Clinically Relevant Magnetic Resonance Imaging and Spectroscopic Imaging Development

by

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Abstract

As one result of this thesis, a single slab 3D fast spin echo imaging (3DFSE) method has been implemented and optimized. This involved sequence design and implementation, SAR considerations, parameter adjustments and clinical testing. The method can deliver 3D T1 or T2 weighted brain image with isotropic 1mm$^3$ voxel resolution in approximately 10 minutes. The ability to obtain high spatial resolution in reasonable time periods has wide clinical applications such as improvement of treatment planning protocols for brain tumor patients, precise radiotherapy planning, and tissue segmentation for following the progression of diseases like multiple sclerosis.

The other part of this thesis is devoted to developing and implementing spectroscopic imaging methods, which include 2D chemical shift imaging (2DCSI) methods, 2D line scan spectroscopic imaging (2D LSSI) methods, spin echo planar spectroscopic imaging (SEPSI) methods and single shot line scan spin echo planar spectroscopic imaging (SSLSEPSI) method. The former two methods are applied to oil phantoms and bone marrow studies. The SEPSI method can provide simultaneous spectroscopic measurements, $R_2$ and $R_2'$ images and field distribution images. A time domain spectral analysis method, LP-HSVD was implemented and applied to spectroscopic imaging studies. The SEPSI method was applied to get lipid characterization of bone marrow as well as to get the $R_2$ and $R_2'$ brain images. The SSLSEPSI method can provide instant line spectroscopic imaging which might be useful to image moving objects and can provide high temporal resolution for dynamic studies. With further development, both SEPSI and SSLSEPSI methods may prove useful for trabecular bone studies as well as functional magnetic resonance imaging (fMRI) studies.

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Chapter 1

Introduction

1.1 Motivation and Background

1.1.1 3D Single Slab Fast Spin Echo Imaging Method

High signal-to-noise, high spatial resolution, true T2-weighted or T1-weighted 3D images through the entire brain in clinically acceptable scan times should improve treatment planning protocols for brain tumor patients. High spatial resolution 3D data sets are also needed for precise radiotherapy planning. Tissue contrast available from 3D single slab spin echo images may improve tissue segmentation currently performed on multi-slice spin-echo imaging for following the progression of diseases like multiple sclerosis (MS).

Though this has long been recognized, the large number of phase encoding steps used for 3D MRI (e.g. 160 × 160) has largely mandated that 3D MR studies be performed with short repetition time (TR), low flip angle, gradient echo sequences to maintain clinically acceptable scan times of approximately 10 minutes[28, 80]. Such sequences suffer from lower inherent signal-to-noise than long TR spin-echo sequences. They also have sub-optimal tissue contrast features compared to spin-echo methods and can demonstrate severe artifacts near bone/tissue or tissue/air interfaces where magnetic susceptibility differences are encountered[82, 15, 78, 86]. Because of the problems with 3D gradient echo imaging, there is a recognized need for designing
and developing long TR spin-echo sequences with better signal-to-noise and tissue contrast properties, as well as reasonable scan times.

The Fast Spin Echo (FSE) method utilizes multiple echoes for distinct phase encode steps and has proven most useful for standard 2D spin-echo imaging in the interleaved multi-slice format[58, 66, 87, 62, 35]. With recent gradient hardware upgrades on clinical 1.5 T systems, it has become possible to consider FSE sequences with very short echo spacings of 5 ms or less. Typical FSE echo spacings with the slower gradient systems typical of older MR imaging systems were on the order of 15 ms. With the factor of 3 reduction in echo spacing, some 3 times as many echoes can be collected with the same, acceptable degree of T2-weighting encountered in standard FSE imaging. Thus long echo trains of 80 echoes or more may be utilized for T2-weighted spin-echo imaging, making 3D FSE imaging with high spatial resolution and high signal-to-noise a possibility in clinically acceptable scan times of approximately 10 minutes.

One major goal of this thesis is to design, implement and optimize 3D FSE sequences which will allow for isotropic voxel volumes of 1mm$^3$ to cover the entire brain with a signal-to-noise ratio of 20 or greater. The design and implementation of the sequence primarily requires programming modifications of a standard FSE sequence to reduce echo spacings. A number of schemes for doing so are available including altering crusher gradient schemes, eliminating slice selection gradients, and changing the default RF pulses from 3.2 ms selective sinc refocusing pulses to hard 180° pulses.

1.1.2 Rapid Magnetic Resonance Spectroscopic Imaging

In vivo localized NMR spectroscopic techniques for studying bone marrow have potentially important clinical relevance for a number of diseases including cystic fibrosis, Gaucher's disease and leukemia. Studies of some tumors such as liposarcomas, in which alterations in the levels of unsaturation among the triglycerides may be diagnostic of tumor grade would also greatly benefit from conveniently applied in vivo spectroscopic techniques that sample large volumes at high spatial resolution. Thus the development of an optimized fast spectroscopic imaging method for separating
olefinic from water protons and methylene from methyl protons will be of significant clinical utility in bone marrow studies. One result of this thesis is the development of techniques for fast spectroscopic imaging of lipids in vivo.

The goal is to develop options for spectroscopic imaging methods that enable measuring some T2-weighted methyl/methylene ratios and olefinic/methyl ratios from many voxels in bone marrow in scan times on the order of 5 minutes or less. This is a much more challenging target than the usual "fat/water" separation[18] studies commonly used in bone marrow due to the small frequency shift between methyl and methylene protons at 1.5 T. Such a technique would however, be useful for estimating indices associated with saturation levels among triglycerides in marrow, furthering potential clinical applications of MRS.

Of the four options in MRSI developed and implemented in this thesis, the first two utilize direct spectroscopic echo readouts (no spatial frequency encoding gradients) to obtain the spectral information. The difference of these first two methods is in their 2D spatial encoding. The first uses two phase encoding directions. The second use one spatial line selection and one phase encoding. Multiple spin echo acquisitions per TR period, which decrease the scan time as well as introduce $T_2$ weighting[59], are applied to both methods. The third method incorporates a spectroscopic echo planar readout which covers both spatial encoding and chemical shift encoding. The final method is a single shot line scan spin echo planar spectroscopic imaging method that includes additional inversion recovery pulse and water suppression options.

1.1.3 Time-Domain Analysis and Relaxation Mappings

The most common method for spectral analysis is fast Fourier transformation (FFT). However, when there is a limited number of data points in the time series, the FFT suffers low resolution limit. If the signal to noise ratio of the data is high enough, time-domain analysis can be applied to overcome FFT disadvantages. One time domain spectral analysis method, Hankel singular value decomposition (HSVD), is implemented, and used together with FFT for spectral analyses.

The mapping or imaging of relaxation rates such as the effective relaxation rate,
reversible relaxation rate and irreversible relaxation rate are indicators of tissue properties. The reversible relaxation rate is closely related to susceptibility changes caused by paramagnetic substances, while the irreversible relaxation rate is related to more complex time dependent processes such as spin-spin interactions, diffusion, etc. Relaxation mapping provides a useful tool in studies of brain and liver disorder with abnormal iron accumulation[65, 5], trabecular bone and related disease such as osteoporosis[54, 25], and in functional MRI where the neuron activation causes local susceptibility changes through changes in blood hemoglobin oxygenation[63, 64, 44, 5, 22]. In this thesis, a method to retrieve simultaneously several relaxation rate maps is developed, implemented and demonstrated.

1.1.4 Single Shot Line Scan Spin-echo Planar Spectroscopic Imaging

Single shot line scan spin-echo planar spectroscopic imaging can offer a spectroscopic image in the order of 100ms and may prove useful for imaging moving body parts such as liver and heart. In functional magnetic resonance imaging, high temporal resolution can offer dynamic metabolite information. The chemical components involved in brain metabolism such as, N-acetyl aspartate(NAA), choline(Cho) and creatine(Cre) are present in the brain in concentrations on the order of 10mM. Thus, water suppression must be applied to retrieve those low concentrated chemical substances. In addition, the lipid signal from scalp and skull should also be suppressed. The single shot line scan spin-echo planar spectroscopic imaging method developed in this thesis includes an inversion recovery pulse and CHESS packets to suppress fat and water signals.

1.2 Structure of this Thesis

3D fast spin echo(3DFSE) methods are introduced and discussed in chapter 2. The design and implementation of 3DFSE methods are presented in chapter 3. An introduction to 3D chemical shift imaging is given in chapter 4, where the development
and implementation of a spin echo planar spectroscopy imaging (SEPSI) method is described. An implementation of LP-HSVD time domain spectral analysis method is included in chapter 5. The application of SEPSI to bone marrow characterization is presented in chapter 6. The development and implementation of two alternative 2D spectroscopy imaging methods are described in the same chapter. In chapter 7, a method for simultaneously imaging of $R_2$, $R'_2$ and field distribution by SEPSI and LP-HSVD is presented. Finally, The single shot spin-echo planar spectroscopic imaging method (SSLSEPSI) is discussed in chapter 8.
Chapter 2

3D Fast Spin Echo Method

2.1 Principles of Magnetic Resonance Imaging

2.1.1 Physics Background of Nuclear Magnetic Resonance

An atom with unpaired nucleons (protons or neutrons) has an angular momentum $I\hbar$ and a dipolar moment $\gamma \hbar I$, where the constant $\gamma$ is called gyromagnetic ratio and $I$ is half or full integer representing angular momentum. The nuclei that are of interest for biological systems are $^1H$, $^2H$, $^{13}C$, $^{23}Na$, $^{31}P$, and $^{19}F$.

Under static magnetic field $B_o \mathbf{k}$ (where $\mathbf{k}$ is the direction of the field), the Zeeman interaction ($-\gamma B_o \hbar$) between a magnetic dipole and the magnetic field causes energy level splits of $-\gamma B_o \hbar$. If a paramagnetic sample of $N$ nuclei are in thermal equilibrium with an environment described by temperature $T$, the population of each level is described by the Boltzmann distribution. The net magnetization of the sample is[2],

$$M = N \gamma \hbar \sum_{m=-I}^{I} \frac{m \exp (m\gamma B_o \hbar / kT)}{\sum_{m=-I}^{I} \exp (m\gamma B_o \hbar / kT)}$$

At room temperature, where $\gamma B_o \hbar / kT \ll 1$, the net magnetization is described by Curie's law,
\[ M = \frac{N\gamma^2\hbar^2 I(I + 1)}{3kT} B_o \] (2.2)

At equilibrium, \( \mathbf{M} \) is aligned along the direction of the magnetic field. When a transverse(\( \perp \mathbf{k} \)) RF field \( B_1 \cos(\omega_0 t) \mathbf{i} \) with a frequency of \( \omega = \gamma B_o \) is applied, \( \mathbf{M} \) will rotate about \( x \)-axis in the \( y-z \) plane(in rotating frame). Once the RF field is removed after it flips \( \mathbf{M} \) off the \( z \)-axis, \( \mathbf{M} \) starts to precess about the \( B_o \) field at Larmor frequency \( \omega_o = \gamma B_o \), inducing a detectable electro-magnetic signal in a receiving coil [34]. If a unit current in the receiving coil produces a magnetic field with transverse component \( \dot{B}_{1z} \), the processing of a system with a transverse magnetization \( M_o \) and volume \( \Delta V \) will induce electrical magnetic field(EMF) in the coil, which is given by,

\[ \xi = \omega_o \dot{B}_{1z} M_o \Delta V \text{volts} \] (2.3)

When the net magnetization is in the transverse plane, the spin system will restore to its equilibrium value by spin-lattice relaxation which is characterized by a time constant \( T_1 \). Meanwhile, the transverse magnetization will diminish by spin-spin relaxation characterized by a time constant \( T_2 \). The transient behavior of the magnetization under external magnetic field can be described by the Bloch equations[8],

\[
\begin{pmatrix}
M'_x \\
M'_y \\
M'_z
\end{pmatrix} =
\begin{pmatrix}
-1/T_2 & -\Delta \omega & \omega_{1y} \\
\Delta \omega & -1/T_2 & -\omega_{1x} \\
-\omega_{1y} & \omega_{1x} & 1/T_1
\end{pmatrix}
\begin{pmatrix}
M_x \\
M_y \\
M_z
\end{pmatrix} - \frac{1}{T_1}
\begin{pmatrix}
0 \\
0 \\
M_o
\end{pmatrix}
\] (2.4)

where the parameters are expressed in rotating frame.

### 2.1.2 Magnetic Resonance Imaging

In magnetic resonance imaging(MRI), the spin density \( \rho(\mathbf{r}) \) of nuclei in each pixel or voxel is to be determined(may be weighted by other properties, e.g. \( T_1, T_2, T_2', \) diffusion \( D \) and flow, etc.). A magnetic field gradient \( \mathbf{G} \) is introduced to supply a
spatial – frequency mapping,

\[ \omega(r) = \gamma B_o(r) + \gamma G \cdot r \quad (2.5) \]

The signal from a voxel \( dV \) at \( r \) is,

\[ dS(t) = \rho(r)dV \exp[i\gamma t(B_o + G \cdot r)] \quad (2.6) \]

In k-space formalism[49, 50, 51] and in the rotating frame, the signal from the whole volume is,

\[ S(k) = \iiint \rho(r) \exp(i2\pi k \cdot r) \, dr \quad (2.7) \]

where \( k = (2\pi)^{-1} \gamma G t \), is the reciprocal space vector. The spin density is given by the inverse Fourier transform,

\[ \rho(r) = \iiint S(k) \exp(-i2\pi k \cdot r) \, dk \quad (2.8) \]

In general, the magnetic resonance imaging reconstruction processes can be expressed as,

\[ D = FI \]

\[ I' = F^{-1}D \]

where \( I \) is the spatial based object to be imaged, \( D \), the result of observation, is also a map of the object which can be, for example, Fourier based, wavelet based[32, 69, 68], etc. \( F \) is the mapping between the two bases, \( F^{-1} \) is the inverse operation of \( F \) through which the image \( I' \) is reconstructed. Due to the discrete nature of digital signal processing, only a subset of original information about the object (which is in continuous domain) remains. Meanwhile, artifacts and noise are inevitably introduced in the mapping process as well as the detection process. Hence, the image \( I' \) is always an approximation of the object \( I \).
2.2 Introduction to Spin Echo Imaging Method

2.2.1 Spin Echo Imaging

Figure 2-1 shows the conventional spin echo imaging method. One spatial dimension
z is first localized by a slice selective excitation pulse. A slice of spins is excited to
the transverse plane by a 90 degree RF pulse. A multiple step magnetic field gradient
is applied in another spatial direction y as phase encode. During the same time,
a x direction gradient is applied to reach the maximum $k_{x_{max}}$ value. Then a 180
degree RF refocusing pulse is applied at $TE/2$. A spin echo[30] will appear at time
$TE$. The 180° RF pulse also transforms the k trajectory from $k_{x_{max}}$ to $-k_{x_{max}}$. A
read out period is placed symmetrically about the spin echo. A read out gradient is
applied during the acquisition to frequency encode. This frequency encode gradient
will sweep from $-k_{x_{max}}$ to $k_{x_{max}}$. The sequence consists of $n_y$(the number of phase
encode) repetition of pulses described in Figure 2-1 to cover all the k space of a slice.
The repetition time $TR$ is the time between two excitations. If the repetition time
$TR$ is large(e.g. $> 5T_1$), varying TE will give rise to $T_2$ weighted contrast. If $TR$ is
less than $T_1$ and TE is short, $T_1$ weighed contrast will be observed in the image. The
proton weighted image is obtained with short TE and long TR.

For a sufficiently long repetition time, and assuming that the $T_2$ value is much
larger than the duration of the acquisition window of the spin echo, the signal at
$(m,n)$ in k-space is,

$$S(m,n) = \int \int \rho(x,y)e^{i2\pi m_{k_{xo}}x}e^{i2\pi n_{k_{yo}}y}e^{-\frac{TE}{T_2}}dxdy$$  (2.9)

or

$$S(m,n) = S_o(m,n)e^{-\frac{TE}{T_2}}$$

where $\rho(x,y)$ is the spin density in the slice, $k_{xo}$ and $k_{yo}$ are steps of $k_x$ and $k_y$ in
k-space respectively. The term $S_o(m,n)$ represents the ideal image to be obtained
from FT encoding method, though there is still Gibb's artifact[29]. If the local in-
homogeneity $\delta\omega$, which is produced by chemical shift or other field inhomogeneities,
and the transverse magnetization dephasing time $T_2^*$ by both $T_2$ decay and static field inhomogeneities are considered, the signal is then,

$$S(m, n) = \int \int \rho(x, y)e^{im(k_x x + \delta \omega \cdot \tau)}e^{i2\pi nk_y y}e^{-\frac{T_E}{T_2}}e^{-\frac{\gamma B}{T_2}}dxdy$$ (2.10)

where $\tau^1 = k_x/2\pi G_x$ and $G_x$ is the readout gradient strength.

The reconstructed image can be expressed in discrete domain,

$$I_D(x, y) = DFT[S(m, n)] \cdot e^{-\frac{T_E}{T_2}}$$ (2.11)

or

$$I_D(x, y) = DFT[S_o(m, n)] \otimes DFT(e^{i\delta \omega \cdot \tau}) \otimes DFT(e^{-\frac{\gamma B}{T_2}} \cdot e^{-\frac{T_E}{T_2}}$$

or

$$I_D(x, y) = DFT[S_o(m, n)] \otimes PSF(\delta \omega) \otimes PSF(T_2^*) \cdot e^{-\frac{T_E}{T_2}}$$

where PSF is the point spread function. The image intensity is proportional to $e^{-\frac{T_E}{T_2}}$, so that the image is called $T_2$ weighted. If the repetition time is too short for spin to recover fully, $T_1$, the spin lattice relaxation time, will appear through a factor of $(1 - e^{(T_R/T_1)})$, which gives rise to $T_1$ weighted imaging.

If the field gradient caused by the field offset $\delta \omega/(size$ of voxel) is greater than that caused by the readout gradient, the voxel position will be shifted.

The $T_2^*$ will contribute to the blurring and reduction of image intensity (e.g. see chapter 7). When $T_2^*$ is shorter than a half width of the acquisition window, the frequency readout will not faithfully encode the spatial x-dimension. However, the constant time imaging method[26], the single-point imaging method[7] and a multiple echo approach called SPARE (single-point acquisition with relaxation enhancement)[53], in which only one point of a spin echo is collected, can be applied for better results. For simplicity, we will neglect $T_2^*$ effects in the following discussion.
2.2.2 Fast Spin Echo Imaging

In conventional spin echo imaging methods, only one echo is acquired in one repetition time. Fast spin echo imaging is accomplished by acquiring a train of echoes in one repetition[33, 57]. Figure 2-2 shows the sequence diagram of fast spin echo imaging\(^2\).

An echo train consists of one excitation pulse and a series of 180 degree refocusing RF pulses. Each refocusing pulse is equally spaced and produces an echo which is phase encoded separately. Fast spin echo imaging can save scan time by a factor of the echo train length(ETL), which is the number of echoes collected in one excitation. Since the amplitude of echoes along one train decays exponentially, the echo train length(ETL) is limited. As an imperfect 180 degree refocusing RF pulse will cause additional free induction decay(FID), a pair of crusher gradients is applied about the 180 degree pulse to spoil the FID. The signal can be written as,

\[
S(m, n) = \int \int \rho(x, y)e^{i2\pi m k_x o x} e^{i2\pi n k_y o y} e^{-\frac{t}{T_2}} e^{-i\delta wt} dxdy
\]

and the reconstructed image form is,

\[
I_D(x, y) = DFT[S_o(m, n)] \otimes DFT[e^{-\frac{t}{T_2}}] \otimes DFT[e^{-i\delta wt}]
\]

where the variable \( t \) is not an independent variable. A mapping from time to phase encoding is raised. Therefore, the flexibility of manipulating \( T_2 \) contrast by changing TE in fast spin echo imaging is accomplished by changing the \( k_y \) trajectory order[56]. Figure 2-3 shows four different phase encoding orders. The time variable \( t \) in the \( T_2 \) decay term can be mapped to the number of phase encoding \( n:n \in (-\frac{N}{2}, \frac{N}{2} - 1) \). In figure 2-3(a), the mapping follows,

\[
e^{-\frac{t}{T_2}} \mapsto e^{-\frac{(n+N/2+1)TE}{T_2}}
\]

\(^2\)It is also called rapid acquisition relaxation enhanced(RARE) method

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The point spread function (PSF) due to $T_2$ decay can be separated into two terms, one associated with the $T_2$ blurring, and the other with the $T_2$ weighted contrast,

$$DFT[e^{-\frac{1}{T_2}}] = DFT[e^{-\frac{n T_E}{T_2}}] e^{-\frac{(n+1) T_E}{T_2}}$$  \hspace{1cm} (2.15)

In figure 2-3(c), the $t-n$ mapping is shifted by $s$ steps,

$$e^{-\frac{1}{T_2}} \rightarrow \text{shift}(e^{-\frac{n T_E}{T_2}}, s) = \text{shift}(e^{-\frac{n T_E}{T_2}}, s) e^{-\frac{(N/2+1-s) T_E}{T_2}}$$  \hspace{1cm} (2.16)

The corresponding PSF is,

$$DFT[e^{-\frac{1}{T_2}}] = DFT[\text{shift}(e^{-\frac{n T_E}{T_2}}, s)] e^{-\frac{(N/2+1-s) T_E}{T_2}}$$  \hspace{1cm} (2.17)

The $T_2$ weighted contrast can be varied by changing the phase encode order or the $t-n$ mapping. Although only the shift mapping is described here, other mapping orders can be applied to get desired PSF[57]. The $T_2$ weighted contrast is mainly determined by the timing of the zero phase encoding. The trade off is that the ringing artifact is introduced into the PSF due to the phase encode ordering, as shown in figure 2-4.

**2.2.3 3D Single Slab Fast Spin Echo (3DFSE) IMAGING**

In the previous two sections, 2D spin echo imaging and 2D fast spin echo imaging were discussed. To get a 3D image, the third dimension is achieved by slice selection, or direct spatial mapping. Since the TR is usually much longer than the acquisition time, interleaving excitation of different slices can reduce the total scan time by a factor of $TR/(acquisition\ time)$. However, the quality of the images in the slice selective dimension is degraded by the profile of the slice. To get an image with uniform quality along that dimension, phase encoding should be applied. Figure 2-5 is the sequence diagram for a 3D single slab fast spin echo imaging method. As the whole volume is excited in each excitation, the scan time will be longer than that using 2D interleaving. The implementation and optimization of 3D FSE will be discussed next.
Figure 2-1: Sequence diagram for spin echo imaging method. The Gradient $G_z$ is used for slice selection together with the RF pulses. The gradient $G_y$ is used for phase encoding and the gradient $G_x$ is used for frequency encoding. The acquisition is placed at spin echo.
Figure 2-2: Sequence diagram for 2D fast spin echo imaging method (RARE). For each excitation pulse, there is a train of refocusing pulses. Each refocusing pulse is phase encoded separately. The acquisition is placed at each spin echo formed by the refocusing pulse.
Figure 2-3: Signal intensities under different phase encoding order. The 1D phase encoding k-space is covered by one echo train. (a) The phase encoding starts from $k_{\text{min}}$ and sweeps to the $K_{\text{max}}$. (b) The phase encoding starts from middle of the k-space and sweeps to the $K_{\text{max}}$, then from $k_{\text{min}}$ to the middle. (c) The phase encoding starts from the place between $k_{\text{min}}$ and the middle of k-space. (d) The phase encoding starts from the place between $k_{\text{max}}$ and the middle of k-space.
Figure 2-4: Diagrams of PSF (see Eq. (2.15)) of $T_2$ relaxation effect due to different phase encoding orders. Each graph corresponds to a phase encoding order described in Figure 2.3.
Figure 2-5: Sequence diagram for 3D single slab fast spin echo (3DFSE) imaging method. Both the gradients $G_y$ and $G_z$ are used for phase encoding. The gradient $G_x$ is used for frequency encoding.
Chapter 3

Implementation of 3D Fast Spin Echo Method

The 3D single slab fast spin echo (3DFSE) sequence (Figure 2-5) was implemented using a multi-slab 3D FSE template provided by GE. The subject to which this sequence is applied is human brain. The goal of this implementation is to get 3D $T_1$ or $T_2$ weighted brain images with an isotropic $1 \times 1 \times 1 mm^3$ spatial resolution with scan time on the order of 10 minutes. The sequence was written in EPIC 5.7 version and tested on GE Signa 1.5T scanner. Problems encountered in reaching this goal are discussed along with their solutions.

3.1 Scan Time

The field of interest (FOI) of human brain is about $220 \times 160 \times 160 mm^3$. A frequency encoding is applied to the longest dimension ($220 mm$). The receiver bandwidth of acquisition is set at $64 kHz$ to minimize the individual echo times. Among phase encodings of the other two directions, one is placed along the echo train, and the other along the excitation pulse series. The fact that the field inhomogeneity artifacts and $T_2$ relaxation effects are mapped to the frequency encoding direction, while the $T_2$ blurring is mapped to the phase encoding direction which is along the echo train, leads the third direction to not be directly affected by both artifact sources.
For $T_2$ weighted imaging, the echo train length is 80 so that two excitations will sweep the whole range of one phase encoding direction. Every other phase encode number is skipped for each excitation. Thus, to cover the entire 3D k space, 320 excitations are required. The total scan time is 13 minutes for a $T_2$ weighted image set with a $TR$ of 2.5s. For an echo train of 80 echoes, the signal losses in the later echoes are severe, thus the echo spacing must be reduced as short as possible.

For $T_1$ weighted imaging, the number of echoes in one train (echo train length) is 16–20. About 1280–1600 excitations are used to cover the entire field of view (FOV). The total imaging time is about 7.68 – 9.6 minutes with a TR of 600ms.

### 3.1.1 RF Pulses

The RF pulses used in standard 2D-FT sequences are usually slice selective pulses. The duration of the selective refocusing RF pulses is 3.2ms which contributes to the echo space\(^1\) significantly. To reduce the echo space, selective refocusing pulses were replaced by hard pulses of 272\(\mu\)s in length. The excitation pulse is kept selective with a length of 3ms in order to confine the field of view.

### 3.1.2 Gradient Placement

The maximum gradient strength($G_{Max}$) available in the current scanner used in this study is 2.3($G/cm$). The rise time($t_r$) is 300\(\mu\)s. For a spatial resolution of $\Delta$, the maximum phase encoding in k-space is,

$$k_{max} = \frac{1}{2\Delta}$$

(3.1)

The corresponding phase encoding gradient pulse width is,

$$t_p = \frac{2\pi (k_{max} - \frac{\gamma G_{tr}}{2\pi})}{\gamma G_{Max}}$$

(3.2)

\(^1\)echo space is the time between two refocusing pulses

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For a 1mm resolution, the length of phase encoding is about 1ms. In one echo space, a pair of phase encoding gradients, one for the encoding and the other for the rewinding, costs 2ms.

To avoid direct effects of imperfect refocusing pulses\(^2\), a pair of crusher gradient is applied. The crusher strength(\(\kappa\)) is described by the number of cycles per pixel, i.e. \(k_c \Delta\), where \(k_c\) is produced by the crusher gradient. The duration of the crusher gradient can be estimated by,

\[
t_c = \frac{2\pi \kappa}{\Delta \gamma G_{Max}} + t_r
\]  

(3.3)

The total length of a pair of crusher gradients with \(\kappa = 0.6\) is about 1.3ms. The crush can be applied to \(x\)(readout) or \(z\)(the second phase encoding) direction. Figure 3-2 shows the axial images from a water phantom under the effect of crusher gradients in two different directions. By examining images from all view angles, we reach the conclusion that better image quality is achieved by applying the crusher gradient along the \(x\) direction.

The length of readout gradient(\(t_x\)) is determined by the acquisition bandwidth(\(B_w(\text{Hz})\)) and the number of sampling points(\(xres\)),

\[
t_x = \frac{xres}{2B_w}
\]  

(3.4)

For acquisition of 220 points, the acquisition window is 1.8ms at bandwidth of \(\pm 64k\text{Hz}\).

The echo space can be estimated as,

\[
esp = pw_{r/2} + \max(t_c, t_p) + t_x
\]  

(3.5)

where \(pw_{r/2}\) is the width of refocusing pulse. The echo space should be about 4.5ms. However, the preread gradient makes the duration between excitation pulse and the first refocusing pulse larger than one half of the echo space determined by Eq. (3.5),

\(^2\)the pulse without exact 180\(^\circ\) flip angle
thus the actual echo space is determined by the preread gradient width. For a 3\( ms \) excitation pulse and 2.32\( ms \) preread gradient, the actual echo space is 7.64\( ms \), and the total length of 80 echoes is 627\( ms \) which is destructive to the later echoes. To overcome this problem, the first echo space is reserved for the preread gradient and no acquisition is performed during the first echo. According to the \( T_2 \) values of the brain, the signal with an echo time of 4.5\( ms \) is doubled compared to the signal with a 7.64\( ms \) echo space.

### 3.2 Specific Energy Absorption Rate(SAR)

#### 3.2.1 Estimation

Having shortened the echo space, we must also consider the RF deposition problem. The limit of SAR given by the Food and Drug Administration(FDA) is 2\( W/kg \) in heads and 8\( W/kg \) in bodies. The average SAR is calculated as,

\[
SAR_{ave} = \frac{N_{std} \cdot E_{std}}{TR \cdot W} \tag{3.6}
\]

where \( N_{std} \) is the number of standard RF pulses in the sequence, \( E_{std} \) is the energy deposited by a standard RF pulse, \( TR \) is the sequence repetition time and \( W \) is the patient weight.

A standard RF pulse is defined as a rectangular 180\( ^{\circ} \) pulse with duration(\( T_s \)) of 1\( ms \). The strength of magnetic field \( |B| \), which is produced by a standard pulse, is,

\[
|B| = \frac{\theta}{2\pi \gamma T_s} = 0.117(Gauss) \tag{3.7}
\]

and the magnetic field is given by,

\[
B = |B| \cos(\omega t + \phi_o) \tag{3.8}
\]

where \( \omega \) is the RF frequency and \( \phi_o \) is the initial phase.
From Faraday’s law, the induced electrical field in a closed loop is proportional to the time rate and the change of magnetic flux through the loop,

$$
\oint E\,dl = -\frac{d\Phi}{dt}
$$

(3.9)

The specific energy absorption rate is expressed by,

$$
SAR = \frac{\sigma |E|^2}{2\rho}
$$

(3.10)

where $\rho$ denote the mass density of the tissue and $\sigma$ is the electrical conductivity of the tissue.

For a homogeneous tissue sphere with a radius of $R$, the specific energy absorption rate is,[34]

$$
SAR = \frac{\sigma \omega^2 |B|^2 R^2}{20 \rho}
$$

(3.11)

For a homogeneous tissue cylinder with a radius of $R$ the specific energy absorption rate is,[9, 10]

$$
SAR = \frac{\sigma \omega^2 |B|^2 R^2}{8 \rho}
$$

(3.12)

For brain[39], the conductivity($\sigma$) is $0.49(\Omega m)^{-1}$, the radius is $8\times10^{-2}m$ and the density($\rho$) is $1.03\times10^3kg/m^3$. By using cylindrical geometry, the $SAR_{std}$ by a continuous RF pulse, which has the same power as the standard pulse, is $0.088W/kg$.

For a $180^\circ$ hard pulse with duration of 272$\mu$s, the specific energy deposition rate during the RF pulse is,

$$
SAR_{rf} = SAR_{std} \times \left(\frac{1000}{272}\right)^2 = 1.2W/kg
$$

(3.13)

The average specific energy deposition rate during an echo space of 4.5$ms$ is,

$$
SAR_{esp} = SAR_{rf} \times \frac{272}{4500} = 7.3\times10^{-2}W/kg
$$

(3.14)
The average SAR of a \( T_2 \) weighted sequence with 2.5s \( TR \) and ETL of 80 is,

\[
SAR_{T_2} = SAR_{exp} \frac{80 \times 4.5}{2500} = 1.1 \times 10^{-2} W/kg \tag{3.15}
\]

The average SAR of a \( T_1 \) weighted sequence with 600ms \( TR \) and ETL of 26 is,

\[
SAR_{T_1} = SAR_{exp} \frac{20 \times 4.5}{600} = 1.1 \times 10^{-2} W/kg \tag{3.16}
\]

The result obtained directly from Faraday’s law is used in the SAR estimation in this study. The estimated values of SAR are below the FDA limits.

The actual value is dependent on the geometrical and electrical properties of both the tissue and the coil and can be calculated from first principle using Maxwell’s equations,

\[
\nabla \times \mathbf{E} = -i\omega \mu_0 \mathbf{H} \tag{3.17}
\]

\[
\nabla \times \mathbf{H} = i\omega \varepsilon \mathbf{E} + \sigma \mathbf{E} + \mathbf{J} \tag{3.18}
\]

where \( \mathbf{J} \) is the current density in the coil. The effect of the eddy currents is to reduce the magnetic fields that produce them. Therefore, the coil current should be increased to overcome the loss from eddy currents.

### 3.2.2 Temperature Measurement

The heat generated by metabolism is about 1W/kg. The healthy human body is able to remove heat at a rate of 4W/kg. If the heat deposition rate is larger, then the body temperature will rise.

To measure the heat deposition rate from the 3DFSE sequence, we monitored the temperature changes in two phantoms containing Ringer’s lactate. The energy deposition and the temperature change in a system are related by,

\[
\Delta E = c_m m \Delta T + Q \tag{3.19}
\]

where \( c_m \) is the specific heat capacity of the system, \( m \) is the mass of the system,
\( \Delta T \) is the temperature change, \( Q \) is the heat transferred to the surrounding medium, and \( \Delta E \) is the energy deposition into the system. In humans, several processes contribute to the heat transformation for temperature regulation, such as, radiation, conduction, vaporization of sweat, respiration, urination and defecation[23]. For the water phantoms, the heat exchange between the phantoms and their environment is through heat transfer at phantom walls and radiation. Therefore, it is reasonable to assume that the water phantom is a worse heat conductor than the human body. If the same RF energy is deposited, the temperature rise in a water phantom will be larger than that in the human body. Thus, the temperature measurement of the water phantoms provides an upper bound of temperature rise.

During the measurement, one phantom was put in the coil, whereas the other was put outside the coil as a control. The physical properties of the two phantom were exactly the same.

The temperature measurement result is shown in Figure 3-1. Between each temperature measurement, a 3DFSE sequence with 80 ETL, 5.2\( ms \) echo space, 2\( s \) repetition time, and a total scan time of 4\( min \), was run. The temperature measurement takes about 15 – 30\( s \). The results show that there is no detectable temperature rising during the 12 scans. Therefore, the heat deposition is negligible for the 3DFSE sequence.

### 3.3 Testing Images

#### 3.3.1 Crusher gradient adjustment

Figure 3-2 shows the axial images with different crusher gradient approaches. Images are made from a spherical water phantom. In the upper image, the crusher is along the \( x \)-direction(readout). In the bottom image, the crusher is along the \( z \)-direction. In the middle one, both \( x \) and \( z \) direction crusher are turned on. A \( \kappa \) value of 0.6 was used for all images(actually, the crusher of the middle case is the sum of two crushers). The purpose of this test was to determine in which direction the crusher
gradient eliminates artifacts more efficiently. The images were also examined from other view angles. It is shown that the image with crusher gradient along $x$ gradient provides better quality.

The strength of the crusher gradient also affects the image quality. Image with lower crusher gradient shows more artifact. On the other hand, the higher crusher gradient applied, the longer the spin echo space. One of the purposes of the crusher gradient testing is to find the lowest crusher gradient strength which is yet sufficient to overcome the artifacts. The results of testing show that the lowest acceptable crusher gradient was the one with $\kappa \sim 0.6$ cycle per pixel.

3.3.2 Preread Gradient Placement

When the pre-read gradient is placed in the position of the first spin echo, the echo space (ESP) can be as short as $4.5ms$. Without this placement, the ESP will be $7.64ms$. Although, the spin echo space should be $4.5ms$ ideally, the hardware can not meet this challenge. The minimum acceptable spin echo space was $5ms$. Figure 3-3 is a plot of signal intensity as a function of echo space. The signals are taken from single slab 3D FSE with $1mm^3$ resolution at various echo space. The repetition time used was $2.4ms$, the ETL was 80 and the FOV is $220 \times 160 \times 160mm^3$. The values are obtained by averaging an area of 621 $mm^2$ on one of the axial slices. It is shown that the short spin echo space reached by placing the pre-read gradient in a separate spin echo slot can provide more signal.

3.3.3 $T_2$ and $T_1$ weighted brain imaging

Figure 3-4 shows $T_1$ weighted 3DFSE images. The resolution is $1 \times 1 \times 1mm^3$ isotropically. The images show good structure resolution and contrast.

Figure 3-5 show $T_2$ weighted 3DFSE images. The resolution is $1 \times 1 \times 1mm^3$ isotropically. The images in the left column are images with single slice thickness of 1mm. The images in the right column are averages of 4 neighboring slices. The $T_2$ images show good resolution as well as contrast between white matter and gray
matter.
Figure 3-1: Estimate of the heat deposition by 3DFSE sequence by monitoring the change in phantom temperature.
Figure 3-2: Crusher gradient placement testing. All images shown here are in axial direction. Top: $z$-direction crusher gradient is applied. Bottom: $z$-direction crusher gradient is applied. Middle: Both direction crusher gradients are applied.
Figure 3-3: Spin echo space effect. The plot shows the signal intensity as a function of spin echo space. The standard deviation, which indicated as error bar, is obtained by averaging over an area of 621 mm$^2$. The intensity is also averaged on the same area.
Figure 3-4: $T_1$ weighted 3DFSE images. The resolution is $1 \times 1 \times 1 \text{mm}^3$ isotropically. $TR = 600 \text{ms}$, $ETL = 16$, FOV: $220 \times 160 \times 160$. 
Figure 3-5: $T_2$ weighted 3DFSE images. The resolution is $1 \times 1 \times 1mm^3$ isotropically. $TR = 2.4s$, $ETL = 80$, FOV: $220 \times 160 \times 160$. Left column shows the images with $1mm$ thickness. The right column shows the images reformatted to $3mm$ thick slice.
Chapter 4

Spin Echo Planar Spectroscopic Imaging Method

4.1 Introduction to Chemical Shift Imaging

Chemical shift is caused by interactions between the spin angular momentum of nuclei and the local electron clouds. The micro-currents created by the electrons in the magnetic field produce a magnetic shielding for the nuclei so that the Larmor frequency of the nucleus is shifted. Under the static magnetic field $B_0$, the Larmor frequency of a nucleus is expressed as,

$$\omega = \gamma (1 - \sigma) B_0$$  \hspace{1cm} (4.1)

where $\sigma$ is the unitless shielding constant. The above expression is valid for liquid states where the chemical shift is isotropic due to the rapid molecular tumbling. In solids and liquid crystals, the chemical shift is anisotropic when the molecular orbital is not isotropic[11]. Nuclei at different locations may acquire different chemical shifts, and then different precessing frequencies will provide chemical shift labels.

Chemical shift imaging (CSI) provides spectral mapping as well as various dimensional spatial spin density and relaxation images of biological systems. For the past several years, chemical shift imaging has been widely used to map metabolite
levels in human brain and to extract lipid chemical compositional indices in bone marrow[3, 59]. The current chemical shift imaging techniques can be classified into two main groups.

One is the echo-time shifting method[18, 70], in which the chemical shift information is encoded as multiple phase shift steps. The other is the free induction decay method where chemical shift is frequency encoded[48, 27]. The spin echo planar spectroscopic imaging(SEPSI) method discussed later in this chapter belongs to the later category.

In general, the former technique gives high spatial resolution and low spectral resolution, since echo-time shifting is time consuming and only a limited number of shift steps can be performed. On the other hand, the later one gives low spatial resolution and high spectral resolution. However, other factors such as time dependent gradient field design, RF pulse design, relaxation time and acquisition rate will also determine whether echo-time shift type or free induction decay type is appropriate to a particular application.

By acquiring multiple-spin-echoes, we can either decrease spectroscopic imaging (SI) scan time by using a rapid acquisition with relaxation enhancement(RARE) imaging sequence or retrieve $T_2$ relaxation information by using a Carr-Purcell-Meiboom-Gill(CPMG) sequence[19, 59]. An alternative way for the multiple-spin-echos approach is to generate a multiple spin echo train by DANTE RF pulses(e.g. FBI,EBI)[36].

In addition, the combination of the two types may lead J-coupling resolved imaging achievable in applications where the region of interest(ROI) is limited,e.g. single voxel and line 1D or 2D J-resolved chemical shift imaging.

For 3D or multi-slice 2D chemical shift imaging of $N_x \times N_y \times N_z$ spatial voxels and $N_\omega$ spectral points, the total number of data points collected is $N_x \times N_y \times N_z \times N_\omega$. The scan time is limited by data acquisition rate and repetition rate. Multi-slice 2D SI allows shorter scan time than 3D SI does by slice interleaving.

In the following sections, a design and implementation of spin echo planar spectroscopic imaging(SEPSI) method are described. The SEPSI method, which takes advantage of high strength gradients, allows fast acquisition by encoding both chem-
ical shift and one of the spatial dimensions at the same time. Section 4.2 presents a general description of SEPSI. In section 4.3, a variation of k space trajectory is discussed. In section 4.4, two types of acquisition schemes are compared. Finally, the implementation is presented in section 4.5. The applications of SEPSI will be presented in the following chapters.

4.2 Spin Echo Planar Spectroscopic Imaging

The pulse sequence is shown in Figure 4-1. The gradient applied along the x direction is an asymmetric gradient[21]. Fourier-space trajectories are shown in Figure 4-2. The variables $k_x$ and $k_y$ are introduced by frequency encoding and phase encoding respectively. The signal is given by,

$$f(t) = \int \int \int \rho(x, y, \omega) e^{ik_x x} e^{ik_y y} e^{i\omega t} dxdy \omega$$  (4.2)

where $\rho(x, y, \omega)$ is the spin density function, including the spectral dimension.

Let $t_m$ be the time at the beginning of the mth gradient echo, at time t during mth gradient echo, the gradient parameters $k_x(t)$ and $k_y(t)$ satisfy the following periodic conditions,

$$k_i(t) = k_i(t_m + \tau) = k_i(\tau)$$  (4.3)

where $i = x$ or $y$, and $\tau$ is the time index in the first gradient echo. Then Eq.[4.2] can be written as,

$$f(l_x, l_y, l_t) = \int \int \rho(x, y, \omega) e^{il_x k_x o x} e^{il_y k_y o y} e^{i\omega l_o t_o} dxdy \omega$$  (4.4)

where $k_{yo}$ and $k_{xo}$ are phase encoding and frequency encoding steps respectively, $t_o$ is sampling period, and $\{l_x, l_y, l_t\}$ are discrete indices of $\{k_x, k_y, t\}$. For simplicity, we ignore relaxation effects for the moment. The spatial encoding is thus established by using the periodic nature of the gradient echoes. Furthermore, the Fourier conjugate variable of chemical shift is introduced by mapping each gradient echo to a time point.
along the free induction decay (FID) curve. At the nth gradient echo, the time index \( l_t \) can be written as,

\[
l_t = \frac{nT}{t_o} + l_x
\]  

(4.5)

where \( T \) is gradient echo space (GES) time, whose inverse determines the spectral bandwidth. Eq. [4.4] can be written as,

\[
f(l_x, l_y, n) = \int \int \rho(x, y, \omega)e^{i\omega x}e^{i_0 x + \omega t_o}e^{i_0 y}e^{i_0 T}dxdydw
\]  

(4.6)

There is a shift in readout direction, \( \delta x = \frac{\omega t_o}{k_x} \). When \( t_o \) is a few \( \mu \)s’s and \( \omega \) is a few hundred Hz’s, the displacement is less than one pixel.

If \( N \) gradient echoes are used within one spin echo time range, the spectral resolution is given by,

\[
\Delta \omega = \frac{1}{NT}
\]  

(4.7)

2D chemical shift imaging data sets can be obtained by performing a 3D discrete Fourier transform (DFT) on the 3D MR data set. A time-domain spectral analysis, which will be discussed in next chapter, can also be applied to the time dimension of the data set.

### 4.3 Asymmetric and Symmetric Readout Gradient Field

The readout gradient field applied in SEPSI is asymmetric. It can been seen from the \( k \)-space trajectory that every gradient echo starts from the same position in readout frequency encoding direction. An alternative gradient technique using symmetric or trapezoidal oscillation gradient has been proposed by Guilfoyle and Mansfield[27]. Although other gradient modulation methods are available[1], we only focus on the above two methods here.

In a symmetric gradient echo train, the adjacent echoes, namely odd and even echoes start in opposite directions along the readout frequency. As a result, the sam-
pling points along the time direction are not even. The simple relationship between readout frequency index and time index as shown in SEPSI, i.e., Eq. [4.5] does not hold. Instead, it follows,

$$l_r = \begin{cases} \frac{T(n-1)}{t_o} + l_x & n = 2k - 1 \\ \frac{nT}{t_o} & n = 2k \end{cases} \quad 1 \leq k \leq \frac{N}{2} \quad (4.8)$$

It turns out that the even echoes and the odd echoes should be treated separately when retrieving spectral information. Therefore, the bandwidth will be cut by half if only one scan is performed. However, we can analyze the data from odd and even echoes separately, and then average them to increase signal to noise ratio (SNR) by a factor of $\sqrt{2}$. On the other hand, for an asymmetric gradient echo train, only odd gradient echoes are acquired and the even echoes are used for phase rewinding. The full strength of the gradient field is applied to the rewinding gradient so that rewinding time is minimized. There is about a 15 percent gradient echo space (GES) time increase in asymmetric gradient format compared to that with symmetric gradient trains, which converts to a 70 percent increase in bandwidth. For fast chemical shift imaging where only one scan is required, the asymmetric gradient method offers a larger spectral bandwidth. In addition, the reconstruction for the asymmetric gradient method is more straightforward.

If the bandwidth determined by hardware and parameters used with SEPSI is sufficiently larger than that required, the symmetric gradient echo train can be considered as an option for cutting the scan time by half. To do so, the odd and even echoes would be phase encoded with different steps. The same argument can go further to incorporate multiple phase encoding steps, e.g. $m$ steps, in one train so that the scan speed increase $m$ times. Such sequences may have a potential application in functional MRI, as discussed in chapter 8.
4.4 Full Spin Echo and Half Spin Echo Acquisition

We analyze in detail the difference between full spin echo (SE type) and half spin echo (FID type) acquisition in the SEPSI application. Figure 4-5 shows a SEPSI sequence using half spin echo acquisition. The spin echo time (TE) in both half spin echo and full spin echo acquisition sequence determines the pattern of the spectrum. The reason is that the spectral relaxation times of different spin groups are different, so that the selection of spin echo time has the same significance as relaxation contrast in spatial images. For a certain spin group at a given spin echo time, the half spin echo (FID type) signal and related spectra are given by,

\[ S(t) = S_0 e^{-R^* t} e^{i2\pi f_0 t} \quad (t \geq 0) \]  \hspace{1cm} (4.9)

\[ S(f) = \frac{2S_0 R^*}{R^{*2} + (2\pi f)^2} \delta (f - f_0) \]

where the reference time \( t \) starts from the center of spin echo, \( R^* \) is the transverse relaxation rate, \( S_0 \) is the signal intensity at the center of the spin echo, and \( f_0 \) is the off-resonance frequency of the spin group. And the full spin echo (SE type) signal and its spectrum are given by,

\[ S(t) = \begin{cases} 
S_0 e^{-R^* t} e^{i2\pi f_0 t} & t \geq 0 \\
S_0 e^{-R^{**} t} e^{i2\pi f_0 t} & t < 0 
\end{cases} \]  \hspace{1cm} (4.10)

\[ S(f) = S_0 \left[ \frac{R^* - i2\pi f}{R^{*2} + (2\pi f)^2} + \frac{R'^{**} + i2\pi f}{R'^{**2} + (2\pi f)^2} \right] \delta (f - f_0) \]

where \( t = 0 \) at the center of the spin echo and \( R'^{**} \) is the transverse relaxation rate at the left side of the spin echo. Since the spins experience a refocusing process at the left side of the spin echo, \( R'^{**} \) is less than \( R^* \). As a result, if the acquisition time windows are same in both cases, i.e. the echo time of SE type is twice that of FID type, the spectrum width given in the full spin echo case is narrower than that given in the half spin echo by simply comparing Eq.[4.9] and Eq.[4.10], as illustrated.
in Figure 4-3. Furthermore, the full SE type acquisition will give better signal to noise ratio if the acquisition starts at the same time. However, in the half spin echo case, the echo time can be much shorter than one half of the echo time of full spin echo. This provides an advantage to observe the spectral information of spin groups with shorter $T_2$. On the other hand, the full spin echo is better for resolving spectral information of spin groups with longer $T_2$.

4.5 Implementation of SEPSI

The SEPSI sequence was implemented on a GE 1.5T Signa clinical scanner (General Electric Medical Systems, Milwaukee), at the 5.7 hardware/software configuration. The maximum gradient strength was $2.3G/cm$, and the ramp time from zero to full strength was $300\mu s$. Data acquisition bandwidth was $\pm 64kHz$, which allows fast data collection for every $7.8\mu s$. For a 72 sample points acquisition window at field of view (FOV) of 24cm, the gradient echo space is $1.624ms$. The length of echo train with 96 echoes is about $160ms$. The corresponding spectral resolution limited by discrete Fourier transformation is about $0.1ppm$. For the full spin-echo readout, the minimum spin echo time is $165ms$, in which the lengths of an RF refocus pulse, phase encoding wind and rewind steps are included. The number of gradient echoes, the acquisition rate and other parameters can be varied according to the specific application. A smaller FOV will give higher spatial resolution given that the number of sample point remains the same. On the other hand, it will cause lower bandwidth and spectral resolution by increasing gradient rising time and related gradient echo space. The repetition time is about 1-4 seconds, depending on the number of slices chosen. For a single spin echo scan, a 32 by 72 spatial and 96 spectral point single slice data set takes about 1:08min. In addition, an 8 slice data set with the same resolution takes about 1:40min.

Both full spin echo and half spin echo acquisition methods were implemented. For the full spin echo acquisition, the minimum echo time is about $160$ ms for 96 gradient echoes, and $145ms$ for 64 gradient echoes. For the half spin echo acquisition, the spin
echo time can be as short as 10ms.

For a typical SEPSI experiment, the dimension of the data set is 32 (phase encode) x 72 (frequency encode) x 96 (time sample) or 64 (phase encode) x 96 (frequency encode) x 64 (time sample). The typical data frame is 256x256. In a conventional sequence, a frame of 256x256 is assigned for one 2D image data set no matter what the actual resolution is. If we treat a 2D image set, e.g. (32x72), as a frame, then there are too many frames, especially when a multi-slice scan is performed. This problem is solved by placing 6 2D image data (i.e. 6 gradient echo acquisition data) into one frame so that the 96 time samples (each with a 32x72 2D image data set) are allocated into 16 frames. The recovery of individual frames is carried out by off line data processing.

4.6 Conclusion

The spin echo echo planar spectroscopic imaging method is developed and implemented. It takes advantage of the improved gradient system which allows simultaneously encoding the chemical shift as well as one of spatial dimension. We have developed two approaches, one is the full spin echo acquisition SEPSI, and the other is the half spin echo acquisition SEPSI. The application of SEPSI will be covered by later chapters.
Figure 4-1: Pulse sequence diagram for spin-echo planar spectroscopic imaging (SEPSI). The pulse lengths of the 90 degree slice selective pulse and the 180 degree pulse are 3.2ms. Phase encoding is applied in y direction. The gradient train in the x direction gives both x direction frequency encode and chemical shift encode.
Figure 4-2: The trajectory of the 3D k-space for SEPSI acquisitions. The asymmetric frequency encoding echo planar readout leads to $k_z$ traversals all in the same direction, simplifying reconstruction at the expense of lengthening overall readout durations compared to bipolar gradient readouts.
Figure 4-3: Simulated time signals from half SE and full SE. The origin of time axis is 80 ms from the excitation pulse. A reversible $T_2$ of 200 ms and an irreversible $T'_2$ of 50 ms are used. In case that $T'_2 > T_2$, the echo is not apparent even though the decay rates of both sides are different from each other. Here, we assume that the relaxation can be expressed as exponential decay.
Figure 4-4: The spectra of signals in Fig. 3. Plots in left column are spectra of full spin echo (SE type), and those in right column are from half spin echo (FID type). The first row shows magnitude plots, the second one is real part, and the third row is imaginary part.
Figure 4-5: Pulse sequence diagram for spin-echo planar spectroscopic imaging (SEPSI) using half spin echo acquisition. The spin echo is placed at the first gradient echo.
Chapter 5

Spectral Analysis

Fast Fourier transformation (FFT) is the most common and the fastest way to obtain spectra from time domain data.

For a time series \( \{x_n|0 \leq n < N\} \), the discrete Fourier transform (DFT) is given by,

\[
X_m = \sum_{n=0}^{N-1} W_N^{mn} x_n
\]  \( (5.1) \)

where \( W_N^{mn} = \exp \left\{ \frac{-2\pi inm}{N} \right\} \), \( n \) is the time index and \( m \) is the frequency index. For an \( N \) point DFT, \( N^2 \) complex multiplications must be performed. If the data length \( N \) is a power of 2, the fast Fourier transform (FFT) algorithm can be applied so that the number of complex multiplications is reduced to \( N \log 2N \). In fast Fourier transform as described in Eq. \( [5.1] \), exact number (the same number as that of the time points) of frequency components with pre-fixed frequencies are used. The frequencies are determined by the number of data points involved. The result of FFT is a set of coefficients of frequency components, \( X_m \), which gives a spectrum. The time series can be expressed by,

\[
x_n = \sum_{m=0}^{N-1} W_N^{-mn} X_m
\]  \( (5.2) \)

where \( W_N^{-mn} = \exp \left\{ \frac{2\pi inm}{N} \right\} \).

Since the number of frequency components is determined by the number of data
points, limiting the data points limits the spectral resolution. The zero filling method, which is frequently used to improve spectral resolution, yields Gibbs artifacts. Furthermore, as NMR signal is subject to decay (when spins are dephasing) or rising (when spins are refocusing), the amplitudes of frequency components will be not localized to the related frequency, hence the spectral resolution is further deteriorated. To retrieve information such as spectral peak positions, peak amplitudes and peak widths (full widths and half-full widths), a line shape fitting in least square sense must be performed. In addition, the noise content is distributed uniformly throughout the frequency-domain, which is a disadvantage for detecting spectral peaks with small intensities.

The time-domain spectral analysis is used when there is limited data points available and the data has good signal to noise ratio (SNR). In the time-domain analysis, the parameters, such as frequencies, are not predetermined. The best fit frequency components are not subject to a resolution limit as in the FFT case. NMR FID signal is assumed to be composed of many decaying sinusoids. Therefore, the time-domain spectrum analysis starts with a modal function which is a sum of some decaying sinusoids. The task is then to find the parameters in the model which best fit (in least square sense) the experimental data. The number of sinusoids can be adjusted so that a best fit of time data can be achieved. By using a singular value decomposition method, the noise can be reduced. Another advantage of time domain spectral analysis is its capability to retrieve the spectral from a short time series so that the method can be applied to the sequences using multiple spin echo approach where the time saved by limiting the time points of each echo can be used to allocate more spin echoes.

The singular value decomposition method is discussed in the next section followed by a description of its implementation and application.
5.1 Linear Prediction Singular Value Decomposition Method

The purpose of the time domain spectral analysis is to find a linear combination of exponentials to fit the experimental data. For one exponential component, there are four variables, i.e. amplitude, phase, frequency and damping factor. On the other hand, one experimental data point offers two parameters, i.e. the real part and the imaginary part. Prony's method, which was developed by Gaspard Riche, Baron de Prony in 1795, uses $N/2$ damped exponentials to fit exactly $N$ data points. When the data points are more than the exact number of exponentials, least squares method is applied, which leads to the modern Prony's method. The singular value decomposition (SVD) method is used to solve the least squares problem. However, a truncated version of SVD was introduced when the data is noisy [79]. The time domain spectral analysis was first applied to NMR spectral analysis in the mid 1980's [31], and has been explored since then [16, 14].

5.1.1 Time series

Assume that the NMR FID signal $\{x_n | n \in [1, N], N : \text{total data points}\}$ can be expressed by a time series which is a sum of $p$ damped sinusoids:

$$\hat{x}_n = \sum_{k=1}^{p} h_k z_k^{n-1}$$

(5.3)

where, $h_k = A_k \exp(i\theta_k)$, $z_k = \exp(-\alpha_k + i2\pi f_k)T$, $T$ is sampling period, the hat over $x_n$ indicates that $\hat{x}_n$ is an approximation to $x_n$, $p$ is the number of sinusoids. $A_k$, $\theta_k$, $\alpha_k$ and $f_k$ are four parameters, amplitudes, phases, decaying factors and frequencies, respectively.

The matrix form of Eq.(5.3) is:

$$\begin{bmatrix} \hat{x} \end{bmatrix} = \begin{bmatrix} Z \end{bmatrix} \begin{bmatrix} h \end{bmatrix}$$

(5.4)
or
\[
\begin{pmatrix}
\hat{x}_1 \\
\hat{x}_2 \\
\vdots \\
\hat{x}_N
\end{pmatrix} = 
\begin{pmatrix}
1 & 1 & \ldots & 1 \\
z_1 & z_2 & \ldots & z_p \\
\vdots & \vdots & \ddots & \vdots \\
z_1^{N-1} & z_2^{N-1} & \ldots & z_p^{N-1}
\end{pmatrix}
\begin{pmatrix}
h_1 \\
h_2 \\
\vdots \\
h_p
\end{pmatrix}
\]

5.1.2 Least Squares Solution

A frequently used criterion which measure the approximation is the sum of squared errors\[45],
\[
E = \sum_{n=1}^{N} |e_n|^2
\]
where \(e = x - \hat{x} = x - Zh\). The squared errors is given by,
\[
E = e^+e = x^+x - x^+Zx + h^+ZZ^+x + h^+Z^+Zx
\]
The optimal value of \(h\) is found under condition that the squared error \(E\) is minimized.
\[
\frac{\partial E}{\partial h} = 0
\]
which gives that\[1\]
\[
Z^+Z = Z^+x
\]
If \(Z^+Z\) is non-singular, the solution to the least-squares problem is,
\[
h = (Z^+Z)^{-1}Z^+x
\]

---

\[1\] This result can also be obtained by observing \(E\) directly. Write \(E\) as a complete square form,
\[
E = x^+x - x^+Z(Z^+Z)^{-1}Z^+x + (Z^+x - Z^+Zx)^+(Z^+Z)^{-1}(Z^+x - Z^+Zx)
\]
The last term has Hermitian symmetry, and is always real and positive. In order to minimize \(E\), this term must set to zero which gives Eq. (5.8)
When \( Z^+Z \) is singular, and \( \text{rank}(Z^+Z) < p \). By performing SVD(Singular Value Decomposition)\(^2\),

\[
Z^+Z = \mathbf{LAR}^+
\]

(5.10)

where \( A = \begin{pmatrix} \Sigma & \emptyset \\ \emptyset & \emptyset \end{pmatrix}, \) and \( \Sigma = diag(\sigma_1, \sigma_2, \ldots, \sigma_l) \) with \( \sigma_1 > \sigma_2 > \ldots > \sigma_l \).

The pseudoinverse of a singular matrix \( Z^+Z \) is defined as,

\[
(Z^+Z)^* = \mathbf{R} \begin{pmatrix} \Sigma^{-1} & \emptyset \\ \emptyset & \emptyset \end{pmatrix} \mathbf{L}^+
\]

(5.11)

The least square solution is then,

\[
h = (Z^+Z)^*Z^+x
\]

(5.12)

The parameter \( h \) can be calculated from Eq.[5.12] when we know the parameter \( z \)'s.

### 5.1.3 The HSVD method

The Hankel singular value decomposition(HSVD) method is to calculate the parameter \( z \)'s[42, 13]. From the time series \( x_n \), a data matrix can be written as,

\[
X = \begin{pmatrix}
x_2 & \cdots & x_{m+1} \\
\vdots & \ddots & \vdots \\
x_{L+1} & \cdots & x_N
\end{pmatrix}_{L \times m}
\]

(5.13)

\(^2\)SVD definition: Any \( m \) by \( n \) matrix(complex value) \( \mathbf{M} \) can be factored into

\[
\mathbf{M} = \mathbf{LAR}^+
\]

The columns of \( \mathbf{L} \) (\( m \) by \( m \)) are eigenvectors of \( \mathbf{MM}^+ \), and the columns of \( \mathbf{R} \) (\( n \) by \( n \)) are eigenvectors of \( \mathbf{M}^+\mathbf{M} \). The \( l \) singular values on the diagonal of \( \mathbf{A} \) (\( m \) by \( n \)) are the square roots of the nonzero eigenvalues of both \( \mathbf{MM}^+ \) and \( \mathbf{M}^+\mathbf{M} \).
The data matrix can be decomposed into,

\[
X = \begin{pmatrix}
1 & \ldots & 1 \\
z_1 & \ldots & z_p \\
\vdots & \ddots & \vdots \\
z_{L-1} & \ldots & z_{p-1}
\end{pmatrix}
\begin{pmatrix}
c_1 \\
\vdots \\
c_p
\end{pmatrix}
\begin{pmatrix}
1 & z_1 & \ldots & z_{m-1} \\
\vdots & \vdots & \ddots & \vdots \\
1 & z_p & \ldots & z_{p-1}
\end{pmatrix}
\]

or

\[
X = Z_L C Z_m^T
\]

where \( c_i = h_i z_i \).

The matrix \( Z_L \) is a Vandermonde matrix which has the following property,

\[
Z_L^{\text{bot}} = Z_L^{\text{top}} \Lambda
\]

where \( Z_L^{\text{bot}} \) is \( Z_L \) with the top row removed, \( Z_L^{\text{top}} \) is \( Z_L \) with the bottom row removed, and \( \Lambda = \text{diag}(z_1, z_2, \ldots, z_p) \).

The Vandermonde Decomposition can be obtained approximately from the reduced order Singular Value Decomposition(SVD). The SVD of the data matrix is given by,

\[
X = USV^+
\]

where \( U \) is an \((L \times L)\) unitary matrix, \( V \) is an \((m \times m)\) unitary matrix and \( S \) is a \((L \times m)\) diagonal matrix\(^3\). The matrix \( S \) is uniquely determined while the unitary matrices \( U \) and \( V \) are not unique. If the signal has \( p \) sinusoid components, then there will be \( p \) larger singular values associated with signal components. The rest \((m - p)\) smaller singular values are associated with noise. When the signal to noise ratio(SNR) is large(e.g. \( SNR > 100 \)), there exists a sharp transition between the larger singular values and the smaller singular values. So the noise can be reduced by keeping only the larger singular value which forms a \((p \times p)\) diagonal matrix \( S' \). The reduced order unitary matrices \( U' \) and \( V'^+ \) are obtained by keeping the first \( p \)

\(^3\)An unitary matrix \( U \) satisfies that \( U^+ U = I \).
columns of U and the first rows of V⁺ respectively. Hence, the reduced-order SVD of data matrix is,

$$X = U'S'V'^+$$  \hspace{1cm} (5.17)

Since the matrices C and S' are both diagonal matrices with the same rank p, there exist two invertible \((p \times p)\) matrices Q and P such that \(S' = QCP^{-1}\), \(Z_L = U'Q\) and \(Z_L^{top} = U^{top}Q\). From Eq. [5.15], we have,

$$U^{bot} = U^{top}A'$$  \hspace{1cm} (5.18)

where \(A' = QA Q^{-1}\). Then A' is obtained in least square sense,

$$A' = (U'^{top}U'^{top})^{-1}U'^{top}U'^{bot}$$  \hspace{1cm} (5.19)

The eigenvalues of A' is the same as the eigenvalues of A which is \((z_1, z_2, \ldots, z_p)\). Notice that U is unitary, so is U', hence \(U'^{top}U'^{top} = I - uu^+\), where u⁺ is the bottom row of U', and \((U'^{top}U'^{top})^{-1} = I + \frac{uu^+}{1 - u^+u}\).

### 5.1.4 Spectrum

The time-domain fitting series gives information of resonance frequency components, associated amplitudes, damping factors and phases. For a discrete time series of Eq. [5.3], the z-transform is[41],

$$\hat{X}(z) = \sum_{k=1}^{p} \frac{h_k}{1 - z_k z^{-1}}$$  \hspace{1cm} (5.20)

for damping sinusoids,|\(z_k| < 1\). A discrete-time Fourier transform is given by substituting z by exp(\(i2\pi fT\)), where \(T\) is the time interval, and \(-\frac{1}{2T} < f < \frac{1}{2T}\). The damping factors, frequencies, amplitudes and phases are given by,

$$\alpha_k = \frac{\ln|z_k|}{T} (sec^{-1})$$
\[ f_k = \frac{\arctan \left[ \frac{\Im[z_k]}{\Re[z_k]} \right]}{2\pi T} \text{(Hz)} \]  
\[ A_k = |h_k| \]
\[ \theta_k = \arctan \left[ \frac{\Im(h_k)}{\Re(h_k)} \right] \text{(Radian)} \]

The spectrum intensity for a frequency \( f_k \) is \( (A_k/\alpha_k) \), and the bandwidth (to the 6 dB point) is \( \alpha_k/\pi \), thus, the area is about \( A_k \). For a small \( \alpha_k \), a narrow resonance peak results.

5.2 Software Implementation

The computation was implemented using MATLAB software, which is optimal for matrix manipulation.

5.2.1 FID Data

FID data is a sum of decaying sinusoids.

1. Input data: \( N \) data points \( x_n \), sampling time \( T \).

2. Choose data matrix order \( m \) and construct data matrix: \( \mathbf{X} \).

3. SVD of data matrix: \( \mathbf{X} = \mathbf{U} \Sigma \mathbf{V}^* \).

4. Choose the Reduced-order \( p \) and find: \( \mathbf{U}' \).

5. Construct matrix \( \Lambda' \) and compute its eigenvalue \( (z_1, z_2, \ldots, z_p) \).

6. Compute coefficients \( \mathbf{h} \).

7. Compute parameters (amplitudes, frequencies, damping factors, and phases).

8. Adjust \( m \) and \( p \), minimize the errors.
5.2.2 Spin Echo Data

The data on the right half of spin echo is a sum of decaying sinusoids. That on the left half spin echo can be a sum of either rising or decaying sinusoids, depending on the field inhomogeneities and $T_2$ relaxation time. Therefore, the left half and the right half of spin echo data should be treated separately.

1. Input data: $N$ data points $x_n$, sampling time $T$.

2. Select either the left half of the right half of the data.

3. Choose data matrix order $m$ and Construct data matrix: $X$.

4. SVD of data matrix: $X = UV^+$.

5. Choose the Reduced-order $p$ and find: $U'$.

6. Construct matrix $A'$ and compute its eigenvalue $(z_1, z_2, \ldots, z_p)$.

7. Compute coefficients $h$.

8. Compute parameters (amplitudes, frequencies, damping factors, and phases).

9. Adjust $m$ and $p$, minimize the errors.

5.3 Spin echo analysis

Spin echo data can be expressed as,

$$
\hat{x}_n = \begin{cases} 
\sum_{k=1}^{p} h_k z_k^n & n \geq 0 \\
\sum_{k=1}^{p} h'_k z'_k^{-n} & n < 0 
\end{cases}
-\frac{N}{2} \leq n \leq \frac{N}{2} - 1
$$

(5.22)

$$
h_k = A_k \exp(i\theta_k)
$$

$$
h'_k = A'_k \exp(i\theta'_k)
$$

$$
z_k = \exp((-\alpha_k + i2\pi f_k)T]
$$
\[ z'_k = \exp\left[(-\alpha'_k + i2\pi f_k)T\right] \]

where \( \alpha_k = \frac{1}{T_{k2}} + \frac{1}{\tau_{k2}} \) and \( \alpha'_k = \frac{1}{T'_{k2}} - \frac{1}{\tau_{k2}} \) for right and left halves, respectively.

\( T_{k2} \) is the spectroscopic relaxation time\(^{59}\) which describes irreversible spin dephasing process (e.g. diffusion), and \( T'_{k2} \) is the spectroscopic characteristic time describing reversible spin dephasing process (e.g. static field inhomogeneity, susceptibility). The damping factor of the left echo is different from that of the right echo. Through the procedures discussed in the previous section, the two parts can be treated separately to find all parameters. The spectroscopic relaxation time \( T_{k2} \) and the reversible spectroscopic relaxation time \( T'_{k2} \) can then be derived from the spin echo data.

5.4 Application: \( T_2 \) Relaxation Time Measurement

\( T_2 \) relaxation time (without spectroscopic information) measurement is carried out by conventional CPMG method. The results SEPSI measurements developed in the previous chapter, which allow a much shorter scan time, were compared to the \( T_2 \) obtained with the CPMG method. The subject of this experiment was a \( NiCl_2 \) doped water phantom. The \( T_2 \) relaxation time was measured by both CPMG and SEPSI methods. The HSVD time domain spectral analysis was applied to SEPSI data including both FID(half echo) and spin echo(full echo) data.

5.4.1 CPMG Method Measurement

A CPMG 2D-FT slice imaging sequence of 16 spin echoes with echo time interval of 15 ms was performed on the \( NiCl_2 \) doped water phantom. The \( T_2 \) relaxation time, which was obtained by fitting the image intensity data of multiple echoes to an exponential function, was 94 ± 2 ms. The data fitting was performed by MATLAB builtin function.
5.4.2 SEPSI Method Measurement

Full Echo SEPSI

Table 5.1 shows the $T_2^*$ of the phantom obtained by HSVD method. Three different spin echo times, 165ms, 200ms and 250ms were used. Different number of exponential components were used to fit the time data. Since only one frequency component exists in this sample, increasing the number of fitting exponential components should not affect the $T_2$ and $T_2^*$ results as shown hereafter. Each $T_2^*$ value is calculated on the integrated values of 10 voxels. Table 5.2 shows the $T_2^*$ from the left side of the same spin echoes. The standard deviations of data from left echoes are much smaller than that of the right echoes, the reason is that $T_2$ relaxation causes signal attenuation so that the intensities on the right side of echoes are smaller than that on the left. In addition, we note that the the difference between $T_2^*$'s of both left and right echoes is in the range of standard deviation. This indicates that the sample is quite uniform so that there are no susceptibility inhomogeneities detectable by this method. Therefore, the $T_2^*$ value here is very close to the $T_2$ value as calculated via the CPMG technique.

Half Echo SEPSI

The half echo SEPSI method collects several half echoes with different echo times. We use echo times of 10ms, 20ms, 30ms, 40ms, 50ms, 60ms, 70ms, 80ms, 90ms, 100ms. For each spin echo time, the HSVD is applied to calculate the amplitude of the spin echo intensity. The same number of exponential as in the full echo case are used. The spin echo intensities of 10 time points are then fitted by a single exponential function to determine the $T_2$ value. 10 voxels are used to average the data. The results are shown in Table 5.3. Table 5.3 shows the $T_2^*$'s of echo times, 10ms, 20ms, and 30ms, obtained the same way as the right echo in full echo method.

Figure 5-1 shows the fitting of half echo data by one exponential. And Figure 5-2 shows the fitting of half echo data by five exponentials. Since there is only one frequency component in the phantom, the two fitting results from both one exponential and five exponentials are consistent by examining from time domain.

From the results shown in Table 5-1, 5-2 and 5-3, the $T_2$ values by both full echo

70
<table>
<thead>
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<th>TE(ms)</th>
<th>p=1</th>
<th>p=3</th>
<th>p=5</th>
<th>p=7</th>
<th>p=9</th>
<th>p=11</th>
</tr>
</thead>
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<td>165</td>
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<td>89.5 ± 9.8</td>
<td>91.3 ± 9.1</td>
<td>93.1 ± 8.8</td>
<td>91.6 ± 12.3</td>
<td>87.1 ± 16.1</td>
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<td>200</td>
<td>88.6 ± 3.8</td>
<td>87.3 ± 4.2</td>
<td>87.4 ± 4.5</td>
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<td>87.0 ± 4.6</td>
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<tr>
<td>250</td>
<td>90.6 ± 4.0</td>
<td>91.3 ± 6.9</td>
<td>91.0 ± 5.5</td>
<td>90.9 ± 7.1</td>
<td>91.4 ± 6.7</td>
<td>90.7 ± 9.3</td>
</tr>
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</table>

Table 5.1: $T_2^*$ s of NiCl$_2$ doped water from the right half of the spin echos. Three echo times, 165ms, 200ms, and 250 ms are used. The fitting exponential numbers, $p$, are chosen as 1, 3, 5, 7, 9, 11.

<table>
<thead>
<tr>
<th>TE(ms)</th>
<th>p=1</th>
<th>p=3</th>
<th>p=5</th>
<th>p=7</th>
<th>p=9</th>
<th>p=11</th>
</tr>
</thead>
<tbody>
<tr>
<td>165</td>
<td>88.7 ± 2.3</td>
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<td>89.4 ± 2.6</td>
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<td>89.3 ± 3.3</td>
</tr>
<tr>
<td>200</td>
<td>90.5 ± 2.4</td>
<td>89.8 ± 1.8</td>
<td>89.5 ± 1.9</td>
<td>89.9 ± 3.8</td>
<td>89.7 ± 3.5</td>
<td>89.1 ± 2.3</td>
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<tr>
<td>250</td>
<td>88.2 ± 2.7</td>
<td>88.3 ± 2.8</td>
<td>88.4 ± 2.9</td>
<td>88.0 ± 3.7</td>
<td>88.0 ± 5.3</td>
<td>88.6 ± 2.9</td>
</tr>
</tbody>
</table>

Table 5.2: $T_2^*$ s of water from the left half of the spin echos. There echo times, 165ms, 200ms, and 250 ms are used. The fitting exponential numbers, $p$, are chosen as 1, 3, 5, 7, 9, 11.

<table>
<thead>
<tr>
<th></th>
<th>p=1</th>
<th>p=3</th>
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<th>p=7</th>
<th>p=9</th>
<th>p=11</th>
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<tbody>
<tr>
<td>p=1</td>
<td>89.8 ± 1.1</td>
<td>90.1 ± 1.0</td>
<td>88.8 ± 1.5</td>
<td>88.9 ± 2.1</td>
<td>89.3 ± 1.3</td>
<td>88.7 ± 2.0</td>
</tr>
</tbody>
</table>

Table 5.3: $T_2$’s of water from half echo method. Ten echo times, from 10 to 100 ms with 10 ms interval, are used. The fitting exponential numbers, $p$, are chosen as 1, 3, 5, 7, 9, 11.
Figure 5-1: Half echo data and time domain fitting by one exponential. The solid line is the experimental data. The dash line is the fitting. And the dot line is the residues.

and half echo analysis are consistent. However, the $T_2$ value from SEPSI method is slightly shorter than that from CPMG method. The lengthening of $T_2$ by CPMG method maybe due to the imperfect selective RF pulses which excite extra spins at the edge of the slice profile and cause stimulated echoes[33].

5.5 Conclusion

The time domain spectral analysis method, LP-HSVD, was implemented using MATLAB. The algorithm to analysis spin-echo data was also implemented. The SEPSI,
Figure 5-2: Half echo data and time domain fitting by five exponentials. The solid line is the experimental data. The dash line is the fitting. And the dot line is the residues.

developed in the previous chapter, together with the LP-HSVD were applied to the $T_2$ measurement of the NiCl$_2$ doped water. The results were consistent with that with the CPMG method.
Chapter 6

Spectroscopic Imaging Methods for Fast Lipid Characterization in Bone Marrow

Lipid characterization of bone marrow in vivo with proton MR spectroscopy is performed using a Spin-Echo Planar Spectroscopic Imaging (SEPSI) sequence. In vivo spectra suitable for measuring lipid indices reflecting saturation levels among triglycerides in bone marrow were acquired in a 32 × 72 spatial matrix in only 68 s. The method readily separated olive oil from corn oil on the basis of lipid compositional indices accessed from the spectra. In vivo spectra and spectroscopic images of the different lipid peaks within human bone marrow in the knees of healthy volunteers were generated and lipid indices reflecting unsaturation levels were estimated from the data. The volume coverage, spatial resolution, speed of acquisition and spectral quality of the technique should make it attractive for clinical studies of diseases affecting normal lipid chemical composition.

Section 6.1-6.4 describe the development and the application of the Spin-Echo Planar Spectroscopic Imaging (SEPSI) sequence.

Two alternative fast 2D spectroscopy imaging methods, 2D fast chemical shift imaging and 2D line scan spectroscopic imaging, will be described in section 6.5-6.8.

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6.1 Introduction

Echo planar spectroscopic imaging sequences have been contemplated, implemented, and demonstrated over the last several years[48, 52, 81, 71, 72]. The most recent implementations and demonstrations have focused on the important area of proton spectroscopy in the brain where water suppression and low concentrations of observable metabolites make spectroscopic imaging particularly challenging[71, 72]. To our knowledge, echo planar spectroscopic imaging of bone marrow has not been considered. In general, however, even conventional proton spectroscopic studies of marrow[74, 24, 40, 4, 77, 37, 60] have garnered less attention than studies of brain for several obvious reasons. Most significantly, marrow can be sampled directly via biopsy much more easily than brain and with less potential for damage. Furthermore, treatment planning for medical conditions affecting the central nervous system more readily justifies the use of expensive, advanced MR technology than those involving bone marrow. Some medical conditions do exist, however, which may benefit from proton spectroscopic imaging studies of marrow. These include diseases like leukemia in which measurements of marrow cellularity are of interest. In this case a fat/water index reflecting overall cellularity may be made from MR spectroscopic imaging exams. This has been suggested as a means for reducing the number of invasive needle biopsies performed and for increasing the volume coverage sampled compared to marrow biopsy. Most published reports of proton spectroscopic techniques in marrow have focused on this MR based cellularity measurement through a quantitative fat/water index.

Lipid characterization with proton spectroscopy of marrow is also a recognized possibility with interesting potential[61, 59]. In particular, indices related to the levels of unsaturation among the triglycerides become available with properly designed proton spectroscopic imaging scans. Ratios of the methylene to methyl or olefinic to methyl are examples of such indices, though others are also available. The utility of performing such measurements in studies of diseases affecting lipid chemical composition such as cystic fibrosis [12, 43], coronary heart disease[73], or in some
tumors such as liposarcomas[55], will remain unknown without the development and demonstration of techniques designed to measure lipid indices efficiently in a clinical setting.

In this work we examine the feasibility of performing spin-echo planar spectroscopic imaging methods for measurement of selected lipid indices in bone marrow at 1.5T. The volume coverage, spatial resolution, speed of acquisition and spectral quality of the technique suggest that it may prove quite useful for clinical studies of diseases affecting normal lipid chemical composition in bone marrow while also MR based cellularity measurements.

6.2 Materials and Methods

Studies were performed with a 1.5T Signa scanner (General Electric Medical Systems, Milwaukee, WI) operating at the 5.7 software/hardware configuration. This system is equipped with echo planar imaging capabilities with a maximum gradient strength of 23mT/m and a rise time of 300μs. The spin-echo planar spectroscopic imaging sequence(SEPSI) is presented in chapter 4. The spin-echo was acquired from a selected slice of 1 cm thickness using standard slice selective excitation and refocusing pulses. A phase encoding step following the refocusing pulse preceded the echo planar spectroscopic readouts which consisted of 96 asymmetrically acquired gradient echoes separated by 1.62ms with 72 frequency samplings per gradient echo and a 64 kHz receiver bandwidth. For echo times less than 165ms, half-echo readouts were performed which began at the center of the spin echo. For TE's of 165ms or greater, full echo readouts symmetrically deployed about the spin echo center were utilized. The spectroscopic resolution with these readouts was 6.4 Hz. With 32 phase encoding steps and a 20cm field-of-view, in-plane spatial resolution was 0.63x0.28cm². A 2-dimensional k-space consisting of the spectral dimension and the frequency encoded spatial dimension is generated with each echo planar spectroscopic readout. The full 3-dimensional k-space acquisition, obtained by repeating the readout 32 times with 32 different phase encoding steps, is shown in Figure 6-2. With a 2s TR and two
dummy scans, the 2D CSI acquisition is completed in 68s. The sequence can be run in multi-slice mode for sampling 8 slices within this TR period.

Reconstructions were performed using Matlab software (The Math Works, Inc., Natick, MA). Standard Fourier transform reconstruction was performed as was a time domain fitting routine based on linear prediction algorithms (chapter 5). The latter required an input of the total number of damped sinusoids within the data. This was estimated by visually inspecting the Fourier transform spectra from which an estimate of the appropriate number of peaks to be fit was made. For full-echo acquisitions at later TE's, only the second half of the echo was used for the linear prediction analyses. Amplitudes from the linear prediction analyses were calculated for the methylene, methyl, olefinic resonances as well as the intra-allylic resonance around 2.9ppm. These were used to evaluate ratios of methylene, olefinic, and intra-allylic to the methyl resonance to form the indices defined as M, U and P, respectively.

Phantom studies were performed using a vial of olive oil contained within a larger vial of corn oil. According to the food labels on the oil products, the corn oil contained 14.29% saturated, 64.29% polyunsaturated, and 21.43% monounsaturated triglycerides and the olive oil contained 14.29% saturated, 14.29% polyunsaturated and 71.42% monounsaturated triglycerides. A quadrature head coil was used for the oil studies. Studies were also performed with two adult female volunteers whose knees were scanned with a linear transmit/receive extremity coil. Informed consent was obtained from the volunteers in accordance with the internal review board of Children's Hospital.

6.3 Results

Figure 6-2 a-d are SEPSI results obtained from the oil phantoms. The image in Figure 6-2 a has been reconstructed from the 9th gradient echo of a SEPSI acquisition (TE = 20ms) and shows the spatial resolution obtained for these 2D CSI experiments in 1 minute and 8 seconds. The olive oil is in the center of the image (bright signal) and is surrounded by corn oil. Spectra obtained by Fourier Transform for voxels along the
central horizontal line outlined in Figure 6-3 a are shown in Figure 6-3 b-d as acquired with separate acquisitions using TE's of 20 ms, 80 ms and 165 ms, respectively. A full echo readout was used for the 165 ms TE and half-echo readouts for the shorter TE's. All spectra show a separation of methyl from methylene resonances at -0.9 and -1.3 ppm, respectively. In the 20 ms TE data, the glycerol resonance is observed around 4.2 ppm and there is a resonance appearing at 2.8 ppm in the corn oil spectra which is not readily detectable in the olive oil spectra. This peak arises from the internally allylic protons in polyunsaturated triglycerides making up a large percentage (64 %) of the corn oil and only a small percentage (14 %) of the olive oil. At TE's of 80 ms and 165 ms, quantization of the three major resonances from olefinic, methylene and methyl resonances is quite feasible from the spectra. The top plots in Figure 6-3 a and b show representative corn oil spectra at TE's of 20 ms and 165 ms along with linear prediction fits in the lower panels. Amplitudes provided by the linear prediction fits to 20 ms TE spectra from five locations in corn and olive oil yielded the M, U, and P values listed in Table 1.

Figures 6-4 a - d show results obtained in the knee of a healthy volunteer using the same format as Figure 6-3. Spectra are taken from voxels along the horizontal line outlined in Figure 6-4a as acquired with TE's of 20, 80 and 165 ms, respectively. A substantial water peak is observed at some locations along this line due to muscle, though in regions of marrow the water peak is generally quite small. The separate quantization of water from olefinic and methyl from methylene was possible in most all the marrow spectra, though more overlap was observed at the shorter echo times with half-echo readouts. The 165 ms TE, full echo readout acquisitions yielded narrow lines with a T₂-weighting that helped reduce the overwhelming signal intensity of methylene compared to methyl observed in the shorter echo time spectra. Table 2 provides the lipid indices M, U and P for the 20 ms TE data and M and U from the 165 ms TE data as calculated with the linear prediction algorithm from 10 marrow spectra. The intra-allylic peak at 2.9 ppm was too small to reliably evaluate in the long TE spectra. The spectral T₂ value for the methylene resonance was measured to be 136 ± 4 ms (N = 10 marrow voxels) as measured from the half-echo linear prediction amplitudes.
Figure 6-1: Plot of the methyl amplitude from linear prediction fits as function of echo time for 10 marrow voxels showing J-coupling oscillations.

...at echo times of 20, 80, 140 and 200 ms. The methyl resonance showed a distinct J-coupling modulation over these same echo times. Figure 6-1 is a plot of the methyl resonance amplitude (magnitude linear prediction estimates) as a function of echo time taken from the 10 marrow voxels sampled. A distinct minimum is observed at a TE of 80 ms. Methyl T2 estimates made from the 1st and 3rd echoes which appear "in-phase" were in the 235 to 265 ms range.

6.4 Discussion

The ability to generate two-dimensional spectral/spatial data sets in "single shots" with closely spaced gradient echo trains requires echo planar imaging capabilities which are now becoming widely available on many commercial scanners. With such capabilities, many spectroscopically based MR inquiries previously considered but not performed due to clinical time constraints may be reconsidered. Echo planar spectroscopic imaging studies of the brain have already been demonstrated[71, 72]. In this work we focused on demonstrating the utility of spin-echo planar spectroscopic imaging methods for extracting lipid indices in bone marrow from many voxels in brief
scan times.

Triglycerides in bone marrow and adipose tissue are composed of a polar head group attached to three long hydrocarbon chains containing, typically, between 16 and 20 carbons. Let us consider a completely saturated hydrocarbon chain with a terminal methyl group and 17 CH$_2$ groups, one of which is adjacent to a carboxyl group in the polar head. The resonant frequency of this CH$_2$ group is shifted out of the primary methylene resonance at 1.3 ppm and is detected as a minor peak around 2.3 ppm. The CH$_2$ group is also shifted, but only to 1.6 ppm. We shall assume that this group contributes to the amplitude of the 1.3 ppm resonance as quantified with our current methods. Thus, for this case there are 16 CH$_2$ groups, or 32 protons, contributing to the 1.3 ppm peak and 3 protons contributing to the terminal methyl signal at 0.9 ppm. An M value of 10.7 is then expected for this hydrocarbon chain in a relaxation free spectrum. With no double bonds in the saturated chain, U and P are identically zero.

The creation of a single double bond along the chain removes two protons from the molecule and shifts the two olefinic protons to 5.4 ppm. Four protons are so removed from the 1.3 ppm resonance of this monounsaturated chain. In addition, the 4 protons in the two CH$_2$ groups adjacent to the double bond are shifted to 2.0 ppm and are detectable as a minor resonance differentiable from the 1.3 ppm signal. The sum effect of the single double bond is to decrease the pool of primary methylene protons, as quantified with the 1.3 ppm resonance, from 32 to 24 with a decrease in M of 10.7 to 8.0. The relaxation free U value for this monounsaturated chain is 2/3 = 0.66. P remains zero until the creation of a second double bond to form the lowest order of a polyunsaturated chain. The second double bond most commonly forms 3 bonds from the first, leaving an inter-olefinic CF$_2$ group between the two double bonds which resonance at 2.9 ppm. Quantization of this peak provides the P index once normalized to the three protons of the terminal methyl resonance. Two double bonds increase the U index to 4/3 = 1.32 and the P index is 0.66. Arguments similar to those used for the octadecenoic chain lead to an M value for this octadecadienoic chain of 8. All of the above arguments are based on the absence of relaxation or
J-coupling effects which cause variations in the observed lipid indices as a function of echo time. Also, within a marrow voxel a distribution of triglycerides with different chain lengths and degrees of unsaturation will be found. The lipid indices measured will reflect this distribution rather than an idealized single chain length hydrocarbon. Overall, however, increasing the degree of unsaturated triglycerides will lower M and raise the U and P values observed.

The lipid indices in Table 1, taken from 20ms TE data to minimize relaxation effects, clearly differentiate corn oil from olive oil. The lower M value in corn oil is consistent with the higher percentage of polyunsaturated oils. Taking the P value of 0.66 for the idealized 18 carbon disaturated chain just discussed, one can predict a P value of 0.42 for the corn oil from the 0.64 fraction of polyunsaturated oils provided by the manufacturer. This is in close agreement with the measured value of 0.45 given in Table 1, suggesting that most of the polyunsaturated triglycerides in the corn oil have two double bonds. In the bone marrow, M, U and P values from the 20ms echo time spectra are in between those found for corn and olive oil. The use of a longer echo time of 165ms with a full echo readout reduces the M and U values to nearly half their 20ms echo time values. The longer $T_2$ of the methyl resonance compared to the methylene or olefinic resonances is most responsible for this effect though $J$-coupling will clearly influence these values at different echo times as well (Figure 6-1).

We utilized an asymmetric readout gradient so that all $k_x$ lines were acquired in the same direction in k-space. Though lengthening the overall readout time compared to bipolar gradient readouts, the asymmetric readout approach generally simplifies reconstruction and avoids the need to separately reconstruct spectral data from odd and even echoes or perform other schemes such as oversampling[71, 72]. Using a spin-echo rather than a free induction decay echo planar spectroscopic readout following a single excitation pulse can allow for spectral $T_2$ measurement by collecting data sets at different echo times. Several other advantages are gained with the spin-echo planar approach. Even at relatively short echo times, the phase encode gradient lobe preceding the half-echo readout does not preclude sampling directly from the start of the half-echo acquisition. This avoids spectral phase errors caused by the phase encode.
lobe when FID sampling is used in CSI formats. The flexibility of a variable spin-echo time also allows one to apply a $T_2^*$ filter to the data to control the spectral information. For example, if the compositional indices M and U are of primary interest, a long echo time such as 165 ms will allow for full echo acquisitions with minimal overlap between methyl and methylene resonances or water and olefinic resonances. The full echo readouts in this case give narrower lines than the half-echo readouts at shorter echo times. Overall the longer echo times simplify spectral interpretation, a situation analogous to long echo time vs short echo time spectroscopic studies of brain. The long echo time spectra should also be important in studies of red marrow or diseased marrow where a higher water content prevails than in healthy yellow marrow, obscuring the olefinic resonance. The use of linear prediction methods, or for that matter other time domain analyses, appears useful for bone marrow spectroscopic data. This is true particularly for the short echo time lipid spectra in which the smaller resonances tend to be dominated by overlapping wings of the methylene resonance.

In conclusion, SEPSI allows large volumes of bone marrow to be sampled at moderately high spatial resolution in realistic clinical scan times to obtain lipid chemical compositional information. The growing availability of EPI equipped scanners may help accelerate the medical application and clinical utility of efficiently performed proton spectroscopic studies of bone marrow.

<table>
<thead>
<tr>
<th></th>
<th>M</th>
<th>U</th>
<th>P</th>
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</thead>
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<tr>
<td>Corn Oil</td>
<td>7.79 ± 1.22</td>
<td>1.56 ± 0.24</td>
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<td>Olive Oil</td>
<td>11.02 ± 2.21</td>
<td>1.09 ± 0.26</td>
<td>0.045 ± 0.015</td>
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</table>

Table 1: Lipid indices available from the linear prediction fits to 20 ms TE spectra of corn oil and olive oil (means and standard deviations from five spectra of each oil).

The lipid indices in Table 1, taken from 20 ms TE data to minimize relaxation effects, clearly differentiate the corn from the olive oil. The lower M value in corn oil is consistent with the higher percentage of polyunsaturated oils. Taking the P value of 0.66 for the idealized 18 carbon disaturated chain just discussed, one can predict a P value of 0.42 for the corn oil from the 0.64 fraction of polyunsaturated oils provided.
by the manufacturer. This is in close agreement with the measured value of 0.45 given in Table 1, suggesting that most of the polyunsaturated triglycerides in the corn oil have two double bonds. In the bone marrow, the overall effect of lengthening echo time is to reduce the observed lipid indices since the methyl signal.

<table>
<thead>
<tr>
<th>TE(ms)</th>
<th>M</th>
<th>U</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>20</td>
<td>9.01 ± 1.61</td>
<td>1.24 ± 0.26</td>
<td>0.27 ± 0.06</td>
</tr>
<tr>
<td>165</td>
<td>5.92 ± 1.03</td>
<td>0.63 ± 0.29</td>
<td>—</td>
</tr>
</tbody>
</table>

Table 2: Lipid indices available from the linear prediction fits to 20 ms TE spectra of yellow marrow (means and standard deviations from 10 marrow spectra).

The method utilized asymmetric readouts so that all kx lines are acquired in the same direction in k-space. Though lengthening the overall readout time compared to bipolar gradient readouts, the asymmetric readout approach generally simplifies reconstruction and avoids the need to separately reconstruct spectral data from odd and even echoes or perform other schemes like oversampling[71, 72]. Using a spin-echo rather than a free induction decay (FID) echo planar spectroscopic readout following a single excitation pulse allows for spectral $T_2$ measurement with the collection of data sets at different echo times. Several other advantages are gained with the spin-echo planar approach, as discussed previously by Pauli et al for 631P CSI acquisitions. At even relatively short echo times, the phase encode lobe preceding the half-echo readout does not preclude sampling directly from the start of the half-echo acquisition. This avoids spectral phase errors caused by the phase encode lobe when FID sampling is used in CSI formats. The flexibility of a variable spin-echo time also allows one to apply a $T_2$ filter to the data to control the spectral information. For example, if the compositional indices M and U indices are of the primary interest, a long echo time like 165ms will allow for full echo acquisitions with minimal overlap between methyl and methylene resonances or water and olefinic resonances. The full echo readouts in this case give narrower lines than the half-echo readouts at shorter echo times. Overall the longer echo times simplify spectral interpretation in a manner reminiscent of long echo time vs short echo time brain spectra. The long echo time spectra should
also be important in studies of red marrow or diseased marrow where a higher water content prevails than in healthy yellow marrow, obscuring the olefinic resonance. The use of linear prediction methods, or for that matter other time domain analyses, appears useful for bone marrow spectroscopic data. This is true particularly for the short echo time lipid spectra in which the smaller resonances tend to be dominated by overlapping wings of the methylene resonance. Minor improvements in spectral quality can be made to obtain better definition of the smaller lipid resonances, possibly with multiple signal averaging. Such improvements made in conjunction with linear prediction analyses can make possible clinical studies of the level of polyunsaturated triglycerides in vivo using the 2.9 peak as a marker and evaluation of the P index. The advantages of performing such studies with a widely available fast proton based spectroscopic imaging technique over the $^{13}C$ based, non-imaging techniques previously suggested for this application are obvious.

In conclusion, SEPSI allows large volumes of bone marrow to be sampled at moderately good spatial resolution in realistic clinical scan times to obtain lipid chemical compositional information. The growing availability of EPI equipped scanners may help propel the medical application and clinical utility of efficiently performed spectroscopic studies of bone marrow.

### 6.5 2D Fast Chemical Shift Imaging

#### 6.5.1 Method

Figure 6-5 shows the 2D fast chemical shift imaging (2D FCSI) sequence. The sequence is a variation of 3D FSE (chapters 2 and 3). The two image dimensions are phase encoded. The chemical shift information is encoded within spin echos. The RARE method is implemented to increase imaging speed. Multiple spin echo of 3 and 5 spin echoes are studied.

The spin echo acquisition window width is 79.87 ms. 156 data points are collected in each spin echo with acquisition band width of 1 kHz. The related resolution of
proton spectroscopy is 0.196 ppm at 1.5T. In the GE Signa scanner where this method is implemented, the 156 point data set is zero filled to 256 points. Thus, the effective resolution of reconstructed spectrum is 0.12 ppm.

6.5.2 Phantom Study Result

The oil phantom was studied with a FOV of 20 cm. The slice thickness was 10 mm. The spatial matrix size was 32 x 32. With a repetition time of 1.5 seconds, a 5 spin echo RARE 2D CSI sequence takes 6:28 minutes, while a 3 spin echo RARE 2D CSI takes 9 : 40 min. Figure 6-6 shows the 2D images. The image from 5 spin echo has poor image quality. One of the reasons is that the T2 decay of the sample kills a lot of signal in the later echoes. The small number of phase encoding is another reason. Figure 6-7 shows the spectrum. The spectrum from 3 spin echo acquisition is of better quality than that from 5 echo. The spectral leakage from neighboring pixels is obvious from the 5 echo spectrum, creating spurious peaks.

6.6 2D Line Scan Spectroscopy Imaging

6.6.1 Method

Figure 6-8 shows the line scan spectroscopy imaging (2D LSSI) sequence. The 2D image plane is covered by multiple parallel lines. A line scan spectroscopy imaging is performed on each line. The line is selected by two planes excited by a 90 degree excitation pulse and a 180 degree refocus pulse. The two excited planes are at 45 and 135 degrees respectively to the image planes, so that the selection of one line will not cause saturation of the neighboring lines. To avoid saturation of next line caused by pulse imperfection, an interleave factor of 4 was used.

The line is phase encoded by 64 steps. The spin echo acquisition window width is 79.87 ms with acquisition band width of 1 kHz so that spectroscopic resolution was identical to that in 2D fast chemical shift imaging method. The RARE method was also implemented for this sequence using 3 and 5 echoes with scan times of 4 minutes.
6.6.2 Phantom Study Result

The same phantom as used in 2D FCSI is used in this study. To cover the 2D image, 32 lines are used, each with 64 steps phase encoding. The thickness of two orthogonal plains is 5mm, which in turn gives 7mm line width. Both 3 echo and 5 echo RARE methods were studied. The scan time in both cases were approximately 4 minutes. The repetition time was 5 seconds. The images are shown in Figure 6-2, and the spectrum are shown in Figure 6-3.

6.7 Discussion

6.7.1 Scan Time

Though both 2D LSSI and 2D FCSI utilize RARE methods to accelerate spatial encoding, 2D LSSI is more time efficient than 2D FCSI. The time saving is from interleaved excitation of lines. The LSSI also offers longer effective TR, so that the spin saturation is reduced.

6.7.2 Image Quality

The images from 2D LSSI are much better than those from 2D FCSI. In the direction where line scan is cruising, the leakage artifact is minimized. On the other hand, the small number of the phase encoding in the same direction as in 2D FCSI causes Gibbs artifact and substantial signal bleed from voxel to voxel.

6.7.3 Spectral Quality

In general, 2D FCSI gives better signal to noise ratio(SNR), as can be observed in Figure 6-3. The digital noise in 5 echo 2D LSSI is shown clearly while the digital noise in 5 echo 2D FCSI is still negligible. However, the 2D FCSI suffers some information leakage artifact, especially, in 5 echo case. Both 3 echo 2D LSSI and 3 echo 2D FCSI spectrum are good compare to 5 echo cases.
Because the effective echo time in the 5 echo case is longer than that in the 3 echo case, and methyl has longer $T_2$ than methylene, the relative intensity of methyl to methylene in 5 echo case is larger than that in 3 echo case. This can be seen from Figure 6-3.

6.8 In Vivo Study

2D spectroscopy imaging of knee is performed using both 2D LSSI and 2D FCSI. Figure 6-9 shows the image of the experiments.

The spectrum of fat, muscle and bone marrow are shown in Figure 6-10. The 3 echo 2D LSSI shows the best image and spectrum qualities compared to 5 echo 2D LSSI and 5 echo 2D FCSI. Due to the fact that 5 echo 2D FCSI takes 9:40 minutes, 5 echo 2D FCSI has not been used in this study.

6.9 Conclusion

We have developed, implemented and tested three fast spectroscopic imaging methods, namely, the spin-echo planar spectroscopic imaging(SEPSI), fast chemical shift imaging(FCSI) and line scan spectroscopic imaging(LSSI). The phantom studies and in vivo studies show that the SEPSI method is superior to the other two methods in terms of scan time and imaging quality. The advantage is provided by the high speed EPI acquisition rate. We have shown that the line scan method has the advantage of line interleaving to cover a 2D plane, therefore saves the scan time limited by repetition time. A method which takes the advantage of both line scan and EPI acquisition will be discussed in chapter 8.
Figure 6-2: Top left(a): Image of the oil phantoms reconstructed from one of the SEPSI gradient echo images showing the spatial resolution obtained with the sequence parameters used. Central vial is olive oil, outer concentric vial is corn oil. Clockwise from top right(b,c,d): Fourier transformed magnitude spectra from the horizontal line outlined in the image at spin-echo times of 20, 80 and 165 ms, respectively.
Figure 6-3: Top plots; Fourier transformed spectra of corn oil at TE of 20 ms (left:a) and 165 ms (right:b). Lower panels are the spectra obtained from linear prediction fits of the same data assuming 7 peaks (left:c) and five peaks (right:d).
Figure 6-4: Top left(a): Image of an axial slice through the knee of a volunteer reconstructed from one of the gradient echoes of a SEPSI acquisition showing the voxels from which spectra are acquired. Clockwise from top right(b,c,d): TE = 20 ms, 80 ms, and 165 ms spectra, respectively, from the horizontal line outlined in the image.
Figure 6-5: 2D FCSI sequence. Phase encodings are applied in y and x direction, slice selection is in z direction. RARE scheme of 3 echoes is shown here.
Figure 6-6: Spatial image, acquired by adding all the spectral components. Top left: image from 5 echo 2D LSSI; low left: image from 3 echo 2D LSSI; top right: image from 5 echo 2D FCSI; low right: image from 3 echo 2D FCSI.
Figure 6-7: Spectrum from pixel (15,90). Top left: spectrum from 5 echo 2D LSSI; low left: spectrum from 3 echo 2D LSSI; top right: spectrum from 5 echo 2D FCSI; low right: spectrum from 3 echo 2D FCSI.
Figure 6-8: 2D LSSI sequence. The plain excited by 90 degrees pulse is orthogonal to the plain selected by 180 degrees refocus pulses. RARE scheme of 3 echoes is shown. Phase encoding is along the line(y direction).
Figure 6-9: In vivo knee spectroscopy image. Left: image from 3 echo 2D LSSI; middle: image from 5 echo 2D LSSI; right: image from 2D FCSI
Figure 6-10: In vivo knee spectroscopy image. Left column: from 3 echo 2D LSSI; middle column: from 5 echo 2D LSSI; right column: from 5 echo 2D FCSI. Top row: spectrum of fat; middle row: spectrum of muscle; bottom row: spectrum of bone marrow.
Chapter 7

MRI for Magnetic Field Distribution, and the Reversible and Irreversible Transverse Relaxation by SEPSI

7.1 Introduction

In this chapter we describe the application of SEPSI for magnetic field mapping and for studying reversible and irreversible transverse relaxation behavior. In particular, the suitability of using a previously discussed model for separately measuring the reversible and irreversible transverse relaxation rates in brain is tested with the SEPSI approach.

7.1.1 Magnetic Field Distribution Mapping

The SEPSI method can provide fast 2D spectroscopic imaging, as shown in the previous chapter. For each pixel in the 2D image, the chemical shift information is efficiently encoded. For a 64 × 96 pixel image over a field of view (FOV) of 24 × 24 cm², typical spectral resolutions achieved by Fourier transform were on the order of 0.1 ppm.
with time domain spectral analyses potentially offering even better resolution in high signal-to-noise situations. Thus the SEPSI may prove useful for rapid magnetic field measurement over large volumes and so prove useful for automated shimming procedures. In section 7.3.1, we demonstrate an experiment where SEPSI is applied to measure the magnetic field distribution of a NiCl\(_2\) doped water phantom in which a major field distortion is introduced by placing a metal clip placed just outside of the phantom.

7.1.2 The Reversible and Irreversible Relaxation Rate Measurements

Transverse relaxation processes are generally separated into two categories, reversible and irreversible, depending on whether a refocusing pulse will cause transverse dephasing resulting from a given process to rephase (reversible) or not to rephase (irreversible). Separate measurement of reversible and irreversible relaxation processes have been suggested as useful in a number of clinical situations. These include functional imaging, where local changes in magnetic susceptibility occur with activation, and in bone marrow studies where changes in trabecular bone architecture, such as those accompanying osteoporosis, cause changes in magnetic susceptibility[46, 20, 47, 84, 85].

Conventionally, the irreversible relaxation rate \(R_2\) is measurable with Carr-Purcell-Meiboom-Gill(CPMG) multiple spin-echo imaging sequences while gradient echo trains may be used to measure \(R_2^{*}\), taken as a sum of the irreversible \(R_2\), and reversible \(R_2'\), relaxation rates. Thus a combination of CPMG methods and gradient echo methods can, in principle, be used to measure both the reversible and irreversible relaxation rates. From a clinical perspective such dual acquisitions are clearly inefficient. Recently, Ma and Wehrli[46], and later Yablonskiy and Haake[85] demonstrated spin echo/gradient echo combination sequences with the potential to measure both \(R_2\) and \(R_2^{*}\) separately from a single acquisition. The implicit assumption for the success of the technique to make meaningful measurements of these parameters is that a
pure exponential decay for both the reversible and irreversible processes is appropriate. Not having fast gradient capabilities which allows SEPSI acquisitions like those we have demonstrated in the previous chapters, the initial demonstrations of the $R_2$, $R'_2$ mapping methods collected only a few (less than 7) gradient echoes on either side of the spin echo. Furthermore, the gradient echoes were all sampled with relatively large echo spacings greater than 4 ms, making for rather small spectral bandwidths. The full echo SEPSI method we have implemented with EPI gradient switching capabilities is capable of measuring 32 gradient echoes on both the left and right side of a spin echo centered around 140 ms after the excitation, all with a 1.928 ms echo spacing. This allows for considerably greater sampling of the time evolution of both halves of a spin echo and so allows for a more realistic determination of whether simple exponential relaxation processes are in fact taking place. If this is indeed found to be the case than separate measurement of the reversible and irreversible relaxation rates may be made with a single, rapid imaging acquisition with SEPSI. More complicated theoretical models are required when the simple exponential decay regime is not appropriate, as discussed by Yablonskiy and Haake and others. Even in this case, however, the improved experimental measurement offered by SEPSI can prove a valuable tool in collecting data for more detailed theoretical treatments.

In the SEPSI method which samples both halves of the spin echo, the case of simple exponential behavior leads to an effective relaxation rate of $R_2 - R'_2 (R_{2l})$ for the left half of the spin echo and an effective relaxation rate of $R_2 + R'_2 (R_{2r})$ for the right half of the echo. In this case, the reversible and irreversible relaxation rates can be retrieved by adding or subtracting the two parameters, $R_{2r}$ and $R_{2l}$.

In section 7.3.2, we will test the appropriateness of simple exponential decay for the reversible and irreversible transverse relaxation in brain and demonstrate measurements of the reversible and the irreversible relaxation rates with SEPSI in regions which allow for such measurements.
7.2 Method

7.2.1 Imaging Method

The SEPSI method described in Chapter 4 was utilized with the following parameters. Images were acquired using 96 frequency encoding steps and 64 phase encoding steps with a field of view (FOV) of $24 \times 24cm^2$. There are 64 gradient echoes within one spin echo which spans approximately 140ms. The full set of 64 gradient echo images were acquired in 1 minute and 40 seconds using a repetition time (TR) of 1.5 seconds. The echo spacing between gradient echoes was $1.928ms$.

7.2.2 Data Processing and Analysis

Image data was collected in complex raw data form and processed offline using MATLAB software. A 2D FFT is first performed along the two spatial dimensions of the 3D data set so that a time domain representation of the full spin echo (both halves) can be extracted from each of the $64 \times 96$ voxels in the image.

In the case that both the reversible and the irreversible relaxation processes behave as simple exponential decays, gradient echoes from the left and right sides of the spin echo are analyzed separately to get the effective relaxation rates, i.e. $R_2 - R'_2$ from the left side and $R_2 + R'_2$ for the right side. For each of the 32 images on the left and 32 on the right, regions were chosen to sample the time domain representation of the full spin echo. For each half, the time domain analysis[14, 17] was applied to the 32 data points to retrieve the damping factors. Specifically the LPHSVD method was used for the brain study, a detailed description of this method having been provided in chapter 5.

In regions where the relaxation behavior was clearly not appropriately described by exponential decay, the reversible and the irreversible relaxation rates cannot be separately measured. In this case, as in some locations of the water phantom study, the FFT method over the entire spin-echo still allows for an accurate determination of the frequency shift at each pixel over an extended spectral bandwidth of 500 Hz.
In some regions of the brain, in particular above the nasal cavity, the damping is also not appropriately described by an exponential function, most probably due to the complex magnetic field distribution caused by air/tissue interface near the nasal cavity. In this case we still used the exponential model simply to get damping factors with the LPHSVD method over the entire image. However, we also employed the technique suggested by Yablonskiy and Haake[85] in which the irreversible relaxation rate is first evaluated from both halves of the spin echo and then, a function, non-exponential, representing the time decay due to the reversible relaxation is evaluated.

7.3 Result and Discussion

7.3.1 Field Mapping for Water Phantom with Metal Clip

Figure 7-1(a) shows the experimental configuration in which a metallic object, a paper clip, was placed by a NiCl₂ doped water ball phantom. In chapter 5 we reported the $T_2$ and $T'_2$ of this same phantom. The inhomogeneity for this phantom is minimal as detected with SEPSI and is largely confined to the edges of the sphere. By placing the paper clip adjacent to the phantom, however, we introduce a considerable magnetic field inhomogeneity. Figure 7-1(b) shows the spin echo image extracted as the central gradient echo image in the train of 64 gradient echo images straddling the spin echo.

Figure 7-2(a) shows the local frequency distribution obtained by fast Fourier transform (FFT) over the entire echo. The local frequency distribution images as shown are representative of the magnetic field over the FOV with the major frequency distortion caused by the metal clip being larger than 20 ppm (note that the spectral bandwidth used did not cover this wide a range of frequencies but the Matlab wrap-around function easily corrected for aliasing as the field distribution is fairly smooth). For comparison, the frequency distribution without the present of the clip is shown in Figure 7-2(b).

We look at the individual spin echo time information in more detail along the line of pixels indicated by the two boundary lines in Figure 7-1(b). Figure 7-3 shows the
actual spin echo from each pixel along the line extending from very close to the clip to the other side of the sphere, far removed from the field distortions created by the clip. The slice thickness is 1cm and the pixel size is $0.375 \times 0.25cm^2$. Figure 7-4 shows 4 curves in greater detail taken from the data in Figure 7-3. Far from the clip, at pixel 18, a smooth single exponential decay indicates that the reversible relaxation rate is very small, i.e. $T_2 \sim T_2^*$, as previously shown for this phantom in chapter 5. The relaxation rate of this pixel is $11s^{-1}$. The closer the pixel is to the clip, e.g. pixel 45 and pixel 60, the greater is the signal attenuation, particularly at the time zones further removed from the center of the spin echo. The damping factors in the region close to the clip are clearly not simple exponential decay as shown in the figure, e.g. pixel 45, pixel 60, pixel 70. For pixel 45 and pixel 60 in Figure 7-4, three line fittings, 'L', 'R' and 'C' are used to fit the different region of the signal. It is interesting to note that there exists a flat region around the spin echo. As the pixel position moves closer to the clip, this flat region gets smaller. In any event, the departure of the signal from monotonic decays on either side of the spin echo indicates a departure from reversible relaxation expected from a Lorentzian distribution of frequencies. As shown by Yablonskiy and Haake and reproduced by us (data not shown), the spin echo shape is a sinc function when a linear field gradient along one spatial axis is applied. In the case of the more non-linear field distortion caused by the clip, sinc-like features still appear though neither an exponential or pure sinc function can account for the actual shape of the echo. In the region very close to the clip, where the frequency shift is very rapidly varying, the sampling rate of the SEPSI method as currently implemented is not high enough to record the modulation in appropriate detail to allow for a meaningful analysis, as seen in Figure 7-3.

7.3.2 The Reversible and the Irreversible Relaxation Rates Measurement for Brain

The reversible and the irreversible relaxation rate measurements in brain were first conducted by Ma and Wehrli[46] using GESFIDE(gradient-echo sampling of FID and
echo). In that method, the dephasing and the rephasing portions of a Hahn echo were collected from each side of the refocusing pulse. In such an approach, the information around the spin echo is missing due to the placement of the excitation RF pulse and imaging gradients. The SEPSI method we are using here overcomes this problem, offering a full spin echo measurement. Furthermore, the SEPSI method provides higher temporal resolution (64 time points separated by 1.928 ms) than the GESFIDE (12 time points separated by 4.65 ms) does. Hence, the spin echo is better sampled.

Figure 7-5(a) shows a spin echo image of a brain which is the middle image (#33 in Figure 7-6) from the train of 64 gradient echo images. The spin echo time is 140 ms so that the image appears as a $T_2$ weighted spin echo image. The other images in the train are $T_2^*$ weighted images with various gradient echo times. Figure 7-6 shows 16 images of the 64 images in one spin echo range.

Following the steps described in chapter 5, the 32 images on the left side of the spin echo were used to get the factors of $R_2 - R_2'$ and the 32 images on the right side of the spin echo were used to get the factors of $R_2 + R_2'$. Finally, the factors of $R_2$ and $R_2'$ were separated for each pixel. Figure 7-5(b,c) shows the $R_2$ mapping and $R_2'$ mapping.

The $R_2$ and $R_2'$ values in two different regions of 9 pixels each, labeled in Figure 7-5(a) as 'A' and 'B', are calculated for each region. For the region 'A', $R_2'$ value is $1.6 \pm 1.2 s^{-1}$, the $R_2$ value is $12.7 \pm 1.9 s^{-1}$. The bright round spot in the $R_2'$ mapping (Figure 7-5(c)) is caused by the nasal cavity below the brain. The average $R_2'$ value in this region is $28.8 \pm 5.8 s^{-1}$, whereas the average $R_2$ is $9.8 \pm 2.4 s^{-1}$. The susceptibility effects caused by air cavities are prominent in $R_2'$ mapping rather than in $R_2$ mapping.

The values just reported, of course, assume that the exponential regime applies to all the human brain regions sampled. Since the spin echoes are so well sampled with the SEPSI method, this assumption can be put to a more rigorous test than previously attempted. Figure 7-7 shows the gradient echo intensities as a function of time for the regions 'A' and 'B' as indicated in Figure 7-5(a). For region 'A', the time
evolution show that the exponential model is reasonably well-justified as straight lines on the semi-log plots are observed. However, for region 'B', the single exponential model is not valid. The spin echo time evolution in this region is similar to the one we observed in the study of the NiCl₂ doped water phantom with the metal clip (Figure 7-4, pixel 60). This indicates that there is a strong inhomogeneity source nearby, in this case, the nasal cavity.

In region 'B' of the brain study and from pixel locations 45, 60, and 70 in Figure 7-3 of phantom study, we have shown that the exponential model does not apply. It remains to be shown what kind of information can be extracted in this case from SEPSI sampling. Yablonskiy and Haake[85] have suggested a model in which the reversible relaxation is not exponential but is symmetric about the spin-echo center and the irreversible relaxation is exponential. In this case, an $R_2$ value can be extracted along with a measure of the degree to which the irreversible relaxation is exponential. Then, the shape of the reversible relaxation can be separated from the irreversible relaxation, as we now do for some regions we have found that do not show exponential decay on either side of the echo. The contribution of the reversible relaxation to the signal is first described by a general function $f(t)$. On the left side of the echo, the signal is given by,

$$S_l(t) = S(0)exp(-R_2t)f(t)$$  \hspace{1cm} (7.1)

for $t < TE/2$, and on the right side of the echo,

$$S_r(t) = S(0)exp(-R_2t)f(t - TE)$$  \hspace{1cm} (7.2)

for $t > TE/2$. The function $f(t)$ is symmetric about the spin echo position ($t = TE/2$) and satisfies,

$$f(t) = f(TE - t)$$  \hspace{1cm} (7.3)

by reversing the $S_r(t)$ data,

$$S'_r(t) = S(0)exp(R_2t)f(TE - t)$$  \hspace{1cm} (7.4)
the irreversible relaxation rate can then be retrieved by,

\[ \exp(-2R_2t) = S_l(t)/S'_r(t) \] (7.5)

or

\[ -R_2t = \frac{1}{2} \log[S_l(t)/S'_r(t)] \] (7.6)

and

\[ f(t) \sim S_l(t)/\exp(-R_2t) \] (7.7)

The suitability of the exponential for the reversible relaxation rate can be checked by line fitting the \( \log(f(t)) \) as a function of time. Figure 7-8 shows the plots of \((-R_2t)\) vs time and \( \log(f(t)) \) vs time for the data from regions 'A' and 'B' as indicated by Figure 7-5(a), where \( t < TE/2 \). For region 'A', the '+' represents the reversible relaxation(\( \log(f(t)) \)) and the 'o' represents the irreversible relaxation(\((-R_2t)\)). For region 'B', the '*' represents the reversible relaxation and the 'square' represents the irreversible relaxation. In region 'B', we observed that the reversible relaxation rate deviates from the simple exponential decay with the actual shape of \( f(t) \) determined by the specific magnetic field inhomogeneity. The plots of \((-R_2t)\) vs time and \( \log(f(t)) \) vs time for the data corresponding to pixels in Figure 7-4 are shown in Figure 7-9, where the 'o' represents the reversible relaxation and the '+' represents the irreversible relaxation. It is shown that even in the high inhomogeneity regions, e.g. pixels 45, 60 and 70 as well as region 'B', the simple exponential decay is reasonable for describing the irreversible relaxation. The measurement of \( f(t) \) by SEPSI provides the information about the inhomogeneity whose origin can be further studied by fitting the experimental data with theoretical modeling and simulation.

7.4 Conclusion

The SEPSI method has been applied to obtain higher temporal sampling than previously obtained of spin echoes from many small voxels in brief scan times. The
information can be used in several ways that may prove of clinical utility. High spatial resolution magnetic field maps for automated shimming can be performed. Also of importance is the potential to determine the appropriateness of exponential decay models and to extract simultaneous measurements of the reversible and the irreversible relaxation rates when such modeling is appropriate.
Figure 7-1: Left(a): Illustration of phantom setup. Right(b): Spin echo image at TE of 145 ms. The relaxation properties of the selected line is explained in the text.
Figure 7-2: Left(a): The frequency shift mapping in the presence of the metal clip. Right(b): The frequency shift mapping without the metal clip.
Figure 7-3: Spin echo intensities along the selected line (as indicated in Figure 7-1(b)) as the function of time.
Figure 7-4: Spin echo intensities from the selected pixels along the line indicated by Figure 7-1(b). Four pixels are selected. Pixel 18 is far from the clip. Pixel 45 and 60 show non-single-exponential decay on both sides of spin echo. Three line fittings were made in corresponding region for pixel 45 and 60. An center lines, C's, show the 'flat' pattern. Pixel 70 shows the severe dephasing.
Figure 7-5: Above(a): Spin echo image of brain at TE of 145ms. Two regions, 'A' and 'B', are marked for relaxation rates measurement as described hereafter. Each box contain 9 pixels. Left(b): $R_2$ mapping of the brain(a). Right(c): $R_2$ mapping of the brain(a).
Figure 7-6: Gradient echo images of brain in one spin echo range about 130ms. The location of each image in a train of 64 images is indicated by '#'1. The middle image(#33) is formed at spin echo position.
Figure 7-7: Gradient echo intensities variation as functions of time. The circle 'o' is from one pixel of region 'A' as in indicated in Figure 7-5a. The 'square' is from one pixel of region 'B' as indicated in Figure 7-5a. The line fittings are performed on each side of the spin echos separately.
Figure 7-8: Separation of the irreversible relaxation rate and reversible relaxation rate from a full spin echo. Plots of $(-R_2t)$ vs time and $log(f(t))$ vs time for the data from regions 'A' and 'B' as indicated in Figure 7-5(a). For region 'A', the '+' represents the reversible relaxation and the 'o' represents the irreversible relaxation rate. For region 'B', the '*' represents the reversible relaxation and the 'square' represents the irreversible relaxation. Line fitting is performed on each data set.
Figure 7-9: Separation of the irreversible relaxation rate and reversible relaxation rate from a full spin echo for NiCl$_2$ doped water phantom experiment. Plots of $-R_2t$ vs time and $\log(f(t))$ vs time for the data corresponding to pixels in Figure 7-4, where the 'o' represents the reversible relaxation and the '+' represents the irreversible relaxation. Line fitting is performed on each data set.
Chapter 8

Single Shot Column Spin-echo Echo Planar Spectroscopic Imaging Method

8.1 Introduction

Line scan spectroscopic imaging can provide one dimensional spatial images with obtained spectra for each voxel along the column. Line scan spectroscopic imaging [75, 60, 61, 19, 67, 38] has been developed by using Carr-Purcell-Meiboom-Gill (CPMG) sequences [83, 76]. Even though this method can be performed in RARE mode where three to five echoes with different phase encoding are acquired in one repetition time, multiple excitations are needed to cover the phase encoding range of the line. Hence, the scan time of the multiple echo approach is not favored in applications which involve motions, e.g. liver or heart spectroscopic imaging, and in those cases where the temporal resolution of the metabolite information might prove important, e.g. functional magnetic resonance imaging (fMRI).

In this chapter, we describe the development and testing of a single shot line scan spectroscopic imaging method (SSLSEPSI).
8.2 Materials and Methods

Figure 8-1 shows the pulse sequence diagram for single shot column spin-echo planar spectroscopic imaging. The line selection is completed by selectively exciting two orthogonal planes. The two orthogonal planes are selected by the excitation pulse and the refocusing pulse respectively. Both pulses are 3.2 ms duration sinc pulses with one cycle. After the line selection, the spin-echo planar spectroscopic imaging sequence(SEPSI) is followed. The SEPSI sequence consists of a train of gradient echoes. Data acquisition is performed for each gradient echo which is frequency encoded for the same selected line. A full gradient rewind is applied between every two gradient echoes. The spectral information is encoded by a time series of the gradient echo trains. An option for a chemical selective suppression(CHESS) sequence is implemented which can be applied before the excitation as a means to suppress water. The chemical selective suppression sequence consists of three soft pulses each followed by a pair of crusher gradients. The other option is an 180° non-selective inversion recovery pulse to suppress fat signal using an inversion time of 150ms.

The sequence with water suppression option is tested on the knee for a bone marrow study. The acquisition bandwidth is ±64kHz which gives a dwell time of 7.8 µs. The spectral bandwidth is determined by the time space between two adjacent gradient echoes(GES), and can be adjusted by varying field of view(FOV) and spatial resolution. By varying the number of gradient echoes in the train, one can control the spectral resolution which is the spectral bandwidth divided by the number of gradient echoes.

The sequence with water suppression was tested on a spherical water phantom containing 20mM N-acetyl aspartate(NAA), 10 mM choline(Cho),and 10mM creatine(Cre). The length of each of the three soft pulses in CHESS is defaulted at 30ms which corresponds to a 42Hz cut-off bandwidth, and can be varied to give the optimal suppression effect.

Both water suppression and fat suppression were applied for the brain study. The inversion recovery time(IR) was set to 150ms to reduce the signal from the lipid
within the skull. Scans with different number of signal averaging were acquired to determine the signal sensitivity and image quality.

The SSLSEPSI sequence has been implemented and tested on a 1.5 T Signa system (General Electric Medical System, Milwaukee, WI) with EPI capable gradient set (2.3G/cm), operating at the 5.7 configuration. Extremity coil was used for knee study and head coil was used for phantom and brain study. The raw data matrices involved in this study are zero-filled and then reconstructed to 256 by 256 matrices by Signa on-line reconstruction software.

8.3 Results and Discussion

8.3.1 Knee study

Figure 8-3 shows the knee image and result of one dimensional spectroscopic imaging from a single shot line spin echo planar spectroscopic imaging method (SSLSEPSI). The locations of selected lines are displayed in Figure 8-2.

48 data points were sampled within a field of view of 24 cm. The spatial resolution was 0.5 cm. The cross section dimension of the line was 2 cm × 2 cm. The voxel size was 2 cm³. 128 gradient echoes were acquired with gradient echo space (GES) of 1.144 ms, which gives a spectral resolution of 0.11 ppm. Figure 8-3(a, b) show spectra without water suppression. The water peak and the olefinic peak are separated by about 40 Hz. In Figure 8-2(c, d), water suppression is applied. The RF pulse width of CHESS is 60 ms which corresponds to a selective spectral width of 20 Hz (0.3 ppm). Therefore, the olefinic peak survived despite the water suppression pulse.

Figure 8-4 shows the result with smaller voxels. The spatial domain was sampled by 72 points and the line cross section was 1 cm × 1 cm. The voxel size was 0.33 cm³. The gradient echo space was 1.412 ms and the number of gradient echoes was 128 so that the spectral resolution was 0.088 ppm.

The image quality by SSLSEPSI is as good as those by SEPSI, FCSI and LSSI methods explored in chapter 6. Similar to LSSI method, a two spatial dimensional
spectroscopic imaging can be obtained by scanning multiple lines covering a 2 dimensional plane. The interleave scheme can allow the scan time to be reduced by a factor 10 comparing to that in 2D SEPSI method described in chapter 6. The trade-off is the reduction in signal to noise ratio. As for 3D case, the line scan SEPSI may be less efficient than interleaved 2D SEPSI.

8.3.2 Brain Metabolite Phantom

Figure 8-5 demonstrates the result of one dimensional spectroscopic images with various numbers of signal averaging and the two acquisition approaches, namely, half echo acquisition and full echo acquisition. Figure 8-5 a, c, e and g are voxel spectra taken from the corresponding lines shown in the spectroscopic images of b, d, f and h. The voxels are located at 12cm as in the coordinate displayed in the spectroscopic images. The column was selected to pass through the center of the phantom ball with a diameter of 15cm. The line cross section was 2cm x 2cm. 48 sampling points were used to cover a FOV of 48 and the spatial resolution was 0.75cm. The voxel size was 3cm³. The number of gradient echoes was 128. With an echo space of 1.144ms, the spectral resolution was 0.11ppm. The water suppression RF pulse width is 40ms which gives a suppression bandwidth of 31Hz.

Although one acquisition was performed in Figure 8-5(a,b), the spectral peaks arising from the methyl group of N-acetyl-aspartate(NAA), choline(Cho) and creatine(Cr) are detectable at approximately 2.0ppm, 3.2ppm and 3.0ppm respectively. Averaging spectroscopic images by factors of 2 and 16 is demonstrated in Figure 8-5(c-f). The noise was suppressed by the square root of the number of averages. In Figure 8-5(a-f), the echo time was 20ms and the acquisition started right at the spin echo which is called half echo acquisition. Another acquisition arrangement which is called full echo acquisition is to place the spin echo at the center of the gradient echo train. More detailed description of both acquisition methods is given in chapters 4.6. Figure 8-5(g,h) shows the results of the full echo acquisition scheme where the echo time was 160ms and the number of averaging was 16. The signal intensity of each spectral component depends on its spectral relaxation rate and spin echo time(TE).
Thus, different TE causes the variation among the signal intensities of various spectral components. In this experiment, the signal intensity from choline is significantly decreased when a longer TE is used as in the full echo acquisition measurement.

8.3.3 Brain study

Figures 8-6 and 8-7 show the result of brain study on a 33 year old healthy man. Lines selected are displayed in Figure 8-2. The top row figures in Figure 8-6 resulted from the line 'A' and the bottom row figures were from the line 'B', as described in Figure 8-2. The water suppression RF pulse width was 40ms. The spectral resolution was 0.11ppm derived from 128 gradient echoes with 1.144ms gradient echo space. The images in Figure 8-6 were taken as an average of 16 scans. Scan time was 32s with 2s repetition time. The cross section of the line was 2cm × 2cm. The spatial resolution was 0.5cm and the voxel size was 2cm³. The figures on right are spectra with a line segment of 2cm as indicated in figures on left. The volume corresponding to the spectra was 8cm³. The NAA, choline and creatine peaks are detectable in both voxel spectra and spectroscopic images.

The top row of Figure 8-7 shows results from line location 'A'. The low row were results from line 'B'. An 180 non-selective pulse were applied before CHESS to suppress lipid signal from the skull. The time period between the inversion pulse and the excitation pulse was set to 150ms so that the signal from fat was suppressed effectively. However, the inversion pulse also caused the reduction of signals from other spectral components. For the top row images, 16 averages were applied. The spatial and spectral parameters were as the same as those described for Figure 8-6. For the lower row, only a single shot was applied. However, the voxel size was enlarged to 13.3cm³. The line cross section is 4cm × 4cm and 48 sampling points was used to cover a FOV of 40cm. The spectral resolution was 0.12ppm , and 128 gradient echoes were acquired with 1.04ms separation.

The spectra along the line show bending structure which results from the magnetic field inhomogeneities, e.g. primarily magnetic field inhomogeneity.
8.4 Conclusion

In this work, we have developed and tested a single shot spin echo planar spectroscopic imaging method. The purpose of the knee study was to assess the image quality from this method compared to those from other spectroscopic imaging methods. The results from the phantom study and brain study show that this method is feasible for brain metabolite studies. The limited sensitivity of the head coil prohibits the SSLSEPSI operating in single shot mode when the voxel is small (< 10cm³). We have demonstrated that for larger voxels, single shot acquisitions are possible. However, it may be feasible to sample smaller voxels by using more sensitive coils such as surface coils and, of course higher magnetic fields. In a word, this method offers instant measurement of one dimensional spectroscopic images which are potentially useful for imaging of body parts in motion and dynamic studies of brain metabolite.
Figure 8-1: Single Shot Line Scan Spin-echo Planar Spectroscopic Imaging (SSLSEPSI) sequence. The sequence consists of IR, CHESS and SEPSI.
Figure 8-2: Left: Image of knee. The two lines selected are shown. Right: Image of brain. Two lines 'A' and 'B' are selected for spectroscopic imaging study.
Figure 8-3: SSLSEPSI of knee. Voxel size is 2cm$^3$. Spectral resolution is 0.11 ppm. Left column: without water suppression. Right column: with water suppression. Top row displays the same object as the bottom row with different view point.
Figure 8-4: SSLSEPSI of knee. Voxel size is 0.33cm$^3$. Spectral resolution is 0.088ppm. Left column: without water suppression. Right column: with water suppression.
Figure 8-5: SSLSEPSI of water phantom. NEX = 1 for a and b. NEX = 2 for c and d. NEX = 16 for e-h. Voxel images for a, c, e and g. Spectroscopic images for b, d, f and h. Half echo acquisition in a, b, c, d, e and f. Full echo acquisition in g and h.
Figure 8-6: SSLSEPSI of brain without inversion pulse. Top left: spectroscopic image of line 'A' in Figure 8.2. Top right: spectrum of segment between two lines of the left figure. Bottom left: spectroscopic image of line 'B' in Figure 8.2. Bottom right: spectrum of segment between two lines of the left figure.
Figure 8-7: SSLSEPSI of brain with inversion pulse and inversion recovery time of 150ms. Top left: spectroscopic image of line 'A' in Figure 8.2. Top right: spectrum of segment between two lines of the left figure. Bottom left: spectroscopic image of line 'B' in Figure 8.2. Bottom right: spectrum of segment between two lines of the left figure.
Bibliography


