimates R2’ values directly from the sampled data. In the past few decades, many fast scan R2 mapping methods based on a single shot method such as EPI have been introduced to reduce the acquisition time. However, such single-shot methods suffer from geometric errors due to the field inhomogeneities as well as ghosting artifacts. Although sacrificing computational convenience, SE-SS-PARSE is totally free of such geometric or ghosting errors. Moreover, SE-SS-PARSE is capable of producing quantitative image parameter measurements. It should be emphasized that the amount of the data sampled in SE-SS-PARSE is associated with the time TE. Longer TE (consistent with expected T2 values) allows for more data points and thus, theoretically more accurate estimations. Optimal choices of TE for estimation accuracy remain to be determined.

SE-SS-PARSE may be of significant value in fMRI research. The BOLD fMRI signal induced by the neural activities consists of a change in the local T2* values. A
single-shot GE technique is normally used to obtain the dynamically changing T2*-weighted images in fMRI. The GE method is easy to implement and has high sensitivity in detecting local signal changes. However, the GE technique is also sensitive to field inhomogeneities induced by large draining veins. At high magnetic field, favored for increased sensitivity for fMRI, the field inhomogeneity problems such as through-slice dephasing, becomes worse, limiting the applications of GE methods. On the other hand, in the SE sequence, the 180 degree rf pulse refocuses the static intra-voxel dephasing around large vessels and hence reduces their contribution to the BOLD response [2]. By producing R2 values instead of R2* values with rapid data acquisition, SE-SS-PARSE is well-suited to detect BOLD effects in fMRI studies.

In summary, a spin echo version of SS-PARSE (SE-SS-PARSE) technique has been developed and validated with tissue-equivalent phantom. It was shown that the simulation results were close to the actual values, even at high noise level with SNR of 20dB. The experimental results on a four-tube phantom were also highly correlated with the results from standard reference techniques. Future work will include application and development of the technique for in vivo studies, and acceleration of the offline reconstruction algorithm.

ACKNOWLEDGMENTS
The authors gratefully acknowledge support from NIH EB003292 and the Alabama Eyesight Foundation.

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Fig. 1. Timing diagrams for the SE-SS-PARSE sequence (time axis not to scale). \( \tau_0 \), \( \tau_1 \) and \( \tau_2 \) were short delays. Note that the actual “phase” and “frequency” encoding readout gradients were sums of two sinusoids. For clarity, only a zoomed section of the waveform is shown in the figure.
Fig. 2. The clock phantom used in the simulations. The table indicates the actual input parameter values for each disk of the clock phantom.

<table>
<thead>
<tr>
<th>Disk #</th>
<th>$R_2$(sec$^{-1}$)</th>
<th>$R_2'$(sec$^{-1}$)</th>
<th>Frequency(Hz)</th>
<th>Magnitude</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-4</td>
<td>5</td>
<td>10</td>
<td>10</td>
<td>1</td>
</tr>
<tr>
<td>5-8</td>
<td>20</td>
<td>0</td>
<td>0</td>
<td>0.9</td>
</tr>
<tr>
<td>9-12</td>
<td>15</td>
<td>10</td>
<td>-10</td>
<td>0.8</td>
</tr>
<tr>
<td>Central disk</td>
<td>5</td>
<td>10</td>
<td>0</td>
<td>1</td>
</tr>
</tbody>
</table>
Fig. 3. Simulation results with 4 noise levels. Each column of this figure shows the estimation results, including magnitude map, frequency map and relaxation rates maps, of the clock phantom with a specific noise level, as indicated by the SNR. Noise was introduced into the simulation signal model. Four representative rectangular areas of interest were chosen from the estimated parameter maps, as shown as the black areas in the upper-left corner magnitude map. Mean and standard deviations of $R2$ and $R2'$ were computed from these areas to compare with the actual values.
Fig. 4. Actual values vs. estimated values for relaxation rate $R_2$ (A) and $R_2'$ (B) in the 4 selected areas of the clock phantom [see Fig. 3]. The actual input $R_2$ and $R_2'$ values are indicated by the solid black line. The blue error bars are the mean and standard deviations calculated from the four representative areas from both small and big disks of the clock phantom.
Fig. 5. Estimated parameter maps with the SE-SS-PARSE technique and reconstructed parameter maps with ME-GE/SE technique. A, B, C and D are the estimated $M_{xy0}$ map, $f$ map, $R2$ and $R2’$ maps from SE-SS-PARSE technique. E and G are the $R2$ and $R2^*$ maps from non-linear fitting of the multi-echo GE and SE magnitude images. F is the $R2’$ map calculated by subtracting the $R2$ map from the $R2^*$ map. Note that there are some ringing artifacts in E, F and G. These may be caused by systematic Gibbs ringing, or by phantom shaking during the data acquisition.
Fig. 6. Convergence history of R2 (left column) and R2’ (right column) estimates in the iterative search for one pixel in each tube of the four-tube phantom. Numbers in the bracket at left side of the figures denotes the (x, y) coordinates of each pixel.
Fig. 7. The phantom results from SE-SS-PARSE and ME-GE/SE technique are highly correlated. A represents the mean of R2 values calculated from the 100 selected areas with both techniques. B illustrates the comparison between R2’ values. The correlation coefficients are 0.9636 for R2 and 0.9788 for R2’.
Fig. 8. Estimated and reference R2 (A) and R2’ (B) values at row 45 of the 4-tube phantom. Estimated values from all shots in SE-SS-PARSE are illustrated as dotted line while the reference values are represented by the solid line. The area outside of the phantom was shown as zero in the standard technique, while the corresponding sections for SE-SS-PARSE demonstrate noisy background. The variations in the reference profiles come from Gibbs ringing artifacts, and possible phantom shaking during the data acquisition.
Fig. 9. Estimated mean and standard deviations over multiple shots in SE-SS-PARSE compared with reference values. The variations in the reference profiles come from Gibbs ringing artifacts, and possible phantom shaking during the data acquisition.
<table>
<thead>
<tr>
<th>Tube #</th>
<th>Agarose</th>
<th>FeSO₄</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>3%</td>
<td>0.325%</td>
</tr>
<tr>
<td>2</td>
<td>2%</td>
<td>0</td>
</tr>
<tr>
<td>3</td>
<td>4%</td>
<td>0</td>
</tr>
<tr>
<td>4</td>
<td>3%</td>
<td>0.975%</td>
</tr>
</tbody>
</table>

Table 1. R2 and R2’ value modifier concentration in 4 tubes.
COMPARISON OF FAST SPIN ECHO AND ULTRAFAST SPIN ECHO SS-PARSE FOR RAPID MR IMAGING OF IRREVERSIBLE TRANSVERSE RELAXATION RATE (R2)

by

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ABSTRACT

Irreversible transverse relaxation rate (R2) maps of the brain can provide information on neural functional activity and neurodegenerative diseases. This information can be directly applied in functional MRI studies, neuroimaging and diagnosis of neural diseases. The recently described SE-SS-PARSE method is capable of ultrafast R2 mapping by sampling whole image MR data in the k,t-space followed a single excitation. This paper compares SE-SS-PARSE with a commonly used and rapid R2 mapping method, fast spin echo, using experimental phantoms with in-vivo-like R2 values. The results indicate that SE-SS-PARSE provided equivalent accuracy in R2 mapping compared to fast spin echo, but with a much shorter acquisition time. It is shown that a fat saturation pulse added to SE-SS-PARSE produces a more accurate R2 estimation in a biological sample containing fat than without fat saturation. The conventional spin echo method provides reference R2 values throughout the paper.

Keywords: Rapid R2 mapping, SE-SS-PARSE, Fast spin echo; Fat-saturation

INTRODUCTION

Rapid and accurate irreversible transverse relaxation rate (R2) mapping is of significant interest to neuroscience researchers and clinicians. In functional MRI (fMRI), R2 maps reflect the neural activities induced blood oxygen level dependence (BOLD) responses more accurately than the net relaxation rate R2* [1-5]. Clinically, R2 maps are valuable for detecting neurodegenerative diseases due to iron deposition [6-10]. The conventional spin echo technique has been routinely used to produce T2 (1/R2) maps to distinguish normal and diseased tissue. However, the scan time is typically too long for practical studies of dynamically changing R2, as in fMRI.

Many rapid R2 mapping methods have been proposed in the past few decades. One way to reduce the scan time uses small angle radiofrequency (RF) excitations with shorter repetition
time (TR). Snapshot FLASH imaging [11] is such a technique allowing quantitative T1 and T2 maps to be acquired in less than 30 sec [12]. Another method utilizes the steady state free precession (SSFP) property of MRI signals to reduce the data scan time. Based on the linearity of SSFP signal, Driven equilibrium single pulse observation T2 (DESPOT2) permits efficient post-processing and rapid data acquisition with only two different flip angles [13]. The T2 fast acquisition relaxation mapping (T2-FARM) technique can reconstruct T2 maps directly from k-space data acquired in 3 seconds [14].

The last type of method decreases the scan time by acquiring multiple k-space lines following single RF excitation. This type of method reduces scan time most efficiently, is widely used and has been developed in many forms. One representative is the fast spin echo (FSE) or turbo spin echo (TSE) technique [15]. By applying multiple refocusing pulses, FSE reduces the scan time by a factor equal to the number of 180 RF pulses. Several studies have demonstrated good image quality with FSE acquisitions [16-18]. Therefore, the FSE sequence has replaced the conventional spin echo sequence for many clinical applications. Instead of obtaining multiple k-space lines, the single-shot (SS) technique traverses the whole k-space after a single RF pulse. The Half-Fourier single-shot turbo spin echo (HASTE) [19] is a SS version of FSE that uses the near-Hermitian property of k-space data to reconstruct images. Another widely used SS method is echo planar imaging (EPI) [20]. EPI changes the direction of frequency and phase encoding gradient iteratively, allowing a whole image data acquisition in less than a second. Although these SS techniques dramatically shorten the scan time, they usually suffer from geometric or blurring artifacts [21-24] due to the off-resonance effect.

The recently developed spin echo single-shot parameter assessment by retrieval from signal encoding (SE-SS-PARSE) [25] is an ultrafast and direct R2 mapping method. Because it models signal changes during the data acquisition, SE-SS-PARSE is free of geometric errors and blurring artifacts. An iterative algorithm searches the parameter space to provide R2 maps directly from the raw k-space data, along with R2’ maps, frequency maps and magnitude maps at
the same time. The purposes of this study were to compare SE-SS-PARSE with FSE in R2 quantification and assess potential errors for both techniques. Conventional spin echo acquisitions were used as references. Additionally, the use of fat saturation with SE-SS-PARSE is addressed in this paper.

METHODS

For all experiments, data were sampled on the 4.7T 60cm-vertical-bore Varian primate MRI system (Varian Inc., Palo Alto, CA), using a stripline resonator quadrature volume coil (Insight Neuroimaging, Worcester, MA). Initial experiments were conducted on an 8 cm diameter water beaker containing a set of four 1.6 cm diameter tube phantoms filled with varying concentration of agarose gel (Table 1.). The concentrations were selected to span a physiologically relevant range of R2 values in human brain. “Gold Standard” reference R2 values were determined using the conventional SE (CSE) method by collecting data at different echo times (TE). The CSE sequence used a TR of 600 ms and a set of TE of [12, 14, 20, 30, 60] milliseconds. R2 was calculated as the nonlinear least-squares fit of the decay rate of the signal amplitude over the sampled echo times, using Matlab (Version 7.5; The MathWorks, Inc., Natick, MA).

The SE-SS-PARSE experiments were implemented with a maximum gradient strength of 3.8 gauss/cm. Using the method of Zhang et al.[26], a pingpong ball phantom filled with water was used to calibrate the rosette k,t-trajectory. Then data were collected along the calibrated trajectory with 8 different agarose gel concentration tubes. FOV was 12.8cm and image matrix was 64 by 64. Slice thickness was 2mm. TR was 6 sec and TE was 98 milliseconds. The total acquisition time for a single shot was 148ms. The R2 maps were estimated by the PLCG algorithm implemented in Matlab running on a
dedicated 8 AMD Opteron 880 dual-core processor computer with 64 GB of Random Access Memory (Xi Computer Corp).

The FSE experiments were performed on the same phantom with the same FOV, image matrix and slice thickness as used in SE-SS-PARSE. For each FSE sequence, 8 refocus pulses were used to produce 8 spin echo signals with an echo spacing of 12ms and a TR of 2 sec. To obtain T2-weighted images at all 8 echo times, 64 FSE shots with echo train length=8 were obtained, with phase encoding incremented at each shot.

The mean and standard deviation (SD) in R2 maps from all three SE methods of a region of interest (ROI) in each tube, containing at least 40 pixels, were calculated. Pixels at tube edges were not included to avoid errors induced by partial volume and susceptibility effects. Two other quantities were determined: 1. Mean accuracy was calculated as the absolute mean difference between the R2 values estimated from SE-SS-PARSE or FSE with reference R2 values from all 8 tubes. 2. Mean precision was computed as the SD divided by the mean R2 values from all tubes.

R2 measurements were also taken from a biological sample (a single fresh, white, chicken egg) at approximately room temperature using SE-SS-PARSE sequence with and without fat saturation. Since SE-SS-PARSE uses a signal model with a single frequency component at each voxel, the existence of both fat and water in a single voxel can lead to inaccurate parameter estimations. In principle, fat suppression can prevent these estimate errors. To investigate this, we applied a fat suppression pulse consisting of a 90 degree RF pulse followed by a spoiler gradient before the excitation pulse. The sequence diagram including fat saturation pulse is illustrated in Fig.1. All the other experiment parameters were the same as in the four-tube phantom studies. R2 maps computed from
CSE were used as reference values. ROIs were selected separately from the yolk and white parts for comparison.

**RESULTS**

Phantom study

All R2 maps obtained from three SE methods were computed after data acquisition in Matlab. After obtaining the raw k-space data, SE-SS-PARSE technique employed the PLCG algorithm to estimate R2 maps directly, which took a relatively long time. On the other hand, FSE and CSE method compute R2 maps indirectly from raw k-space data in two steps. Firstly, raw k-space data were Fourier Transformed to produce T2-weighted images. R2 maps were then determined pixel-by-pixel by the least square fitting of the mono-exponential signal intensity decay. Fig. 2 shows R2 maps obtained from SE-SS-PARSE, FSE and CSE technique with two four-tube phantoms containing 8 different tubes. Eight ROIs with the same area were selected from each tube shown in Fig. 2. Mean, SD, mean accuracy and mean precision for each tube among the three SE techniques are summarized in Table 1. The total data acquisition time for SE-SS-PARSE, FSE and CSE were 148ms, 2 min 32 ms and 6 min 48 ms, respectively. In interpreting the comparison in Table1, it is worth emphasizing that SE-SS-PARSE acquired the whole dataset using only a 1/800 time required for FSE.

The agarose gel was distributed approximately uniformly in all tubes as seen in the reference R2 maps. The relatively large SD in R2 maps of FSE and SE-SS-PARSE technique thus represented largely the estimation errors. Significant ringing artifacts can be observed in the R2 maps from FSE method (see Fig. 2), which may be the result of
motion during the relatively long data acquisition time. Obvious ringing, observed in tubes 5 to 8, are associated with large SD in Table 1. Fig. 3 shows the estimated magnitude maps, frequency maps and R2’ maps along with the R2 maps from SE-SS-PARSE measurements. Some areas failed to fully converge [25, 27]. These areas, indicated by the white arrows, are associated with the far off-resonance area in the frequency map. Other areas with relatively large SD, indicated by the black arrow, have a relatively non-uniform distribution, which may due to the bias errors arising from signal model discrepancies [25, 27]. The next section will discuss the types of errors in each technique and potential error sources in detail.

Biological samples

Fig. 4 demonstrates the four parameter maps obtained using SE-SS-PARSE of a single fresh egg: with and without fat saturation pulse. Image results without fat saturation pulse possess obvious variations in the fat-containing yolk part not seen in the images with fat suppression. These significant variations were very possibly from failure of the single-frequency signal model to adequately model the mixed fat and water signal. Fig. 5 compares R2 maps estimated from SE-SS-PARSE methods with the reference R2 map computed from CSE data. Distinct ROI were chosen from yolk and white part of all three R2 maps. Table 2 summarizes the mean and SD calculated from ROIs. Clearly, the fat suppressed R2 map possesses a smaller SD and is more close to the reference R2 values than the non-fat suppressed R2 map. Although the fat-suppression pulse was not applied to the CSE, the relatively small fat signal may not have affected the results.
DISCUSSION

This paper has demonstrated the ability of SE-SS-PARSE to produce accurate R2 maps with a short data acquisition time, typically a few hundreds of ms. Two other frequently used R2 measurement methods have also been used to compare with SE-SS-PARSE. One of them is the CSE method, which produces the most accurate R2 measurements but requires a relatively long data acquisition time. The other method, FSE, accelerates the data acquisition time by sampling multiple spin echoes after a single excitation and has been used often in clinical applications for rapid R2 mapping. However, motion artifacts, blurring and hyperintensity of fat may degrade the final images. Because of their longer minimum acquisition times, neither of these multiple-shot acquisition methods are suitable for direct estimation of the rapid dynamic changes in R2 and R2’ in fMRI and dynamic contrast studies. Using the R2 maps from CSE as the reference, this paper compares R2 measurement of experimental phantoms, biological samples and in vivo subject between the more rapid FSE and SE-SS-PARSE methods.

Other ultrafast single-shot R2 mapping methods, such as SE-EPI, can generate R2 maps from acquisitions as brief as a few seconds in duration. However, such techniques are susceptible to geometric errors induced by the off-resonance phase shift accumulated during the relatively long period of data collection for each signal. The geometric errors become worse as the field strength increases and can be severe in areas close to air spaces. In addition to geometric distortions, R2 maps are indirectly computed in SE-EPI by least square fitting of multiple T2-weighted images. Thus variations in image intensity due to variations in Mxy can cause errors in the R2 calculation. As an alternative approach, SE-SS-PARSE estimates R2 maps directly from the raw k,t-space data. Because SE-SS-
PARSE considers the signal phase and amplitude changes during data collection, and also because the SE-SS-PARSE estimates R2 maps from k,t-space raw data directly, it is free of geometric errors due to phase evolution and decay.

The ultrafast R2 mapping provided by SE-SS-PARSE may benefit the neural activity detection and location in fMRI. In fMRI studies, brain functions are identified by observing changes in the blood oxygen level dependent (BOLD) effects. Such changes consist of changes in local R2 and R2’ values, usually detected by changes in the signal intensity in T2- and T2* -weighted MR images. BOLD related R2 changes usually occur dynamically over a short time scale. Rapid R2 mapping methods, such as FSE, may not be sufficiently rapid to capture dynamic BOLD responses and thus may fail to detect brain functions accurately. On the other hand, SE-SS-PARSE acquires the whole image dataset within a sub-second time scale. The ultrafast data acquisition not only captures the instantaneous changed BOLD signal, but also minimizes image artifacts caused by motions and incidental physiological changes. The ultrafast R2 mapping may also be applied to cardiac imaging to minimize effects of heartbeat and blood flow induced movements.

The R2 maps computed from FSE and SE-SS-PARSE are both close to the reference R2 values in most of the cases examined, as indicated in Table 1. However, some of the values deviate relatively far from reference R2 values. For FSE, ringing artifacts seen may be induced in part by motions during the long data acquisition time. Specifically, the large gradient amplitudes and fast slew rate can result in vibrations in the fluid-filled phantom. In addition, imperfect refocusing pulses could lead to a range of errors in the measured R2 decay [28].
Estimation errors in SE-SS-PARSE can be categorized into bias errors and random errors. Bias errors in SE-SS-PARSE derive from various sources [25, 27], such as signal model discrepancy and k-band mis-match. Random errors in parameter estimates propagate from random measurement noise. In locations with large off-resonance frequencies, convergence of the PLCG to the proper solution may be difficult to achieve. For this reason, great care was taken in adjusting field shims before data collection.

Although R2 mapping from SE-SS-PARSE is subject to various kinds of errors, it should be emphasized that the R2 values are estimated from a data length of only 148 milliseconds. The accuracy of the parameter estimates, being influenced by noise propagated from random measurement noise, is expected to improve with increased total acquisition time, due to signal averaging. Thus in terms of signal-to-noise ratio, the FSE acquisition could be compared to the average of 64 shots of SE-SS-PARSE results. Nevertheless, the 64 shots, 8 echo train length FSE usually takes more than 2 minutes to collect the data required to compute R2 maps. Even with a much shorter data collection time, SE-SS-PARSE provides accuracy equivalent to FSE, indicated by the same level of SD and mean accuracy in Table 1. A multi-shot version of SE-PARSE with a larger k-space bandwidth could in principle produce higher-resolution parameter maps with only a few acquisitions, promising higher-resolution and potentially more selective neural activity identification in fMRI [29]. SE-SS-PARSE achieves ultrafast data sampling but requires a relatively long data reconstruction time. The PLCG estimation required approximately one hour on our computational platform. Acceleration of the
reconstruction algorithm and faster computer hardware are expected to significantly speed the estimations.

ACKNOWLEDGEMENT

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Table 1. Chemical concentrations and statistical values of estimated R2 values in the four-tube phantom study.

<table>
<thead>
<tr>
<th>Tube #</th>
<th>Agarose Concentration</th>
<th>$R^2$+SD</th>
<th>Mean Accuracy</th>
<th>Mean Precision</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>SE-SS-PARSE</td>
<td>CSE (Reference)</td>
<td>SE-SS-PARSE to Reference</td>
</tr>
<tr>
<td>1</td>
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<td>16.33±1.12</td>
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<tr>
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<td>6.98±0.47</td>
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</tr>
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<td>2.5%</td>
<td>12.40±0.88</td>
<td>12.52±1.23</td>
<td>13.00±0.64</td>
</tr>
<tr>
<td>7</td>
<td>1.2%</td>
<td>17.04±1.13</td>
<td>16.50±1.38</td>
<td>18.94±0.27</td>
</tr>
<tr>
<td>8</td>
<td>3%</td>
<td>8.43±0.91</td>
<td>9.23±1.47</td>
<td>11.05±0.50</td>
</tr>
</tbody>
</table>
Fig. 1. The SE-SS-PARSE sequence diagram (time axis not to scale). After the pre-delay, a 90 degree pulse followed by a spoiler gradient suppressed the fat signal. The water signals were collected after the 90 and 180 degree excitation pulses. $\tau_0$, $\tau_1$ and $\tau_2$ were short delay periods during which signals were not sampled. For clarity, only zoomed sections of the “phase” and “frequency” encoding gradients are shown in the figure. The actual waveform is a combination of two sinusoids.
Fig. 2. Comparison of R2 maps from SE-SS-PARSE, FSE and CSE in four-tube phantom studies. A, B and C show R2 maps estimated and reconstructed from SE-SS-PARSE, FSE and CSE, respectively for tubes 1 to 4. D, E and F demonstrate R2 maps estimated and reconstructed from SE-SS-PARSE, FSE and CSE, respectively for tubes 5 to 8. The black circle in B represents the example ROI selected from tube 1.
Fig. 3. Four image parameters estimated from SE-SS-PARSE in four-tube phantom studies. A, B, C and D are magnitude map, frequency map, R2’ map and R2 map of tube 1 to 4. E, F, G and H are magnitude map, frequency map, R2’ map and R2 map of tube 5 to 8. Chemical concentrations of individual tubes can be found in Table 1. White arrows in F indicate areas with the relatively far off-resonance. Corresponding areas in H experienced convergence difficulties. The black arrow in D points out the area with relatively large variability in estimates representing bias errors.
Fig. 4. Four image parameters estimated from SE-SS-PARSE with and without fat saturation pulse in the biological sample studies. A, B, C and D are magnitude map, frequency map, R2’ map and R2 map estimated from water signal only. E, F, G and H are magnitude map, frequency map, R2’ map and R2 map estimated from water and fat signals. Significant irregularities can be observed in the fat-containing yolk part in F, G and H.
Fig. 5. R2 maps from SE-SS-Parse and CSE in the biological sample study. A and B are R2 maps estimated from SE-SS-Parse with and without fat-saturation, respectively. C is the R2 map computed from the conventional multiple echo SE method. Two ROIs were selected from yolk and white part distinctly. Mean and standard deviation computed from ROIs are summarized in Table 2.
Table 2. Mean and standard deviation of yolk and white part in R2 maps. FATSAT signifies use of a fat-saturation pulse.

<table>
<thead>
<tr>
<th></th>
<th>R2±SD</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>SE-SS-PARSE w FATSAT</td>
<td>SE-SS-PARSE w/o FATSAT</td>
<td>CSE</td>
</tr>
<tr>
<td>Yolk</td>
<td>20.13±1.98</td>
<td>16.93±2.78</td>
<td>22.75±0.58</td>
</tr>
<tr>
<td>White</td>
<td>5.81±0.62</td>
<td>7.94±4.08</td>
<td>5.48±0.48</td>
</tr>
</tbody>
</table>
SUMMARY

This dissertation research investigated and developed a novel fast scan MRI method, the SE-SS-PARSE technique, in estimating four useful image parameters, $M_{xy0}$, $f$, $R_2$ and $R_2'$, quantitatively and simultaneously. In the process, five significant contributions were made. First, the signal model of the SE-SS-PARSE was specially designed to describe three different signal evolutions: FID, ascending part of spin echoes and descending part of spin echoes. The sign of the effective time evolution for irreversible transverse relaxation rate $R_2$ remains the same, while the sign of the effective time evolution for reversible transverse relaxation rate $R_2'$ alters twice after the refocusing RF pulse. Second, the SE-SS-PARSE method has been tested in computer simulations under various noise conditions and a range of different signal magnitudes, frequencies and decaying rates. For all cases investigated in computer simulations, SE-SS-PARSE produced accurate image parameter estimations. Third, SE-SS-PARSE was validated in experiments by comparing the estimates from SE-SS-PARSE with the “gold standard” estimates from CSE using a four-tube phantom. The highly correlated results between SE-SS-PARSE and CSE indicate that SE-SS-PARSE is capable of generating
accurate and reliable estimates. Fourth, R2 mapping in SE-SS-PARSE was compared with FSE, a commonly used R2 mapping method in clinical environments. The ultrafast R2 mapping provided by SE-SS-PARSE may benefit fMRI studies and cardiac imaging. Finally, a fat-suppressing pulse was applied in the SE-SS-PARSE method and was tested using a biological sample containing both fat and non-fat parts. The estimates with fat saturation presented more uniform distributions in the fat-containing part than the estimates without fat saturation.

Different from conventional MRI methods, PARSE MRI models signal amplitude decay and phase evolution during the signal acquisition. This characteristic of PARSE MRI is particularly helpful in accurately describing the signal change during the relatively long data acquisition time in the SS techniques. Geometric errors, a major disadvantage in SS MRI, are caused by the presence of far off-resonance frequencies. A great many methods have been proposed to correct geometric artifacts by field mapping or phase compensation [55-58]. As an alternative, PARSE MRI samples data in k,t-space and models purely temporal signal changes in the data collection process, leading to more reliable and robust data measurements. The SE-SS-PARSE method developed in this dissertation is based mainly on PARSE MRI, and thus promises more accurate data interpretation than existing SE methods. In addition, by coding multiple image
parameters in the signal model, SE-SS-PARSE is capable of producing estimates of multiple image parameters at the same time.

In SE-SS-PARSE, data were sampled along a specially designed rosette k,t-trajectory [30]. These types of trajectories are suitable for the PARSE data sampling because they make the signal highly sensitive to the temporal evolution of the magnetization magnitude and phase [31]. Due to several reasons, such as imperfect gradient performance and eddy currents, the actual k-sampling locations usually deviate from their ideal location. For this reason, the effective k,t sampling locations in this work were calibrated (i.e. determined experimentally) using the method proposed by Zhang et al [59]. An example of the calibrated rosette trajectories for FID and echo part is illustrated in Fig. 1. There were ramp-up and ramp-down sections at the beginning and the end of the readout gradient waveforms to return the gradient to zero. It should be mentioned that the calibration procedure is only required once, and does not need to be repeated until the gradient system hardware is changed or readjusted.

Calibration can also calculate the timing for experiments. Accurate timing plays an important role in parameter estimations of SE-SS-PARSE. The present PARSE methods employ the PLCG algorithm to estimate all image parameters. The general
process of the PLCG algorithm is demonstrated in Fig. 2. The starting values for the parameters are usually set to zero. Then the CG algorithm is applied to a partial data length by iteratively searching the parameter space to minimize the difference between the model signal and the experimental signal. Once the difference, characterized by the least square subtraction, is smaller than a user-defined threshold, the algorithm is applied to a longer data length. This process is repeated until the entire signal length has been searched. In order to consistently match the model signal with experimental signal, durations of the RF pulses, and gradient on and off times need to be determined precisely and substituted into the model. These time durations can be measured once in the calibration process and they will only change if the rf-pulses or gradients change.

Nevertheless, careful design of the signal model does not promise a smooth convergence of the PLCG algorithm. The iterative searching process usually takes a long time and may fail to converge at locations with large off-resonance frequencies. For this reason, great care is taken in adjusting the shim currents before obtaining data. Furthermore, the algorithm may be optimized by shortening the progressive data lengths over which successive estimations are performed. Reduced data length may increase the accuracy of estimates, but in theory could lead to convergence to a secondary minimum. However, it has been shown that proper choice of progressive lengths can effectively
prevent this problem [32]. Another way to improve the estimation accuracy is to lower the stopping tolerance. The algorithm stops the search for each data length when it meets the criterion of stopping tolerance. A smaller tolerance is associated with longer search duration, but also potentially a more precise estimation. In addition, adjusting parameter weighting factors may speed up the algorithm, especially when the parameters for decay rates or frequencies are not in the same value scale. Proper weighting factors can effectively balance the size of the search gradients for decaying rates and frequencies. Faster computing hardware, such as the Graphical Processing Units (GPU), may greatly accelerate the whole estimation process in SE-SS-PARSE.

Besides the convergence issue, several other aspects of estimation errors merit discussion. Although the SE-SS-PARSE results were highly correlated to the “gold standard” technique, it should be noted that SE-SS-PARSE results include relatively large variance compared to the reference values. This is to be expected because SE-SS-PARSE collected data much faster than the standard technique. However, the source of estimation errors needs to be investigated. From our previous studies, the estimation errors can be categorized into two major types: the bias errors and random errors. Because the SE-SS-PARSE estimates parameters by matching the model signal with the experimental signal, any discrepancy between the signal model and experimental signal may lead to the bias
errors [32]. For example, the local signal model in SE-SS-PARSE does not account for the non-exponential effects of dephasing across the voxel that may exist in the actual object. For another example, the evaluation k-band is a square while the acquisition k-band is a disc, leading to under- or over-estimates of high spatial frequencies from the gap between two k-bands. These bias errors may be reduced [32], but may not be eliminated.

For all cases investigated in this dissertation, including computer simulations and experimental studies, SE-SS-PARSE demonstrated the ability to yield adequate R2 maps with a rapid data acquisition. Two other commonly used R2 mapping methods, CSE and FSE, were executed to compare with SE-SS-PARSE. As described in the introduction, CSE produces the most accurate R2 mapping but requires a long data acquisition time. Any changes such as motion during the data collection may degrade final images. Another frequently used R2 mapping method, FSE, accelerates the total data sampling time by collecting data from multiple spin echoes after a single excitation. This approach decreases the total data acquisition time, however, extends the time required after a single excitation, potentially leading to ringing artifacts in the final images, as seen in Fig. 3. From our observations, ringing artifacts may result from vibrations in the fluid-filled phantom due to the large gradient amplitudes and fast slew
rate. In addition, multiple imperfect inversion pulses in FSE could lead to a range of errors in the measured R2 decay [60]. In contrast, SE-SS-PARSE estimates R2 values directly from the raw k-space data, obtained within a few hundred milliseconds. The ultrafast data collection in SE-SS-PARSE not only reduces motion artifacts, but also minimizes the adverse effects of physiological changes, such as flow, respiratory and heartbeat effects.

Rapid R2 mapping may benefit cardiac mapping [61-64] and recording dynamic BOLD responses applied in neural imaging and fMRI studies [65-68]. In cardiac imaging, breath-hold methods are usually applied to prevent movements from respiration. However, effects of motions and blood flow variations related to the cardiac cycle are difficult to prevent. The SE-SS-PARSE collects data in a sub-second time scale, and thus can effectively minimize the effect of movements or changes from any source. Furthermore, instead of measuring the commonly used R2* values for BOLD fMRI, the R2 mapping in SE-SS-PARSE reflects the local tissue mapping more accurately by avoiding non-homogeneity effects caused by large draining veins. Similarly, BOLD-based fMRI usually detects and locates brain functions by measuring the rapid R2* decays. However, the intravascular and extravascular effects in and around large vessels can be prominent in BOLD signal [69-71]. The R2*-weighted images thus cannot reflect
the BOLD responses originating from the parenchyma (ex. the capillary-level vasculature within active gray matter) accurately. BOLD related R2 changes occur dynamically over a time scale of seconds. Most of the rapid R2 mapping methods are based on indirect non-linear fitting of separately acquired intensity images, and thus may fail to capture such dynamic signal changes. As an alternative, SE-SS-PARSE samples the whole image data with an ultrafast speed, typically a few hundreds of millisecond. Rapid data acquisition not only effectively captures the instantaneously changed BOLD signal but also minimizes effects from random head movements and cyclic blood flow in large draining veins.

As discussed above, various sources contribute to the estimation error in R2 mapping from SE-SS-PARSE. However, it is worth mentioning that R2 maps are estimated from a data length equal to 148 milliseconds in our experiments. In contrast, the 64-shots FSE reconstructed R2 maps from a data length equal to about 2 minutes. The image accuracy, being influenced by random measured noise propagation, is expected to increase as the total acquisition time increases, due to signal averaging. With the same noise bandwidth, the image SNR is proportional to the square root of the total acquisition time, and this should be reflected in the relative accuracy of estimations. Theoretically, SE-SS-PARSE very possibly could yield more accurate R2 maps than FSE when taking
signal averaging over 64 shots. In addition, a multiple shot version of SE-PARSE may produce higher resolution parameter maps with only a few acquisitions, with the potential to identify more selective neural activities in fMRI studies [72].

To sum up, this dissertation research developed an ultrafast MRI scan method, SE-SS-PARSE, as well as evaluated the accuracy of image parameter estimations by comparing SE-SS-PARSE with conventional MRI methods. For all cases investigated in this dissertation, including computer simulations, phantom experiments and biological-sample studies, SE-SS-PARSE demonstrated the ability to produce accurate parameter maps of reversible and irreversible transverse relaxation constants with a rapid data acquisition. Sources of estimation errors in SE-SS-PARSE have been investigated and discussed. Possible directions for optimizing the reconstruction algorithm have been described. A positive feature of SE-SS-PARSE is that it can be installed into modern MRI systems without hardware alteration. The ultrafast R2 mapping ability of SE-SS-PARSE may be applied to a number of clinical applications, and may be especially useful in brain functional studies or neural imaging.
Fig. 1. One of the calibrated rosette k,t-trajectories used in this dissertation research. A and B are the 2-dimensional version trajectories for collecting data in FID and spin echo signals. C is the 3-dimensional view of the rosette in (k_x, k_y, t)-space. Small lead-in and lead-out sections at the beginning and the end of rosette trajectories are shown in A and B.
Fig. 2. The procedure of the PLCG algorithm applied to the parameter estimations in SE-SS-PARSE. Initially, all parameter values are set to zero in the signal model. Then the PLCG algorithm searches the parameter space and updated estimated parameter values after each iteration. Once the cost, defined as the fractional least square difference (LESD), becomes smaller than a manually set threshold, PLCG stops and begins searching over a longer data length. This process is repeated until the whole data length is searched and the newest updated image parameters are used as the final estimates.
Fig. 3. The R2-weighted maps and fitted R2 map from FSE experiment of the four-tube phantom. A, B, C, D, E, F, G, H are R2-weighted image acquired at effective echo time of [12, 24, 36, 48, 60, 72, 84, 96] ms using a FSE sequence with echo train length of 8. R2 map in I was computed as the intensity decay of R2-weighted images at different TE. Obvious ringing artifacts can be observed in the R2-weighted images, and in the R2 map.
GENERAL LIST OF REFERENCE


[43] Li N, Bolding M, and Twieg DB. Spin Echo SS-PARSE: A PARSE MRI Method to estimate frequency, R2, and R2’ in a single shot, Magn Reson Imag 2010 [in press].


APPENDIX A

SEQUENCE CODE OF SE-SS-PARSE (C)

/***************************************************************************/

separse.c

spin echo parse sequence
adapted from palm.c from Rose.c from episs.c
waveforms are pre-computed externally in matlab or your favorite enviroment
written 24 Feb 2009 -- msbolding and nzli

sequence timeline.
wait for TR - seqtime
optional fat sat block - not added yet...
excitation block
    turn on slice select gradient, gss
    wait for rise gss rise time
    wait rof1, pi/2 pulse transmitter for p1 ms, wait rof2
    turn off all gradients
    wait for gss fall time
    turn on refocus pulse, gssr
    wait for rgss rise
    wait for tssr
    turn off refocus gradient
    wait for fall time, rgssr
acquire fid data
    while playing ro and pe gradients for te_delay time
        collect fid data
spin echo block
    turn on slice select, and ro and pe crushers
    wait for slice select and crusher rise time
    wait for tcrush
    turn off crusher

97
wait for crusher fall time
wait rof1, pi pulse for p2 ms, wait rof2
turn on crusher
wait for crusher rise
wait for tcrush
turn off all gradients
wait for gradient fall
acquire echo
collect data for (at-te_delay)

#include "standard.h"
#include "group.h"
#define MAX_DAC_VAL 32767.0 /* system max DAC value */

pulsesquence()
{
    /* our variables for this sequence */
    double  seqtime; /* sequence length */
    double  rgss; /* ramp time of slice select gradient */
    double  tssr; /* time of slice select refocus */
    double  tcrush1,tcrush2; /* crusher length */
    double  tcrushf; /* crusher fraction, tweaker */
    double  tcrush; /* crusher rise time */
    double  fid_dur,s_e_dur; /* length of the shaped gradients in seconds*/
    double  te_dur1,te_dur2,te_dur3; /* the three parts of the te delay. */
    double  grate; /* gradient slew rate */
    double  predelay; /* delay before execution for TR */
    int fid_np,s_e_np; /* number of acq pts before and after 180 */
    char ro_fid_file[MAXSTR], pe_fid_file[MAXSTR]; /* fid gradient table file path */
    char ro_s_e_file[MAXSTR], pe_s_e_file[MAXSTR]; /* spinecho gradient table file path */
    char *home_dir;
    char calib[MAXSTR]; /* calibration flag */
/* bring in varian defined vars */
initparms_sis();

/* select varian variables **************************
tr  repetition time of sequence
te  echo time
gmax  maximum gradient strength
trise  rise time to gmax
gss  slice select gradient strength
np  number of points of data to acquire
gpe  phase encode gradient str
gro  read out grad str, should equal gpe
tcrush  crusher length
***************************/

/* load the gradient tables */
if ((home_dir = (char *) getenv("HOME")) == NULL)
{
        abort_message("Error in determining HOME environment variable\n");
}
getstr("ro_s_e_file",ro_s_e_file);
getstr("pe_s_e_file",pe_s_e_file);
getstr("ro_fid_file",ro_fid_file);
getstr("pe_fid_file",pe_fid_file);

/* get any other variables from the environment */
fid_dur = getval("fid_dur"); /* get the shaped gradient durations */
s_e_dur = getval("s_e_dur");
tcrushf = getval("tcrushf"); /* get crusher tweaker */

/* calculate constants */
grate  = trise/gmax;  /* gradient rate */
rgss  = grate*fabs(gss); /* gss rise time */
rcrush  = grate*fabs(gss); /* crush rise time */
gcrush  = gss;      /* use gss as crush strength for now */
tcrush1 = tcrush;      /* pre 180 crusher duration */
tcrush2 = tcrush*tcrushf; /* post 180 crusher duration */
/* time and np bookkeeping *******************************************/

seqtime total time needed to execute sequence
tssr time of slice refocus pulse plateau, set to make refocus integral = 1/2 ss
integranal
te_dur1 time from middle of excite to start of fid acq
te_dur2 time of fid acq
te_dur3 time from end of fid acq until middle of 180 pulse
predelay time to wait until execution, padding for TR
fid_np np before 180
s_e_np np after 180
*/

tssr = p1/2.0 + rof2 - rgss/2.0;
seqtime = 6.0*rgss + 2.0*rof1 + p1 + 2.0*rof2 + tssr + at + p2 + tcrush1 + tcrush2 + 2.0*rcrush;
te_dur1 = p1/2.0 + rof2 + 3.0*rgss + tssr;
te_dur3 = rgss + rof1 + p2/2 + tcrush + rcrush;
te_dur2 = te/2.0 - ( te_dur1 + te_dur3 );
if (te_dur2 < 0.0)
{
    abort_message("%s: Requested te too short. Min te = %f ms",seqfil,te_dur1+te_dur3);
}

predelay = tr - seqtime;
if (predelay < 0.0) /* is TR long enough? */
{
    abort_message("%s: Requested tr too short. Min tr = %f ms",seqfil,seqtime*1000.);
}

fid_np = (int) te_dur2*sw*2;
s_e_np = np - fid_np;

/* PULSE SEQUENCE ***************************************************/

status(A);
/* Phase cycle: Part I **********************************************/
mod2(ct,v3); /*0101 0101*/
dbl(v3,v3); /*0202 0202*/
hlv(ct,v4); /*0011 2233*/
mod2(v4,v4); /*0011 0011*/
add(v3,v4,v1); /*0213 0213*/
assign(v1,oph);
add(one,v1,v2);
assign(zero,v10);
assign(zero,v12);
/* tr delay ******************************************************/
delay(predelay);
msloop(seqcon[1],ns,v13,v14); /* Slice loop ***********/
rotate(); /* hardware based coordinate frame rotation */
poffset_list(pss,gss,ns,v14); /* set slice offset frequency */
/* 90 degree RF excitation section *******************************************/
observepower(tpwr1);
if (calib[0] == 'r') obl_gradient(gss,0.0,0.0);
if (calib[0] == 'p') obl_gradient(0.0,gss,0.0);
if (calib[0] == 'n') obl_gradient(0.0,0.0,gss);
delay(rgss);
shapedpulse(p1pat,p1,v1,rof1,rof2); /* actual excitation */
zero_all_gradients();
delay(rgss);
/* slice refocus section *******************************************/
if (calib[0] == 'r') obl_gradient(-gss,0.0,0.0);
if (calib[0] == 'p') obl_gradient(0.0,-gss,0.0);
if (calib[0] == 'n') obl_gradient(0.0,0.0,-gss);
delay(rgss);
delay(tssr); /* refocus time */
zero_all_gradients();
delay(rgss);
obsoffset(resto); /* put the receiver back on freq */
/* fid acquisition section *******************************************/
if (calib[0] == 'r') obl_shapedgradient(ro_fid_file,"","",fid_dur,gro,0.0,0.0,1,NOWAIT);
if (calib[0] == 'p') obl_shapedgradient("",pe_fid_file,"",fid_dur,0.0,gpe,0.0,1,NOWAIT);
if (calib[0] == 'n')
obl_shapedgradient(ro_fid_file,pe_fid_file,"",fid_dur,gro,gpe,0.0,1,NOWAIT);
acquire(fid_np,1.0/sw); /* acquire data from fid before spin echo */
/* spin echo 180 degree RF section *******************************************/
obspower(tpwr2);
poffset_list(pss,gss,ns,v14); /* move transmitter to slice offset frequency */
if (calib[0] == 'r') obl_gradient(0.0,gcrush,gcrush);
if (calib[0] == 'p') obl_gradient(gcrush,0.0,gcrush);
if (calib[0] == 'n') obl_gradient(gcrush,gcrush,0.0);
delay(rcrush);
delay(tcrush1);
if (calib[0] == 'r') obl_gradient(gss,0.0,0.0);
if (calib[0] == 'p') obl_gradient(0.0,gss,0.0);
if (calib[0] == 'n') obl_gradient(0.0,0.0,gss);
delay(rgss);
shapedpulse(p2pat,p2,v2,rof1,rof2); /* 180 excitation */
if (calib[0] == 'r') obl_gradient(0.0,gcrush,gcrush);
if (calib[0] == 'p') obl_gradient(gcrush,0.0,gcrush);
if (calib[0] == 'n') obl_gradient(gcrush,gcrush,0.0);
delay(rcrush);
delay(tcrush2);
zero_all_gradients();
delay(rgss);
/* spin echo acquisition section *******************************************/
obsoffset(resto); /* put the reciever back */
if (calib[0] == 'r') obl_shapedgradient(ro_s_e_file,"","",s_e_dur,gro,0.0,0.0,1,NOWAIT);
if (calib[0] == 'p')
obl_shapedgradient("",pe_s_e_file,"",s_e_dur,0.0,gpe,0.0,1,NOWAIT);
if (calib[0] == 'n')
obl_shapedgradient(ro_s_e_file,pe_s_e_file,"",s_e_dur,gro,gpe,0.0,1,NOWAIT);
acquire(s_e_np,1./sw); /* acquire data from spin echo */
zero_all_gradients();
endmsloop(seqcon[1],v14);
APPENDIX B

ROSETTE GENERATION CODE (MATLAB)

%roser2.m
% takes gmax,fov,nres,gam, computes k-trajectory kss for simulation tests
% D Twieg 8/06
% modified by inwhere@uab.edu 9/08
% play around with values in the lead-in -out section to tweak the initial and final
% sections of the trajectory. The gradients should start and end near zero as should the
% k-trajectory

% which trajectory
% wtraj = 'pre15'; % Spline or Trapazoid for now

% hardware
MAX_DAC_VAL=32767.0;% DAC max integer, corresponds to gro, gpe
GDELT=1e-05; % gradient waveform DAC speed
WAVEFORM_RESOL = 5.0e-2;
GRAD_UPDATE_TIME = 10;
MAX_RAMP_RES = 50;

% constants
gam=4258.;
twopi=2*pi;
sq2=sqrt(2);

defaults
circum=1; % circumscribed (=1) or not (!=1).
gmax=3.8; % maximum read gradient to be used.
pre_emph=1.05; % pre emphasise to compensate for high freq attenuation, increase this can reduce
the whole thing.
fov=12.8; % field of view in cm
nres=64; % resolution
kf=nres/(2*fov);

wtraj = 't65';

% other parameters of desired trajectory
switch lower(wtraj)
    case 't65'
        Ta=.065;  % gradient duration in seconds without lead-in and -out
    case 't15'
        Ta=.015;  % gradient duration in seconds without lead-in and -out
    case 't30'
        Ta=.030;  % gradient duration in seconds without lead-in and -out
    case 'test'
        Ta=.030;  % gradient duration in seconds without lead-in and -out
    case 't40'
        Ta=.040;  % gradient duration in seconds without lead-in and -out
    case 't45'
        Ta=.045;  % gradient duration in seconds without lead-in and -out
    case 't80'
        Ta=.080;  % gradient duration in seconds without lead-in and -out
    case 't85'
        Ta=.085;  % gradient duration in seconds without lead-in and -out
    case 't95'
        Ta=.095;  % gradient duration in seconds without lead-in and -out
    case 't120'
        Ta=.120;  % gradient duration in seconds without lead-in and -out
    case 'epi3'
        Ta=.040;
    otherwise
        error('please set wtraj')
end

delt=1./(gam*gmax*fov); % ADC sample rate
Na=floor(Ta/delt); % number of acquisitions
tim=(0:Na-1)*delt; % vector of time points

%%% generate trajectory
switch lower(wtraj)
case 'epi3'

%% generate vector of gradient values for epi
kra = kf;
Ne = nres;

nv = nres; % number of k-space lines
etl = nv; % echo train length
center_echo = etl/2;

%% calc gradient wave forms
gpeint = 1/(fov*gam); % grad integral for 1 unit step in k-space
blip_int = gpeint; % integral of one phase enc blip
gped_max = nv/2; % max mult fact on gped;
rise_time = 195/1000; % min rise time for gradients FIXME: lookup on scanner
grate = gmax/rise_time; % max gradient rate

gpe = sqrt(blip_int/grate); % phase encode gradient
gped = sqrt(gpeint/grate);
gro = 1/(delt*fov*gam); % read out gradient
if (gro > gmax)
    disp('WARNING: gro > gmax, increase dwell or fov')
end
if (abs(gpe) > abs(gro))
    disp('WARNING: phase enc grad > readout grad, increase readout gradient')
end
% calculate ramp parameters
rgro = abs(gro)*grate; % read out gradient minimum rise time
rgpe = abs(gpe)*grate; % phase enc minimum rise time
dwint = gro*delt; % required gradient area per point
np = nres; % number of points in one read out line
np_ramp = 0;
np_flat = np;
at_flat = np_flat * delt; % minimum acq time on flat
flat_cc = ceil(at_flat*1.0e6/WAVEFORM_RESOL);
rgro_res = rgro*1.0e6/GRAD_UPDATE_TIME;
if ( rgro_res < MAX_RAMP_RES )
    rgro_res = round(rgro_res + 0.5);
else
    rgro_res = MAX_RAMP_RES;
cc_pp = ceil(1.0e6*rgro/(rgro_res*WAVEFORM_RESOL));

Gread = tim;
Gphase = tim;
gs = Gread + 1i * Gphase;
otherwise
  if circum == 1     % circumscribed or not
    kra=sqrt(2)*kf;
    Ne=2*round(sqrt(2)*nres/2);
  else
    kra=kf;
    Ne=nres;
  end
  om1=gam*gmax/kra;
  om2=(41.1/nres)*om1;
  gs=kra*(1.042*(om1+om2)*(cos((om1+om2)*tim+pi/2)+1i*sin((om1+om2)*tim+pi/2))...
      + (om2-om1)*(cos((om2-om1)*tim+pi/2)+1i*sin((om2-om1)*tim+pi/2)))/(2*gam);
end
% generate lead-in and lead-out
% play with the internal points of the trapezoids or splines to get the
% lead-in and -out correct.
num_pts = 100;
pts = 1:num_pts;
switch lower(wtraj)
case 't65'
  L = [ 2.065+1i*(-1.64)  2.63+1i*(0.7) ;  % lead in tweakers
       -0.77+1i*(2.31)  -2.4+1i*(-0.48)];  % lead out tweakers
  ctl_pts_x = [0 num_pts/3  2*num_pts/3 num_pts];
  gs_li = spline(ctl_pts_x,[ 0 L(1,1) L(1,2) gs(1) ],pts);  % lead-in
  gs_lo = spline(ctl_pts_x,[ gs(end) L(2,1) L(2,2) 0 ],pts);  % lead-out
  if true
    case 't15'
      L = [ 2.045+1i*(-1.59091)  2.53+1i*(0.70248) ;  % lead in tweakers
            -1.745+1i*(0.83)  -2.9+1i*(-1.4)];  % lead out tweakers
      ctl_pts_x = [0 num_pts/3  2*num_pts/3 num_pts];
    end
gs_li = spline(ctl_pts_x,[ 0  L(1,1)  L(1,2)  gs(1) ],pts); % lead-in
gs_lo = spline(ctl_pts_x,[ gs(end) L(2,1)  L(2,2)  0 ],pts); % lead-out

case 't30'
L = [ 2.175+1i*(-1.64091)  2.53+1i*(0.70248) ; % lead in tweakers
     -1.435+1i*(0.8)   -2.2+1i*(-1.9) ]; % lead out tweakers
cntl_pts_x = [0 num_pts/3  2*num_pts/3 num_pts];
gs_li = spline(ctl_pts_x,[ 0  L(1,1)  L(1,2)  gs(1) ],pts); % lead-in
gs_lo = spline(ctl_pts_x,[ gs(end) L(2,1)  L(2,2)  0 ],pts); % lead-out

case 'test'
L = [ 2.045+1i*(-1.59091)  2.53+1i*(0.70248) ; % lead in tweakers
     -1.245+1i*(0.13)   0.1+1i*(-1.4) ]; % lead out tweakers
cntl_pts_x = [0 num_pts/3  2*num_pts/3 num_pts];
gs_li = spline(ctl_pts_x,[ 0  L(1,1)  L(1,2)  gs(1) ],pts); % lead-in
gs_lo = spline(ctl_pts_x,[ gs(end) L(2,1)  L(2,2)  0 ],pts); % lead-out

case 't40'
L = [ 1.81+1i*(-1.62)   2.88+1i*(0.68) ; % lead in tweakers
     0.19+1i*(1.9)    -0.23+1i*(0.45) ]; % lead out tweakers
cntl_pts_x = [0 num_pts/3  2*num_pts/3 num_pts];
gs_li = spline(ctl_pts_x,[ 0  L(1,1)  L(1,2)  gs(1) ],pts); % lead-in
gs_lo = spline(ctl_pts_x,[ gs(end) L(2,1)  L(2,2)  0 ],pts); % lead-out

case 't45'
L = [ 1.81+1i*(-1.62)   2.88+1i*(0.68) ; % lead in tweakers
     -0.84+1i*(0.49)   -0.98+1i*(-1.01) ]; % lead out tweakers
cntl_pts_x = [0 num_pts/3  2*num_pts/3 num_pts];
gs_li = spline(ctl_pts_x,[ 0  L(1,1)  L(1,2)  gs(1) ],pts); % lead-in
gs_lo = spline(ctl_pts_x,[ gs(end) L(2,1)  L(2,2)  0 ],pts); % lead-out

case 't80'
L = [ 1.63+1i*(-1.48)   3.07+1i*(0.55) ; % lead in tweakers
     0.29+1i*(0.67)   -1.77+1i*(0.22) ]; % lead out tweakers
cntl_pts_x = [0 num_pts/3  2*num_pts/3 num_pts];
gs_li = spline(ctl_pts_x,[ 0  L(1,1)  L(1,2)  gs(1) ],pts); % lead-in
gs_lo = spline(ctl_pts_x,[ gs(end) L(2,1)  L(2,2)  0 ],pts); % lead-out

case 't85'
L = [ 1.76+1i*(-1.48)   2.93+1i*(0.55) ; % lead in tweakers
     1.19+1i*(2.57)    -2.04+1i*(2.04) ]; % lead out tweakers
cntl_pts_x = [0 num_pts/3  2*num_pts/3 num_pts];
gs_li = spline(ctl_pts_x,[ 0  L(1,1)  L(1,2)  gs(1) ],pts);  % lead-in
gs_lo = spline(ctl_pts_x,[ gs(end) L(2,1)  L(2,2)  0 ],pts);  % lead-out

```
case 't95'
    L = [ 1.63+1i*(-1.48)  3.07+1i*(0.55) ;  % lead in tweakers
          1.65+1i*(0.31)  -1.06+1i*(-0.14)];  % lead out tweakers
    ctl_pts_x = [0 num_pts/3  2*num_pts/3 num_pts];
    gs_li = spline(ctl_pts_x,[ 0  L(1,1)  L(1,2)  gs(1) ],pts);  % lead-in
    gs_lo = spline(ctl_pts_x,[ gs(end) L(2,1)  L(2,2)  0 ],pts);  % lead-out

```
case 't120'
    L = [ 1.7+1i*(-1.14)  3+1i*(0.2) ;  % lead in tweakers
          2.55+1i*(-0.08)  0.17+1i*(3.83)];  % lead out tweakers
    ctl_pts_x = [0 num_pts/3  2*num_pts/3 num_pts];
    gs_li = spline(ctl_pts_x,[ 0  L(1,1)  L(1,2)  gs(1) ],pts);  % lead-in
    gs_lo = spline(ctl_pts_x,[ gs(end) L(2,1)  L(2,2)  0 ],pts);  % lead-out

```
case 'epi3'
    gs_li = zeros(size(pts));
    gs_lo = zeros(size(pts));
```
otherwise
    error('Unknown method. Check lead in and out code.
end

```
gs = [gs_li gs gs_lo];  % put the lead-in -out and gradient wave together
gs_max=max(abs(gs));
gmax=gs_max;

% predict k trajectory vector by integrating gs
ks2=kra+gam*delt*cumsum(gs);
ks2=ks2-ks2(1);  % assume start at zero

% compute resampled and scaled output vectors for UnityInova hardware
Q=10000;  % we resample at P/Q rate, P, Q must be pos. int.
P=round(Q*delt/GDELTA);  % downsample because grad DAC is slower than ADC
dac = gs*MAX_DAC_VAL/gs_max;  % use computed max dac value not gmax (problem?)
% dac_r=resample(real(dac),P,Q);  % actual values sent to hardware
% dac_i=resample(imag(dac),P,Q);
dac_r=real(dac);  % actual values sent to hardware
dac_i=imag(dac);
% show that puppy
len_d=100; % number of points to display on lead-in and -out dac
len_d_k=900; % number of points to display on lead-in and -out ktraj

figure(1)

subplot(3,3,1); % plot dac
plot(dac_i,dac_r);
title(['dac gs_m_a_x=' num2str(gs_max)]);

subplot(3,3,2); % dac start
plot(dac_r(1:len_d),dac_i(1:len_d),'o',...
    real(dac(1:round(len_d*Q/P))),...
    imag(dac(1:round(len_d*Q/P))));
hold on
plot(L(1,:)*MAX_DAC_VAL/gs_max,'r+')
hold off
title('dac start ');

subplot(3,3,3); % dac end
plot(dac_r(end-len_d+1:end),dac_i(end-len_d+1:end),'o');
hold on
plot(L(2,:)*MAX_DAC_VAL/gs_max,'r+')
hold off
title('dac end ');

subplot(3,3,4); % plot ks
plot(ks2)
title(['ks ' wtraj])

zm=[-1 1 -1 1]*0.82646; % zoom in to center
subplot(3,3,5); % ks start
plot(ks2(1:len_d_k))
hold on
plot(ks2(1:2),'+r')
hold off
title(['ks start ' num2str(ks2(1))])
axis(zm)

subplot(3,3,6); % ks end
plot(ks2(end-len_d_k:end))
hold on
plot(ks2(end-2:end),'+r')
hold off
title(['ks end ' num2str(ks2(end))])
axis(zm)

ks2_diff=[ks2 ks2(end)]-[ks2(1) ks2];
subplot(3,3,7) % ks diff
plot(ks2_diff(1:len_d_k))
hold on
plot(ks2_diff(end-len_d_k+1:end),'+g')
hold off

subplot(3,3,8); % ks start
plot(ks2(1:len_d_k),'+o')
hold on
plot(ks2(1:len_d_k/10),'+r')
hold off
title('ks start')

subplot(3,3,9); % ks end
plot(ks2(end-len_d_k+1:end),'+o')
hold on
plot(ks2(end-len_d_k/10:end),'+r')
hold off
title('ks end')