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Magnetic Resonance Imaging at Ultra High Field: Initial Experiences with an 8 Tesla Whole Body System

DISSERTATION

Presented in Partial Fulfillment of the Requirements for the Degree Doctor of Philosophy in the Graduate School of The Ohio State University

By

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* * * * *

The Ohio State University

2000

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ABSTRACT

In this dissertation, several aspects of the initial experiences using the world’s first clinical ultra high field system are examined. These include intrinsic signal to noise, high resolution imaging and relaxation time measurements.

The ultimate motivation for increasing clinical field strengths is to provide an enhanced signal to noise ratio. Therefore a comparison of intrinsic signal to noise at 8 Tesla versus 1.5 Tesla is presented using a single RF coil with identical pulse sequences and identical imaging parameters except TR(Repetition Time) and TE(Echo Time). These measurements were performed on mineral oil, water and chloroform phantoms and on the human brain in vivo. The TR and TE were selected for each individual phantom according to their $T_1$(Longitudinal Relaxation Time) and $T_2$(effective Transverse Relaxation Time) values. A better than linear dependence of the intrinsic signal to noise on field strength has been obtained.

The higher signal to noise observed at 8 Tesla can be converted to increased spatial resolution at the microscopic level. Therefore, a series of high-resolution in vivo MR images of the rodent (rat), feline (cat) and human brain are presented using a 1.5 Tesla GE Signa and the ultra high field 8 Tesla whole body system. High resolution images obtained at 1.5 Tesla using a three dimensional imaging technique enabled the effective discrimination of tumors in the rats. The 8 Tesla gradient echo images are characterized by high signal to noise and strong susceptibility contrast.
The enhanced signal to noise ratio and strong $T_2^*$ based contrast at ultra high field enabled the visualization of small vascular structures. Both the human and rodent MR images demonstrated excellent vascular structure detail in the cortex and in the deep brain. Comparative Spin echo and gradient echo images of the feline brain at the same anatomical level are obtained. The Spin Echo images are observed to be less affected by susceptibility at this field strength. A good visualization of the cochlea in the temporal lobe of the cat is illustrated as an example. Gradient echo images, on the other hand, exhibit considerable geometric distortion at the air/tissue interfaces near the temporal lobe. The receiver bandwidth is shown to have a major effect on chemical shift artifacts at 8 Tesla.

$T_1$ and $T_2$ values are important parameters to optimize contrast at 8 Tesla. Due to the highly complex and heterogeneous nature of biological tissue, predictions of relaxation times based on theoretical model are not available, one must rely on experimental means to accurately determine the relaxation times in the human brain in vivo at ultra high field strengths. Therefore, measurements of $T_1$ and $T_2$ were conducted at 8 Tesla. Average $T_1$ values of $1,635\pm169\text{ms}$, $1,370\pm128\text{ms}$, $3,950\pm650\text{ms}$ were obtained for gray matter, white matter and CSF in the human brain in vivo. Likewise, average $T_2$ values of $41\pm5.6\text{ms}$, $33\pm4.7\text{ms}$, $128\pm12.5\text{ms}$ were obtained for gray matter, white matter and CSF(Cerebro-Spinal Fluid), respectively. Within the limitations of the progressive saturation and multi-echo techniques, these findings are in agreement with the estimated $T_1$ and $T_2$ values for cortical gray matter and white matter extrapolated from the literature values at lower field strength and from the
measurements obtained from animals at similar field strengths. These preliminary estimates of relaxation times can provide important guidelines for contrast optimization in ultra high field imaging studies of the human head.
To my parents
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It is a privilege to have the unique opportunity to work on the 8 Tesla whole body system. I would like to thank my advisor, Dr. Pierre-Marie L. Robitaille, for his insight, courage and intelligence in making the 8 Tesla project possible and successful. I am also grateful for his guidance, encouragement and advice in my research.

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Y. Yu, A.M. Abduljalil, R. Gilbert, P.M.L. Robitaille. “Intrinsic Signal to Noise Analysis at 8 Tesla”. *manuscript in preparation*

**Talks and Posters**


**FIELDS OF STUDY**

Major Field: Biomedical Engineering

Studies in:

Magnetic Resonance Imaging  Dr. Pierre-Marie L. Robitaille
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CHAPTER 1

INTRODUCTION

1.1 The History of MR

Over the course of the past two decades, clinical magnetic resonance has witnessed a rapid growth in both imaging and spectroscopy. To understand these applications, it is helpful to recall the historic development of magnetic resonance. The first person to utilize the term “Nuclear Magnetic Resonance” (NMR) was Isidor I. Rabi who studied and described the splitting of molecular beams within magnetic fields [129]. Rabi was credited with the discovery of the nuclear spin and awarded Nobel Prize in physics for his work. In his setting however, the lattice was absent. The lattice is critical to longitudinal spin relaxation in magnetic resonance imaging and spectroscopy. The Russian scientist E.K. Zavoisky is generally acknowledged as the discoverer of Electron Spin Resonance (ESR) [176, 177]. He discovered the NMR signal as early as 1941. Zavoisky was the first to recognize the importance of applying a perpendicular magnetic field to excite the spins. He was also the first to observe the magnetic resonance phenomenon in the presence of a lattice. Soon after, Felix Bloch [19] and Edward M. Purcell [128] independently succeeded in discovering NMR signal in condensed matter using the nuclear induction method. They shared the 1952 physics
Nobel Prizes for their contribution to the field. As a theoretical physicist, Bloch described the nuclear behavior mathematically through an equation that now bears his name. Erwin L. Hahn discovered the spin echo [64] and the free induction decay [63]. Chemical shift was discovered by Proctor in 1950. Chemical shift is the basis for ESR and NMR spectroscopy and is widely used in academic research in physics, chemistry and biochemistry.

In 1972, Raymond V. Damadian patented the first instrument that could be used to scan the human body [41] after which MR scanners soon became available commercially and clinically. He also observed a distinct difference in $T_1$ relaxation time between normal and malignant tissues in 1971 [40]. This observation stimulated much interest in the relaxation time studies within the in vivo setting and in vitro tissues. His contribution to MR has made magnetic resonance a standard modality for whole body medical scanning and diagnostic imaging.

Magnetic resonance imaging is dependent on the process of spatially encoding the spins. Spatial encoding using a gradient field was proposed independently in 1973 for back projection by Lauterbur [101] and for line scanning by Mansfield [106] in 1976. These authors applied a linear gradient field superimposed on the main magnetic field such that the resonant frequency was made to vary linearly with position in the object to be imaged. Later, this general concept was perfected by Richard R. Ernst with the introduction of phase encoding and two-dimensional Fourier Transform Imaging [96]. This approach is more flexible, has higher sensitivity and is routinely applied on commercial scanners.

Today, clinical MRI (Magnetic Resonance Imaging) scanners operating at 1.5T are in operation all over the world as a result of the power of this non-invasive imaging
modality. MRI has become an indispensable tool in the diagnosis of neurological disorders. The commercial success of MRI scanners has facilitated medical research as well. In search of higher signal-to-noise and improved detectability of pathological conditions, numerous efforts have been devoted to both MRI hardware and software improvements. This has included: the design of new pulse sequences for better contrast and signal-to-noise in a shorter time, the construction of RF coils with improved quality factors (Q value), better homogeneity and the manufacturing of more powerful gradients in order to increase the spatial resolution. Consequently, images with high spatial resolution and better signal-to-noise have been achieved.

Using a combination of specialized RF (Radio Frequency) coils and the GRASE (GRAdient And Spin Echo sequence) imaging sequence, Feinberg et. al. [51] have successfully acquired images of the human brain from a 4 mm thick slice with an in-plane resolution on the order of only 270 μm at 1.5 Tesla despite the relatively lower intrinsic signal to noise available at this field strength. These images were acquired with surprisingly short acquisition times. Nonetheless, attempts to further increase inherent image resolution would be accompanied with significant degradation in image quality as a result of insufficient signal to noise. For fast imaging such as FLASH [62] and RARE [70], this is also the case, since fast imaging protocols are usually accompanied by a degradation in signal to noise. As such, people turned to the ultimate solution of enhancing signal to noise: increasing the field strength.

1.2 High Field

As early as the 1980s, there were debates as to which magnetic field strength was optimal for MR imaging. Initially, it was postulated that the field strength for human
whole body imaging could not exceed 10 MHz (corresponding to about 0.25T) because of RF power deposition, RF penetration and chemical shift artifacts [73]. Soon after, however, images were obtained at 63MHz (corresponding to 1.5T) showing no problems of the RF penetration. In addition, imaging at high field strength (around 1.5T) demonstrated considerable potential to increase the signal to noise ratio and image contrast. Nonetheless, physical and technical limitations could become important when going to higher fields (>3T). These concerns included: 1) human safety factors [144, 145, 183], 2) a possible decrease in the penetration depth within the body such that the signal may not be able to reach the center of the body [139], 3) the expected RF power requirements at high fields [72, 73], 4) the generation of standing waves or dielectric resonances within tissues with high dielectric constants which would compromise homogeneity [14, 15], 5) the degradation of image quality due to geometric distortions at air/tissue or tissue/bone interfaces caused by magnetic susceptibility [49], 6) the diminished $T_1$ contrast because of the lengthening and convergence of $T_1$ values for gray and white matter [52, 121, 157] and 7) chemical shift artifacts.

With these problems anticipated, several research institutions explored the possibility of imaging at 4 Tesla in early 1990 [15, 121, 157]. Images displayed no apparent RF penetration problems. Nonetheless, the images appeared to display dielectric resonance problems as manifested by central brightness on the scans. The amount of RF power was also shown to increase with the square of the field strength in brain, heart and cartilage experiments [43, 44]. An 8-10 fold increase of peak power from 1.5T to 4T using equivalent pulse shapes was reported [44]. In addition, $T_1$ values of white matter, gray matter and CSF (CerebroSpinal Fluid) were found to be much longer than at 1.5T [44, 98, 121]. Moreover, the ratio of gray/white matter $T_1$ values
decreased from 1.5T to 4T. As a result, it was much harder to extract $T_1$ contrast using conventional imaging sequences at higher field.

Nevertheless, promising results have been obtained at high field strength. The signal-to-noise ratio was demonstrated to have approximately a linear relationship from both imaging and spectroscopy results [65, 166]. High resolution anatomical imaging [121, 157], functional imaging [157] and spectroscopy [15, 65, 68, 69] all gained success at 4 Tesla. In addition, it was possible to obtain images with a 270$\mu$m in plane resolution displaying high $T_1$ contrast from a 3mm slice with good signal-to-noise using an inversion recovery pulse sequence [121]. $T_1$ contrast could also be achieved with the MDEFT pulse sequence in the presence of prolonged $T_1$ values [157]. Functional MRI became the most promising aspect of 4T studies because of the increased susceptibility contrast for deoxyhemoglobin and oxyhemoglobin in blood. Visual cortex stimulation obtained by flashing lights [111], auditory cortex stimulation obtained through sound production [18], and other clinical applications were soon explored [115]. A 15% BOLD signal change was observed at 4T compared to only 3-7% at 1.5T [155]. Spectral resolution was greatly improved for spectroscopy. With the help of efficient shimming techniques, such as FASTMAP [61] and a greater separation of spectroscopic resonances, better identification of chemical species was obtained at 4T as a result of the enhanced chemical shift dispersion. This was especially beneficial for the less sensitive nuclei such as $^{31}P$ and $^{13}C$ or the low glutamine signals in proton spectra. The enhanced signal-to-noise at 4T could be traded for a much smaller voxel size in spectroscopic imaging [68] to increase the sensitivity of the metabolites and may therefore improve the accuracy of pathological diagnosis.
From a safety perspective, it was known that human exposure to high magnetic fields could cause sensations such as vertigo and nausea. This was most likely the result of weak eddy currents induced in the inner ear as one moved in the gradient field of the magnet. This sensation was not thought to be physiologically harmful [144, 145]. More and more experimental evidence convinced FDA in 1996 that human exposure to static magnetic fields at or below 4T did not constitute a significant risk to human health in 1996 [183]. As a result, 3T and 4T clinical whole body imaging systems are now available from both Siemens and General Electric. It could be concluded that none of the aforementioned hurdles were insurmountable for imaging or spectroscopy at 4 Tesla. Indeed, it could be concluded that neither technology nor physics was near their inherent limit. The 8 Tesla project was thus inspired to push both MR physics and technology forward in every aspect: magnet design, RF technology, gradient performance, sequence design, RF penetration, RF power limitation, dielectric resonance and clinical applications.

However, the jump in field strength from 4T to 8 T represented a significant leap in technology. At 8 Tesla, the resonant frequency for proton imaging was 340MHz, a frequency approaching the microwave region. Consequently, issues such as susceptibility, dielectric resonances and power deposition were expected to become even more complicated. In addition, the ability to construct a stable magnet, to build suitable RF coils and to assemble all the components so that the system could reach its optimal performance presented another significant challenge. Whether or not the advantages of the higher intrinsic signal to noise at this field strength would be fully realized was not a trivial concern.
<table>
<thead>
<tr>
<th>Site</th>
<th>Field strength</th>
<th>Bore size</th>
<th>Operation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ohio State</td>
<td>8T</td>
<td>80cm</td>
<td>1998</td>
</tr>
<tr>
<td>MGH</td>
<td>7T</td>
<td>90cm</td>
<td>2000</td>
</tr>
<tr>
<td>U of Minnesota</td>
<td>7T</td>
<td>90cm</td>
<td>1999</td>
</tr>
<tr>
<td>U of Illinois</td>
<td>9.4T</td>
<td>80cm</td>
<td>2001</td>
</tr>
</tbody>
</table>

Table 1.1: The availability of the ultra high field whole body systems at different research sites.

Nonetheless, results obtained to date at 8 Tesla once again revealed that none of these problems constituted an insurmountable hurdle to obtaining high quality images at 8 Tesla. The system was successfully designed and assembled [133]. The physical problems, RF penetration [135] and dielectric resonances [86], if they exist at all, were shown not serious enough to impair image quality.

Excellent high resolution anatomical images, approaching a histological level of detail, have been acquired at 8 Tesla [32, 134, 175]. These images were characterized by excellent signal-to-noise and strong $T_2^*$ contrast. Small vessels were more conspicuous at ultra high field than at lower field strength. Presumably, this was because of the significant susceptibility effects of deoxyhemoglobin at higher field. Preliminary measurements of $T_1$ and $T_2$ have been conducted. The contrast within these images appears much different from that obtained for images acquired at lower field strength, partly due to an elongation in $T_1$ and a shortening of $T_2$. In light of the promising results at 8 Tesla, a number of research institutes are in the process of acquiring similar or even higher field strength magnets. Table 1.1 shows the near-term growth of ultra high field whole body systems.
1.3 Organization of the Dissertation

It is the purpose of this dissertation to present initial results of imaging at 8 Tesla. Quantitative comparisons of signal-to-noise at 1.5T and 8T are provided. High-resolution images are presented. Preliminary relaxation time measurements are also reported. Contrast is analyzed qualitatively among conventional sequences. These results can provide useful information on optimization of experimental methods and design. Potential applications can also be derived from these initial results. The organization of this dissertation is as follows.

Chapter 1 provides a brief overview of the important technological events in MR history followed by a discussion of the motivation for going to progressively higher field strengths. The results from high field systems are reviewed. The advantages and concerns of imaging at high field are also discussed.

Chapter 2 reviews the basic physical principles behind MR imaging. This is a foundation for the discussion on signal-to-noise, resolution, relaxation and contrast in later chapters.

Chapter 3 gives a brief overview of the 8 Tesla system and how each individual component is designed and connected to ensure all the components are interfaced properly, thereby maximizing signal-to-noise at 8 Tesla. A description of the materials and methods for the imaging experiments in this dissertation are also presented.

Chapter 4 provides both qualitative and quantitative analysis of the intrinsic signal-to-noise at 8 Tesla. It was believed that the signal-to-noise ratio increases as $B^{7/4}$ [72] for small sample experiments. For human whole body imaging, however, noise is thought to be dominated by the human body, hence some believe that the signal-to-noise ratio could increase by less than $B^{7/4}$. In studies performed at 4T
SNR(signal-to-noise) was found to increase approximately linearly with $B_0$ in human experiments. Therefore, the initial results of this study on intrinsic signal to noise (ISNR) are provided. ISNR is analyzed at 8.0 T relative to 1.5 T on mineral oil, water, chloroform and human brain images.

Chapter 5 presents high resolution anatomical imaging of the rat, feline and human brains at both 1.5 T and 8 Tesla. It is demonstrated that when the signal-to-noise gain is traded for resolution, near histological resolutions can be reached at 8 Tesla. In addition, the resultant images display strong $T_2^*$ contrast. They enable the visualization of the vascular detail with the GRE sequence. The spin echo cat images are observed to be less affected by susceptibility at this field strength. Both susceptibility and chemical shift artifacts can be minimized by selecting proper imaging sequence and acquisition parameters. A good visualization of the cochlea in the temporal lobe of the cat is illustrated as an example.

Chapter 6 examines the mechanisms for relaxation in biological tissue and reports our initial attempts in conducting relaxation time measurements. Relaxation times are essential parameters in optimizing the image contrast and pulse sequence design. Due to the elongation of $T_1$ values and shortening of $T_2$ values at 8 Tesla, contrast at this field strength is different from that obtained at a lower field. The initial report of the measurement and analysis of these relaxation times can act as a guideline for the selection of acquisition parameters in 8 Tesla imaging. The determinants of contrast at ultra high field are examined. The difference in contrast between 1.5T and 8 T as well as the contrast among the images acquired with a number of conventional imaging sequences is compared and discussed.
Chapter 7 presents the conclusion followed by a discussion of the contribution of this dissertation.
CHAPTER 2

THE PHYSICAL PRINCIPLES OF MRI

While magnetic resonance is a quantum mechanical process, it can also be illustrated using classical physics. In this chapter, the classical model is utilized to explain the basics for the MR signal, to introduce the concept of spin relaxation processes and to review the basic principles of image formation.

2.1 The MR Signal

Nuclear Magnetic Resonance (NMR) allows detection of a signal from nuclei that possess a spin angular momentum. The intrinsic spin angular momentum $P$ and the magnetic moment $\mu$ are related by the gyromagnetic ratio as

$$\mu = \gamma P = \gamma h(I(I + 1))^{1/2}$$

where $\gamma$ is the gyromagnetic ratio, a constant that is unique for each nucleus, and $h$ is Planck's constant, $h$, divided by $2\pi$. The nuclear spin quantum number, $I$, is specific for each nucleus and is $1/2$ for the proton. The sensitivity of the MR signal is determined by the strength of the magnetic moment. The proton, $^1H$, having the strongest magnetic moment, is considered the most sensitive nucleus and is most frequently used in MRI.
In the absence of an external magnetic field, the magnetic dipoles are distributed randomly, thus there is no observable net magnetization. However, if they are placed in a magnetic field, some of the dipole moments will become aligned parallel or anti-parallel to \( B_0 \). The spin has lower energy in the parallel state. Thus, the entire system will exhibit a net magnetization. If \( N^+ \) and \( N^- \) correspond to the number of spins that has z components parallel or anti-parallel to \( B_0 \), the difference in the population of these two states in thermal equilibrium can be expressed by Boltzmann distribution.

\[
\frac{N^-}{N^+} = e^{-\Delta E / kT} \tag{2.2}
\]

where \( k \) is the Boltzmann's constant, \( T \) is the absolute temperature in \(^\circ\)K. \( \Delta E \) is the energy separation between the up and down states given by

\[
\Delta E = \gamma \hbar B_0 \tag{2.3}
\]

and \( B_0 \) is the applied static magnetic field. Hence the energy separation is proportional to the applied static field field strength. The population difference can also be influenced by the absolute temperature. At normal physiological temperatures (37\( ^\circ \)C), the population of spins in up and down states is roughly equal. However, at temperature close to absolute zero, most spin would occupy the parallel state, hence more signal will be detected. The magnitude of the magnetization \( M_0 \) is

\[
M_0 = N \hbar^2 \gamma^2 I(I + 1)B_0 / 3kT \tag{2.4}
\]

where \( N \) is the number of spins in the sample. It is important to notice that the net magnetization is a result of the small population difference between the up and the down states and is proportional to the static magnetic field applied.
Since the spins align with the static magnetic field at an angle, the resulting torque causes the magnetic moment to precess around the axis of $B_0$. The frequency of the precession is proportional to the magnitude of the applied field and is denoted Lamar frequency. The Lamar frequency can be expressed as:

$$\omega = \gamma B_0$$

(2.5)

where $\gamma$ is the gyromagnetic ratio and unique for each nucleus. Table 2.1 shows the resonant frequency for biologically important nuclei at 1.5T, 4T and 8T.

At thermal equilibrium, the behavior of the net magnetization can be described by the Bloch Equation:

$$\frac{dM}{dt} = \gamma(M \times B_0)$$

(2.6)

where $M$ is the magnetization vector and $B_0$ is the main magnetic field. This equation states that, at any time, the direction of the movement of the magnetization vector is perpendicular to both $M$ and $B_0$. As a result, the magnetization vector moves in a circular path when there is only an external magnetic field present. This motion resembles that of a top.
2.2 Excitation

The signal formed in MR is usually treated in the reference frame denoted as \((x', y', z')\) which rotates at Larmor frequency \(\omega_0\). In this reference frame, the net spin vector does not move as long as the strength of the magnetic field is equal to \(B_0\). During the MR experiment, the equilibrium is perturbed by an applied \(B_1(x')\) field which lies perpendicular to \(B_0\) and which is generated by the RF transmit coil at frequency \(\omega_0\). The RF irradiation for a certain time period leads to the rotation of the magnetization about \(x'\) to \(-y'\). The flip angle \(\alpha\) is a function of the duration and the amplitude of the RF pulse. It can be described as:

\[
\alpha = \gamma \int_{0}^{\tau} B_1(t) dt
\]  

(2.7)

where \(\tau\) is the duration of the RF pulse. The flip angle is simply a time integral of the applied RF pulse. In general, \(\alpha\) is set to either \(\pi/2\) or \(\pi\). In the rotating frame, assuming the direction of \(B_1\) is along \(x'\), the rotation of the magnetization vector caused by \(B_1\) field can be described by the Bloch Equation[164].

\[
\frac{d\vec{M}}{dt} = \gamma \begin{bmatrix} 0 & 0 & 0 \\ 0 & 0 & B_1 x' \\ 0 & -B_1 x' & 0 \end{bmatrix} \begin{bmatrix} M_{x'} \\ M_{y'} \\ M_{z'} \end{bmatrix}
\]  

(2.8)

Solving this linear coupled differential equation gives.

\[
\begin{bmatrix} M_{x'}(t) \\ M_{y'}(t) \\ M_{z'}(t) \end{bmatrix} = \begin{bmatrix} 1 & 0 & 0 \\ 0 & \cos \alpha & \sin \alpha \\ 0 & -\sin \alpha & \cos \alpha \end{bmatrix} \begin{bmatrix} M_{x'}(0) \\ M_{y'}(0) \\ M_{z'}(0) \end{bmatrix}
\]  

(2.9)

where \(\alpha = \gamma B_1 x' t\) and therefore depends on \(B_1\) field strength and pulse length. Thus moving the magnetization from along \(z'\) to the \(xy'\) plane is seen as a simple rotation.
in the rotating frame. If \( \alpha \) (the nutation angle) is 90°, then the magnetization is along \(-y\) axis after the pulse.

### 2.3 Relaxation

After the pulse, the spin system is no longer in equilibrium. The energy absorbed by the spin system during excitation is then dissipated by the relaxation process after the pulse. Consequently, the MR signal can be detected from a receiver coil oriented perpendicularly to the main magnetic field as the spin emits a radio frequency signal. The magnetization decays transversely and regrows longitudinally. These two relaxation processes are considered approximately exponential. The time constants, \( T_1 \) and \( T_2 \) are used to characterize the longitudinal and transverse relaxation, respectively.

The whole process can be described by the Bloch equation for relaxation:

\[
\frac{d\mathbf{M}}{dt} = \begin{bmatrix}
\frac{-1}{T_2} & 0 & 0 \\
0 & \frac{-1}{T_2} & 0 \\
0 & 0 & \frac{-1}{T_1}
\end{bmatrix} \begin{bmatrix}
M_{x'} \\
M_{y'} \\
M_{z'}
\end{bmatrix} + \begin{bmatrix}
0 \\
0 \\
\frac{M_0}{T_1}
\end{bmatrix}
\] (2.10)

Solving this equation gives:

\[
\begin{bmatrix}
M_{x'}(t) \\
M_{y'}(t) \\
M_{z'}(t)
\end{bmatrix} = \begin{bmatrix}
e^{\frac{-t}{T_2}} & 0 & 0 \\
0 & e^{\frac{-t}{T_2}} & 0 \\
0 & 0 & e^{\frac{-t}{T_1}}
\end{bmatrix} \begin{bmatrix}
M_{x'}(0) \\
M_{y'}(0) \\
M_{z'}(0)
\end{bmatrix} + (1 - e^{\frac{-t}{T_1}}) \begin{bmatrix}
0 \\
0 \\
M_0
\end{bmatrix}
\] (2.11)

Hence it is easy to generalize the Bloch Equation with excitation and relaxation, assuming the RF pulse has an arbitrary phase.

\[
\frac{d\mathbf{M}}{dt} = \begin{bmatrix}
\frac{-1}{T_2} & 0 & -\gamma B_{1y'} \\
0 & \frac{-1}{T_2} & \gamma B_{1x'} \\
\gamma B_{1y'} & -\gamma B_{1x'} & \frac{-1}{T_1}
\end{bmatrix} \begin{bmatrix}
M_{x'} \\
M_{y'} \\
M_{z'}
\end{bmatrix} + \begin{bmatrix}
0 \\
0 \\
\frac{M_0}{T_1}
\end{bmatrix}
\] (2.12)

### 2.4 Spatial Encoding

Spatial information is encoded through a combination of three orthogonal linear gradient fields \( G_x, G_y, G_z \) generated from the X, Y and Z gradient coils, respectively.
The main magnetic field is altered so that the precessional frequency of the spins will become position dependent. The change in frequency or phase can be encoded such that when the signal is processed through Fourier transformation, the different spatial position can be revealed. The gradient field is small relative to the static magnetic field and is usually on the order of 1-3G/cm in a normal imaging experiment. The zero point of the gradient is located at the isocenter of the magnet. Hence no matter what the combinations of the gradients are applied, the magnetic field in the center of the magnet is $B_0$. The following illustration is helped by Keller[91].

### 2.4.1 Slice selection

When the X gradient coil is turned on there is a gradient in the X direction. This gradient determines the thickness of the slice to be imaged and selectively excites the spins that are perpendicular to the direction of the gradient. Hence the resonant frequency of the spins will be:

$$\omega = \gamma (B_0 + G_s z)$$

where $G_s$ is the amplitude of the slice selective gradient, and $z$ is the position along the slice selective gradient from the isocenter.

The RF pulse consists of a band of frequencies. It excites the spins whose resonant frequency lies within that band of frequency. After the RF pulse and the slice select gradient, the signal can be detected from the slice. The gradient amplitude during slice selection, the RF bandwidth and the slice thickness are related as follows.

$$BW_{rf} = \gamma G_s ST$$

where $BW_{rf}$ represents the bandwidth of the RF pulse in Hz, $G_s$ represents the amplitude of slice selective gradient in Guass/cm, $\gamma$ is the gyromagnetic ratio in
Hz/Gauss and ST is the slice thickness in cm. For instance, if a 2ms Gaussian RF pulse is applied, the Fourier transformation of this pulse gives a bandwidth of 1024Hz. If a slice selective gradient strength of 2 Gauss/cm was present during the RF pulse, the slice thickness then is:

\[
\frac{1024}{(4257 \times 2)} = 0.12 \text{ cm}
\]

The center frequency of the RF needs to be changed to excite an off-center slice.

\[
\Delta F = \Delta D \times \frac{BW_{rf}}{ST}
\]  

(2.15)

where \(\Delta D\) is the distance between the center of the slice imaged to the isocenter. For example, to excite a 5cm-thick slice 10cm from the isocenter, the center frequency of the RF pulse is shifted by

\[10 \times \frac{1024}{5} = 2048\text{ Hz}.\]

In this way, it is possible to prescribe any slice desired along the slice direction. If a thinner slice is preferred, it can be achieved through increasing the gradient amplitude or decreasing the RF pulse bandwidth. This translates to an increase in the duration of the RF pulse. Such selections are now built-in functions for most MRI systems.

### 2.4.2 Frequency encoding

The frequency encoding gradient together with phase encoding gradient determines the field of view (FOV). These two gradients are used to encode the spatial information within the excited slice. Proper application of RF pulses and gradients can result in the formation of an echo signal that can be sampled by opening the receiver. When the frequency encoding gradient is on, the signal received in the receiver will be comprised of the different frequencies for the spins. The echo signal in
the acquisition window is the projection of the image along the readout axis. The amplitude of the frequency encoding gradient is related to the receiver bandwidth as follows [91],

\[ BW_{rc} = \gamma G_r FOV_r \]  

(2.16)

where \( BW_{rc} \) is the receiver bandwidth and \( G_r \) is the amplitude the frequency encoding gradient. By the Nyquist theorem,

\[ BW_{rc} = N_r / T \]  

(2.17)

where \( N_r \) is the total points sampled and \( T \) is the sampling time. For instance, if the matrix size is 256 \( \times \) 256 and the receiver is open for 5ms, then the receiver bandwidth is 256/0.005 = 51KHz. Combining equations [2.16] and [2.17], we have.

\[ \gamma G_r FOV_r = N_r / T \]  

(2.18)

Clearly, if the FOV decreases, the readout gradient will increase. Hence to image a very small structure, the requirement on gradient can be very stringent. Rearranging equation [2.18] gives.

\[ FOV_r / N_r = 1 / (T \gamma G_r) \]  

(2.19)

This illustrates that the image resolution in the readout direction can be increased through increasing \( G_r \) or by increasing the acquisition time.

2.4.3 Phase encoding

The phase encoding gradient is applied before the acquisition window is open. Hence it can not change the frequency of the detected signal. However, the change
in the phase information is preserved. The phase change induced depends on the amplitude, duration of the gradient and the position of the spins along phase encode direction. Once the spins are placed in the transverse plane, the incremental phase change during each phase encoding step can be described as,

$$\Delta \phi = 2\pi \gamma \int \frac{G_p}{N_p} dt = \frac{2\pi \gamma G_p T_p}{N_p} \quad (2.20)$$

where \(N_p\) is the number of phase encoding steps, \(T_p\) is the duration of the phase encoding gradient and \(G_p\) is the maximum amplitude of the phase encoding gradient. Taking into consideration the sampling theory, the phase change caused by each incremental change in the phase encoding gradient must be between \((-\pi, \pi)\). The following equation is obtained,

$$\gamma G_p FOV_p T_p = N_p \quad (2.21)$$

where \(FOV_p\) is the field of view in the phase encoding dimension. The pixel size is therefore,

$$FOV_p/N_p = 1/(\gamma G_p T_p) \quad (2.22)$$

Thus, the resolution along phase encoding direction can be improved by increasing the strength of the phase encoding gradient or by increasing the duration of the phase encoding gradient.

### 2.5 Image Formation

At any point in time, the resonant frequency of the spin in three dimensional space in the presence of the three orthogonal gradients is,

$$\omega(x, y, z) = \gamma(xG_x + yG_y + zG_z) \quad (2.23)$$
where \( x, y, z \) are the position in three-dimensional space, and \( G_x, G_y \) and \( G_z \) are the three orthogonal gradients. In a typical two-dimensional MR experiment, a slice of a certain thickness perpendicular to the static magnetic field is selected in the presence of the slice select gradient and the selective RF pulse. The signal from the transverse magnetization of this excited slice at position \((x,y)\) as a function of time can be described as.

\[
S(t) = \int \int \rho(x, y) e^{i \int \omega(x, y, t) dt} dx dy
\]  

(2.24)

where \( \rho(x, y) \) is the magnetization from position \((x,y)\) within the excited slice, \( \omega(x, y, t) \) is the local processional frequency of the magnetization at position \((x,y)\) at time \( t \). Considering the \( T_1 \) and \( T_2 \) relaxation processes, the above equation becomes,

\[
S(t) = \int \int \rho(x, y) e^{i \int \omega(x, y, t) dt} dx dy (1 - e^{-TR/T_1}) e^{-TE/T_2}
\]

(2.25)

The resulting signal is then encoded under the influence of the frequency encoding gradient and phase encoding gradient,

\[
S(t) = \int \int \rho(x, y) e^{i \gamma (xG_xt_x + yG_yt_y)} dx dy (1 - e^{-TR/T_1}) e^{-TE/T_2}
\]

(2.26)

The two dimensions on the image are the readout direction and phase encoding direction, corresponding to the two encoding gradients. The pixel size is determined by the field of view and matrix size. The signals in each pixel are summed. On the image, signal intensity within each pixel is expressed through the brightness of that pixel.
CHAPTER 3

SCANNER ASSEMBLY AND EXPERIMENTAL METHODS

3.1 The 8 Tesla Whole Body System

The driving forces to higher magnetic field strengths include enhanced intrinsic signal-to-noise ratio, increased susceptibility contrast and increased chemical shift dispersion. However, in order to achieve the desired signal-to-noise and resolution, the system needs to be carefully designed and assembled to reach its optimal performance. Otherwise the intrinsic signal-to-noise advantages at this field strength might be compromised completely. Since ultra high field systems are not available commercially at present, the 8 Tesla system offers a unique opportunity to reexamine the physical and technical challenges imposed by the 4T systems. This chapter briefly reviews the key components of the 8 Tesla system and presents the materials and methods for the imaging experiments carried out in this dissertation. For more detailed design and assembly information on the 8T system, please refer to the presentation of Robitaille et. al.[133]
3.1.1 The 8 Tesla magnet

A stable magnet with excellent field homogeneity is crucial to the success of imaging and spectroscopy. Homogeneity requirements become even more stringent with higher field strength. The risks brought by the increased force on the windings of the magnet, including stronger loop forces and associated risks of quenching, is higher with larger magnet. In addition, the fringe field becomes stronger. This increased fringe field leads to a requirement for more extensive magnetic shielding.

The 8 Tesla magnet at the Ohio State University (OSU) was manufactured by Magnex Scientific Limited (Abingdon, England). It is a superconducting magnet made of niobium titanium operating at liquid Helium temperature (4° K). The Helium reservoir contains 1600 liter Helium with a boil off rate specified at 0.171/hr. The field homogeneity is better than ±2.5ppm over a 40cm diameter spherical volume subject to a minor drift of less than 0.015ppm/h. A total current of 200 A is required to drive the field up to 8 Tesla. The total inductance of the coils is 4155H. To confine the fringe field, 200 tons of steel were utilized to shield the magnet. Immediately outside the magnet room, the stray field is approximately 50 Gauss, while it is about 10 Gauss at the operator console. Shimming is achieved by a set of superconducting shim coils for lower order correction and passive shim trays for high order correction.

3.1.2 Gradient coil

Gradient coils are used to produce the three linear orthogonal gradient fields. Gradient strength, gradient linearity and rise/fall time are the parameters to characterize the gradient quality. Failure to meet the desired standards may cause image
distortion and inability to reach the expected resolution. The demand on the gradient design at ultra high field strength can be challenging because of the increased mechanical torque, acoustic noise and heating of the coil. Due to the short $T_2$ or $T_2^*$ values at 8 Tesla, gradient strengths and rise times need to be improved in order to apply short TE values. This requirement can be even more stringent for fast imaging sequences at ultra high field. Lowering coil inductance helps to lower rise times at the expense of weaker gradient strength. Actively shielding the gradient helps to reduce the induction of eddy currents within the gradient formers.

To date, only a head gradient insert has been used in the imaging experiment. An actively shielded asymmetric torque free gradient coil design [3] is utilized. To reduce the acoustic noise, a thicker former is employed. The gradient coils provide a rise time of $415\mu s$ and a maximal gradient strength of $59.3\,\text{mT/m}$ for the X and Y gradients channels. Similarly, a $200\mu s$ rise time was achieved for a gradient of $68\,\text{mT/m}$ on the Z gradient channel. This gradient amplitude and rise time enabled many fast imaging sequences at 8 Tesla. The head insert gradient has a linearity of -5.2 to 3.5% over a 22cm diameter spherical volume.

3.1.3 Gradient amplifiers and RF amplifiers

A good gradient amplifier system is essential to the gradient performance, including the gradient strength and speed. To implement fast imaging sequences such as Echo Planar Imaging (EPI), powerful gradient amplifiers are required. High power RF amplifiers with short rise times are required in order to deliver the required RF power.
On the 8 Tesla system, the gradients are driven by Techron 8745 amplifiers (Crown International, Elkhart, IN). The current output linearity for these amplifiers is better than 15mA. This system is also able to deliver 320V/400A on each gradient axis. Eight high power RF amplifiers surround the 8 Tesla system. Four high band RF amplifiers (245MHz-345 MHz) are available for imaging and spectroscopy with $^1H$. They are characterized with a 63dB gain and with a 2.5 kW power output with rise times of less than 200ns. Four low band RF amplifiers (10MHz-140 MHz) are also available for $^{23}Na$ and $^{31}P$ experiments. They provide 60dB gain, 2kW power output with a rise time of less than 500ns.

3.1.4 The RF front end

The RF front end includes the preamplifier and TR switch. These components are crucial for the determination of the noise figure of the system because they constitute the first stage of amplification of the signal. Hence, a low insertion loss non-magnetic T/R switch and minimal noise figure narrow-band preamplifiers are desired.

In the 8 Tesla system, the T/R switch has a $10\mu$s switching speed with 2 kW peak power. It has a 0.2 dB insertion loss and its isolation is greater than 63dB. Instead of using the standard Bruker broad band preamplifiers, non-magnetic narrow-band GaAs FET pre-amplifiers with a noise figure of less than 0.5dB (Advanced Receiver Research, Harwinton, CT) were utilized. Four preamplifiers were available for each of $^1H$, $^{31}P$ and $^{23}Na$ nuclei. This front-end configuration provides a maximum signal-to-noise.
3.1.5 The RF coil

Volume coil

The radio frequency (RF) coil directly excites and receives signals from the spins. Therefore, it must be properly optimized in order to fully utilize the signal-to-noise advantage of high field systems. For a whole body MR system at any field strength, the requirement for an efficient RF coil involves high sensitivity, low losses and uniform $B_1$ field distribution. However, this is much easier to achieve at low field than at high field strength ($> 3$T) since the size of the coil is only a small fraction of a wavelength at low field as compared to a wavelength at high field.

The birdcage [67] has been a highly successful transmit/receive RF head coil design at 1.5 T. characterized by high $B_1$ field homogeneity, high signal-to-noise ratios and good quality factors. The birdcage coil can be easily understood with a quasi-static circuit design concept and can be constructed with conductive struts in conjunction with capacitors on a cylindrical former. The capacitors can be evenly distributed on the end rings (high pass) or on each conductive strut (low pass). A standing wave of the desired mode is set up at the resonant frequency along the end rings. Each vertical strut, in connection to the end ring, has a constant phase shift of $2\pi/N$, where $N$ is the number of struts. The uniform current distribution on the struts enables the generation of a uniform transverse $B_1$ field. The higher the number of struts, the better the simulation of a continuous sinusoidal current distribution on the surface of the coil and thus a more homogeneous $B_1$ field. The $B_1$ homogeneity can also be enhanced by increasing the length of the coil. The rotational symmetry of the coil enables excitation and reception in quadrature and, thus, the production of a circular polarized $B_1$ field. Besides optimizing the $B_1$ field, quadrature excitation also
provides a \( \sqrt{2} \) gain in signal-to-noise and one half of the required power to achieve 90° excitation. However, this is under the assumption of perfect isolation between the two channels. Otherwise the coupling between the two channels will result in a degradation of the theoretically achievable signal to noise gain [156].

At low frequency, the current distribution for the birdcage coil is close to uniform on all the struts, therefore the \( B_1 \) field distribution is uniform. As the RF frequency increases (> 3T), however, the size of the conductive strut becomes comparable to the RF wavelength, and the coil resembles more of a radiating antenna. A standing wave will be set up on the struts, the current distribution is no longer uniform and the phase shift for each strut becomes even more complicated. The radiative loss of the coil increases dramatically with the frequency. The decreased skin depth will increase the resistance of the conductor at high field as well. It has been calculated [74] that with a typical head coil and a spherical physiological sample, the coil loss is approximately 20% of sample loss at 63MHz, whereas at 150MHz, the two losses are approximately equal. In the presence of a head at 200MHz, the current distribution is significantly distorted due to the dielectric interaction between the coil and the head [77].

However, with careful design and implementation, a 3T quadrature driven balanced birdcage coil (diameter = 17.5cm) for knee imaging demonstrated a 2.7 times greater SNR than a linear coil at 1.5T and good structural detail of cartilage [113]. A new hybrid shielded birdcage (a mixture of high pass and low pass) design has been proposed for head imaging at 170MHz [13] with an optimized coil diameter, coil length, balun and shield spacing. This hybrid design is able to decrease the conductor
length on the struts to a small fraction of a wavelength, hence minimizing the wavelength effect at high frequency. A configuration of a birdcage transmit and surface coil receive system has been demonstrated to facilitate the use of the phase array and surface coil. This configuration resulted in a five-fold higher SNR and CNR than the transmit/receive birdcage at 4T [13].

Since the shape of most body parts resembles an ellipse, elliptical birdcage coils have been found to have a better filling factor than the circular coils and thus an improvement in signal-to-noise [102, 104]. However, due to the inherent asymmetry of the ellipse, a sinusoidal current distribution as used in the standard birdcage coil will not generate a homogeneous $B_1$. Hence, the current distribution needs to be numerically optimized to find optimal strut locations. It may also be necessary to adjust the phase of the excitation pulse to obtain a homogeneous $B_1$ field distribution. Nonetheless, an optimized linear elliptical birdcage with a circular shield is reported to have 55% higher SNR than a linear circular birdcage coil at 3 Tesla [104].

However, one drawback of the birdcage coil design is that it suffers from a strong coupling between the coil and the sample due to the utilization of discrete elements. As the frequency increases, the radiative losses from the coil, dielectric losses as a result of coil/patient coupling and the conductive losses from the conductive nature of the human body all increase dramatically. The coil/sample interactions also become significant. This is reflected in a substantial degradation of Q value when such coils are loaded with samples. Shielding appears to be necessary to reduce the radiative losses for the birdcage and to some extent, could be used to obtain a more homogeneous $B_1$ field by optimizing the induced current on the shield flowing in the opposite direction [178].
The free element design [167] and the TEM transmission line design [159] are other successful volume coil designs proposed for high field imaging. They were designed in an attempt to minimize the radiative loss of the coil and the coupling between the head and the coil which occurs with conventional birdcage designs. These coils utilize a more distributed circuit design approach comprising the transmission line and cavity concept instead of lumped elements.

The free element resonator [167] consists of a circular array of inductively coupled resonant elements surrounded by a shield. Each resonant element is a rectangular resonant circuit, the tuning of which is achieved by adjusting the value of a variable capacitor. Tuning of the coil is then achieved by rotating these inductively coupled resonant elements along their individual axes uniformly and therefore changing their mutual inductance. In the presence of an asymmetric load such as a head, tuning of each resonant element individually is necessary to compensate for the non-uniform $B_1$. A nearly four fold higher loaded Q value is observed with this coil compared to the birdcage design at 170MHz.

The TEM resonator [159] utilizes multiple resonant elements evenly distributed around two end rings that in turn are connected to a shielded cavity wall. Each resonant element consists of a central conductor inserted into a dielectric tube. Coarse tuning for each resonant element is achieved by sliding the central conductor and fine tuning is achieved by adjusting the variable capacitor. The wave travels along the struts and the field surrounding the struts are coupled to each other. There are $N/2 + 1$ modes in the resonator, with mode 1, the TEM mode, generating the desired homogeneous transverse homogeneous $B_1$. The TEM mode produces a homogeneous $B_1$ field distribution for the empty coil. However, when loaded with the human
head, the TEM mode changes and mixes with other hybrid modes which are not homogeneous [184]. Since the only discrete elements in this design are the matching capacitors, the distributed approach minimizes the losses due to the coupling. It is relatively easy to transform the TEM resonator into a doubly tuned RF coil by tuning the even and odd struts to two differing frequencies. The extension of this approach has been successfully applied to the design of a body coil at 4.1T for cardiac imaging [163].

At 8 Tesla, the resonance frequency is approaching the microwave region. The wavelength effect is becoming more conspicuous. The following table provides an illustration of how the wavelength changes as a function of field strength and medium. A dielectric constant of 1 is assumed in the air, 80 in water and 50 in the human head [182], respectively. The wavelength in the human head is 66.4 cm at 1.5 Tesla whereas the wavelength is only 12.4 cm at 8 Tesla.

<table>
<thead>
<tr>
<th>$\omega_0$ (MHz)</th>
<th>$\lambda$ in air (cm)</th>
<th>$\lambda$ in water (cm)</th>
<th>$\lambda$ in head (cm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.5T</td>
<td>63.8</td>
<td>470</td>
<td>52.5</td>
</tr>
<tr>
<td>8T</td>
<td>340.6</td>
<td>88</td>
<td>9.84</td>
</tr>
</tbody>
</table>

Table 3.1: Wavelength as a function of frequency and medium

A typical RF head coil has a diameter of 30 cm while a body coil has a diameter of 60 cm. At 8 Tesla, the coil dimension becomes comparable to the RF wavelength. The birdcage design is not suitable at 8 Tesla since the value of the capacitance needed is similar to the stray capacitance. A distributed transmission line design is more appropriate. As a result, since the TEM resonator is relatively easy to construct and

29
since it has a large tuning range. Its design was selected as the template for the 8 Tesla coil. The detailed description of the construction of this coil has been presented [136]. A picture of this coil is displayed in figure 3.1. It was designed to operate in quadrature.

Precise machining was found to be critical to the performance of the TEM resonator. Inaccuracy in the position of the struts, even if only a few millimeters, causes the resonant peak to split. This problem is especially pronounced for small coils or for coils with more struts. The distance between the struts and the shield determines the separation of the resonance modes. The TEM resonator is tuned such that the
I and Q channels are identical. This is a time consuming process and usually has to be performed in an iterative fashion. Most of magnetic field energy in the TEM resonator resides in the space between the struts and the shield. The magnetic fields in the center are relatively uniform and weak in amplitude for the empty coil [12]. However, simulations have demonstrated that the $B_1$ field distribution becomes inhomogeneous when the coil is loaded at 8 Tesla due to the coupling between the RF coil and the human head [78]. In addition, because the TEM resonator is so sensitive to its load at high field, different head sizes were observed to have quite different loading effects on the coil. Typically, the tuning of the TEM resonator has to be adjusted for each subject in order to obtain an optimum tuning and matching.

Two sizes of TEM resonators have been utilized in the imaging experiments described in this dissertation. The larger coil has an outer diameter of 34.6cm and an inner diameter of 23.5cm. This resonator is used for human head imaging as well as for large phantoms. Since the head is an asymmetric object, it is usually harder to tune than phantom samples. The smaller coil (outer diameter = 18cm, inner diameter = 12cm) was optimized for small animal and extremity imaging. High resolution cat brain images and wrist images were obtained from this coil.

**Surface coils**

The first surface coil was developed by Ackerman [6] who utilized a single turn flat loop as both a transmit and receive coil to study $^{31}P$ metabolism. Since then, the surface coil has been widely used in imaging and spectroscopy. This is a result of its higher sensitivity compared to the volume coil since the surface coil receives noise from only a small region of interest, which also contributes to the signal. However, because of its non-uniform $B_1$ field, the surface coil is used usually as a receive only coil in
conjunction with a body coil for transmission. In addition, the lack of symmetry and the stray capacitance of the surface coil lead to a non-uniform current distribution and to strong coupling with the sample for this coil. Utilizing a more distributed capacitance and balanced matching have been proven to improve the sensitivity of the surface coil. Such approaches also act to reduce coupling to the sample.

At a field strength greater than 4 Tesla, a body coil is currently not available. As mentioned above, since the dimension of the body coil is also on the order of the wavelength, the strong coupling between the coil and the body will result in a distorted $B_1$ field. Another reason for the lack of a body coil at high field is the possibility of violating the specific absorption rate (SAR), since large RF coils require more RF power.

By using a surface coil as a transmit/receive coil, one is able to overcome many of the limitations of the absent body coil. Furthermore, adiabatic excitation [16] can be used to generate a homogeneous excitation with such coils and therefore can provide an alternate means of achieving a high signal-to-noise throughout the region of interest. However, there are problems associated with the design of surface coils at high field. In a manner that is similar to the volume coil, a circuit design that is based on lump elements will suffer from non-uniform current and $B_1$ field distributions. Even a more distributed circuit will experience significant radiation loss since coil radiation loss is a function of $\omega^4$ [161]. In addition, when the surface coil is loaded, dielectric loss and conductive loss will also be significant as a result of capacitive coupling between the sample and the coil. Radiation losses can be minimized using a properly designed RF shield and a transmission line as a reactance and conductance element in the circuit. However, the distance between the shield and the coil affects
the $B_1$ field distribution and the coil $Q$. Furthermore, reducing the radiation loss by employing a shield may unfavorably increase the dielectric loss [119].

The idea of using a shielded transmission line design for a surface coil was proposed by Roschmann in 1988 [140]. He used solid-sheath cables to form a bipartite loop. This configuration decreased dielectric losses in the patients. This design was further refined by Vaughan [161] by using a hybrid $\lambda/4$ distributed circuit as a building block to construct a symmetrical circuit such that the electric field is minimized and the magnetic field is maximized along the virtual ground plane in the center of the coil. However, no images have been acquired with this coil. Recently, shielded quadrature surface coils and half volume cavity resonators have been proposed for imaging and spectroscopy at 300 MHz [7, 8] to minimize effectively the radiation loss at ultra high frequency. A similar performance was observed between the shielded coil and cavity resonator design.

Once the surface coil is successfully designed and constructed, a head coil transmit/surface coil receive system can increase further the available SNR [13]. Surface coils used in the imaging experiment at 8 Tesla have been confined to less than 50mm. They were successfully built by using lower resistance silver wire with distributed capacitance. The tuning and matching capacitors were soldered in close contact with the loop. These coils were used in rat brain imaging and phantom imaging and spectroscopy at 340 MHz. An effort was also made to construct a human head size surface coil. While not yet fully successful, this has provided a worthwhile experience. This design and testing could be used as guidance for future coil development. The larger surface coil utilized a microwave substrate layered with double-sided copper. The dielectric material was either Teflon ($\varepsilon = 2$) or Duroid ($\varepsilon = 10.2$). After the coil
was machined to a circular shape of desired size, the copper was etched selectively on both sides so that the resulting coil has an overlapped area of copper and a gap. With this design, tremendous coupling between the coil and the sample was observed. This was reflected by the 7 or 8 MHz frequency shifts and the large degradation of Q values observed when the coil was loaded. Shielding the coil was also implemented. However, a distortion of $B_1$ field was experienced and the frequency response became indeterminate. This was probably due to an incorrect shielding distance and to the shape of the shield, which needs to be improved for future development.

### 3.1.6 Image acquisition and processing

The 8 Tesla 80cm magnet was interfaced to a Bruker AVANCE console (Billerica, MA). All images presented in this dissertation are acquired from the Bruker console. It is equipped with 4 transmitters and 4 receivers. The graphical user interface in Paravision Software allows for interactive acquisition and processing. This spectrometer is able to support basic acquisition sequences such as the conventional spin echo, gradient echo, ultra-fast imaging, 3D imaging, etc. In addition to displaying and processing images on the Bruker console, the raw data (FIDs) were also retrieved through a network connection to a Linux environment to be processed and analyzed for the signal-to-noise, relaxation time and contrast studies.

### 3.2 Subject

To guarantee the safety of the human subject, the potential risks regarding exposure to a high magnetic field must be considered even though there is no defined safety limit of static field strength. Based on the experimental data available at static field strengths of 3T-4.23 T [144, 145], it can be concluded that human field exposure
up to 4T does not constitute a health hazard. The FDA has recently revised its regulation on these safety thresholds and has designated all field strengths below 4 T as nonsignificant risk exposures[184].

At 8 Tesla, the effects on static field exposure to normal human volunteers and to swine were studied [87]. Results showed no statistically significant changes in cardiac output, myocardial contractility and concentration of body electrolytes in swine. Cognitive, ECG and physiological studies on 10 human subjects prior to and after an exposure of one hour in the isocenter in the magnet reveals that the static field does not produce adverse effects on physiological function and cognitive performance in this setting.

Radio frequency power requirements were predicted to increase with the square of the field strength in magnetic resonance [73]. Experimental data at 4T confirmed this prediction [166]. Given known RF power requirements at 1.5 Tesla, the FDA regulation on SAR levels could be violated easily at 8 Tesla. The SAR is classically thought to be related directly to the conductivity and the electric field within tissue and to the way in which the heat is transferred. It is usually associated with tissue heating and tends to be higher near the area where there is high susceptibility. Even though in a recent High Field Engineering workshop, “the power required for a 90° pulse at the origin is less than that predicted by the traditional formula”[75], it seems high power is still generally expected at 8 Tesla. However, initial results at OSU showed that the power to reach the 90° excitation is significantly lower than expected. It takes only 90W to achieve 90° excitation for a 5mm thick slice with 4ms two lobe Sinc [137]. Later, spin echo images and RARE images were successfully acquired at 8 Tesla without SAR violation [2, 88].
3.2.1 Human

All human subjects participating in the imaging experiments in this dissertation were normal healthy volunteers in an age range from 22 to 50. They were recruited from physicians, professors and medical students at The Ohio State University. The subjects were given a tour at the facility followed by explanation of the imaging experiment. All had been given informed consent under the guidelines of The Ohio State University institutional review board. For each subject, basic vital signs (heart rate, ECG, temperature and blood pressure) were monitored prior to and following each imaging session. The subjects were in communication with the staff during each imaging session. For each subject, the RF coil was tuned and matched outside the magnet. All studies utilized a TEM (transverse electromagnetic coil) resonator. The subjects were asked to maintain their positions in the tuned coil as best as they could relative to that on the bench outside the magnet.

3.2.2 Animals

OSU’s institutional animal care and use committee approved all studies involved in this dissertation. Normal healthy animals including cats, dogs and rats were studied at 8 Tesla. Rats implanted with lymphatic tumors were also studied at 1.5T. These animals were anesthetized with ketamine and/or maintained on isofloraine during the entire imaging session. An optimized small TEM resonator [174] was specially designed and built for the cat study. Rats were imaged with a custom designed receive-only surface coil at 1.5T, and with a transmit/receive surface coil at 8 T. The RF coils used to study these animals were tuned and matched outside the magnet, then the resonance was confirmed once the animals were at the isocenter of the field.
3.3 Sequence

During the initial stage of ultra high field imaging, the Gradient Echo and Spin Echo sequences proved to be methods of choice because of their well understood and well defined contrast at lower field strength. In the Bruker Paravision software, they can also be integrated with many other optional modules, such as inversion recovery, fat saturation, etc. As such, most of the images are acquired with gradient echo sequence (GRE), spin echo sequence (SE) and their derivatives.

3.3.1 The GRE sequence

Unlike the case of spin echo sequence, in which a pair of RF pulses are needed, gradient echo can be formed by a single RF pulse in combination with gradient reversals. As such, the phase shift due to the static field inhomogeneity can not be corrected. Hence the images are usually characterized by $T_2^*$ contrast. There are many versions of gradient recalled echo sequence. Figure 3.2 shows a representative diagram of this sequence on the Bruker console.

In this gradient echo sequence, a slice is selected by applying an RF pulse with an arbitrary flip angle in the presence of a slice select gradient. During this period, the spins acquired different phase along the selected slice. Therefore a rephaser, a gradient with an opposite sign and one half of the area of the slice selected gradient, is applied to unwind the phase shift so that identical phase can be achieved within the selected slice. The echo signal can be maximized in this fashion. Likewise, the spins in the transverse plane are dephased by a negative gradient before the receiver is open. The area under this gradient is one half the area of the frequency encoding gradient during signal acquisition. The spins are in phase in the center of the acquisition window and
maximum echo can be observed. Phase encoding is achieved by incrementing the phase encoding gradient strength during each application of the sequence. To reduce the echo time, thereby minimizing the susceptibility artifacts, a combination of the three orthogonal gradients can be applied simultaneously when the gradients affect only the phase of the spins. However, when the RF pulse is applied or the acquisition window is open, no other gradients can be applied. At 8 Tesla, a minimum TE of 6 ms can be achieved in this manner. If a small flip angle is used, most of the longitudinal magnetization remains undisturbed, and therefore little saturation occurs. For short TR sequences, a stronger signal should be observed by using Ernst angle $\alpha$,

$$\cos \alpha = e^{-TR/T_1}$$

(3.1)
This is the precise principle of FLASH (Fast Low Angle Shot) except that the gradient application in FLASH provides spoiling of residual transverse magnetization. This sequence can usually be completed within several hundred milliseconds. Varying the flip angle also enables the contrast manipulation.

The three-dimensional Gradient Echo Sequence was also used at 8 Tesla to increase the signal-to-noise ratio and spatial resolution. With 2D imaging, there are potential cross talk problems between slices resulting from the non-ideal shape or truncation of the RF pulse. It is possible to overcome this problem in part by prescribing slices in an interleaved fashion or by leaving a sufficient spacing between the slices. However, these problems do not exist in 3D imaging since a slab of spins is selected.

A typical 3D GRE sequence diagram is shown in Figure 3.3. The RF pulse is implemented with an adiabatic half passage in order to achieve a homogeneous excitation with a surface coil.

3.3.2 SE sequence

The spin echo sequence is similar to the gradient echo sequence except that a 180° refocusing pulse is used instead of a gradient reversal. A typical spin echo sequence is displayed in Figure 3.4. The function of the rephaser gradient along the slice selection axis and the dephaser gradient along the frequency encoding axis are the same as in the GRE sequence. Since the 180° pulse reverses the phase of the spins, the two gradients along the frequency selection axis are of the same sign. The rewinding gradient along the phase encoding direction acts to counteract the effect of the phase encode gradient, thereby ensuring that the transverse magnetization is completely dephased after acquisition.
Unlike gradient echo sequence, spin echo sequence is invariant to field inhomogeneity. In the presence of a short $T_2$ values and even shorter $T_2^*$. spin echo images can be readily differentiated from gradient echo images at 8 Tesla based on contrast and susceptibility artifacts. On almost every gradient echo head image at 8 Tesla, most of the signal is lost near the skull base, while in the spin echo images, more of this signal is recovered.

With long $T_2$ values, RARE (Rapid Imaging with Relaxation), also named FSE (Fast Spin Echo), is useful in imaging tissues. It offers good $T_2$ contrast with short acquisition times. It is therefore a useful sequence for ultra high field imaging.
Figure 3.4: A representative SE sequence for the Bruker console
3.3.3 Evaluation of the sequences

Contrast appears to be significantly better on the gradient echo images than for the spin echo images. This is simply because there are more variables to manipulate within the gradient echo sequence, most notably, the flip angle. In addition, while susceptibility causes image degradation and loss of signal in the skull base or cerebellum, it also can provide inherent contrast. FLASH offers fast imaging with relatively high signal-to-noise. However, using the Ernst angle does not necessarily guarantee the optimum contrast in FLASH. As seen on the FLASH images, the gray/white matter differentiation is not optimal. Nonetheless, unless a 90° excitation is necessary, such as in the $T_1$ measurement with the progressive saturation method, it is often preferable to utilize a low flip angle RF pulse in order to decrease partial saturation effects and RF power requirement. $T_2^*$ contrast can be enhanced by lengthening the TE value, while saturation effects can be adjusted by changing the flip angle and the TR value. Intra-voxel dephasing can be minimized by increasing resolution, thereby reducing voxel size and shortening the TE value[172].
CHAPTER 4

INTRINSIC SIGNAL TO NOISE AT ULTRA HIGH FIELD

4.1 Introduction

Based on equations [2.2], [2.3] and [2.4], the separation of energy between the two energy states is proportional to $B_0$, and hence the population difference is a linear function of $B_0$. The net magnetization per unit volume is therefore proportional to $B_0$, providing the temperature of the system does not change. In addition, according to Faraday's law of electromagnetic induction, the induced signal is proportional to the rate of change of the magnetic flux, therefore the induced MR signal is proportional to the precessional frequency. Omitting the details, assuming the $B_1$ field is homogeneous, the signal in the presence of an RF pulse and relaxation can be shown as [72]:

$$S(t) \propto \omega_0 B_1 M_0 \cos(\omega t) \exp(-t/T_2)$$

(4.1)

where $\omega_0$ is Larmor frequency, $B_1$ is the magnetic field generated by unit current in the transmit coil, $M_0$ is the net magnetization, $T_2$ represents the transverse relaxation time. It can be readily observed that the signal is proportional to $B_0^2$ and $B_1$. In MR, noise is a result of random motion of electrons and is generated from within the
patient body. RF coil and/or the receiver chain. The RMS noise intensity can be expressed as,

\[ N = \sqrt{k\Delta fRT} \]  

where \( k \) is the Boltzmann constant, \( \Delta f \) is the receiver bandwidth, \( R \) is the effective resistance of the coil and \( T \) is the absolute temperature.

While the noise is dominated by the coil and receiver chain for small samples or at low field strength, from mid to high field on the whole body scanner, noise becomes dominated by the patient body. This implies that although the SNR can be enhanced by cooling the RF coil, preamplifier and receiver for small samples, the same method will not apply for the whole body scanner at high field.

From a classical standpoint, the noise observed at the coil can be separated into three sources\[74\]: the radiative loss (\( R_c \)) due to coil resistance, dielectric loss due to the capacitive coupling\( (R_c) \) between the coil and the patient and inductive loss \( (R_e) \) as a result of eddy currents within the conductive patient. The three losses all increase substantially with the field strength. Hence it is essential to minimize the radiative loss in RF coil designs at 340MHz.

The signal to noise ratio increases as \( B^{7/4} \) \[72\] for small sample experiments when the coil resistance dominates the losses. For human whole body imaging, when the noise is dominated by the human body, the signal to noise ratio was thought to increase only linearly with field strength\[72, 166\]. In addition, power was predicted to increase with the square of the field strength \[74\]. These predictions have been compared with experimental data and were found to be in agreement at fields up to 4T. For example, an 8-10 fold increase in the power requirement for a 90° excitation was reported in human brain, heart and cartilage at 4.0 Tesla [166]. Signal to noise
measurements also revealed that the intrinsic signal to noise ratio (ISNR) has an approximately linear dependence on field strength, if not lower. As such, it appears that at least up to 4.0 Tesla, the dependence between signal to noise, field strength and power (ISNR=\(B_o^2/\sqrt{P}\)) does indeed hold.

Signal to noise also depends on the selection of sequences and the choice of imaging parameters, image resolution, the effect of relaxation times and system noise figure. Since signal to noise is dependent on so many factors, the concept of an intrinsic signal to noise ratio [46] was formulated in an attempt to characterize SNR in the absence of \(T_1, T_2, \) system noise figure, and the choice of the sequence and imaging parameters. Intrinsic signal to noise was described by Elderstein as,

\[
pixel SNR = \psi_s \rho V \sqrt{N T_2 (1 - e^{-T_R/T_1})} e^{-T_E/T_2}
\]

where \(\psi_s\) represents the measured SNR including the electrical loss in the coil and subject and the effect of an imperfect preamplifier. \(T_s\) is the sampling time and is equal to \(1/\text{bandwidth}\). \(N\) is the number of excitation, \(\rho\) is the proton density of the tissue, \(V\) is the voxel volume. \(T_R\) is the repetition time and \(T_E\) is the echo time. \(T_1\) and \(T_2\) are the longitudinal and transverse relaxation times, respectively. It can also be shown that

\[
\psi_I = \frac{\psi_s \left[10^{NF/20}\right]}{\left[1 - \frac{Q_L}{Q_E}\right]^{1/2}}
\]

where \(NF\) is the noise figure in decibles. \(\psi_I\) is the intrinsic SNR, \(Q_L\) is the coil loaded \(Q , \) \(Q_E\) is the coil unloaded \(Q . \) These two equations were formulated for the saturation recovery sequence, but they can be applied to gradient echo sequences when \(T_2\) is substituted with \(T_2^*\). Based on these two equations, it is possible to perform
an intrinsic signal to noise comparison at 1.5T and 8 Tesla given a knowledge of the SNR on the images and all the other parameters in these two equations.

Despite many concerns at ultra high field strength mention in Chapter 1, excellent results have been obtained. In particular, the RF power was found to be lower than expected [137] with a 90 excitation achieved using only 90W for a 5mm thick slice with 4ms-two-lobe-Sinc pulse. RF penetration and dielectric resonance [86, 135], if they exist at all, were not serious enough to impair the image quality.

Once the 8 Tesla scanner became operational, the OSU group immediately reported our signal to noise comparison on Gradient echo images [4], FLASH [31] images and the high resolution images at 8 Tesla [134]. The measurements yielded at least a 10-fold increase in signal to noise than at 1.5T. Unfortunately, imaging parameters for signal to noise comparison at 1.5T and 8 T in these studies were not identical. Hence the effects of $T_1$ and $T_2$ were not fully taken into account [4, 31, 134]. In addition, these studies were performed on scanners with different noise figures. Moreover, a TEM resonator was utilized at 8 Tesla measurements while a GE birdcage coil was utilized for 1.5T measurements. With so many different variables, it was difficult to evaluate properly the ISNR. Therefore, the study described below was undertaken to obtain a more accurate and meaningful comparison of intrinsic signal to noise at 8 Tesla versus 1.5 Tesla.

### 4.2 Materials and Methods

At 1.5T, all phantoms and human brain images were acquired from a GE Signa commercial scanner (Milwaukee, WI). At 8 Tesla, images were acquired from a whole
Figure 4.1: A schematic diagram on noise figure test

body scanner previously described in Chapter 3. A simple gradient echo sequence was used for all image acquisitions.

The noise figure measurement of the receiver chain on the Bruker AVANCE console was performed by examining the noise performance at both room temperature and liquid nitrogen temperature using a liquid nitrogen dip test (Figure 4.1). The acquisition data points equaled to 4K. In Chapter 3, we mentioned that the narrow band preamplifier exhibited a noise figure of less than 0.5dB and that the T/R switch was characterized by a < 0.3dB insertion loss. These two key components minimized the noise losses in the receiver chain.

Noise figure tests were performed on different days of a total of four times when the experiments were performed. The noise figure was calculated with a number of different bandwidths. The results were shown in Figure 4.2. This plot demonstrated that the system noise figure was approximately constant throughout the range of the receiver bandwidths and that the hardware system was stable. The measurement established that the complete receive path had a noise figure of 1.68 ± 0.2dB at 32KHz where all the images were acquired. This is a good system performance given a frequency of 340MHz.
Figure 4.2: Noise figure as a function of receiver bandwidth
The noise figure for the receiver chain the GE Signa 1.5T was supplied by General Electric as 1.2dB.

To further characterize the system performance, noise images were acquired as a function of receiver gains. The results were summarized in Figure 4.3.

The noise intensity increases with the receiver gain approximately in a linear relationship. This measurement further demonstrated that the hardware system was stable and produced reproducible results.

In order to permit intrinsic signal to noise measurements in a manner that was independent of coil type, transverse electromagnetic (TEM) resonators were constructed for operation at both 1.5T and 8T from previously published procedures. The TEM resonators operated as a linear device both at 1.5T and 8T. The same 16 struts TEM coil was used. The tuning to the desired resonant frequency was achieved by interchanging two set of resonant elements. One set of resonant elements could be tuned to 63.86MHz while the other set could be tuned to 340MHz. A Q of 160 and 100 is observed in an unloaded case at 1.5T and 8T, respectively. The loaded Q and return loss (RL) for each phantom and human head are summarized in table 4.3 and table 4.4.

Mineral oil, water, and chloroform were considered for phantom studies at 1.5T and 8T. Having a dielectric constant of around 80, water exhibits pronounced dielectric resonance artifacts at 8 Tesla, although it can produce excellent images at 1.5T. However, water might exhibit no or little dielectric resonance artifacts when the size of the phantom is sufficiently small. Hence, a ping pong ball filled with copper sulfate doped water was used as the water phantom. The purpose of adding copper sulfate to water was to decrease the $T_1$ relaxation time and lessen the total imaging time.
Figure 4.3: Noise intensity as a function of receiver gain
Mineral oil has a relative permittivity of 2.5. Consequently, it can not support any significant dielectric resonance from 63-340 MHz range. In addition, mineral oil is not lossy (conductivity < 0.1 Siemens/m) and can not present RF penetration problems. However, mineral oil has two resonant peaks due to the different chemical shift of its constituent protons. The separation of the two peaks is 136Hz at 8 Tesla and 25Hz at 1.5 Tesla. This chemical shift dispersion can modulate the SNR significantly when mineral oil is used as a phantom. At 8 Tesla, the two resonances of mineral oil become completely antiphase at 3.6ms, 10.8ms, 17.9ms. Maximum signal is thus expected at a multiple of TE = 7.3ms. A demonstration of this signal modulation is displayed in an acquisition of FID from the mineral oil (Figure 4.4). It can be observed clearly that the signal from these two peaks constructively interfere at TE equal to 7.3ms and 14.7ms. Likewise, the two resonances of mineral oil become completely inphase at a multiple of TE = 39.1ms at 1.5T. Two different sizes of mineral oil phantoms were used in the SNR measurements. One is the size of a ping pong ball, the other is a 18.5 diameter cylindrical container.

Chloroform (CHCl₃) appears to be a good candidate for SNR studies. It has a dielectric constant of only 4.8 and therefore it can not support a dielectric resonance at either 1.5T or 8 T. In addition, it has very low conductivity and thus is not lossy. The disadvantage of using chloroform as a phantom is that it is toxic and volatile. Nonetheless, chloroform was carefully prepared and imaged in a well sealed cylindrical glass container.

Each of these phantoms was placed in a TEM RF coil which in turn was tuned to 63.86MHz at 1.5T and 340.6MHz at 8T and was matched to 50Ω. Since neither mineral oil, water or chloroform is lossy, the loaded Qs at 1.5T and 8T are similar to
Figure 4.4: The two resonances of mineral oil at 8 Tesla
the unloaded case. However, the human head is more lossy than the above phantoms, hence the loaded Qs for human heads were the lowest among all the measurements.

Each phantom and human brain was imaged three times independently on the 1.5T and the 8T scanners to obtain a more reliable SNR measurement. For instance, after an imaging session of chloroform was completed, the phantom was taken out from the coil. Another phantom, for example, the mineral oil ping pong ball, was placed into the coil, so that an independent tuning and matching was obtained. In this manner, the uncertainty resulting from tuning, matching and positioning of each phantom was eliminated.

Except TR and TE, other imaging parameters were maintained throughout the imaging experiments for each phantom at 1.5T and 8T. The individual acquisition parameters were listed in Tables 4.3 and 4.4. The same excitation pulse, a 3ms 2-lobe-Sinc. was utilized in all the experiments.

Measurements of $T_1$ and $T_2^*$ were performed on each phantom and in the human brain. A progressive saturation method was used for $T_1$ measurements from a series of gradient echo images with varying TRs. $T_2^*$ was calculated from a series of gradient recalled echo images with increasing TEs. From these images, the signal intensity was read from a region of interest comprising most of the image. Average $T_1$ and $T_2^*$ values were then fitted using these values.

The processed images at 1.5T were transferred across The Ohio State University Hospital firewall to a PC under Linux environment. The raw data (FIDs) at 8T were also transferred to the same environment. A custom written program in Yorick was used to calculate the SNR of all of the images.
The use of a Fermi Filter is standard on a GE Signa scanner. For consistency of comparison at 1.5 Tesla and 8 Tesla, all 8 Tesla images were processed using a Fermi filter. 

\[ W(k,l) = \frac{1}{1 + e^{(r FR)/FW}} \]

where FR is the Fermi radius and FW is the Fermi width. This low pass digital filter was used to remove high frequency noise and can improve image SNR a factor of about 20% over the unprocessed image.

Signal to noise was measured as the mean of the signal in the ROI over mean of noise. The signal ROI was drawn as a circle encompassing most of the image. The noise ROI was drawn as a circle where only background noise is present. The signal to noise is reported as mean ± standard deviation.

A slice through the center of all phantoms was imaged with a single slice Gradient Echo sequence. In all human studies, single slice gradient echo axial images at 1.5T and 8T were obtained in a region well removed from the base of the brain (no CSF and ventricles) such that susceptibility effects could be minimized. To ensure that ISNR was accurately obtained, fully relaxed gradient echo images were obtained and \( T_2^* \) were corrected with measured values.

### 4.3 Results

Extensive measurements in water and mineral oil were conducted previously using a gradient recalled echo sequence at 1.5T GE Signa to quantify the effect of slice thickness on the signal to noise. The results are summarized in Table 4.1. Other imaging parameters besides those listed in the tables were TR=1000ms, receiver bandwidth =32KHz, FOV=24×24cm. Similar experiments were also conducted at 8T with a
Table 4.1: SNR on mineral oil images with various slice thickness at 1.5 Tesla

<table>
<thead>
<tr>
<th>Image number</th>
<th>Filename</th>
<th>Sequence</th>
<th>Matrix size</th>
<th>ST(mm)</th>
<th>TE(ms)</th>
<th>SNR</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
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<td>GRE</td>
<td>256 x 256</td>
<td>10</td>
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<td>224±15</td>
</tr>
<tr>
<td>2</td>
<td>E31478S1I2</td>
<td>GRE</td>
<td>256 x 256</td>
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<td>4.5</td>
<td>138±5</td>
</tr>
<tr>
<td>3</td>
<td>E31478S3I1</td>
<td>GRE</td>
<td>256 x 256</td>
<td>2.5</td>
<td>4.5</td>
<td>85±2</td>
</tr>
<tr>
<td>4</td>
<td>E31478S4I1</td>
<td>GRE</td>
<td>256 x 256</td>
<td>10</td>
<td>8.4</td>
<td>153±7</td>
</tr>
<tr>
<td>5</td>
<td>E31478S5I1</td>
<td>GRE</td>
<td>256 x 256</td>
<td>5</td>
<td>8.4</td>
<td>93±3.5</td>
</tr>
<tr>
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<td>E31478S6I1</td>
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<td>8.4</td>
<td>50±1.6</td>
</tr>
<tr>
<td>7</td>
<td>E31478S7I1</td>
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<td>42±1.6</td>
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<tr>
<td>9</td>
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<td>14.7</td>
<td>22±1.4</td>
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</table>

Table 4.2: SNR on mineral oil images with various slice thickness at 8 Tesla

<table>
<thead>
<tr>
<th>Image Number</th>
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<td>4</td>
<td>14</td>
<td>1.25</td>
<td>496±20</td>
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</table>

gradient recalled echo sequence. Images were acquired with TE fixed at 14ms. varying slice thickness at 10mm, 5mm, 2.5mm and 1.3mm with the same receiver gain. Other imaging parameters were identical. The results are shown in Table 4.2.

It is interesting to examine the effect of varying slice thickness on SNR. Clearly, a linear relationship does not exist on both scanners between slice thickness and signal. Indeed, all images obtained at a 10mm slice thickness have less SNR than expected.
from 2.5mm and 5 mm images as illustrated by the signal to noise measurements on these images. The signal intensity remains approximately the same for each image. However, the background noise is amplified to a different level for each image. Apparently, this is caused by the automatic optimization of receiver gains by the console prior to image acquisition with the receiver gain favoring thinner slices. In addition, when the signal to noise is over 100, the measured noise background is not pure noise, but is contaminated with signal. The spreading of the signal into the noise floor leads to signal to noise measurements with lower than expected values. For instance, the signal to noise ratio for the slice thickness 10mm, 5mm, 2.5mm were well under 100 with a TE of 14.7ms at 1.5T. Hence, the signal to noise ratio with 2.5mm is half of that with 5mm thickness which is in turn half of the 10mm slice. On the other hand, with a TE of 4.5ms at 1.5T, the SNR from a 2.5mm thick slice is 62. reason for this non-linearity between signal to noise and slice thickness is that the slice profiles may not be identical with slices of different thickness.

4.3.1 Mineral oil

At both 1.5T and 8T, a careful analysis of the effect of chemical shift dispersion on mineral oil was conducted. At 8 Tesla, gradient recalled echo images were acquired with TE varying from 6.5 to 20ms in 0.5ms steps while maintaining the same receiver gain. Other imaging parameters were TR = 1500ms, bandwidth = 32kHz, FOV=24x24cm. Maximum signal was observed at TE equals to 7.3ms and 14.7ms. Similarly, at 1.5 Tesla, gradient recalled echo images were acquired with TE varying from 4ms to 120ms in 3ms steps while maintaining the same receiver gain. Other
<table>
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<th>Field Strength</th>
<th>Phantom diameter(cm)</th>
<th>Q value(1)</th>
<th>Q value(2)</th>
<th>Q value(3)</th>
<th>Return loss(dB)(1)</th>
<th>Return loss(dB)(2)</th>
<th>Return loss(dB)(3)</th>
<th>T₁(ms)</th>
<th>T₂(ms)</th>
<th>TR(s)</th>
<th>TE(ms)</th>
<th>FOV(cm)</th>
<th>Slice thickness(mm)</th>
<th>BW(KHz)</th>
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<th>SNR(1)</th>
<th>SNR(2)</th>
<th>SNR(3)</th>
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<td>116</td>
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<td>792</td>
<td>171</td>
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<td>8</td>
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<td>19.73 ±1.39</td>
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<td>20.35 ± 1.44</td>
</tr>
<tr>
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<td>78</td>
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<td>30</td>
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<td>140</td>
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<td>251.82 ± 18.71</td>
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<tr>
<td></td>
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<td>82</td>
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<td>589.28 ± 181</td>
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<td>586.38 ± 186</td>
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Table 4.3: Experimental Parameters for Copper Sulfate Doped Water and Mineral Oil
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<th>Chloroform</th>
<th>Human head</th>
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<td></td>
<td>8 T</td>
<td>8 T</td>
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<td><strong>Phan. dia.(cm)</strong></td>
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<td>11.5</td>
<td>18</td>
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<td><strong>Q value(1)</strong></td>
<td>155</td>
<td>57</td>
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<tr>
<td></td>
<td>81</td>
<td>23</td>
</tr>
<tr>
<td><strong>Q value(2)</strong></td>
<td>138</td>
<td>51</td>
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<tr>
<td></td>
<td>79</td>
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<td><strong>Q value(3)</strong></td>
<td>114</td>
<td>44</td>
</tr>
<tr>
<td></td>
<td>86</td>
<td>*</td>
</tr>
<tr>
<td><strong>RL(dB)(1)</strong></td>
<td>38</td>
<td>39</td>
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<tr>
<td></td>
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<td>35</td>
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<tr>
<td><strong>RL(dB)(2)</strong></td>
<td>47</td>
<td>38</td>
</tr>
<tr>
<td></td>
<td>44</td>
<td>37</td>
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<tr>
<td><strong>RL(dB)(3)</strong></td>
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<td>38</td>
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<tr>
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<td><em><em>T₂</em>(ms)</em>*</td>
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</tr>
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<td></td>
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<tr>
<td></td>
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<td>22</td>
</tr>
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<td><strong>ST(mm)</strong></td>
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<td><strong>matrix size</strong></td>
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</tr>
<tr>
<td></td>
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<td>256x256</td>
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<tr>
<td><strong>SNR(1)</strong></td>
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<td>185.92± 42.86</td>
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<td><strong>SNR(2)</strong></td>
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<tr>
<td><strong>SNR(3)</strong></td>
<td>17.37 ± 1.17</td>
<td>169.84 ±23.27</td>
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</table>

Table 4.4: Experimental parameters for chloroform and human Brain
Figure 4.5: Representative mineral oil bottle images obtained with a Gradient Echo sequence at 1.5T(A) and 8T(B). Imaging parameters for A: TR = 3000ms, TE = 5ms. Slice thickness = 2mm, FOV =16 x 16cm, Matrix size =256 x 256. Receiver bandwidth = 32KHz. excitation = 3ms 2-lobe Sinc. Imaging parameters for B: TR = 3000ms. TE = 7.3ms. Slice thickness = 2mm. FOV =16 x 16cm. Matrix size =256 x 256. Receiver bandwidth = 32KHz. excitation = 3ms 2-lobe Sinc.

imaging parameters were TR = 250ms. bandwidth = 32kHz. FOV=24x24cm. Maximum signal was observed at TE equals to a multiple of 39ms. Both measurements agreed well with our previous calculations.

Therefore, the comparison of ISNR at these two field strengths was carried out using a TE of 5ms at 1.5T and a TE of 7.3ms at 8 T. Due to the short $T_1$ for mineral oil, the TRs at both fields are sufficiently long. Hence, a $T_1$ correction is not necessary. To correct for $T_2^*$, we need to multiply the SNR by a factor of $(e^{TE/T_2^*})$ at both field strengths, which is equal to 1.34 at 8T and 1.13 at 1.5T. The ratio of ISNR for mineral oil at 8T and 1.5T is obtained by averaging the three SNR measurements at 8T and
Figure 4.6: Representative mineral oil pingpong ball images obtained with a Gradient Echo sequence at 1.5T(A) and 8T(B). Imaging parameters for A: TR = 3000ms, TE = 5ms, Slice thickness = 2mm, FOV = 24 x 24cm, Matrix size = 256 x 256, Receiver bandwidth = 32KHz, excitation = 3ms 2-lobe Sinc. Imaging parameters for B: TR = 3000ms, TE = 7.3ms, Slice thickness = 2mm, FOV = 24 x 24cm, Matrix size = 256 x 256, Receiver bandwidth = 32KHz, excitation = 3ms 2-lobe Sinc
<table>
<thead>
<tr>
<th></th>
<th>8T SNR (before correction)</th>
<th>8T SNR (after correction)</th>
<th>1.5T SNR (before correction)</th>
<th>1.5T SNR (after correction)</th>
<th>SNR ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>min. oil b(1)</td>
<td>589.28±181</td>
<td>789.6 ±242.54</td>
<td>85.54± 3.81</td>
<td>96.66 ±4.3</td>
<td>7.73</td>
</tr>
<tr>
<td>min. oil b(2)</td>
<td>596.05±149</td>
<td>798.7±199</td>
<td>94.92±3.75</td>
<td>107.2±4.23</td>
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</tr>
<tr>
<td>min. oil b(3)</td>
<td>586.38±186</td>
<td>785.7±249</td>
<td>91.67±3.31</td>
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<tr>
<td>min. oil pp(1)</td>
<td>269.61±20.73</td>
<td>361.3±36.5</td>
<td>47.39± 1.6</td>
<td>53.55±1.8</td>
<td>7.14</td>
</tr>
<tr>
<td>min. oil pp(2)</td>
<td>262.76±18.92</td>
<td>352.3±25.3</td>
<td>45.69±1.81</td>
<td>51.63±2.04</td>
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</tr>
<tr>
<td>min. oil pp(3)</td>
<td>251.82±18.71</td>
<td>337.4± 25.1</td>
<td>43.91±1.73</td>
<td>49.61±1.95</td>
<td></td>
</tr>
</tbody>
</table>

Table 4.5: Computation of intrinsic SNR for the mineral oil phantom

1.5T and then by taking the ratio of these two values. The results are listed in Table 4.5.

The average ISNR at 8 Tesla over 1.5 Tesla is then 7.73 for the mineral oil bottle phantom and 7.14 for the mineral oil ping pong ball phantom. These values do not take into account corrections for Q values and noise figures, both of which favor the 8 Tesla scanner.

### 4.3.2 Chloroform

Chloroform phantom images were obtained with a gradient echo sequence at 1.5T and 8T. Three identical studies were performed at each field strength. At both field strengths, a 2mm-thick-slice through the center of the phantom was selected and a 90° pulse was used for spin excitation. The signal to noise was measured using the Yorick program at 1.5T(\(TR = 14000\)ms, \(TE = 5\)ms, \(ST = 2\)mm, \(FOV = 24 \times 24\)cm, matrix size=256 × 256, \(BW=32\)KHz) and 8T(\(TR = 30000\)ms, \(TE = 6\)ms, \(ST = 2\)mm, \(FOV = 24 \times 24\)cm, matrix size=256 × 256, \(BW=32\)KHz) and is listed in Table 4.4.
Representative chloroform images are displayed in Figure 4.7. The results of intrinsic signal to noise ratio for these two field strengths are listed in Table 4.6.

The 8 Tesla images are not as homogeneous as the 1.5T images due to the imperfect $B_1$ field. This is also reflected in the large standard deviation in the signal to noise measurement. Representative images of 1.5T and 8T are shown in Figure 4.7.

Given the values of $T_1$ and $T_2^*$ for chloroform at 1.5T and 8T (at 1.5T, $T_1 = 2280$ ms, $T_2^* = 91.8$ ms; at 8T, $T_1 = 6130$ ms, $T_2^* = 53.2$ ms), no correction is needed for the comparison of SNR at 1.5T and 8T. Hence, the ratio of ISNR for chloroform at 8T versus 1.5T is therefore 9.07 without correcting for differing system noise figures and Q values. The latter two corrections would once again favor the 8 Tesla scanner.
Table 4.6: Computation of intrinsic SNR for the chloroform phantom

<table>
<thead>
<tr>
<th></th>
<th>8T SNR (before correction)</th>
<th>8T SNR (after correction)</th>
<th>1.5T SNR (before correction)</th>
<th>1.5T SNR (after correction)</th>
<th>SNR ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chlorof.(1)</td>
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<td>185.92±42.86</td>
<td>21.12 ±1.51</td>
<td>21.12 ±1.51</td>
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<tr>
<td>Chlorof.(2)</td>
<td>178.38±29.65</td>
<td>178.38±29.65</td>
<td>20.39±1.28</td>
<td>20.39±1.28</td>
<td></td>
</tr>
<tr>
<td>Chlorof.(3)</td>
<td>169.84±23.27</td>
<td>169.84±23.27</td>
<td>17.37±1.17</td>
<td>17.37±1.17</td>
<td></td>
</tr>
</tbody>
</table>

4.3.3 copper sulfate doped water in a pingpong ball

Copper sulfate doped water was contained in a ping pong ball to minimize the effect of dielectric resonances. The ping pong ball was then imaged with a gradient echo sequence at 1.5T and 8T. The measurements for the three identical studies are listed in Table 4.6. At both field strengths, a 2mm thick slice through the center of the phantom was selected and a 90° pulse was used for spin excitation. The signal to noise was measured using the Yorick program at 1.5T( TR = 14000ms, TE = 5ms, Slice thickness =2mm, FOV = 8×8cm, matrix size=256 × 128, BW=32KHz) and at 8T( TR = 30000ms, TE = 6ms, Slice thickness =2mm, FOV = 8×8cm, matrix size=256 × 128, BW=32KHz). Representative copper sulfate doped water images are displayed in Figure 4.8. The images at both field strength showed an absence of dielectric resonance artifacts. The signal to noise ratios measured are listed in Table 4.7.

Given the values of $T_1$ and $T_2$ for water at 1.5T and 8T(at 1.5T, $T_1$=792ms, $T_2$=171ms; at 8T, $T_1$=2370ms, $T_2$ = 221ms), no correction for $T_1$ and $T_2$ is needed for the comparison of SNR at 1.5T and 8T. Therefore, the ratio of ISNR for copper sulfate doped water at 8T versus 1.5T is 9.91.
Figure 4.8: Representative water Ping Pong ball images obtained with a gradient echo sequence at 1.5T(A) and 8T(B). Acquisition parameters for A: TR = 14000ms, TE = 5ms. Slice thickness = 2mm, FOV = 24 x 24cm, Matrix size = 256 x 128, Receiver bandwidth = 32KHz, excitation = 3ms 2-lobe Sinc. Acquisition parameters for B: TR = 30000ms, TE = 6ms, receiver bandwidth = 32KHz, FOV = 24 x 24cm, matrix size = 256 x 128, excitation = 3ms 2-lobe Sinc.
<table>
<thead>
<tr>
<th></th>
<th>8T SNR (before correction)</th>
<th>8T SNR (after correction)</th>
<th>1.5T SNR (before correction)</th>
<th>1.5T SNR (after correction)</th>
<th>SNR ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Water(1)</td>
<td>216.52±8.34</td>
<td>216.52±8.34</td>
<td>21.47±1.33</td>
<td>21.47±1.33</td>
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<tr>
<td>Water(2)</td>
<td>201.4±17.67</td>
<td>201.4±17.67</td>
<td>20.35±1.44</td>
<td>20.35±1.44</td>
<td></td>
</tr>
<tr>
<td>Water(3)</td>
<td>192.78±4.5</td>
<td>192.78±4.5</td>
<td>19.73±1.39</td>
<td>19.73±1.39</td>
<td>9.91</td>
</tr>
</tbody>
</table>

Table 4.7: Computation of intrinsic SNR for the doped water phantom

4.3.4 Human head

Axial images at 1.5 T and 8.0 T were obtained in a region well removed from the base of the brain (no ventricles) such that susceptibility effects could be minimized. A simple gradient echo sequence was utilized. To ensure that ISNR was accurately obtained, imaging parameters were selected in a manner that could minimize the effect of $T_1$ and $T_2^*$ values on the resultant images. Hence, fully relaxed images were acquired at each field strength. The TE value selected was limited by the sequence and the gradient strength on the Bruker and the Signa systems. Three identical proton density images were acquired at 1.5T using TR=5000ms, TE=5ms, flip angle=90°, matrix size = 256 x 256, receiver bandwidth =32kHz, field of view=22x22cm, slice thickness=2mm, excitation = 3ms 2-lobe Sinc. Similarly, proton density images acquired at 8T using TR=6000ms, TE=6ms, flip angle=90°, matrix size = 256 x 256, receiver bandwidth =32kHz, field of view=22x22cm, slice thickness=2mm, excitation = 3ms 2-lobe Sinc. Shimming was performed over the entire head before image acquisition. A 90° excitation pulse was applied. This pulse was adjusted by observing the maximum echo signal on the free induction decay. The representative human brain images at 1.5T and 8T are displayed in Figure 4.9. The SNR on these images are
Figure 4.9: Representative human brain images with a gradient echo sequence at 1.5T(A) and 8 T(B). Acquisition parameters for image A: TR = 5000ms, TE = 5ms, flip angle =90, matrix size = 256 x 256, receiver bandwidth =32kHz, field of view=22x22cm, slice thickness=2mm, excitation = 3ms 2-lobe Sinc. Acquisition parameters for image B: TR = 6000ms, TE = 6ms, flip angle =90, matrix size = 256 x 256, receiver bandwidth =32kHz, field of view=22x22cm, slice thickness=2mm, excitation = 3ms 2-lobe Sinc

listed in Table 4.8. With an average $T_1$ of 1530ms for both white matter and gray matter at 8T and 1.5T, respectively, it is not necessary to correct for partial saturation if a 6s TR is utilized. Likewise, there is no correction for $T_1$ at 1.5T. However, the $T_2^*$ at 8 Tesla is only 22.6ms. The correction for $T_2^*$ involves multiplication by a factor of $e^{(TE/T_2^*)}$ or 1.3. At 1.5T, the correction for $T_2^*$ requires the multiplication of 1.077 given a $T_2^*$ of 67.3ms. The calculated results are summarized in Table 4.7. The ratio of ISNR at 8T versus 1.5T is calculated as 8.08.
<table>
<thead>
<tr>
<th></th>
<th>8T SNR (before correction)</th>
<th>8T SNR (after correction)</th>
<th>1.5T SNR (before correction)</th>
<th>1.5T SNR (after correction)</th>
<th>SNR ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brain(1)</td>
<td>231.85±108</td>
<td>301.4±140.4</td>
<td>38.29 ±6.01</td>
<td>41.23±6.46</td>
<td>8.08</td>
</tr>
<tr>
<td>Brain(2)</td>
<td>254.74±119</td>
<td>331.2±154.7</td>
<td>36.75±7.08</td>
<td>39.57±7.62</td>
<td></td>
</tr>
<tr>
<td>Brain(3)</td>
<td></td>
<td></td>
<td>33.99±4.47</td>
<td>36.6±4.81</td>
<td></td>
</tr>
</tbody>
</table>

Table 4.8: Computation of intrinsic SNR for the human brain

4.4 Discussion

In an ideal situation, the comparison of the ISNR should be performed on the identical consoles. Unfortunately, this opportunity was not available for these experiments. However, these studies were designed and performed with reasonable care. The TEM coils for each measurement have been fully characterized on a network analyzer (HP4195A) on the bench outside the magnet. The coils were properly tuned and matched to 50Ω. Measurements of system noise figures were verified over the period the imaging experiments were conducted. The performance of the coils and systems has been reproducible and consistent.

The low permittivity and conductivity of mineral oil and chloroform eliminated the artifacts caused by dielectric resonances or RF penetration. The water ping pong ball phantom doped with copper sulfate was shown to present no dielectric resonance artifact.

Each phantom has been imaged three times independently. The measurements of the signal to noise were also performed independently. The SNR from all the images was calculated from the same Yorick program. This decreases the statistical and systematic errors.
Since the conversion on slice thickness and field of view does not follow a linear relationship as described in Equation [4.3], all the acquisition parameters have been selected to be identical at these two field strengths. The experiments were also designed to be fully relaxed according to the $T_1$ relaxation time for each phantom and human brain. The echo time (TE) was limited by the console, gradient amplifiers and other acquisition parameters. The TE used in the imaging experiments was the minimum TE allowed on the scanner in the presence of other parameters. However, the $T2^*$ was measured for each phantom, and proper conversion was applied.

To avoid the problem of cross talk and magnetization transfer among slices, only one slice was selected and imaged in the study. For the phantoms, the chosen slice was located at the center of the phantom. For the human studies, the slice was chosen to be one without the ventricle.

For a comparison of SNR, a linear drive TEM resonator was utilized at 1.5T and 8T. However, the $B_1$ field distribution in a linear drive TEM resonator is less homogeneous than a quadrature drive TEM coil, especially at higher frequency. As shown in these images, the 1.5T images were relatively homogeneous, manifested in the smaller standard deviations. On the other hand, the inhomogeneity was obvious on the 8T images. There was a gradual dropping of the signal intensity along the drive point on all the 8T images. In particular, the signal was almost lost completely in the frontal area in the 8T human brain image. The inhomogeneity was also reflected in the large standard deviation on these images.

For all the 1.5T and 8T images, the region of interest was drawn to be a circle comprising most of the images. Hence, the SNR values from the 8T images were an average of the region with high signal intensity and low signal intensity. Therefore,
even though $B_1$ field inhomogeneity existed in the 8T images, an accurate SNR comparison can still be performed using this approach. In this experiment, it is assumed that the gradient echo sequence on the Signa Console is implemented exactly the same way as implemented on the Bruker console, although it is quite common that different vendors implement their sequence slightly differently.

Nonetheless, even in the presence of the aforementioned uncertainty, the conclusion can be safely drawn that the ISNR has a better than linear relationship with field strength. Based on a linear relationship, the signal to noise at 8 Tesla would outperform the signal to noise at 1.5T only by a factor of 5.3. However, our studies showed an improvement of 7.14-9.91. In addition, the system noise figure and the coil quality factor were in favor of the signal to noise at 8 Tesla. If Equation (4.4) is applied to convert the system noise figure and the coil quality factor, a ratio higher than 7.14-9.91 is expected. Indeed, 7.14 is the lower limit of the signal to noise ratio at 8T versus 1.5T. In [22], a greater than linear relationship of SNR with field strength was observed. Simulations [118] have also shown that a super-linear dependence of SNR on field strength could be obtained by optimizing the $B_1$ field distribution in the human body.

Predictions for power and signal to noise were initially based on frequencies below 100MHz, and therefore a quasi-static approximation was assumed. Moreover, the linear relationship of signal to noise versus field strength is formulated with a solenoid or a saddle coil [72]. With these simple coil designs, the coil losses (radiation loss, dielectric loss and inductive loss) increase dramatically with frequency.

However, by using a multiple transmission line design concept [159] and by using a proper shield, these losses could be minimized even at ultra high frequency. Therefore.
the aforementioned three losses might not follow the behavior observed in a simple solenoid or saddle coil with an increased frequency.

It is complicated to calculate quantitatively the amount of loss allowed with these high frequency coils. The TEM coil, for instance, has a more complicated geometry, shape and dimension than a simple solenoid design. Theoretical analysis for an empty case already take a considerable amount of time and effort, as does the coil loaded with a human head [12]. With the unclear electrical properties of the human head at ultra high frequency, it is difficult to study this problem theoretically. Even with simulations, the exact $B_1$ field distribution in the presence of human head may be difficult to determine due to the heterogeneous nature of human tissue.

In conclusion, ISNR measurements at both 1.5T and 8 T were performed. Results showed a better than linear relationship at ultra high field strength.
CHAPTER 5

HIGH RESOLUTION IMAGING AT 1.5 TESLA AND 8 TESLA

5.1 In Vivo High Resolution Rat Brain Imaging at 1.5 Tesla: Tumor Evaluation

5.1.1 Introduction

Over the course of the past decade, MR microscopy has provided a powerful extension to clinical imaging [81]. Microscopic techniques can enhance spatial resolution. This increased resolution directly benefits from the enhanced signal to noise ratio. In turn, the increased signal to noise is achieved generally using a small-bore high field micro-imaging magnets with field strengths in excess of 9 Tesla and equipped with dedicated small gradient coils. These gradient coils can offer high gradient strengths and short rise time. Other approaches involve the design of small optimized RF coils, three dimensional sequences [37] and the application of echo reduction techniques [55, 170]. Surface coil [6, 53], phased array [138] or implanted coils [11] usually offers higher sensitivity than birdcage coils of comparable size. Pulse sequences can also substantially increase the resolution and contrast. For instance, 3D imaging sequences may yield advantages because the signal is coming from the whole selected volume during each excitation rather than from a single slice. Hence, when there is a need to
increase spatial resolution, 3D imaging techniques can provide a good choice of pulse sequences. In addition, 3D imaging enables the visualization of the desired structure from any angle and view. Echo time reduction within 3D imaging can reduce the signal loss due to susceptibility, thereby increasing signal to noise.

Using a combination of the above-mentioned techniques, it is possible to obtain resolution for micro-imaging on the order of 50 μm [103]. As such, even as early as in 1986, a single human cell had been imaged [9].

The use of rat subject is inexpensive, easily available, and has been used widely in various disease models [50]. The 9L glioma brain tumor affects a large population in this country. MRI, with its unique capability to diagnose normal tissue from cancerous tissues, offers a powerful tool for this type of tumor using high resolution and high contrast methods as previously demonstrated. In addition, MRI provides an accurate way to monitor the growth of tumor volume non-invasively over a critical period.

Many tumors are characterized with elevated $T_1$ and $T_2$ relaxation times [40]. In principle, tumors will appear dark on $T_1$ weighted images. Edema, having long $T_1$ values, will also appear dark on $T_1$ weighted images. Hence, it is fairly difficult to identify the tumor with $T_1$ weight sequences alone. However, on $T_2$ weighted images, tumors will appear dark while edema will appear bright. Therefore tumors can be readily discriminated from edema. Contrast agents are relatively nontoxic paramagnetic materials that act to reduce the relaxation times of tissue. Under normal conditions, the blood brain barrier (BBB) prevents the contrast agent from entering the brain. However, under cancerous conditions, the contrast agent will leak...
into tumor tissue as a result of the disruption of the BBB, thereby enhancing the lesion.

This study was undertaken to acquire high resolution images in a clinical 1.5 Tesla magnet using rats previously injected with tumor cell lines and to monitor tumor evolution over a certain time interval. The goal of the study was to obtain high-resolution MR images of live rat brains and skull base structures in order to evaluate tumor development in these animals.

5.1.2 Materials and methods

Image acquisition: 16 rats were studied. Two of these animals were controls. The 9L glioma tumor was previously implanted by surgical intervention. Imaging was performed using a 1.5 Tesla GE, Signa MR system (Milwaukee, WA). A custom designed 1 inch receive-only surface coil was placed over the rat skull. It was not tuned for each rat since the variation of tuning and matching across the rats are relatively small.. T$_1$-weighted images with and without contrast enhancement and T$_2$-weighted images were acquired. The T$_1$-weighted images were acquired with a 3D spoiled gradient echo pulse (3D-SPGR) sequence using the following parameters: TR=25ms, TE=4.7ms, flip angle=40°, 2 signal averages, FOV= 6cm with a 512x256 matrix size (0.12mmx0.23mm pixel size, interpolated to 0.12mmx0.12mm) and 0.6mm slice thickness interpolated to 0.3mm. For the contrast enhanced images, 100μl of Gd-DTPA (Omniscan) was injected either intravenously or intraparenchymaly. T$_2$-weighted images were acquired using a prototype segment interleaved motion compensated acquisition in steady state [97]. Acquisition parameters were: TR=22ms, TE=3.5ms, flip angle=40°, 4 excitations, FOV=7cm, 512x256 matrix (0.13mm×0.27mm pixel
size, interpolated to 0.13mm x 0.13mm) and 0.6mm slice thickness interpolated to 0.3mm. Tumor tissue was identified and then traced to define the tumor volume.

5.1.3 Results

Normal Rats

Both the $T_1$ weighted and the $T_2$ weighted sequences demonstrated certain anatomic structures to best advantage. The $T_1$ weighted sequences demonstrated the fat spaces, and the internal brain anatomic structures very well (Figure 5.1). The SIMCAST technique easily enhanced the fluid spaces including CSF, endolymph and perilymph (Figure 5.2). It was possible to visualize accurately the cochlea, vestibule, internal auditory canal, and semi-circular canals of the temporal bone. It was possible to define the ventricular and cisternal spaces in great detail. Both of the sequences demonstrated certain anatomic structures in a manner similar to that observed in humans. The $T_1$ images allowed for visualization of many detailed structures including the ventricles, cisterns, optic nerves, olfactory nerves, colliculi, optic chiasm, pituitary, pituitary stalk, lobes, geniculate bodies, hippocampus, cerebellum, carotid and vertebral arteries.

9L Glioma Rats

Representative images are shown in Figure 5.3 and 5.4. Tumor was identified as a dark area on $T_1$ weighted images and also as a dark area on $T_2$ weighted images. The tumor was then traced on each slice. The number of pixels was counted within the boundary of the tumor. The resolution on this images was 130x130x300$\mu$m. The tumor volume was calculated as the sum of the number of pixels times 0.13x0.13x0.13. This gives a total volume of 5.07 $mm^3$. 

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Figure 5.1: The $T_2$ weighted image (right) demonstrates visualization of the cochlea (C), vestibule (V), and the internal auditory canal (IAC). The $T_1$ weighted image (left) does not demonstrate the fluid spaces of the otic capsule well as anticipated, but there is excellent visualization of the fourth ventricle (FV), the external auditory canal (EAC), and the brain stem (BS). The mm scale is seen at the left side of each image.

In the tumor bearing rat, the ventricles appeared enlarged on both $T_1$ and $T_2$ weighted images. Below the tumor cell injection site, a dark area appeared on the unenhanced $T_1$ image. This region remained dark on the $T_2$ weighted images indicating an area of hemorrhage rather than fluid collection (edema). Adjacent to this area, there was a region with variable slightly increased signal on the $T_2$ weighted images. This area was strongly enhanced and appeared bright on the contrast $T_1$ images indicating that this was the area of predominant tumor infiltration.
Figure 5.2: The $T_1$ weighted images of a live rat demonstrate excellent detail of the cerebral aqueduct (CA), the hippocampal formation (HF), the ambient cistern (AC), and the oral cavity (OC). The $T_2$ sequence demonstrates the CSF spaces, the ambient cistern (AC) and the cerebral aqueduct (CA) very well. The detail in the brain is not as good. Overall the image quality of each sequence is excellent for sub mm voxel volumes and comparable to lower resolution human images. The mm scale is seen at the left side of each image.
Figure 5.3: Reformatted images showing the tumor and the hemorrhage. Left image: $T_1$ weighted contrast enhanced image. Right image: $T_2$ weighted image.
Figure 5.4: A series of high resolution images acquired with a 3D-SPGR sequence. The left image was acquired with a $T_1$ weighted sequence without contrast enhancement. The right image was acquired with a $T_2$ weighted sequence without contrast enhancement. The middle image was acquired with a $T_1$ weighted sequence with the administration of contrast agent.

5.1.4 Discussion

One limitation of the utilization of small animals for research has been the inability to image them with a resolution that is sufficiently high to be comparable to human imaging in quality. These images demonstrate that it is possible to acquire images with quality similar to many existing human imaging units, but at a scale which is much smaller (sub mm resolution). The standard imaging sequences that are successful in humans appear to have similar advantages for small animals.

These results demonstrate that excellent quality images can be obtained even using a relatively low field clinical scanner (1.5T) and without special gradient coils. The costs associated with this type of imaging are less than dedicated animal magnets since the experimental setting is compatible with routine scanner components.
However, RF coils have to be optimized to achieve maximum sensitivity, usually by the employment of surface coil and phase array concepts. The choice of sequence and imaging parameters could also play an important role on the signal to noise and contrast. These images demonstrate that it is possible to have a detailed imaging evaluation of anatomic structures that are sub mm with laboratory animals that could be used for evaluation of experimental surgical procedures. This study has also demonstrated that tumor-bearing animals can be well characterized using these high resolution $T_1$ and $T_2$ weighted images.

Acknowledgments: I wish to thank Professor Michael Caligiury for providing the animals for these studies. I also wish to thank Dr. Chakeres for his assistance.
5.2 Comparative Mammalian Cortical Vascular Anatomy at 8 Tesla: Insight from High Resolution Imaging Studies of the Rodent and Human Brains

5.2.1 Introduction

Image quality in MRI is achieved through a combination of signal to noise, image contrast and resolution. At a given field strength, however, attempts to enhance image quality through increased resolution can become limited significantly by a lack of adequate signal to noise [46]. This limitation can be overcome in part using three dimensional Fourier transform (3DFT), multiple averages and through the optimization of pulse sequences and acquisition parameters [55, 170]. In addition, increased sensitivity is often achieved using surface [6], phased arrays [124] or implanted coils [11, 143] which provide higher RF coil quality factors (Q) and filling levels. Moreover, digital decimation techniques can increase the sensitivity of the receiver greatly. Image processing techniques [165, 171] can further enhance signal to noise, although this usually occurs at the expense of inherent resolution through increased edge blurring.

Using a combination of specialized RF coils and pulse sequences, Feinberg et. al. [51] have successfully acquired images of the human brain from a 4 mm slice thickness with an in-plane resolution on the order of 270 μm at 1.5 Tesla despite the relatively lower signal to noise available at this field strength. These images were acquired with surprisingly short acquisition times. Nonetheless, attempts to further increase inherent image resolution would be accompanied with significant degradation in image quality as a result of insufficient signal to noise.

Signal to noise is expected to increase substantially with field strength as a result of the Boltzman distribution. As such, increases in field strength can be used as
an advantage in further enhancing image resolution. Such an approach has proven
fruitful in in vivo experiments conducted at higher field strength. Hence, at 4.1 Tesla
[121] an in-plane resolution of 400-500 μm has been obtained with excellent gray-white matter contrast even from a 3mm slice. A further increase in magnetic field
to 8 Tesla has enabled an even greater increase in resolution. Initially for instance,
using simple gradient echo imaging schemes and a 2 mm slice thickness it has been
possible to obtain 1k x 1k images with a 215 μm in-plane resolution which display
both excellent contrast and signal to noise [32]. Shortly thereafter, resolution was
further increased to 100 μm in-plane resolution through a 2000 × 2000 matrix [134].
This constitutes nearly a microscopic level of detail within the living human brain.

Although high field whole body MR systems can enhance signal to noise, their
use is complicated by the presence of significant magnetic susceptibility artifacts in
gradient echo imaging [1] and by increased longitudinal (T₁) relaxation times [173].
Ingenious acquisition schemes however can be utilized to reduce the geometrical dis-
tortions associated with magnetic susceptibility [168]. Furthermore, simple echo-time
reduction techniques [55, 170] may be applied to decrease the time for T₂* dephasing
in gradient echo based sequences thereby reducing susceptibility effects. Nonetheless,
it is important to note that the high magnetic susceptibility present at 8 Tesla can act
as a powerful contrast mechanism at this field strength [30, 32, 175]. The enhanced
signal to noise ratio and strong T₂* based contrast at ultra high field enabled the
visualization of small vascular structures. At the same time, the higher spatial reso-
lution obtainable at high field can be used to reduce intra-pixel dephasing artifacts,
which can occur at lower fields when resolution is more limited [172]. In this section,
a series of high-resolution in vivo MR images of the rodent (rat) and the human brain
are presented using the same ultra high field 8 Tesla magnet and gradient system. Similarities of the anatomical detail and cerebral cortical vascular structures are then compared.

5.2.2 Materials and Methods

Equipment: High-resolution images were obtained from an 8 Tesla whole body scanner previously described[133]. The 8 Tesla 80cm magnet (Magnex. England) was interfaced to a Bruker AVANCE console (Billerica. MA). An actively shielded asymmetric torque free gradient insert [3] was utilized. The gradients were driven by Techron 8745 amplifiers (Crown International, Elkhart. IN). The gradient coils provided a rise time of 415μs and a maximal gradient strength of 59.3 mT/m for the X and Y gradients channels. Similarly, a 200μs rise time was required to achieve a gradient of 68 mT/m for the Z gradient channel.

Rat: Normal healthy animals were utilized. OSU institutional animal care and use committee approved all studies. Prior to image acquisition, animals were anaesthetized. They were then supported in the prone position on a shaped foam cradle. To optimize signal to noise, a custom designed 19 mm diameter surface coil was then positioned superior to the head of the animal. Since this device generated an inhomogeneous $B_1$ field, a 4 ms adiabatic half passage excitation [16] was used for spin excitation. Images were acquired with a 3D gradient echo sequence optimized for contrast and high resolution as follows: TR = 1200ms, TE = 18ms, FOV = 4cm x 4cm x 1.5cm, matrix size = 512 x 512 x 16. NEX = 1. A total acquisition time of 2.7 hours resulted in a 3D resolution of 78 x 78 x 913 μm.
Human: All images were acquired from healthy human volunteers who had previously given informed consent under the guidelines of The Ohio State University institutional review board. For each subject, basic vital signs (heart rate, ECG, temperature and blood pressure) were monitored prior to and following each imaging session. A modified quadrature drive volumetric TEM resonator was used for signal transmission and reception. This RF coil was specifically tuned for each subject examined. In order to retain reasonable acquisition times, images were acquired with a simple 2D gradient echo sequence. Acquisition parameters were as follows: TR = 750ms, TE = 17ms, FOV = 20cm, Slice Thickness = 2mm, NEX = 1. Matrix size = 1024 x 1024. The images of the human and rat brain were compared using vascular atlases of the brain [122, 150].

5.2.3 Results

High-resolution MR images obtained from a normal rat brain were obtained with a 19 mm surface coil and adiabatic spin excitation (Figures 5.5,5.6). Pixel relative intensity was strongest near the surface coil (the superior portion of the brain). Signal intensity was thus maximal in the region close to the vertex and decreased slightly with increasing penetration through the brain. Nonetheless, an estimate of total signal to noise in these images could be obtained by selecting a region of interest that encompassed most of the area of the brain and comparing this region to the background noise. As such, the signal ROI was chosen to be a circle covering both hemispheres. SNR was then calculated as mean intensity of the signal over standard deviation of background noise. The signal to noise was greater than 110 for 930 μm thick slices. Given that an in-plane resolution of 78 μm x 78 μm was utilized to
acquire these images in conjunction with a 930 μm slice thickness, a net voxel volume of 0.0057 mm$^3$ was obtained.

In the rat brain images, the gray white matter contrast differentiation was not optimal. Measurements of the thickness of the cortex were performed (approximately 1.3 mm) based on the location of the ventricles, which were seen as lower signal regions and were very small. Essentially all of the vessels (both large and small or arterial or venous) demonstrated low signal. The deep venous system was located centrally within the deep cisternal spaces. Importantly however, the cortical vasculature was well demonstrated. Numerous small vessels running perpendicular to the cortex diving towards the central brain were clearly visible. These vessels stopped near the lateral ventricle. The diameter of these vessels was on the order of about 50 μm with a length near 1.2 mm maximally.

In Figure 5.8 and 5.9, histological views [122] are presented which are similar to the MRI slices. These corresponding histological sections of the rat brain are displayed which present a magnification of the vascular details.

Human images are displayed in Figure 5.10, 5.11 and 5.12. These 2mm thick images have a signal to noise ratio on the order of 100 with a 200 μm in plane resolution. Images from the vertex region were evaluated. The image quality was excellent. There was no significant degradation by bulk magnetic susceptibility, flow or chemical shifts artifacts. The cerebral spinal fluid (CSF) spaces demonstrated the highest signal intensity followed by gray and white matter. The non-motor or sensory cortex measured approximately 2.1-2.6 mm in thickness. The image contrast between the gray and white matter structures in humans was superior to that obtained in the rat brain.
Figure 5.5: Group of eight coronal slices obtained from a normal rat brain using a 19 mm surface coil and a 3D Gradient Echo Sequence at 8 Tesla (TR=1200ms, TE=18 ms, FOV=4 x 4 x 1.5 cm, matrix=512 x 512 x 16, in-plane resolution=78 μm). The excitation was achieved by a 4ms half passage adiabatic pulse.
Figure 5.6: Magnified view of Figure 5.5F. The gray white matter differentiation is not optimal. The interhemispheric fissure, the gray matter, the white matter and the corpus callosum are labeled. A dotted white line displays the thickness of the gray matter. These images demonstrate clear visualization of many vessels penetrating cerebral cortex (short white arrows) running perpendicular to the surface of the brain towards the deep brain. The vessels appear to stop at the white matter junction. Note that they course perpendicularly to the surface of the white matter in a “spoke” like fashion.
Figure 5.7: Magnified view of Figure 5.5C. This image demonstrates similar findings. Short white arrows also highlight the many small radial-perforating vessels. The frontal lobe and interhemispheric fissure are labeled. A 1 mm scale is seen at the corner of the image for comparison.
Figure 5.8: This is a histological section of the rat brain in coronal plane centered through the corpus callosum. The section is stained for neurons. This image can be compared to Figure 5.6. The thickness of the gray matter is shown as a dotted black line. The white matter, interhemispheric fissure, corpus callosum are labeled.
Figure 5.9: This is a corresponding coronal histological section of the rat brain at a similar location as Figure 5.7. Note the many small perforating vessels (short black arrows) running perpendicular to the surface of the gray matter. These correspond to the MR low signal regions in Figure 5.7. These vessels are known to follow the course of the nerves. The diameters of these vessels are on the order of about 50 \( \mu m \). Labeled structures include the gray matter thickness (black dotted line) and the white matter. A 1 mm scale is seen at the corner of the image for comparison. Figure 5.8 and 5.9 were taken from [122]
The human images demonstrated excellent vascular structure in the cerebral cortex and in the internal brain. The cerebral cortical vessels demonstrated nearly identical micro-vascular appearances for the human and the rodent brain. The cortical vessels entered the cortex perpendicular to the surface and coursed towards the center of the brain. The vessels stopped near the gray white matter interface. All of the intra-parenchymal vessels were seen as signal voids. Hundreds of individual vessels were visible. No substantial flow artifacts were observed.

In Figure 13 and Figure 14, corresponding MRI and histological sections of the human brain are displayed which presents a magnification of the vascular details. A single gyrus within the human brain was found to be on the order of 1.5 cm, comparable to the size of a rat brain.

5.2.4 Discussion

Ultra high field imaging has previously revealed unique anatomic demonstration of the microvasculature of the human brain [132, 150, 169]. In order to expand on these findings, this work is sought to make a comparison between high resolution images obtained from the rodent and human brain. The rodent brain images demonstrate that it is possible to acquire high quality, sub-millimeter resolution images using a whole body instrument at 8 Tesla. It is also possible to image the rodent and the human with comparable resolution. Both the human and rodent MR images demonstrated excellent vascular structure detail in the cortex and in the deep brain. Thus, while the rodent brain measures 1.6 cm in diameter and its gray matter cortex measures 1.3 mm, its total size is comparable to one human gyrus in scale.
Figure 5.10: This is a human axial MR image acquired at 8 Tesla (2D GRE, TR = 750ms, TE = 17ms, FOV = 22cm) through the superior portion of the cerebral cortex near the vertex. Overall, the image quality is excellent for a sub mm pixel size. The image demonstrates excellent detail of the cerebral cortex vascular structures. The CSF has the highest signal followed by the gray matter then the white matter.
Figure 5.11: This image is a magnified view of Figure 5.10 comprising the center of the brain. The CSF, the gray matter and the white matter structures are labeled. There are many small low signal intensity leptomeningeal vessels in the sulci. Multiple small perforating vessels are visible coursing perpendicular to the surface of each gyrus (short black arrows). The vessels stop at the gray-white matter junction just as seen with the rat images. Note that the configuration between the human and rat vessels are identical for each individual gyrus.
Interhemispheric Fissure

Figure 5.12: This image is another magnified view of Figure 5.10.
Figure 5.13: This image displays a magnified view of a single human gyrus. (2D GRE, TR = 750ms, TE = 17ms, FOV = 22cm)
Figure 5.14: This image displays a light photomicrograph of 100 μm celloidin section with alkaline phosphatase vascular stain, counterstained with cresyl violet acetate and light green. The cortical arterioles penetrate the cerebral surface perpendicular to the surface. The gray matter demonstrates a higher density of vessels than the white matter. Note that the largest vessels tend to stop at the gray-white matter junction in a fashion identical to that seen on the 8 Tesla images. The photomicrograph was taken from [114]
Indeed, the cerebral cortex of the human and rat brain are different in thickness, but in general have a similar configuration of the vessels and relationship to the white matter. The rat cortex measures approximately 1.3 mm in thickness. The reported human cortex for the motor cortex is 3.9 mm and 1.8 mm for the sensory cortex [29]. These two cortical thicknesses are not representative of most of the cortex, which is intermediate in thickness. The sensory cortex in general is the thinnest and the motor cortex is the thickest. The human cortex measurement (see Fig. 5.11) on the 8 Tesla images measures 2.1-2.6 mm, which is in the normal range [113].

The anatomic configuration of the perforating vessels of the human brain are similar to that observed in the rat whose vessels coursed perpendicular to the surface extending towards the white matter in a radial pattern as shown in Fig. 5.11. There are more vessels in the cortex than in the white matter. The vessels bend at the gray/white matter junction. With this level of resolution, the known vascular anatomy configuration of human and rodent brains appear to be similar. The dimensions of the cerebral cortex of human and rodent brains are slightly different, but the general configuration again is similar. Both demonstrate straight penetrating vessels that course perpendicular to the surface of the brain towards the center of the brain and these perforating vessels stop near the gray/white matter junction. Both the arterial and venous structures have a similar pattern although the veins frequently continue deeper into the white matter tracts to connect with the deep venous medullary system. Both the rat and human images demonstrate the vessels as low signal regions [76, 152]. The increase in signal to noise, flow and the high susceptibility effects of deoxyhemoglobin may account for the contrast between gray/white
matter and small vessels at higher field. The striking presentation of small cerebral vessels has been previously noted and discussed in works at 4.1T [121].

This study confirms that small vessels are even more conspicuous at ultra high frequency. As a result, UHFMRI can resolve the micro-anatomy of the cerebral cortex vasculature of human and rodent cortex. This is particularly true for the venous system. The visualization of this micro-angiographic level vasculature can serve as a means for angiographic studies of vascular pathology [116] in a non-invasive manner. Such experimental studies could aid in the evaluation of intra-vascular chemotherapy[59], brain tumor vasculature, infarcts and radiation changes. This provides a non-invasive way to evaluate vascular brain injury on a small scale and may lead to an improvement in the accuracy of radiological diagnosis.
5.3 High Resolution Feline Brain Imaging

5.3.1 Introduction

High resolution anatomical imaging[121], functional imaging [157] and spectroscopy [15, 65, 69] have all gained success at 4 Tesla as a result of enhanced inherent signal to noise (SNR) ratio, high susceptibility contrast and increased chemical shift dispersion at this field strength. However, the increase in field strength from 4T to 8 T represents a challenging leap in technology. We have succeeded in demonstrating the viability of human and animal imaging at 8 Tesla[137]. The initial human studies have shown excellent image quality despite some image artifacts. In this regard, high resolution MR imaging demonstrated anatomic structures previously seen only histologically. In this work, such studies were extended to the feline head in order to test the hypothesis that 8 Tesla imaging can provide an excellent research tool for small animal research by further defining the human findings at ultra-high fields.

Results obtained to date revealed that there have been no insurmountable problems to obtaining high quality images at 8 Tesla. The system was successfully designed and assembled at 8 Tesla [133]. Imaging with a FLASH sequence demonstrated at least a 10 fold increase in signal to noise compared to that at 1.5 Tesla [31], thereby enabling an much greater increase in image resolution. Ultra high resolution images with 215 \( \mu \text{m} \) and 100\( \mu \text{m} \) in plane resolution yielded good contrast and signal to noise ratio. They could be obtained a simple gradient echo imaging scheme and a 2mm slice [4]. A 78 \( \mu \text{m} \) in plane resolution in the rat brain was also achieved using a 3D gradient echo sequence [175]. All images are characterized by an enhanced signal to noise ratio and strong \( T_2^* \) based contrast.
However, high field images are usually accompanied by magnetic susceptibility artifacts and chemical shift artifacts. Magnetic susceptibility at high field can act as a powerful contrast mechanism resulting in a better visualization of vascular structures for high resolution imaging. However, substantial geometrical distortion in the air/tissue or tissue/bone interface is expected especially from gradient echo based sequences. For instance, gradient echo acquisition from a human head [4] with a TE of only 10ms will result in almost complete signal loss in the region of the frontal lobe and the sinuses, thus making it extremely hard to image structures like the inner ear that are surrounded by air[146].

Chemical shift artifacts are a result of the difference in resonance frequency between the water and fat proton. They cause the misregistration of the fat and water interface along the frequency encoding direction of MR images. Chemical shift artifacts can be affected by the receiver bandwidth, the gradient strength, the field of view, the resolution and the magnetic field strength. At 8 Tesla, the 3.5ppm chemical shift difference between water and fat (1190Hz) is expected to cause significant artifacts on the images.

Feline models are used extensively in neuroscience research as models for human neuro-degeneration [147], vascular disease [147] and AIDS [125, 126]. As such, the acquisition of feline brain images at 8 Tesla can help establish the usefulness of such images in a variety of experimental settings. Consequently in this study, we acquired a series of high-resolution gradient echo and spin echo feline brain images at ultra high field.
5.3.2 Materials and methods

A 4 kg, male specific pathogen-free cat was housed according to National Institutes of Health Guideline for The Care And Use Of Laboratory Animals for this experiment. Prior to each scan, the cat was premedicated with ketamine (10 mg/kg IM), a cephalic intravenous catheter placed, induced with diprivan (5-10 mg/kg IV to effect, (10 mg/ml) for endotracheal intubation, maintained on isoflurane anesthesia (1.5 - 2). The cat was placed in sternal position for scanning of the brain. High-resolution images were obtained from an 8 Tesla whole body scanner. Briefly however, the 8 Tesla 80cm magnet (Magnex, England) was interfaced to a Bruker AVANCE console (Billerica, MA). An actively shielded asymmetric torque free gradient insert was utilized. The gradient coils were driven by Techron 8745 amplifiers (Crown International, Elkhart, IN). The gradient coils provided a rise time of 415μs and a maximal gradient strength of 59.3 mT/m for the X and Y gradients channels. Similarly, a 200μs rise time was achieved for a gradient of 68 mT/m for the Z gradient channel. A custom designed quadrature drive TEM resonator [174] (15.5 cm diameter and 35 cm length or 12.5 cm and 40 cm length) was used for signal transmission and reception. The size, length and number of struts of the coil are optimized for the homogeneity and signal to noise of this experiment. A return loss (S11) of 35dB was obtained on both ports. Typical loaded Q values of 60 were obtained.

The imaging parameters were chosen in order to optimize contrast and signal-to-noise while still maintaining reasonable imaging times. Detailed analysis of contrast with varying changes with pulse sequences parameters has not yet been completed at 8 Tesla. A series of 12 slice high-resolution 512 × 512 gradient echo and spin echo images were acquired from the feline head with one signal average. Spin echo
images were acquired with the following parameters: TR = 3700 ms, TE = 13 ms, slice thickness = 3 mm and field of view = 10 cm. This resulted in a total acquisition time of 31.5 minutes. Gradient echo images were acquired with the following parameters: TR = 750 ms, TE = 10 ms, flip angle = 45°, slice thickness = 2 mm. This resulted in a total acquisition time of 6.4 minutes. These parameters produced in-plane resolution of approximately 200 μm on both sets of images. Brain structures were identified according to a stereotaxic atlas of the cat brain [149].

5.3.3 Results

Four images from a set of 12 multi-slice high resolution spin echo images acquired are displayed in Figure 5.15. The in-plane resolution of these images is 195 μm. Overall, these spin echo images demonstrate excellent B1 field homogeneity and contrast with minimal magnetic susceptibility and chemical shift artifacts at this field strength. In general, the image contrast for the brain is highly proton density weighted. There are no serious phase encoded artifacts from either blood or CSF flow. The blood vessels in general are all represented by a low signal intensity voids.

Detailed anatomy of the brain, skull base, and the head of the cat is visible. The subcutaneous fat spaces were seen outlining some of the muscles of mastication, the pinna, and the mandible. There were only minor chemical shift artifacts. The scalp could be seen as a multi-layered structured. The CSF containing spaces had the highest intracranial signal intensity. The gray matter had higher signal intensity than the white matter, but lower signal intensity than the cerebrospinal fluid (CSF). At the level of the frontal lobe and nasal cavity, the olfactory tract that enters the calvarium and connects to the rhinencephalon can be observed (figure 5.15A). Signal voids
corresponding to the small carotid arteries, the deep venous system, and the cavernous
sinus are demarcated in figure 5.15B. The microvascularity of the cerebral cortex
was not seen. In figure 5.15C, the concentric rings of the cochlea and vestibule are
discernable. The periaqueductal gray matter surrounding the mesencephalic aqueduct
is visible. Discrete brain stem nuclei are also apparent, including the trapezoid body
and trigeminal nuclei of the pons (figure 5.15D).

Figure 5.16, a SE image centered at the level of the cochlea and vestibule, is dis­
played. The individual turns of the cochlear are visible on this image and the magnetic
susceptibility artifact is minimal. The adjacent brainstem and cerebral aqueduct are
seen. Note that the subcutaneous fat is shifted only slightly to the left. Note also
that the subcutaneous low signal fascial plane is visible on the cat’s right, but not
on the left due to this shift. Other regions of fat are seen surrounding the structures
of the mouth. The air way is visible. The muscles are homogeneous and slightly
lower in signal intensity than the brain. The skull is of low signal intensity. The CSF
spaces (cerebral aqueduct) is high signal intensity. The gray matter is slightly higher
in signal intensity than the white matter. The overall image quality is excellent and
quite homogeneous. Figure 5.17 is a gradient echo image at a similar level. The arti­
facts due the magnetic susceptibility are much greater with distortions of the adjacent
regions. The brain demonstrates somewhat similar contrast relationships. Note that
the deep venous system is also producing intracranial artifacts. Figure 5.18 is a SE
image centered at the third ventricle. The corpus callosum, lateral ventricles, and the
cerebral hemispheres are well seen. The gray and white matter structures are labeled.
The carotid artery is seen as a small signal void. The thalamus is relatively homoge­
neous. The muscles of mastication are outlined in part by high signal intensity fat.
Figure 5.15: Figure A. A spin-echo transverse image at the level of the frontal lobe in a normal cat. 1=Olfactory tract connecting to rhinenencephalon; 2=Falx cerebri; 3= Frontal lobe gyrus; and 4=Nasal cavity. Figure B. A spin-echo transverse image at the level of the thalamus in a normal cat. 1= Internal capsule; 2=Corpus callosum; 3 = Cingulate gyrus; 4 = Lateral ventricle; and 5 = Third ventricle. Figure C. A spin-echo transverse image at the level of the mesencephalon in a normal cat. 1=Tympanic bulla; 2=Cochlea of the inner ear; 3=Caudal colliculus; 4=Rostral colliculus; 5= Mesencephalic aqueduct; and 6=Periaqueductal gray matter. Figure D. A spin-echo transverse image at the level of the mylencephalon in a normal cat. 1=Trapezoid body; 2=Pontine nuclei of the trigeminal nerve; 3=Medial cerebellar penduncle; 4=Cerebellar vermis; 5=Pyramidal tracts; and 6=Basilar artery.
Figure 5.16: A Spin Echo image at the brainstem level. Acquisition parameters were: TR = 3700ms, TE = 13ms, Slice thickness = 3mm, FOV = 10 x 10 cm, Matrix size = 512 x 512, Receiver bandwidth = 100KHz.
Figure 5.17: A Gradient Echo image at the brainstem level. Acquisition parameters were: TR = 750ms, TE = 10ms, Slice thickness = 2mm, FOV = 12 x 12 cm. Matrix size = 512 x 512.
Figure 5.18: A Spin Echo image at the level of the third ventricle. Acquisition parameters were: TR = 3700ms, TE = 13ms, Slice thickness = 3mm, FOV = 10 x 10 cm. Matrix size = 512 x 512, Receiver bandwidth = 100KHz.
Figure 5.19: A Gradient Echo image at the level of the third ventricle. Acquisition parameters were: TR = 750ms, TE = 10ms, Slice thickness = 2mm, FOV = 12 x 12 cm, Matrix size = 512 x 512.
Note that the skin at the vertex of the skull has a multi-layer pattern demonstrating the high resolution nature of the images. Figure 5.19 is the corresponding gradient echo image. Large artifacts at the skullbase and near the pinna are once again observed. The third ventricle, and gray and white matter structures are labeled. Note that the micro vasculature of the brain is not visible as small linear signal voids [34]. Also note that there are lower signal changes in the lateral basal ganglion probably due to the iron deposition [30]. Such iron containing regions are better highlighted on the gradient echo sequence. The gradient echo images also demonstrated substantial magnetic susceptibility artifacts even with a TE of only 10ms. Most of the signal is lost near the nasal cavity, sinuses, and temporal bones and nearby structure are distorted. For example, the details of the temporal bone otic capsule structures and the olfactory bulb structures was lost on the GE images. Susceptibility changes were seen near the tentorium and deep veins. The intracranial image contrast is similar to the SE images and it is T2 weighted. The signal differences between CSF, white matter and gray matter is even greater for the GE images. There were also greater changes in the signal intensity within the basal ganglion structures. The fat spaces demonstrated low signal intensity.

5.3.4 Discussion

Our results demonstrated excellent signal to noise and reasonable contrast in both spin echo and gradient echo images of the feline head at 8 Tesla. The RF coil utilized has an optimized filling factor and geometry offering a better homogeneity of the images and signal to noise. This gain in signal to noise can be converted to increase
spatial resolution at the microscopic level. The increase in signal to noise and higher resolution will also enable the observation of fine structures.

Contrasts on these images are different from that obtained at lower field strength due to the increased longitudinal \( (T_1) \) relaxation times [173] and shortening of \( T_2 \) and \( T_2^* \) [173]. The extremely short \( T_2^* \) value, only on the order of 13ms, will influence any gradient echo technique due to \( T_2^* \) weighting. In addition, due to the lengthening of \( T_1 \), a conventional sequence with TR less than 3000ms will be \( T_1 \) weighted. Hence under the normal range of imaging parameters, the images will demonstrate a combination of both \( T_1 \) and \( T_2 \) weighting. The preliminary measurement of longitudinal relaxation times yielded \( T_1=1650\pm169 \text{ms} \) for gray matter and \( T_1=1370\pm128 \text{ms} \) for white matter [173]. Compared to an average of 1250ms for gray matter, 940ms for white matter at 4T [43, 98, 121], and 960ms for gray matter and 660ms for white matter at 1.5 T [26, 27], the ratio of \( T_1 \) value for gray matter and white matter has been decreased from approximately 1.7 to 1.2. This points to the increased difficulty of obtaining \( T_1 \) weighting at this field strength.

Susceptibility is found to be prominent on gradient echo images while minimal on the spin echo images for the cat. In addition, the structures near the temporal bone are very well characterized in these images, yet they show up poorly in the human images. This finding is most likely due to the difference in presence of air in the temporal bones and anatomical structures between these species.

Novel acquisition schemes can be utilized to reduce the geometrical distortions associated with magnetic susceptibility at higher field to compensate for the \( T2^* \) based dephasing that occurs on gradient echo sequences [55, 170]. Nonetheless, the simplest method to reduce magnetic susceptibility is to use a spin echo pulse sequence
to refocus the spin dephasing due to $B_0$ inhomogeneity. A successful implementation of spin echo pulse sequences however, requires excellent $B_1$ homogeneity. Good $B_1$ homogeneity is difficult to achieve because of coupling between the sample and the RF coil. Using a small optimized TEM resonator as RF coils seems to adequately deal with these problems.

Minimal chemical shift artifacts were observed on the spin echo images of the feline brain. The extent that chemical shift artifacts are present is not only related to the field strength, but also to the receiver bandwidth. The bandwidth used in this study was large at 100KHz, hence the shift was minimal. The fat tends to have a high signal intensity on the spin echo images making the chemical shift artifacts more prominent. On the gradient echo images the fat tends to be suppressed due to its inherent short $T_2^*$. These findings were also observed in human studies.

The cerebral vasculature within the feline brain was not well seen in this study. In humans, the venous structures in particular are seen very well particularly microvasculature of the brain[32, 134]. It is suspected that vessels are highlighted at 8 Tesla due to the presence of deoxyhemoglobin and its natural paramagnetic properties leading to short $T_2^*$ relaxation times. This change leads to marked loss of signal of the microscopic vessels. In this study this was not the case probably as a result of the short TE values utilized. Although the resolution on these cat images are comparable to human images at 8 Tesla (both approximately 200μm), the microvascular structure clearly observed on the human images, it is absent on these cat images. This is because of a shorter echo time for the cat images (TE=10ms) is utilized compared to that on the human images (TE=17ms). This study confirms that excellent ultra-high field MR images can be obtained for feline brain at 8 Tesla. The availability of such
images become important both in the practice of clinical veterinary medicine and in the future neuroscience research at ultra high field strength.
There are two relaxation processes. The spin-lattice relaxation and the spin-spin relaxation. The spin-lattice (longitudinal) relaxation process is a thermal process. It is characterized by the exchange of energy between the spin and the lattice consisting of the other nuclei and electrons so that the spins are brought to equilibrium after a RF pulse. $T_1$ is the time constant used to characterize the spin-lattice relaxation process.

In the spin-spin (transverse) relaxation process, energy is transferred only within the spin system itself. This process is characterized by the redistribution of energy within the spin system. For instance, lower energy spins exchange energy and states with higher energy spins. Although the spins lose their phase coherence, the population of spins occupying the energy levels is approximately constant. The spin-spin relaxation contributes to the width of the absorption spectrum. $T_2$ is the time constant used to characterize the spin-spin relaxation process.
The effective transverse relaxation is the transverse relaxation in the presence of both field inhomogeneity and spin-spin interaction. It causes additional signal loss due to the dephasing as a result of the magnetic field inhomogeneity. $T_2^*$ is the time constant used to characterize the effective transverse relaxation process. $T_2^*$ is related to $T_2$ as follows.

\[
\frac{1}{T_2^*} = \frac{1}{T_2} + \frac{\gamma \delta B_0}{2}
\]

(6.1)

where $\delta B_0$ represents the static field inhomogeneity. $T_2^*$ losses depend on both the specific scanner and the particular load. Unlike the $T_2$ dephasing, $T_2^*$ dephasing can be recovered by the use of a spin echo sequence.

Theories and models have been developed over the last several decades to gain an understanding of the relaxation mechanism at a microscopic level. The relaxation phenomenon was first explored by Bloembergen, Purcell and Pound (BPP)[20] in oxygen containing liquids and paramagnetic solutions. They formulated a theory that the relaxation time was related to dipole-dipole interaction and the rotational and vibrational motion of molecules. The BPP theory successfully explained the relaxation phenomenon in homogeneous liquids, viscous liquids and solids. The local field of one of the two protons in the water molecule is influenced by the magnetic moment of the other proton, causing dephasing to occur. In solids such as ice, the tumbling motion of the molecules modulates the local magnetic field of the proton, hence having a $T_2$ of only several milliseconds, much shorter than $T_1$. However, in the case of liquid, due to the thermal motion, the local dephasing was averaged out and thus the $T_2$ appears much longer and similar to $T_1$. 

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The frequency of the thermal motion of the molecules covers a wide range of the spectrum. Only the frequency that is equal to the resonant frequency contributes to the relaxation. In other words, the fraction of the protons oscillating at resonant frequency and the total number of protons at all frequencies determines the relaxation time. For solid and viscous liquid, changing the resonant frequency through a magnetic field strength can change the fractional spectral distribution and thus change the relaxation times.

The relaxation times depend on the molecular tumbling rate, which can be represented by correlation time ($\tau_c$). It can be conceived as the time for a molecule to tumble for one radian. It is the inverse of the maximum cut-off frequency in the frequency distribution spectrum. The correlation times are $\tau_c \approx 10^{-5}$s, $\tau_c \approx 10^{-12}$s and $\tau_c \approx 10^{-9}$s for solid, liquid and viscous liquid, respectively.

The relaxation times in simple solution were thought to be dependent on the resonant frequency and the correlation time. It can be described in the following two equations [108],

$$1/T_1 = K \left[ \frac{\tau_c}{1 + \omega_0^2 \tau_c^2} + \frac{4 \tau_c}{1 + 4 \omega_0^2 \tau_c^2} \right]$$ (6.2)

$$1/T_2 = K/2 \left[ 3 \tau_c + \frac{5\tau_c}{1 + \omega_0^2 \tau_c^2} + \frac{2 \tau_c}{1 + 4 \omega_0^2 \tau_c^2} \right]$$ (6.3)

where $K$ is proportionality constant, which is a function of the gyromagnetic ratio, Planck’s constant, the magnetic moment for a specific nucleus and the dipole dipole separation. $\tau_c$ is the correlation time and $\omega_0$ is the resonant frequency.

The above two equations can be depicted in the following graph.
Figure 6.1: Relaxation times as a function of correlation time and field strength. (Taken from[108])
At typical NMR frequencies, for instance, \( \omega_0 \tau_c << 1 \) for liquids, the \( T_1 \) and \( T_2 \) are similar. In addition, the relaxation times tend to be constant with the change of resonant frequency, while for solids, where \( \omega_0 \tau_c >> 1 \), the \( T_2 \) appears much shorter than \( T_1 \). These relations can be utilized to derive the relaxation times with a prior knowledge of the correlation time and the resonant frequency. In addition, correlation times may facilitate the study of molecular motion.

Relaxation times have been related to temperature, field strength and the presence of paramagnetic ions. Increasing temperature will decrease correlation time and will lengthen the relaxation times. In the presence of paramagnetic ions, the water proton will experience an extra magnetic field, which causes rapid dephasing of spins and therefore shortens the relaxation times.

While relaxation time has been relatively well characterized quantitatively in simple solutions, limitations began to arise when theories attempted to explain the motion of water in biological tissue.

Tissue is composed primarily of 60-80% water and of proteins suspended in water. The study of the relaxation time is complicated by the presence of the macromolecules and the complex structure of the biological tissue. The values of the relaxation times in biological tissue were found far smaller than predicted theoretically. This was thought to be a result of the increased relaxation rates due to increased viscosity, the bonding of free water to macromolecules and presence of paramagnetic substance in biological tissues [57].

The free water molecule can bind to proteins in several forms. First, it exists as free water. Second, it can be bound to the proteins through a single bond, where the water molecule can still rotate, or through a double bond, where the water molecule
can not rotate. According to the fast exchange model[57], the water molecule is undergoing fast exchange between these several states. The overall relaxation rate is the weighted relaxation rate of the three fractions of water molecules. The rate depends on the fraction of the state of water and the relaxation rate of that particular state. The anisotropic motion of water that is bound to macromolecules in biological tissue was thought to account for the shortening of $T_2$ in biological tissue [17, 58]. This anisotropic motion of water is represented by the $3\tau_c$ term in equation 6.3. In solvents and simple solutions, the isotropic motion of the water molecule averages out this term and has a long $T_2$ similar to $T_1$.

In addition to the complex composition of tissue, the complex environment of biological tissue in vivo also has a strong influence on the relaxation behavior of the water molecule. The substances are not distributed homogeneously; they form microscopic compartments. Hence, the fast exchange is absent for a voxel. In this case, it is not possible for a voxel to have a single unique relaxation rate. Thus, the voxel need to be separated into different compartments. Within each compartment, there is fast exchange, but fast exchange does not exist between different compartments. In addition, there is fast exchange between free water and water bound to macromolecules among different molecular environments [95]. Due to the heterogeneity of the biological tissue and possible compartmentalization of intracellular water, it appears that the relaxation process is more likely to be multi-exponential. A multi-exponential model to fit the relaxation data was employed and is shown to achieve a better characterization of the brain and skeletal muscle [56, 142].

It is clear that CSF has a much larger $T_1$ than gray and white matter: because there is more free water in CSF.
The $T_1$ values in excised mammalian tissues have been collected as a function of frequency and have been found to have an exponential dependence on frequency up to $100\,\text{MHz}$ [24, 52, 99]. In [24], a formula is generalized to predict the frequency dependency of $T_1$ values. It was described as

$$T_1 = A\nu^B$$

(6.4)

where $A$ and $B$ were tissue specific constants and $\nu$ is the Larmor frequency. This simple formula was found to have a good agreement with the experimental data and a better fit than other more complex formulas in the range $1$-$100\,\text{MHz}$. In [52], it was demonstrated that the frontal white matter and gray matter converged at the frequency above $100\,\text{MHz}$ due to the abnormal dispersion of white matter at a high frequency. As a result, the discrimination of contrast between these two tissue types is harder at higher field strengths.

Measurements on tissue samples in the 1980s demonstrated that $T_2$ was independent of frequency [24]. However, recent measurements conducted at high field strength ($>3T$) on excised tissue and in vivo mammalian tissues showed a decrease in $T_2$ value. This finding was attributed to water molecules diffusing through the gradient [57] and fast chemical exchanges between macromolecule and hydrogen in water [39].

Accurate measurement of relaxation time has become a reliable means to characterize tissue type [24], evaluate tumor tissue [23, 40], optimize contrast [89] and obtain other diagnostic information [100]. Due to the highly complex and heterogeneous nature of biological tissue, the understanding of the relaxation process at a molecular level is imperfect. It appears that there is no analytical model available to predict the $T_1$ and $T_2$ in human tissue in vivo at ultra high field strength. Therefore,
accurate measurement is needed to determine experimentally the relaxation time at 8 Tesla.
6.2 Longitudinal ($T_1$) Relaxation Time Measurement

While the exact mechanism of the relaxation process is not fully understood, field strength is shown to be a major determinant of longitudinal relaxation times. Up to 4.1 Tesla, the longitudinal relaxation time in the human brain in vivo has been published throughout the literature. Above 4.1 Tesla, relaxation time measurements from animal studies, rats primarily, or human tissue in vitro were available. The value of the longitudinal relaxation time from 1.5 Tesla to 7 Tesla are summarized in table 6.1. At 1.5 Tesla, an average value of 547-664ms for white matter, 944-1080ms for gray matter, 2000-4000ms for CSF is observed. The few published studies at 4T reported the range of longitudinal relaxation time being 1228-1730ms for cortical gray matter, 886-1043 ms for white matter, 4550±800ms for CSF. Obviously, there are overlaps between the values of white matter and gray matter obtained at different sites.

The variations in the measurements in the values of $T_1$ resulted mainly from the different acquisition methods of the measurements. Inversion recovery and progressive saturation methods are routinely used in spectroscopy to measure relaxation times. However, measurement of $T_1$ on an image on a whole body scanner usually takes a much longer time, although it can give better precision on these values. Hence, numerous optimizations on the methods have been developed in an effort to improve the accuracy and reduce the scan time. For instance, fast imaging techniques have been used for this purpose. However, the accuracy of the measurement is usually dependent on the technique and is often compromised in exchange of speed.
<table>
<thead>
<tr>
<th>White matter</th>
<th>1.5T</th>
<th>2T[38]</th>
<th>3T</th>
<th>4T</th>
<th>4.1T</th>
<th>7T</th>
</tr>
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<tr>
<td>Cortical Gray matter</td>
<td>998 ± 55[26, 27]</td>
<td>1724 ± 5[143, 80]</td>
<td></td>
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<tr>
<td>Caudate nucleus</td>
<td>1157 ± 78[26, 27]</td>
<td>1425 ± 88[98]</td>
<td>1329.4 ± 76.5[121]</td>
<td></td>
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</tr>
<tr>
<td>Putamen</td>
<td>1027 ± 79[26, 27]</td>
<td>1289 ± 51[98]</td>
<td>1372 ± 60[43, 80]</td>
<td>1444.4 ± 59.2[121]</td>
<td></td>
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</tr>
<tr>
<td>Thalamus</td>
<td>950 ± 60[26, 27]</td>
<td>1215 ± 56[98]</td>
<td></td>
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</tr>
<tr>
<td>Substantia nigra</td>
<td>957.6 ± 75.0[121]</td>
<td></td>
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<td></td>
<td></td>
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</tr>
<tr>
<td>CSF</td>
<td>4000 ± 2000[154]</td>
<td>2610 ± 110[154]</td>
<td>3752 ± 368[105]</td>
<td>4550 ± 800[43, 80]</td>
<td>3285.6 ± 331.8[121]</td>
<td>3386 ± 460[107]</td>
</tr>
</tbody>
</table>

All values are in ms

Table 6.1: Longitudinal($T_1$) relaxation times at various field strengths

One example of a fast acquisition technique is the two point method. The two point method[79] acquired two gradient echo images with two different flip angles, and derives the $T_1$ based on the two flip angles. By selecting a reasonable TR, the total experimental time can be conducted within minutes. However, much optimization needs to be performed in such a case. In addition, the accuracy of these measurements depends on the accuracy of the flip angle, which has a demand on the homogeneity of the $B_1$ field and the slice profile. It is also sensitive to susceptibility differences.

While a TurboFLASH with centric reordering technique can ensure image acquisition within a single breathhold, the accuracy depends on the choice of flip angle and inversion time(TI). Furthermore, the low flip angle and short TR contributes to the degradation of SNR, which would lead to the errors in fitting process [21, 38]. The
IR-EPI technique [120] can even reduce the scan time to a few seconds and thereby reduce motion artifacts, but it suffers from low spatial resolution and low SNR which affect the accuracy of the measurement of the $T_1$ values.

Despite the concern of imaging at 8 Tesla, promising results have been obtained. The images demonstrated that there is no apparent RF penetration or dielectric resonance problems on the 8 Tesla images. The high resolution images showed that the images are homogeneous and that the images are characterized by high signal to noise and high susceptibility contrast. The inherent signal to noise enhancement at 8 Tesla will be somewhat compensated by the increase in $T_1$, the shortening of $T_2$ and the high susceptibility. Nonetheless, imaging at ultra high field strengths has been demonstrated to be not only possible, but to deliver excellent quality images can be obtained [32, 134, 175]. These images are characterized by high signal to noise and high susceptibility contrast. The overall image contrast is determined by $T_1$, $T_2$ and susceptibility. However, optimizing pulse sequences in order to extract the inherent contrast at this field strength depends on accurate relaxation time measurements.

It would be an advantage to use fast scan protocols for $T_1$ measurements. However, all these methods have limited accuracy due to statistical and systematic errors. Considering the simplicity and availability of the pulse sequences at the Ohio State University, progressive saturation with gradient echo sequences are used for the $T_1$ measurement. When using progressive saturation methods, the accurate measurement of longitudinal relaxation times is critically dependent on the homogeneity of the $B_1$ field utilized in generating the imaging results. Error in the determination of the $90^\circ$ excitation in turn can lead to large variations in measured $T_1$ values. For this reason, it is often more prudent to obtain longitudinal relaxation values using
inversion recovery methods. These methods have larger dynamic ranges and are dependent on proper spin inversion. Therefore any problems in spin excitation are easily reported. Nonetheless, full inversion recovery methods are extremely time consuming to perform and as such, progressive saturation methods are often utilized to obtain preliminary estimates, prior to the completion of more definitive inversion recovery measurements.

The $T_1$s at 4T has been reported by several institutions. However, field strengths higher than 4.1T are confined to animal studies and in vitro measurements. The goal of this study is to quantitatively determine the $T_1$ value of gray matter, white matter and CSF for human brain in vivo at 8 Tesla and to compare the contrast with that at 1.5Tesla. In these studies, we used a progressive saturation technique. A slice selective 90° pulse is applied in a gradient echo sequence with a list of varying TR and a fixed TE. The signal from tissue with longer $T_1$ will be partially relaxed between the interval of 90° pulses with the decrease of TR. The resulting signal intensity on an image is therefore a function of TR. The signal intensity on an image is given by:

$$S(x, y) \propto M_0 e^{-TE/T_2^*}(1 - e^{-TR/T_1})$$

(6.5)

where $M_0$ is the net initial magnetization at equilibrium and $T_2^*$ is the effective transverse relaxation time. The TE and TR are echo time and repetition time, respectively. The precision of the measurement may be improved by using more points and more widely varied TRs. As such, in this work, initial longitudinal relaxation times are presented for CSF, gray and white matter at 8 Tesla using progressive saturation methods.
6.2.1 Materials and Methods

Imaging was performed on an 8 Tesla whole body scanner previously described in chapter 3. The 8 Tesla 80cm magnet (Magnex, England) was interfaced to a Bruker AVANCE console (Billerica, MA). An actively shielded asymmetric torque free gradient insert is utilized. The gradients were driven by Techron 8745 amplifiers (Crown International, Elkhart, IN). The gradient coils provided a rise time of 415\(\mu\)s and a maximal gradient strength of 59.3 mT/m for the X and Y gradients channels. Similarly, a 200\(\mu\)s rise time was required to achieve a gradient of 68 mT/m for the Z gradient channel.

All images were acquired from healthy human volunteers who had previously given informed consent under the guidelines of The Ohio State University institutional review board. For each subject, basic vital signs (heart rate, ECG, temperature and blood pressure) were monitored prior to and following each imaging session. A modified quadrature drive volumetric TEM resonator was used for signal transmission and reception. This RF coil was specifically tuned for each subject examined.

A group of 15 normal subjects (age from 22-34) were studied. The subjects wore ear plugs during all the imaging sessions. The longest of these scans with TR 6000ms required a total of 23 minutes to acquire. Conventional gradient recalled echoes were used for acquisition. Ten(10) slice images were obtained in all the experiments with a matrix size of 256 x 256, a receiver bandwidth of 33kHz, a field of view of 22cm, slice thickness of 5mm and an inter-slice spacing of 5mm. RF pulse was implemented with a 4ms 3-lobe-Sinc. One signal average is used. Shimming was performed over the entire head before image acquisition.
90° flip angle excitation pulse was used and determined by observing the maximum echo signal on the free induction decay. Transmit power and receiver gain were maintained across individual measurements within each series of the experiment. $T_i$ was measured using a TE value of 8ms. To improve the accuracy of the measurement, TR was selected across a wide range of the values ($TR = 230ms, 500ms, 800ms, 1500ms, 2000ms, 3000ms, 6000ms$). The first TR was the minimum that could accommodate the number of slices without violating the duty cycle. The ideal longest TR should be five times of $T_i$ to guarantee the magnetization is fully relaxed, however, in order to retain reasonable acquisition times, the longest TR was limited to 6000ms.

The duration for the each imaging session was approximately an hour and fifteen minutes.

6.2.2 Results

The raw data (FIDs) were transferred to a Linux workstation. A fitting program, written in Yorick, Fourier transformed the complex data, applied the baseline correction and ensured identical scaling on the each data set within the image series. The 256 x 256 x 7 data points for each subject were analyzed then with a nonlinear least square fitting algorithm written in Yorick. While a total of 15 subjects were examined in this study, only half subjects remained immobile sufficiently long to enable the acquisition of all images without motion artifacts, especially during the longest scan TR=6000ms which takes 23mins. This points to the difficulty of obtaining full inversion recovery experiments under this experimental setting. Nonetheless, good
motion free data during the entire imaging session was obtained from at least 4 sub-
jects so that a pixel-by-pixel $T_1$ map could be fitted. A set of such representative
data is displayed in Figure 6.1.

The overall quality of these images is good. SNR was in excess of 1200 on the
image with TR=6000ms. The images demonstrated good homogeneity. The gray
white matter contrast was not able to be differentiated on short TR value images.
The signal intensity is slightly higher in the frontal lobe. resulting in a fitted $T_1$ value
which was slightly higher in the frontal lobe. The Yorick program allows the selection
of an individual ROI on each image first, the 7 ROIs are then fitted using the software.
The ROI for white matter and cortical gray matter usually consists of 5-15 pixels.
the intensities on the image inside ROI are averaged.

As such, the average $T_1$ value was determined using the $T_1$ map. The value of
each pixel map was calculated independently of the spin density and the transverse
relaxation using least square fitting. The $T_1$ map generated from these images is
displayed in Figure 6.2. The $T_1$ value was fitted using a three parameter exponential
fit $M(t) = M_0 * (1 - Ae^{-TR/T_1})$ and then $T_1$ map obtained by the same exponential
fitting using Yorick. In addition, the $T_1$ value was also determined by the fitting of
ROIs over the tissue of interest. The intensities on the image inside ROI are averaged.
CSF values were obtained from the ROI fitting.

Figure 6.4 displayed a series of gradient echo images acquired at the level of
ventricle. Two regions of interest were drawn on the TR=6000ms image. Each region
of interest comprised of 10-18 pixels. The same ROI was selected on the seven images.
An average signal intensity was then computed within the ROI on these images and
fitted using the Yorick program. The $T_1$ of the white matter ROI was fitted and
Figure 6.2: A group of 7 axial gradient recalled echo images acquired for the determination of longitudinal relaxation times at 8 Tesla. Images were acquired with repetition times corresponding to 6.0, 3.0, 2.0, 1.5, 0.8, 0.5 and 0.23 seconds.
Figure 6.3: This image shows the corresponding $T_1$ map.
Figure 6.4: A group of 7 axial gradient recalled echo images at the level of ventricle acquired for the determination of longitudinal relaxation times at 8 Tesla. Images were acquired with repetition times corresponding to 6.0, 3.0, 2.0, 1.5, 0.8, 0.5 and 0.23 seconds.
Figure 6.5: A typical $T_1$ value for a white matter ROI at 8 Tesla displayed in Figure 6.5. A $T_1$ value of 1380 ms was obtained for this ROI. The error bar represented the standard deviation of the signal intensity. Similarly, the $T_1$ of the gray matter ROI was fitted and displayed in Figure 6.6. A $T_1$ value of 1627.4 ms was obtained.

The $T_1$ value was obtained from both approaches, namely, reading the pixel value of the $T_1$ map and fitting of the selected ROI. The values obtained from these two approaches are in good agreement. An average Gray matter $T_1$ value of $1625\pm196$ ms
Figure 6.6: A typical $T_1$ value for a gray matter ROI at 8 Tesla
Figure 6.7: A group of 7 axial gradient recalled echo images at 1.5T acquired for the comparison of contrast of longitudinal relaxation. Images were acquired with repetition times corresponding to 6.0, 3.0, 2.0, 1.5, 0.8, 0.5 and 0.23 seconds.

was obtained. Similarly, an average $T_1$ value of $1,370\pm 137\text{ms}$ was obtained for white matter. CSF had an average $T_1$ value of $3,950\pm 650\text{ms}$.

6.2.3 Discussion

A disadvantage of using the progressive saturation technique is that the error is dependent on the shape of the selected slice profile and $B_1$ filed inhomogeneity.

The fourier transformation of 3-lobe-Sinc is not ideally square. Therefore, unless the correction can be made with prior knowledge of the slice profile, it will affect the
accuracy in the $T_1$ measurements. This non-ideal slice profile will cause an overestimation of the signal intensity for TR values much shorter than $T_1$ which in turn will cause an underestimation of $T_1$.

As Figure 6.1 and Figure 6.3 demonstrated, there is slight variation of signal intensity on the images. This is probably due to the inhomogeneous $B_1$ field distribution of the RF coil. This contributes to the error in defining the 90° pulse on the selected slices, which will cause the fitted value deviated from the ideal situation from equation 6.5.

The resolution on this set of image is 859$\mu$m x 859$\mu$m x 5mm given the FOV of 22cm, a slice thickness of 5mm and a matrix size of 256. It could be possible that there exists partial volume artifact, giving another source of errors when reading the values from the map.

Another possible source of error are those introduced while using multi-slice technique, as has been suggested in [83]. An average $T_1$ of gray matter and white matter around 1400ms is anticipated prior to the acquisition of images. This requires the longest TR to be at least 6000ms which takes 23min in this experiment. A total of 1hr and 15mins of imaging time is needed for the entire acquisition during which the subject had to remain motionless for a perfect fit at each pixel in order to compute $T_1$ map. At the time of the experiment, a patient table was not available. It took enormous efforts for the subjects to remain still over the entire imaging session. As a result, while a single slice imaging using progressive saturation is usually preferred because we can further decrease TR for the first point, to avoid wasting data even in the presence of motion between the imaging session, 10 slices were acquired in an interleaved fashion with only 2 mm slice spacing so that even the subjects moved,
A reasonable fit using the ROI approach would still be achieved. Although slice cross talk is eliminated with this interleaved approach, magnetization transfer between the slice might still be present and motion artifacts could be more pronounced than single slice excitation.

$T_1$ is shown to increase substantially with field strength. Extrapolation of the available data at lower field strength and using equation 6.4 gives the estimated $T_1$ value at 8 Tesla to be 1720ms for cortical gray matter and 1650ms for white matter. In comparison, our values of gray and white matter are slightly lower than the extrapolated values.

1.5T images looked more homogeneous than the 8T images. The 8T images, however, showed center brightness, susceptibility artifact and chemical shift artifacts. In addition, the contrast on the 8T images is different from those at 1.5 Tesla. For TR < 2000 sequence, the 8T images look flat because of the saturation of the magnetization. The 1.5T images, however, showed much better contrast differentiation between white matter and gray matter at all values of TR. It seems that the contrast between the white matter and the gray matter can not extracted for relatively short TR. While the ratio of $T_1$ values for gray and white matter is almost 1.7 at 1.5 Tesla, it is only 1.2 at 8 Tesla. Hence, the $T_1$ contrast is diminishing in the conventional $T_1$ weighted sequence. However, using MDEFT sequence[117], it has been shown that superb $T_1$ contrast can be obtained. Contrast can also be enhanced by changing the order of phase encoding.
Table 6.2: Transverse($T_2$) relaxation times at various field strengths

<table>
<thead>
<tr>
<th>Tissue</th>
<th>1.5T [26, 27]</th>
<th>3T [35]</th>
<th>4T</th>
<th>4.7T</th>
<th>7T</th>
<th>9.4T [93]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Internal Capsule</td>
<td>65±4</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gray matter</td>
<td>91±6</td>
<td>88±7</td>
<td>63±6.2$^{[43]}$</td>
<td>77±0.8$^{[14]}$</td>
<td>61$^{[153]}$</td>
<td>52$^{[131]}$</td>
</tr>
<tr>
<td>Corpus callosum</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Thalamus</td>
<td>71±4</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Caudate nucleus</td>
<td>75±4</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Putamen</td>
<td>68±2</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hippocampus</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White matter</td>
<td>68±6</td>
<td>49.8±2.2$^{[43]}$</td>
<td>62±0.65$^{[14]}$</td>
<td>34$^{[153]}$</td>
<td>35$^{[112]}$</td>
<td>21</td>
</tr>
<tr>
<td>CSF</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

6.3 Transverse Relaxation Time Measurement

The $T_2$ value was considered by most researchers to be independent of frequency in the early days of MR imaging. However, recent data showed a decrease of $T_2$ with the frequency, especially when the field strength was sufficiently high. The $T_2$ value has been a very important parameter in determining the acquisition parameters to optimize image contrast. In addition, quantitative $T_2$ measurements have been used as a marker to characterize ischemia$^{[151]}$, sclerosis$^{[10, 100]}$ and tumors$^{[84]}$ at various field strengths.

In vivo human brain $T_2$ measurements up to 4.1 Tesla has been published. $T_2$ measurements on excised tissue and live rats at 7T-9.4T have also been reported. These data are summarized in the following table. As the trend of the data suggests, there is a considerable decrease in $T_2$ value from 1.5 Tesla to 9.4 Tesla.
The purpose of this study was to obtain accurate value of $T_2$ in human brain at 8 Tesla and to obtain a $T_2$ map. The value of $T_2$, together with the $T_1$ measured earlier, can serve as important guides in optimizing the sequence parameters at ultra high field imaging.

6.3.1 Materials and methods

The hardware configuration for this experiment was the same as in the $T_1$ measurement as described above. Two subjects were studied. They were previously given informed consent under the guidelines of The Ohio State University institutional review board. For each subject, basic vital signs (heart rate, ECG, temperature and blood pressure) were monitored prior to and following each imaging session.

Ten(10) axial slices were acquired from Spin Echo sequence. A multi-slice single echo and a multi-slice multi-echo sequences were applied in this study. The single echo method gives less error in the presence of an imperfect 180° pulse. In the multi-echo sequence, however, the error due to the imperfect 180° pulse would accumulate in the acquisition of the subsequent echoes. The multi-echo method takes much less time than the single echo method and can thus minimize the motion from the subject. Nonetheless, both methods were used in this study. Using the single echo method, the images were acquired using the following parameters: matrix size = 256 x 256, receiver bandwidth = 47KHz, FOV = 20 x 20 cm, TR = 2000ms, TE varies from 13ms, 25ms, 40ms and 60ms, Slice thickness = 5mm, excitation pulse = 4ms Guassian. For the multi-echo sequence, the measurement was performed using a TR of 1000ms while keeping other imaging parameters the same. Six echo images were collected with TE varying from 15ms to 90ms with a step size of 15ms.
6.3.2 Results

Similar to the data processing for $T_1$, the raw data were transferred to a Linux workstation. A program, written in Yorick, Fourier transformed the complex data, performed the baseline correction and applied identical scaling on the six 256x256 data sets. Each pixel intensity was fitted with a nonlinear least square algorithm written in Yorick. The multi-echo data set had a better fit than the single echo data set, because there is slight motion on one of the signal echo data set. Figure 6.8 shows six spin echo images corresponding to the six TEs from the same slice containing the ventricle.

The images showed low signal in the front of the head. Apparently, there is slight $B_1$ field inhomogeneity on these image due to the tuning of the RF coil. This leads to the imperfect 90 and 180 pulse. The contrast on these images are good for the long TE. Signal to noise was in excess of 500 in the first echo image. Compared to Gradient echo images, there are much less susceptibility artifacts. The fat layer in the skin and the region of frontal sinus are well visualized. Nonetheless, the overall quality of these images is good enough to perform an accurate $T_2$ measurement.

The Yorick program allows the fitting on each pixel and generation of a $T_2$ map, however, due to inhomogeneous $B_1$ field at the anterior portion of the head, the fitting software failed at the pixels where there is low signal intensity. Apparently, the signal intensity in those areas does not follow the expected change as the TE varies. Nonetheless, the fitting program on Bruker is more robust in the presence of $B_1$ inhomogeneity. The $T_2$ map was thus generated using Bruker software.

The $T_2$ value was obtained by selecting six corresponding ROIs and then by fitting the average value inside the corresponding ROIs. The ROIs of cortical white matter
and gray matter were identified by comparing to the human anatomy book and with the help of the OSU radiologists. The typical size of an ROI contained 5-15 pixels. The signal intensity of all the pixels within an ROI was averaged.

As such, the \( T_2 \) value was fitted using a two parameter mono-exponential fit \( M(t) = M_0 \cdot (e^{-TE/T_2}) \). A pixel-by-pixel \( T_2 \) map was generated from the six echo images and is displayed in Figure 6.9. In addition, \( T_2 \) was calculated by the fitting of ROIs over the tissue of interest on these echo images.

The \( T_2 \) value was determined by fitting the corresponding ROIs. An average \( T_2 \) value of \( 41\pm5.6\text{ms} \) and \( 33\pm4.7\text{ms} \) was obtained for gray matter and white matter, respectively. Likewise, an average \( T_2 \) of \( 128\pm12.5\text{ms} \) was obtained for CSF.

### 6.3.3 Discussion

Due to the availability of volunteers and the restrictions of the institutional review board, only two subjects were imaged for the determination of \( T_2 \). Obviously, more subjects need to be imaged to obtain a more accurate statistical distribution of \( T_2 \). However, the same measurements were also performed on at least three dogs. The \( T_2 \) values for the gray matter and white matter between these two species were found to be similar.

The accurate measurement of \( T_2 \) values requires a homogeneous \( B_1 \) field distribution and the precise determination of the 90° and 180° pulse. The multiple echo approach in \( T_2 \) measurements makes a heavy demand on the accuracy of the 180° pulse. Because the imperfect 180° will accumulate the inaccuracy on the measurements, the last echo image would have the largest deviation from the true 180° pulse.
Figure 6.8: A group of six axial images obtained with different TEs using a Multi-echo SE sequence for the determination of transverse relaxation time at 8 Tesla. Images were acquired with the following echo times: 15ms, 30ms, 45ms, 60ms, 75ms and 90ms.
Figure 6.9: Corresponding $T_2$ map at 8 Tesla
The imperfect profile of the slice selective 90° and 180° pulse could also cause an underestimation in the $T_2$ value. This underestimation, however, can be minimized by making the first echo time as long as possible. The chosen value for echo spacing, 15ms, appears to be in a reasonable range for this study. A single slice pulse is also suggested by Joseph et. al. [82] such that a non selective 180° pulse can be used to minimize the systematic error in measuring the $T_2$ value.

In conclusion, in this work the initial attempt to estimate in vivo relaxation times of human brain at 8T is presented. Within the limitations of the progressive saturation and multi-echo techniques, particularly possible errors in exactly determining the 90° and 180° excitation, these findings are in agreement with the estimated $T_1$ and $T_2$ values for cortical gray matter and white matter extrapolated from the literature values at lower field strength, as well as the measurements obtained from animals at similar field strengths. These preliminary estimates of relaxation times can serve as important guides for ultra high field imaging studies of the human head at both 7 and 8 Tesla.
CHAPTER 7

CONCLUSION

It has been demonstrated earlier in our laboratory that dielectric resonance, RF penetration limitations are not serious enough to impair the image quality at 8 Tesla. In addition, power requirement has been found to be much lower than the square dependence on the field strength as previously expected. Based on these findings, three aspects of the issues on ultra high field imaging at 8 Tesla were further examined in this dissertation. These include measurements of the intrinsic signal to noise, high resolution imaging and relaxation time measurements.

The ultimate motivation for increasing clinical field strengths is to provide an enhanced signal to noise ratio. Therefore, issues concerning intrinsic signal to noise ratio at 8 Tesla on mineral oil, copper sulfate doped water solution, chloroform and human brain were investigated. The system noise figure, noise performance with the receiver gain, noise performance with the receiver bandwidth are characterized prior to each experiment. A comparison of intrinsic signal to noise at 8 Tesla versus 1.5 Tesla was presented with identical field of view, slice thickness, matrix size, receiver bandwidth and excitation pulse. A simple gradient echo sequence was applied at both 1.5T and 8T. $T_1$ and $T_2^*$ values were measured for each phantom. The repetition time was chosen to obtain a fully relaxed images for each phantom. The echo time was
selected as the minimum echo time limited by the hardware system. The ratio of signal to noise at 8 Tesla and 1.5 Tesla was calculated with proper conversion when necessary. A better than linear dependence (7.14-9.91) of the intrinsic signal to noise ratio on field strength for the aforementioned phantoms has been found. This may be partly the result of a more distributed design in the TEM resonator, thereby minimizing the losses at ultra high field. The ISNR measurement provides useful information of how far the signal to noise ratio at 8 Tesla can be improved without being limited by the fundamental physical factors.

In addition to signal to noise ratio, contrast to noise ratio and limitation of artifacts are important to determine the image quality. The sequence parameters that could optimize the signal to noise ratio usually adversely affect the contrast to noise ratio and can produce susceptibility and chemical shift artifacts. At ultra high field, $T_1$ values are getting much longer and the $T_2^*$ values are becoming significantly shorter. It seems more complicated to obtain a high signal to noise image with true $T_1$ or $T_2^*$ contrast using conventional sequences within a reasonable imaging time. For instance, decreasing TE will increase SNR at the expense of decreasing $T_2^*$ contrast. Likewise, decreasing receiver bandwidths will enhance the signal to noise ratio while increasing the chemical shift artifacts. In these cases, it might be worthwhile to compromise SNR for a better image contrast and the reduction of artifacts.

We then investigated the limit of the resolution while maintaining reasonable image quality at both 1.5T and 8T. At 1.5T, sub-millimeter resolution in the rat brain can be achieved with excellent image quality using a combination of an optimized pulse sequence and a RF coil. Tumors in the rat brain can also be well characterized using a commercial scanner. At 8 Tesla, microscopic resolution can be achieved
when this gain in signal to noise ratio is converted to increasing spatial resolution. Signal to noise can be further optimized by utilizing optimized surface or volume TEM resonators of appropriate size. The signal to noise is in excess of 100 on both the rodent brain and human brain with resolutions of 78\(\mu\)m \(\times\) 78\(\mu\)m \(\times\) 930\(\mu\)m and 200\(\mu\)m \(\times\) 200\(\mu\)m \(\times\) 2000\(\mu\)m, respectively. The human and rodent MR images both demonstrated excellent vascular structures in the cortex and in the deep brain. The configuration of the perforating vessels of human brain and in the rodent brain is similar, both perpendicular to the cortex in a radiating fashion. Small vessels are more conspicuous at ultra high frequency because of the susceptibility of deoxyhemoglobin which is paramagnetic. The resolution achieved has shown the potential application for high resolution imaging at high field. Whereas only normal animals and subjects were studied at 8 Tesla, better discrimination of diseased condition could be made using high resolution imaging. Since small vessels are more conspicuous at ultra high frequency, potential application such as the visualization of micro-angiographic level vasculature could serve as a valuable means for studying vascular pathology in a non-invasive manner. This provides a non-invasive way to evaluate vascular brain injury on a small scale and may lead to an improvement in the accuracy of radiological diagnosis. The adverse effect of susceptibility and chemical shift were studied on feline brains using simple spin echo and gradient echo sequences. The signal to noise is optimized with a custom designed TEM coil. Susceptibility artifacts are prominent on gradient echo images and are the major cause of image inhomogeneity. However, this geometrical distortion caused by susceptibility can be minimized by utilizing a spin echo sequence. Excellent visualization of cochlea in the temporal lobe in the cat with minimal susceptibility artifacts was presented. Receiver bandwidth could be
properly chosen on these spin echo images in a manner to counteract the effect of the field strength to minimize the chemical shift artifacts.

Finally, the initial results on the longitudinal and transverse relaxation time measurements at 8 Tesla were presented. $T_1$ and $T_2$ values are important parameters to optimize contrast at 8 Tesla. Since predictions of relaxation times based on theoretical models are not available, one must rely on experimental means to accurately determine the relaxation times in the human brain in vivo. The $T_1$ values were determined using a progressive saturation technique. Average $T_1$ values of $1.635\pm169\text{ms}$, $1.370\pm128\text{ms}$, $3.950\pm650\text{ms}$ were obtained for gray matter, white matter and CSF in the human brain in vivo. Likewise, average $T_2$ values of $41\pm5.6\text{ms}$, $33\pm4.7\text{ms}$, $128\pm12.5\text{ms}$ were obtained for gray matter, white matter and CSF, respectively using a multi-echo sequence with varying TEs. Within the limitations of the progressive saturation and multi-echo techniques, these findings were in agreement with the estimated $T_1$ and $T_2$ values for cortical gray matter and white matter extrapolated from the literature values at lower field strength as well as with the measurements obtained from animals at similar field strengths. These preliminary estimates of relaxation times can provide important guidelines for contrast optimization in ultra high field in vivo imaging studies of the human brain. The measurements at 8 Tesla also showed a convergence of $T_1$ for gray matter and white matter. $T_1$ contrast would be more difficult to extract at ultra high field strength with a conventional imaging sequence.
APPENDIX A

ABBREVIATIONS AND SYMBOLS

BPP               Bloembergen Pound Purcell theory
BOLD              Blood Oxygen Level Dependent
CSF               CerebroSpinal Fluid
EPI               Echo Planar Imaging
ESR               Electron Spin Resonance
FASTMAP           A fast shimming method
FID               Free Induction Decay
ESR               Electron Spin Resonance
FET               Field Effect Transistor
FLASH             Fast Low Angle SHot
FSE               Fast Spin Echo
GRASE             GRadient And Spin Echo sequence
GRE               Gradient Recalled Echo sequence
ISNR              Intrinsic Signal to Noise Ratio
MDEFT             Modified Driven Equilibrium Fourier Transform
MRI               Magnetic Resonance Imaging
MRS               Magnetic Resonance Spectroscopy
MHz  Mega-Hertz
NMR  Nuclear Magnetic Resonance
OSU  Ohio State University
Q    coil Quality factor
RARE Rapid Acquisition with Relaxation Enhancement
RF   Radio Frequency
SAR  Specific Absorption Rate
SE   Spin Echo sequence
SPGR Spoiled Gradient Echo sequence
SNR  Signal to Noise Ratio
T    Tesla
TE   Time of Echo
TEM  Transverse ElectroMagnetic
TR   Time of Repetition
T1   Longitudinal relaxation time
T2   Transverse relaxation time
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