Magnetic Resonance Imaging of Lungs at Ultra-Low Magnetic Field Strength using Hyperpolarized ^{129}Xe Gas

by

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Abstract

Conventional proton Magnetic Resonance (MR) imaging has been limited to water rich organs and tissues, with limited success in lungs and airways. With the introduction of Hyperpolarized Noble Gases (HNG's), the low spin concentration in gas-spaces is compensated by the extremely high non-equilibrium magnetizations achievable. This magnetization increase allows the use of field strengths much lower than those currently used in clinical MR systems with advantages such as: increased patient accessibility, reduced cost and image artifacts and less siting restrictions.

Until now, the choice of field strength for HNG imaging has been mostly determined by the existing conventional MR systems or on hardware limitations. This work provides a theoretical framework for selection of the optimum field strength for clinical HNG MR imaging systems based on models of the field strength dependence of the achievable signal-to-noise ratio (SNR) and spatial resolution.

A methodology for MR imaging of the lungs at very low field strengths is developed by building a system for hyperpolarized ^{129}Xe (HXe) rat lung imaging that uses the fringe field of a superconducting magnet as the source of the static magnetic field. A passive shimming procedure that improves the fringe field homogeneity to the levels required for imaging is theoretically described and used at two field strengths (8.5 mT and 17 mT).

Spectra and images of HXe gas in phantoms and excised rat lungs are presented and used to validate the obtained theoretical SNR field dependence for small samples. The issues related to clinical HNG imaging at low fields for both gas-space and dissolved-phase imaging are investigated and possible ways to address them in future are discussed.

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List of Abbreviations

2D	Two Dimensional
3D	Three Dimensional
AWG	American Wire Gauge
BO	Bronchiolitis Obliterans
CMRF	Carleton Magnetic Resonance Facility
COPD	Chronic Obstructive Pulmonary Disease
CT	Computed Tomography
DSV	Diameter Spherical Volume
dB	Decibel
DNP	Dynamic Nuclear Polarization
EPI	Echo-Planar Imaging
EMI	Electromagnetic Interference
ESR	Electron-Spin Resonance
FID	Free Induction Decay
FT	Fourier Transform
FWHM	Full Width at Half Maximum
Gd-DTPA	Gadolinium-diethylenetriaminepentaacetic Acid
HXe	Hyperpolarized ^{129}Xe
HHe	Hyperpolarized ^3He
HNG	Hyperpolarized Noble Gas
ML	Maximum Likelihood
MR	Magnetic Resonance

MRI	Magnetic Resonance Imaging
NMR	Nuclear Magnetic Resonance
PFOB	Perfluorooctyl Bromide
PMRI	Pre-Polarized MR Imaging
RF	Radiofrequency
ROI	Region of Interest
SAR	Specific Absorption Rate
SARS	Severe Acute Respiratory Syndrome
SNR	Signal-to-Noise Ratio
SQUID	Superconductive Quantum Interference Device
TE	Echo Time
TR	Repetition Time
VFA	Variable Flip Angle
VOI	Volume of Interest

Chapter 1

Introduction

1.1 Historical Background

1.1.1 Magnetic Resonance Imaging

MR imaging is based on the phenomenon of Nuclear Magnetic Resonance (NMR) discovered in 1946 by Bloch¹ and Purcell², independently. Since the introduction of Magnetic Resonance (MR) imaging by Lauterbur³ in 1973, this technique has become one of the most powerful and promising diagnostic tools in biology and medicine. The power of MR imaging is due not only to its ability to produce high quality anatomical images non-invasively, but also to the extremely rich information content provided in MR images.⁴ The MR signal depends on a number of parameters which strongly depend on the chemical and physiological properties of tissues, such as: nuclear spin density, relaxation times, molecular motion, magnetic susceptibility and electronic environment. This dependence allows images to be obtained that selectively provide information characterizing the structure, physiology and function of hydrogen-rich soft tissues and organs, containing water and/or fat. Despite this success, conventional proton MR imaging has been limited in imaging void spaces of the body (e.g. lungs and airways) due to low spin density.

The need for effective lung imaging techniques is becoming a very important issue since respiratory diseases, such as asthma, emphysema, pulmonary embolism, cystic fibrosis, lung cancer and chronic obstructive pulmonary disease (COPD),^{5,6,7} are among the leading causes of death in many countries. Various factors such as smoking,

increasing air pollution and allergies and new viral diseases such as the Severe Acute Respiratory Syndrome (SARS) emphasize the importance of improving existing lung imaging technologies and developing new ones.

Current radiological techniques for lung imaging include computed tomography (CT) and nuclear ventilation scintigraphy^{5,6} (imaging by measuring radiation from introduced radioisotopes). CT provides excellent depiction of structural changes of the lungs (e.g. architectural distortion and bronchial wall and septal thickening), but functional information can only be obtained indirectly from those structural changes or from the appearance of air trapping on expiration scans.⁶ Nuclear scintigraphy, though widely used to obtain ventilation information to evaluate regionally impaired ventilation and perfusion in various lung diseases (such as pulmonary embolus), has inherent disadvantages due to poor spatial resolution and radiation exposure.^{6,8}

Despite the low density of water and fat in the lungs, proton MR imaging has also been used with limited success in the lungs by exploiting contrast agents to directly or indirectly assess pulmonary structure and function. These imaging techniques include the use of oxygen-enhanced T_1 imaging to evaluate the ventilation-perfusion ratio⁹ and the use of gadolinium-based (Gd-DTPA) aerosols combined with perfusion imaging⁸ to study several pulmonary diseases, such as cystic fibrosis and pulmonary embolism. These techniques are limited by the short transverse relaxation times, the large susceptibility differences at the air-tissue interfaces and respiratory motion. The use of ultra-short echo-time pulse sequences in the future could help overcome some of these disadvantages, but motion will likely still be a concern. Other nuclei, such as ^{19}F (e.g. SF_6) has also been used for MR imaging of the lungs but the low spin density is still a limitation.¹⁰

1.1.2 Hyperpolarized Noble Gas Imaging

The low density of atoms in the lungs and airways can be compensated by the introduction of highly polarized noble gases such as helium and xenon. Using optical pumping, ^3He and ^{129}Xe gas can be polarized to achieve nuclear polarizations typically 4 to 5 orders of magnitude higher than those achieved in standard (thermal equilibrium) MR imaging ($\sim 10^{-5}$). Since the first demonstration of hyperpolarized ^{129}Xe (HXe) gas MR imaging of excised mouse lungs by Albert et al,¹¹ great advances have been made in the use of these Hyperpolarized Noble Gases (HNG's) to obtain anatomical and physiological information regarding the lungs. The potential of HNG techniques has been demonstrated in the diagnosis of several respiratory diseases such as asthma, emphysema, pulmonary embolism, cystic fibrosis, lung cancer and chronic obstructive pulmonary disease (COPD).^{5,6,7} HNG imaging can also be used to evaluate chronic rejection in lung transplant recipients,^{6,7} which commonly develop bronchiolitis obliterans (BO). Early BO is difficult to detect since it can be asymptomatic and traditional methods (i.e. bronchial biopsy and CT) are not very sensitive.⁶

While most recent HNG imaging studies have focused on hyperpolarized ^3He (HHe) due to its stronger signal, HXe has the additional feature of being highly soluble in blood, fat and other body tissues. This feature, together with its strong sensitivity to oxygen concentration and large chemical shifts, makes HXe an excellent blood pool marker and a potential novel contrast agent for perfusion MR imaging.^{12,13,14} Furthermore, ^{129}Xe is relatively cheap and very abundant unlike ^3He which is very rare and expensive.

In HNG MR imaging, the extremely high spin polarizations achievable depend on the laser polarization conditions such as laser power and gas mixture rather than the magnetic

field strength.^{15,16,17} This fact makes low (~ 0.1 - 0.3 T) and ultra-low (<0.1 T) MR systems another attractive option for HNG MR imaging.

1.1.3 Low Field Magnetic Resonance Imaging

Conventional clinical proton MR imaging is currently performed at medium to high magnetic field strengths (0.5 - 1.5 T) with even higher field strengths (3 - 7 T) available for research and preclinical applications. This trend towards higher field strength is largely based on the improved image signal-to-noise ratio (SNR) available at increased field strengths. The increased SNR at higher fields not only improves image quality, but also allows for reduced imaging times. Unfortunately, these high field systems typically rely on superconducting magnet technology which is expensive, requires costly cryogenics and imposes some restrictions on the system geometry.

Provided the low SNR problem can be overcome, MR imaging at lower fields (<0.5 T) may reduce the cost of MR imaging systems since less expensive resistive and/or permanent magnets can be used. MR imaging at low field strengths has several other important advantages including:^{15,18,19} (i) reduced siting restrictions and reduced chemical shift and susceptibility artifacts. (ii) Since low-field systems operate at much lower frequencies there are also advantages from the radiofrequency (RF) point of view. The RF skin depth (the penetration of RF waves in tissue) is larger resulting in more homogeneous excitation fields and less RF power requirements. (iii) Tissue RF heating is also reduced, allowing for more RF intensive pulse sequences without surpassing the safety limits on specific absorption rate (SAR).

Since the early years of MR imaging, there has been interest in using low field strengths,^{18,20} but the low SNR achievable has always been a major limitation. The

development of low field magnets with open geometry has renewed the interest in low field MR due to the increased patient accessibility available for interventional applications and therapy planning.^{21,22} Significant progress has also been made in recent years in pre-polarized MR imaging. This technique uses the non-equilibrium magnetization created by a strong magnetic pulse that polarizes the spins and a lower field strength is used during signal reception.^{19,23}

There have been some advances in the use of ultra-low magnetic fields for both hyperpolarized ^3He (HHe) and HXe imaging. Saam and co-workers²⁴ obtained one-dimensional profiles of HHe gas samples at 3.1 mT. Darrasse et al²⁵ demonstrated HHe human lung imaging at 0.1 T and reported transverse relaxation times on the order of a few seconds, which suggest that fast spin-echo sequences may be advantageous.²⁶

Augustine et al²⁷ imaged HHe and solid HXe at liquid helium temperatures (4 K) and 54 μT using superconductive quantum interference devices (SQUID), which could be an attractive alternative for increasing the sensitivity of detection of the MR signal. Tseng et al²⁸ demonstrated fast 2D imaging of HHe in sealed glass phantoms at 2.1 mT. Wong et al¹⁶ obtained images of HHe in excised rat lungs at 2.1 mT and compared the achievable resolutions at low and high fields. Wong-Foy et al²⁹ used SQUID to obtain images of HXe in porous materials at 2.3 mT with millimetre resolution.

Durand et al³⁰ reported the use of single-shot spin echoes for *in vivo* gas diffusion measurements and ultra-fast imaging of human lungs with HHe at 0.1 T. Venkatesh et al³¹ obtained lung images of rats at 15 mT using HHe and HXe and images of human lungs with HHe. Bidinosti et al¹⁵ measured the apparent diffusion coefficients of ^3He in

human lungs. Those measurements were done on a standing subject using a homebuilt system operating at 3 mT.

Most recently, Mair et al³² reported initial HHe human lung images obtained with an open access magnet operating at 3.8 mT which allows imaging with the subject in different positions. Bidinosti et al³³ used HHe in a whole body scanner operating at reduced current (3.1 mT) to measure the global O₂ partial pressure in human lungs.

The SNR dependence on magnetic field strength for clinical HNG imaging at higher fields has also been investigated. For large coils used in human imaging, where the noise originating from the body begins to dominate the coil noise, it has been experimentally demonstrated by Chronik et al³⁴ that for a solenoid (25.4 cm diameter and 16.5 cm length) the body noise dominates above a Larmor frequency of about 2 MHz. They predicted no SNR improvement for HXe imaging for field strengths beyond 0.2 T (and lower for larger coils).

Cross et al¹⁷ compared the SNR at 8.5 mT and 1.88 T and verified the expected field dependence for HXe imaging of small glass cells. Their results suggested that MR imaging of animal and human lungs using HXe at 8.5 mT may be feasible provided that an increase of the SNR by a factor of 5 could be achieved (for a 0.5 mm resolution and 7% xenon polarization). That increase could be obtained by increasing the field strength or the spin polarization, reducing the noise by improvements to the receiver electronics, optimum filtering or cooling the receiver coil, or by reducing the image resolution.

Furthermore, it has been shown by Brief et al³⁵ that due to the decrease in the apparent transverse relaxation times, T_2^* , of xenon and helium gas in the lungs at higher fields, the signal read-out times must be reduced, resulting in wider bandwidths and

decreased SNR. The reduced T_2^* at high field has been attributed to increased susceptibility-induced field gradients through which HNG molecules rapidly diffuse. Another consequence of the increased susceptibility differences at the gas/tissue interfaces is a decrease in spatial resolution at high fields, for a given acquisition time.¹⁶

Until now, the choice of field strength for HNG imaging has been dictated by the magnet hardware available for conventional clinical proton MR systems. Dedicated MR systems for HNG MR imaging with field strengths much lower than that provided by conventional clinical systems are desirable. Such systems have been developed but their field strength selection has not been optimized in any comprehensive way. The optimum field strength for clinical HNG MR imaging will depend on several factors including choice of nucleus (HHe or HXe), coil geometry, T_2^* and the region to be imaged (e.g. gas vs. dissolved phase; animal vs. human). A generalized theory accounting for these factors is required and needs to be verified experimentally.

The work presented in this thesis continues work previously performed at the Carleton Magnetic Resonance Facility (CMRF) by Mark McDonald for his M.Sc. project³⁶ and by Cross et al.¹⁷

This thesis addresses the following objectives:

1. To provide a theoretical framework for selection of the optimum field strength for clinical HNG MR imaging of the lungs based on achievable SNR and spatial resolution.
2. To develop a methodology for HNG MR imaging of in vivo rat lungs at ultra-low field strengths including magnet, RF and gradient/shim systems, as well as pulse sequences.

3. To experimentally verify the theoretically predicted field strength dependence of the SNR for HXe imaging of rat lungs.
4. To extrapolate the results to the situation of human clinical MR imaging of HXe in both gas-space and dissolved in tissues, at low (0.1-0.3 T) and ultra-low fields (<0.1 T).

1.2 Thesis Overview

The next chapter presents the basic physics of NMR and MR imaging, with emphasis on the details particular to HNG MR imaging. The physical basis of the laser polarization of ^{129}Xe is also described.

In Chapter 3, the theoretical derivation of the magnetic field strength dependence of the SNR and spatial resolution for HNG MR imaging of human lungs is presented. The theory is used to predict the dependence of SNR and spatial resolution on field strength. The optimal field strengths for HNG MR imaging are predicted under various conditions and discussed. In particular, the requirements for rat lung imaging are discussed.

Chapters 4 and 5 describe the ultra-low field MR system developed in this work. Those system components that differ significantly from those used in conventional high field MR are described in detail. In particular, a simple passive shimming method is described theoretically and shown to reduce the fringe field inhomogeneities of a superconducting magnet to a level that can be corrected with standard active shims allowing HXe MR imaging of rat lungs.

Chapter 6 presents the HNG imaging experiments performed with the ultra-low field MR system developed in this work. Images of phantoms and excised rat lungs are

presented and compared to high field images to verify the validity of the SNR theory presented in Chapter 3, for the case of small coils and samples.

Finally in Chapter 7, the results of this thesis are summarized and conclusions are presented. Extrapolation of the results to human lung imaging is made and future directions of this research are also discussed.

Chapter 2

Physics of HNG MR Imaging

2.1 Introduction

This chapter reviews the physical principles of both NMR and MR imaging necessary to understand the work presented in this thesis. In section 2.1, the theory of NMR is explained. Next (section 2.2), the principles of MR imaging are reviewed in the context of HNG imaging. Finally in section 2.3, the theory of laser polarization of ^{129}Xe is presented.

2.2 NMR Physics

Nuclear Magnetic Resonance refers to the interaction of nuclei composed of an odd number of protons and/or neutrons (i.e. possessing spin) with alternating magnetic fields of a given frequency. This frequency corresponds to the natural frequency of gyroscopic precession of the nuclear magnetic moment in the presence of an external static magnetic field. In this section, firstly the spin system is defined quantum mechanically, and then the magnetization (polarization) and excitation of a magnetic system are explained using the simpler classical approach. Next, the relaxation mechanisms of the nuclear system are presented and, finally, the Bloch equations are introduced to describe the time dependence of the magnetization in the presence of a magnetic field.

2.2.1 Nuclear Magnetic Moment in a Static Magnetic Field

Nuclei consist of a number of protons and neutrons each of nuclear spin $I = \frac{1}{2}$ coupled together resulting in a total magnetic moment $\vec{\mu}$ and a total angular momentum $\vec{J} = \hbar \vec{I}$ ($\hbar$ is the Dirac's constant), which are related according to:³⁷

$$\vec{\mu} = \gamma \vec{J} \quad (2.1)$$

where γ is the gyromagnetic ratio that is a scalar constant for a given nucleus (e.g. $20.38 \times 10^7 \text{ rad} \cdot \text{s}^{-1} \cdot \text{T}^{-1}$ for ^3He and $7.45 \times 10^7 \text{ rad} \cdot \text{s}^{-1} \cdot \text{T}^{-1}$ for ^{129}Xe).

In the presence of a static magnetic field $\vec{B}_0 = B_0 \hat{z}$, the nuclei are distributed in one of two states with energies given by the eigenvalues of the Hamiltonian:³⁷

$$\mathcal{H} = -\gamma \hbar B_0 I_z \quad (2.2)$$

where I_z is the component of the spin parallel to the static field. These energy levels are called Zeeman states; for nuclei with spin $I = \frac{1}{2}$, their energies are given by:³⁷

$$E = \pm \frac{1}{2} \gamma \hbar B_0 \quad (2.3)$$

Macroscopically, the bulk magnetization per unit volume M is given by:

$$|\vec{M}| = \left| \sum_{i=1}^N \vec{\mu}_i \right| = \frac{1}{2} N \gamma \hbar P, \quad (2.4)$$

where N is the total number of nuclei per unit volume and μ_i is the magnetic moment of the i th nucleus. P is the polarization, which is the fractional excess of nuclei in the lower energy (i.e. aligned) state:

$$P = \frac{n_- - n_+}{N} \quad (2.5)$$

where n_- and n_+ are the number of nuclei per unit volume in the lower and higher energy levels of Eq. 2.3, respectively.

At equilibrium, the distribution of the nuclei in these two levels follows the Boltzmann distribution according to:³⁷

$$P = \frac{1 - e^{-\hbar\gamma B_0/kT}}{1 + e^{-\hbar\gamma B_0/kT}} \quad (2.6)$$

where k is the Boltzmann constant and T is the absolute temperature of the sample. In the high temperature approximation ($\hbar\gamma B_0 \ll kT$), the equilibrium magnetization is approximately proportional to B_0 and given by:³⁷

$$M_0 = \frac{N\gamma^2\hbar^2}{4kT} B_0 \quad (2.7)$$

For HNG, the polarization achievable does not depend on B_0 , but rather on the laser polarization conditions, which will be reviewed later in this chapter. This polarization is a non-equilibrium state and is typically 4 to 5 orders of magnitude larger ($\sim 10^{-1}$) than the equilibrium magnetization ($\sim 10^{-6}$).

For macroscopic samples, N is large and the system appears continuous. For nuclei with spin $1/2$, a classical description is typically used to explain the NMR phenomenon. This has the advantage that a vector description can be used to represent the interaction between $\vec{M}$ and the applied magnetic fields. The equation of motion of the bulk magnetization in the presence of a magnetic field $\vec{B}$ can be written as:^{4,37}

$$\frac{d\vec{M}}{dt} = \gamma \vec{M} \times \vec{B}. \quad (2.8)$$

The solution of Eq. 2.8 when only the static (i.e. constant) field $\vec{B}_0$ is present is a precession of $\vec{M}$ about the direction of the field (Fig. 2.1), with a frequency given by the Larmor equation:

$$\bar{\omega}_0 = -\gamma \vec{B}_0. \quad (2.9)$$

This is the resonance frequency and corresponds to the difference of energy between the Zeeman states (Eq. 2.3). It can be shown from Eq. 2.3 that this energy difference is:

$$\Delta E = \hbar \omega_0. \quad (2.10)$$

Figure 2.1. Precession of the nuclear magnetization $\vec{M}$ in the presence of a magnetic field $\vec{B}_0$.

2.2.2 Effect of Alternating Magnetic Fields

The effects of time-varying alternating magnetic fields with frequency ω and amplitude B_1 on the spin system are easier to study in a reference system that rotates with the same frequency about the z direction of the laboratory system (Fig. 2.2). In this rotating frame of reference, the nuclei will experience an effective magnetic field $\vec{B}_{eff}$ given by:^{4,37}

$$\vec{B}_{eff} = \vec{B} - \frac{\vec{\omega}}{\gamma} \quad (2.11)$$

If $\vec{B}_1$ is perpendicular to $\vec{B}_0$, $\vec{B}_{eff}$ will then be:^{4,26}

$$\vec{B}_{eff} = \left(B_0 - \frac{\omega}{\gamma} \right) \hat{z}' + B_1 \hat{x}' \quad (2.12)$$

where $\hat{x}'$ and $\hat{z}'$ are unit vectors in the rotating coordinate system and $\vec{B}_1$ is applied along the x' axis (i.e. $\vec{B}_1 = B_1 \hat{x}'$).

Figure 2.2. Rotating magnetic field in the (a) laboratory and (b) rotating frames.

If $\vec{B}_1$ is applied as a pulse of duration t_p (called an RF pulse since its frequency is typically in the RF regime) on or close to resonance, $(\omega - \omega_0)^2 \ll (\gamma B_1)^2$, in the rotating frame the nuclei will only experience the $\vec{B}_1$ field and the magnetization will rotate through an angle given by:^{4,26}

$$\alpha = \gamma \int_0^{t_p} B_1(t) dt \quad (2.13)$$

about the $\vec{B}_1$ direction. This is called nutation and α is referred to as the flip angle. For $\alpha = \pi/2$, this RF 'excitation' pulse nutates $\vec{M}$ entirely into the transverse ($x'y'$) plane.

RF pulses are produced by coils of various geometries. Non-uniformities of the $\vec{B}_1$ field produced by the coil result in non-uniform flip angle distributions over the sample. Another source of non-uniformity is the finite penetration power of the RF field in conductive samples, which decreases with increasing Larmor frequency. This penetration power is typically characterized by the skin-depth parameter, which is defined as the depth at which the amplitude of the RF field is attenuated by a factor of e^{-1} and given by:³⁸

$$\delta = \left[\frac{\mu_0 \mu_s \omega_0}{2\rho_s} \right]^{-1/2}, \quad (2.14)$$

where μ_0 is the permeability of free space and μ_s and ρ_s are the permeability and the resistivity of the sample, respectively. For tissues, ρ_s is small and δ is large and not a great concern at the Larmor frequencies of clinical MR systems. However, for metals δ can be a few μm 's and its effects cannot be neglected (further discussed in Chapter 3).

After the pulse, the magnetization will have components ($M_{x'}$, $M_{y'}$, and $M_{z'}$), given by:²⁶

$$M_{x'} = M_{x',0} \quad (2.15)$$

$$M_{y'} = M_{y',0} \cos \alpha + M_{z',0} \sin \alpha \quad (2.16)$$

$$M_{z'} = -M_{y',0} \sin \alpha + M_{z',0} \cos \alpha \quad (2.17)$$

where $M_{x',0}$, $M_{y',0}$, and $M_{z',0}$ are the components of the magnetization prior to the RF pulse. If the system was in equilibrium before the pulse, then: $M_{x',0} = 0$, $M_{y',0} = 0$, and $M_{z',0} = M_0$.

2.2.3 Longitudinal Relaxation

After the spin system has been perturbed from its equilibrium state by an RF pulse (or by laser-polarization for HXe), it will return to this state through a relaxation mechanism due to the interactions between the nuclear spins and the surroundings.

The process of recovery of the longitudinal magnetization (M_z) to its equilibrium value M_0 is called longitudinal or spin-lattice relaxation. The spin-lattice relaxation mechanism is characterized by an exponential time constant, T_1 , called the longitudinal or spin-lattice relaxation time. This relaxation is produced by the energy exchange between the resonant nuclei and the surroundings.

For a monoatomic gas like xenon, couplings between the resonant nuclei and the surroundings are weak except during infrequent Xe-Xe collisions, where magnetic dipole-dipole interactions occur,³⁹ resulting in a T_1 on the order of minutes. For HXe dissolved in tissues and for HXe gas in the presence of impurities, coupling with electronic dipole moments of paramagnetics (such as molecular O_2) is very important and T_1 is correspondingly lower (on the order of seconds).

The T_1 relaxation depends on the density of lattice states of energies that would produce transitions between the Zeeman levels (corresponding to ω_0), which decreases with increasing frequency.³⁷ Hence, T_1 values will tend to increase with increasing B_0 .

In the rotating frame, the time dependence of M_z in the presence of this relaxation mechanism is described by:^{4,26}

$$\frac{dM_z}{dt} = -\frac{M_z - M_0}{T_1} \quad (2.18)$$

The solution for this equation is:

$$M_z(t) = (M_{z,0} - M_0)e^{-t/T_1} + M_0 \quad (2.19)$$

2.2.4 Transverse Relaxation

The transverse component of the magnetization ($M_{xy} = M_x + iM_y$, $i = \sqrt{-1}$) also returns to its equilibrium value ($M_{xy} = 0$) through a relaxation process that involves (in addition to some of the T_1 relaxation mechanisms) magnetic interaction between neighbouring resonant spins and is characterized by the transverse or spin-spin relaxation time T_2 . This process includes the loss of coherence between neighbouring nuclear spins due to slightly different local magnetic fields which results in a range of resonance frequencies over the sample (broadening of the resonance line).

In the rotating frame, the time dependence of the transverse magnetization is characterized phenomenologically by the equation:^{4,26}

$$\frac{dM_{xy}}{dt} = -\frac{M_{xy}}{T_2} \quad (2.20)$$

The solution of Eq. 2.20 is given by:

$$M_{xy}(t) = M_{xy,0} e^{-t/T_2} \quad (2.21)$$

where $M_{xy,0}$ is the transverse magnetization at time $t = 0$.

In addition to the spin-spin interactions, there are other relaxation processes that reduce the apparent transverse relaxation time such as B_0 inhomogeneities, magnetic susceptibility differences, chemical shift, chemical exchange and diffusion.^{4,16} These

combined effects are represented by a time constant T_2^* , called the apparent transverse relaxation time which is given by:¹⁶

$$\frac{1}{T_2^*} = \frac{1}{T_2} + \frac{1}{T_{2,inh}} + \frac{1}{T_{2,susc}} + \frac{1}{T_{2,diff}} \quad (2.22)$$

The spin-spin relaxation time T_2 for gases is on the order of the longitudinal relaxation time T_1 (several seconds) and its contribution to T_2^* is negligible.⁷

The second term in Eq. 2.22, accounts for the spectral line broadening due to inhomogeneities in the main magnetic field ΔB_0 and is given by:

$$\frac{1}{T_{2,inh}} = \frac{\gamma \Delta B_0}{2} \quad (2.23)$$

This term is mostly independent of the field and can generally be made as small as desired by properly designing the main field source ($\vec{B}_0$) and accurate shimming. At ultra-low fields (< 0.1 T), however, this term can be the dominating factor in T_2^* .

Variations of the magnetic susceptibility, $\Delta\chi$, in the sample also lead to spectral line broadening which depend on the field strength as:¹⁶

$$\frac{1}{T_{2,susc}} = \frac{\gamma \Delta\chi B_0}{2} \quad (2.24)$$

In the lungs, there are strong susceptibility differences ($\sim 10^{-5}$) over very small distances (~ 10 μm) at the interfaces between the gas spaces and tissue. Due to the large number of such interfaces and their very irregular shapes, this effect is much more important for HNG lung imaging than for conventional MR imaging of other regions of the body. This effect is larger for helium than for xenon due to its larger gyromagnetic ratio.

For nuclei diffusing in a region of susceptibility gradients, there is an additional contribution to T_2^* , which for the fast diffusion regime, $(\gamma \Delta \chi B_0)(l^2/D) \ll 1$, is given by:¹⁶

$$\frac{1}{T_{2,diff}} = (\gamma \Delta \chi B_0)^2 \left(\frac{l^2}{D} \right) \quad (2.25)$$

where l is the characteristic length over which χ varies by $\Delta \chi$ and D is the diffusion constant. For HNG MR imaging at the field strengths of interest in clinical MR imaging, this factor seems to be less important than susceptibility broadening (Eq. 2.24). This can be a consequence of the "apparent suppression" of the diffusion coefficient due to motional averaging in the restricted diffusion regime (the alveolar space dimensions are smaller than the characteristic diffusion length).⁷

For xenon dissolved in tissues, the diffusion and susceptibility effects are not as important as for lung HXe gas imaging due to the smaller diffusion coefficient⁴⁰ ($\sim 2.2 \times 10^{-5} \text{ cm}^2 \text{ s}^{-1}$) and reduced susceptibility differences at the boundaries between soft tissues (with the possible exception of the lung alveolar interface). However, other contributions need to be introduced in Eq. 2.22 to account for the line broadening produced by the chemical shift heterogeneity and chemical exchange between the different HXe compartments.^{41,42}

2.2.5 Spin Echoes

Spin-echoes are produced using a refocusing 180° pulse at time $TE/2$ after an initial RF excitation pulse (typically 90°). The effect of this pulse is flip the "pancake" of dephasing spins in the transverse plane (Fig. 2.3). In this way, the spins begin refocusing until the initial transverse magnetization is recovered at time TE , which then proceeds to

dephase with relaxation time T_2^* . If the 180° pulse is repeated, the several spin-echoes obtained will decrease in amplitude with a time constant T_2 . This multi-echo approach is a common technique for estimating T_2 . Not all the T_2^* relaxation mechanisms described in the previous section are refocused by the spin echo sequence. Dephasing due to homogenous line broadening (e.g. diffusion effects for long TE) can not be entirely refocused.^{4,26}

Figure 2.3. Diagram of the magnetization behavior during a Spin Echo sequence.

2.2.6 Bloch Equation

The phenomenological Bloch equation can be obtained by combining Eqs. 2.8, 2.18 and 2.20:^{4,26}

$$\frac{d\vec{M}}{dt} = \gamma \vec{M} \times \vec{B} - \frac{M_x \hat{x} + M_y \hat{y}}{T_2^*} - \frac{(M_z - M_0) \hat{z}}{T_1} \quad (2.26)$$

This equation describes the time dependence of the nuclear magnetization in the rotating frame in the presence of applied magnetic fields (both, static and RF) and includes relaxation mechanisms. The solution of Eq. 2.26 is a Lorentzian absorption/dispersion lineshape with a linewidth in the frequency space given by the Full

Width at Half Maximum,⁶ $FWHM = \frac{\pi}{T_2^*}$.

2.2.7 MR Signal

MR signal detection is based on the Faraday law of electromagnetic induction. The temporal evolution of the sample magnetization induces a voltage in a coil (properly tuned to the resonance frequency). This coil can be the same used to produce the RF excitation pulse or be an independent receiver coil.

Using the principle of reciprocity, the sensitivity of the coil is equal to the transverse field produced by a unit current in the coil, $(B_1)_{xy}$, and the induced voltage can be expressed using Faraday's law of magnetic induction as:^{43,44}

$$V(t) = -\frac{\partial \Phi(t)}{\partial t} = -\frac{\partial}{\partial t} \int_{V_s} (B_1(\vec{r}))_{xy} M_{xy}(\vec{r}, t) dV \quad (2.27)$$

where the integral is calculated over the volume of the sample V_s and $\Phi(t)$ is the magnetic flux crossing the coil at time t .

In general, this voltage contains the range of RF frequencies (i.e. the Larmor frequencies present in the sample) and is modulated in amplitude by the relaxation mechanisms discussed in the previous section. Before the signal can be digitized, it is amplified and the high frequency carrier removed through phase-sensitive detection.^{4,26}

The detected signal, that decays exponentially, is called the Free Induction Decay (FID) and can be written as:^{4,43}

$$S(t) = A \omega_0 \int_{V_s} (B_1(\vec{r}))_{xy} M_{xy,0}(\vec{r}) e^{-t/T_2^*(\vec{r})} e^{-i\Delta\omega t} dV \quad (2.28)$$

where A is a proportionality constant, which depends on factors such as the gain and frequency response of the receiver and the coil filling and geometric factors, and

$$\Delta\omega = \omega(\vec{r}) - \omega_0 = \gamma \Delta B_0(\vec{r}) \quad (2.29)$$

The field inhomogeneity, $\Delta B_0(\vec{r})$, is the difference between the field strength at point $\vec{r}$ and the field strength at the magnet isocentre, $\vec{r} = (0,0,0)$. The inhomogeneity is due to various sources, including imperfections in the magnet's field and magnetic susceptibility differences inside the sample, as well as any applied magnetic field gradients for spatial encoding as described in the next section.

2.3 Physics of MR imaging

In this section the principles of MR imaging are presented. Spatial encoding using field gradients is explained and the use of different imaging pulse sequences is discussed with respect to HNG applications.

2.3.1 Spatial Encoding

Equations 2.28 and 2.29 show that the detected signal contains a number of frequency components produced by non-uniformities in the field. In MR imaging, the field is purposely made non-uniform by using linear field gradients to spatially encode the signal. This is done by superposing additional weaker $\vec{B}$ fields in the same direction as $\vec{B}_0$ but

with amplitude changing linearly with position. For example, an x -gradient (G_x) has a variation in the x direction of the z component of the applied field given by:⁴

$$\frac{dB_z}{dx} = G_x \quad (2.30)$$

For imaging, the field variations produced by the gradients need to be much larger than the other field inhomogeneities in $\Delta B(\vec{r})$. In this case, each frequency of the signal will have a shift in frequency linearly dependent on spatial dimension (x) given by:⁴

$$\Delta\omega(\vec{r}) = \gamma G_x \Delta x \quad (2.31)$$

where Δx is the distance from the magnet isocentre.

The field gradients are typically used as pulses in sequences (combined with RF pulses) with variations in all three directions to obtain two-dimensional (2D) or three-dimensional (3D) images.

2.3.2 2D Spin-Warp MR Imaging

2D images can be obtained by a combination of three encoding processes: (i) slice selection, (ii) phase encoding and (iii) frequency encoding (Fig. 2.4). In slice selection, a field gradient is applied during an RF pulse, such that only a slice of the sample perpendicular to the direction of the gradient is excited. The slice position z' , thickness Δz and shape are determined by the gradient intensity, shape and duration of the RF pulse. For example, for a gradient G_z the selected slice would be given approximately by:⁴

$$z' \pm \Delta z = \frac{\omega' \pm \Delta\omega}{\gamma G_z} \quad (2.32)$$

where ω' is the carrier frequency of the RF pulse and $\Delta\omega$ is the bandwidth of the pulse, which depends on the pulse duration t_p according to:

$$\Delta\omega = \frac{4\pi}{t_p} \quad (2.33)$$

If a second field gradient (e.g. G_x) is applied for a time T_x following slice excitation, and during the sampling of the signal, the signal will have a frequency content given by Eq. 2.28. The Fourier transform (FT) of this signal will be the projection of the slice magnetization in the x direction. A gradient used this way is called a frequency encode or read-out gradient.

Spatial encoding in the third direction is achieved by using a phase-encoding gradient. This gradient (G_y) is applied for a period of time T_y after excitation and before the signal read-out. During T_y , spins at different y -positions will experience different fields and have different Larmor frequencies. After the pulse, all the spins will have again the same frequency but different phases given by:⁴

$$\phi(y) = \gamma G_y y T_y \quad (2.34)$$

The application of a combination of the three gradients (G_x, G_y, G_z) produces a signal from a slice of the sample with spatially dependent frequency and phase content. To obtain the complete 2D image, the sequence of RF and gradient pulses is usually repeated and the signal sampled and digitized. Each signal read out in the time domain corresponds to a line of the corresponding Fourier space of the object, which is referred to as k -space. A 2D FT is used to reconstruct the slice in the x and y directions.

Equation 2.28 can be written using the k -space formulism as:

$$S(t) = A \omega_0 \int_{V_S} (B_1(\vec{r}))_{xy} M_{xy,0}(\vec{r}) e^{-t/T_2^*} e^{-2\pi i [x k_x(t) + y k_y]} dV \quad (2.35)$$

where the spatial frequencies k_x and k_y for constant gradients are given by:

$$k_x(t) = \gamma G_x t \quad (2.36)$$

$$k_y = \gamma G_y T_y \quad (2.37)$$

Figure 2.4. Time diagram of a 2D spin-warp imaging sequence using spin echoes.

Three dimensional (3D) images can also be obtained by replacing the slice-selective gradient by a second phase-encoding gradient in the slice-select direction which is then varied N_z times for each value of the other phase gradient to complete the 3D k-space matrix. The 3D image can then be reconstructed using a 3D FT. Three-dimensional imaging provides an SNR advantage over 2D imaging of a factor of $\sqrt{N_z}$.

2.3.3 Pulse Sequences and Contrast in MR images

Spin echo and Gradient echo sequences are the most commonly used sequences for imaging and, generally, one k-space line is read out for each echo. In the gradient echo sequence, the transverse magnetization is refocused for read-out using bipolar gradient pulses (i.e. pulses with opposite amplitudes) instead of 180° RF pulses.^{4,26}

Multiple gradient echoes can also be obtained as described in section 2.2.5 for spin echoes, but their amplitude decreases rapidly due to the fact that, unlike the spin-echo sequence, the gradient-echo technique does not reverse the effect of T_2^* loss due to field inhomogeneity.

The intensity in the reconstructed image $I(x, y)$ is a function of the distribution of physical parameters of the sample (e.g. spin density and relaxation times). The form of this function depends on the pulse sequence used to obtain the image. The pulse sequence parameters (e.g. tip angle, echo time TE and repetition time TR) can be chosen to accentuate difference in one particular physical parameter between different tissues.

For example, for the spin echo sequence (Fig. 2.4) the image intensity can be written as:⁴

$$I(x, y) = A \rho(x, y) \left[1 - e^{-TR/T_1(x, y)} \right] e^{-TE/T_2(x, y)} \quad (2.38)$$

where $\rho(x, y)$ is the spin density at coordinates (x, y) and A is a proportionality constant.

T_1 -weighted images can be obtained by using short $TE \ll T_2$ and $TR \approx T_1$. By making $TE \approx T_2$ and $TR \gg T_1$, T_2 -weighted images can be obtained.

2.4 MR Imaging of Hyperpolarized Noble Gases

Due to the non-equilibrium nature of the spin polarizations obtained by laser polarization, the spin system does not recover its initial longitudinal magnetization following RF excitation. T_1 relaxation returns the excited spins to their thermal equilibrium polarization, which is negligible compared to the initial non-equilibrium magnetization. Therefore, unlike conventional thermal equilibrium MR, the magnetization available for imaging is non-renewable and with each RF pulse (flip angle α), an amount of magnetization equal to $M_z(1 - \cos \alpha)$ is lost.

Following the Look-Locker notation,⁴⁵ the longitudinal magnetization before (M_n^-) and after (M_n^+) the n th RF pulse of tip angle α_n in a train of pulses separated by a repetition time TR is given by:^{45,46}

$$M_n^+ = M_n^- \cos \alpha_n \quad (2.39)$$

$$M_{n+1}^- = M_n^+ e^{-TR/T_1} \quad (2.40)$$

and the transverse magnetization after the pulse is given by:^{45,46}

$$M_{xy,n}^+ = M_n^- \sin \alpha_n \quad (2.41)$$

Equation 2.40 can be written in terms of the initial longitudinal magnetization prior to the train of pulses M_i , for equally spaced pulses of the same flip angle, as:

$$M_{n+1}^- = M_i (\cos \alpha)^n e^{-(n+1)TR/T_1} \quad (2.42)$$

This equation can be used to estimate both T_1 and α , either simultaneously or in separate experiments.^{45,46}

The signal obtained after the n -th pulse in a pulse sequence decreases after each pulse since it is proportional to the transverse magnetization (Eq. 2.41). This effect produces a modulation on the signal amplitude in addition to the T_1 and T_2 (or T_2^*) relaxation, which generally decreases the image quality. A sequence with variable flip angle (VFA) can be designed to produce the same signal after each pulse (except for relaxation effects). VFA sequences use a 90° pulse at the end of the sequence to employ all the remaining magnetization. The flip angle for a VFA sequence consisting of N pulses follows the expression:³⁹

$$\alpha_n = \tan^{-1} \left(\frac{e^{-(N-n)TR/T_1}}{\sqrt{N-n}} \right) \quad (2.43)$$

2.5 Laser Polarization

The most common methods for hyperpolarization of ^{129}Xe are based on spin exchange with an optically pumped alkali metal vapour using a laser.⁶ Alkali metal spin exchange is capable of achieving moderate levels of spin polarization over a wide range of conditions, such as temperature, gas pressure, gas mix and field strength.⁵ This method is a two-stage process combining the optical pumping of alkali metal atoms with spin exchange between the polarized alkali metal atoms and the noble gas atoms. Rubidium (Rb) is the most common alkali metal used for spin exchange.

2.5.1 Optical Pumping

In the first step, the unpaired electrons of the Rb vapour are optically excited, in the presence of a magnetic field, by applying circularly polarized light tuned to the D_1 transition of Rb (i.e. 794.8 nm), which is the only interaction allowed by the condition

$\Delta m = +1$ (m is the angular momentum). As a result, the $5S_{1/2}$ level becomes populated. Collisions with other Rb vapour atoms equalize the population of the excited-state sub-levels, until a steady state is rapidly reached leaving the metal vapour highly polarized. Nitrogen is usually added to the gas mixture to quench the fluorescence created by the electronically excited Rb atoms, which depolarize the electron spins.^{5,39} Helium is also added to pressure-broaden the Rb resonance to match the laser bandwidth.

2.5.2 Spin Exchange

In the second step, collisions between the Rb atoms with unpolarized Xe gas atoms permit spin exchange via hyperfine coupling between the electronic spin of the alkali metal atoms and the nuclear spin of the noble gas atoms, creating a population of HXe gas nuclei. The process can be represented as:³⁹

The probability of spin exchange interactions depends on the relative velocities of the Rb and Xe atoms and on the spin-exchange cross-section of Xe.^{5,39} The presence of nitrogen in the gas mix increases that probability by providing a third body for momentum transfer during collisions.

The achievable noble gas polarization depends on the efficiency of the hyperpolarization process and on the relaxation of the hyperpolarized atoms, which is mainly a result of collisions of the hyperpolarized gas atoms with other atoms and with the walls of the polarization cell.^{5,6} The characteristic spin exchange time for Rb-¹²⁹Xe ranges from tens of seconds to a few minutes.^{5,6} The wall relaxation time of HXe is typically tens of minutes to a few hours depending on the wall material. Theoretically

these times predict polarizations up to 70-80% are achievable, however, in practice the polarizations typically obtained range between 15 and 20%.^{5,6}

Chapter 3

Theoretical Field Dependence of the Signal-to-Noise Ratio and Spatial Resolution in Hyperpolarized Noble Gas Magnetic Resonance Imaging

3.1 Introduction

The material included in this chapter represents, in large part, a manuscript accepted for publication in *Medical Physics* (manuscript #: 04-284): "Theoretical Signal-to-Noise Ratio and Spatial Resolution Dependence on the Magnetic Field Strength for Hyperpolarized Noble Gas Magnetic Resonance Imaging of Human Lungs".⁴⁷

In this chapter, a theoretical derivation of the magnetic field dependence of the SNR and spatial resolution for HNG MR imaging of human lungs is presented. The calculations use the principle of reciprocity under various imaging conditions and explicitly include the effects of susceptibility differences, transverse relaxation times and diffusion. The theory is used to predict the dependence of SNR and spatial resolution on field strength. The optimal field strengths for MR imaging of HHe and HXe in the lungs and elsewhere are discussed.

3.2 Theory

3.2.1 Signal-to-Noise Ratio

Using Eq. 2.28, the MR signal available after a 90° pulse can be written as:^{43,44}

$$S = K \omega_0 (B_1)_{xy} M_0 V_s \quad (3.1)$$

where: K is the coil geometry factor (discussed further in Chapter 4) and V_s is the volume of the sample. The initial magnetization of the sample M_0 is given by Eq. 2.4 and for HNG MR imaging is field independent.

The noise voltage V_N produced by both the thermal fluctuations in the coil and by sample losses is given by:^{43,44}

$$V_N = (4k \Delta f [T_C R_C + T_S R_S])^{1/2} \quad (3.2)$$

where T_C is the temperature of the coil, Δf is the receiver bandwidth, R_C is the resistance of the coil, R_S is the equivalent resistance of the sample, k is the Boltzmann constant and T_S is the temperature of the sample.

Combining Eqs. 3.1 and 3.2, the SNR expression can be written as:

$$SNR = \left[\frac{\eta N V_s P \gamma \hbar}{2} \right] [K (B_1)_{xy}] [4k \Delta f]^{-1/2} \omega_0 [T_C R_C + T_S R_S]^{-1/2} \quad (3.3)$$

where the filling factor η is the fraction of the coil that is occupied by the gas (from which the signal is derived), N is the number of nuclei per unit volume and P is the polarization.

The first factor in Eq. 3.3 depends on properties of the sample and the polarization (Eq. 2.5) and is independent of B_0 . This is a significant difference between HNG MR and conventional thermal equilibrium MR that leads to a very different field dependence of the SNR.

The second factor is also independent of B_0 and depends on the coil geometry and $(B_1)_{xy}$, the latter of which for a saddle coil with $g=a$ and n turns (Fig. 3.1), can be written as:⁴³

$$(B_1)_{xy} = 0.585n\mu_0/a \quad (3.4)$$

Figure 3.1. (a) Saddle coil and (b) sample geometry and dimensions.

The third factor in Eq. 3.3, containing the bandwidth Δf , is usually taken to be frequency independent for SNR calculations. However, for HNG MR imaging, the large variation in T_2^* over the range of field strengths of interest introduces an additional dependence of the SNR on magnetic field strength. Δf is related to the sampling interval Δt , the acquisition time T_{acq} and the number of samples N_x by:⁴⁸

$$\Delta f = \frac{1}{\Delta t} = \frac{N_x}{T_{acq}} \quad (3.5)$$

and the optimum acquisition time in terms of SNR (minimum bandwidth) is:⁴⁸

$$T_{acq} = \pi T_2^* \quad (3.6)$$

The expression for T_2^* (Eqs. 2.22-2.25) will not be substituted here but the consequences of its field dependence will be discussed later.

The first term in the last factor in Eq. 3.3, contains the coil resistance, R_C which can be calculated to be:^{38,43}

$$R_C = \frac{\zeta r_w R}{2 \delta} \operatorname{Re} \left[(1+i) \frac{J_0((1+i) r_w \delta^{-1})}{J_1((1+i) r_w \delta^{-1})} \right] \quad (3.7)$$

where: ζ is the proximity factor, r_w is the resistivity of the wire, $i = \sqrt{-1}$, Re denotes the real part, J_0 and J_1 are Bessel functions of the first kind and δ is the skin depth (Eq. 2.14) for the wire. $\delta \approx 0.5$ mm at 100 kHz and $\delta \approx 5$ μ m at 10 MHz. R is the resistance of the wire to direct current ($\omega_0 = 0$):

$$R = \frac{\rho_w l}{\pi r_w^2} \quad (3.8)$$

where ρ_w and l are the length and the radius of the wire, respectively.

Equation 3.7 is valid for all frequencies of interest (0-100 MHz), including the very low frequencies (<1 MHz) that are of little interest for conventional MR imaging and neglected in previous studies.^{21,22} No attempt is made here to calculate the proximity factor more accurately, however, this factor can be ignored for single turn coils typically used at most field strenghts^{53,54}. At very low fields it is expected to produce negligible effects since at those low Larmor frequencies, the skin depth is larger than the wire radius

and the current flows through the whole wire cross-section almost unaffected by the field produced by neighbouring wires^{53,54} (this is discussed further in Chapter 6).

For frequencies such that $r_w \gg \delta$ (typically above 5 MHz),^{21,24} Eq. 3.7 indicates that the resistance of the coil depends on $\omega^{1/2}$,^{21,22} while at lower frequencies, Eq. 3.7 becomes:³⁸

$$R_c = R \left[1 + \frac{1}{48} \left(\frac{r_w}{\delta} \right)^4 \right] \quad (3.9)$$

which for $\delta \gg 0.38 r_w$ is a constant given by Eq. 3.8.

The sample noise is due to two main sources:⁴⁴ dielectric and inductive losses. While dielectric losses can be avoided by properly designing the RF coil or by introducing shields, inductive losses are unavoidable. For a saddle coil of radius a , length $2g$ and n turns (Fig. 3.1a), containing a cylindrical sample (Fig. 3.1b) of radius b , and resistivity ρ_s , the sample equivalent resistance due to inductive losses is approximately given by:

44,49

$$R_s = (1 - \eta^{5/2}) \frac{1.37 \pi \mu_0^2 n^2 b^4 g \omega_0^2}{16 \rho_s a^2} \quad (3.10)$$

where $\eta = c^2/b^2$ is the fraction of the sample volume occupied by the lungs (gas space), which is the fraction that contains the HXe but has very low conductivity and produces negligible inductive losses.

For large samples or for small samples at high frequencies the sample noise dominates the last factor of Eq. 3.3. The frequency ω_0' at which the noise goes from the

coil-dominated regime ($R_C > R_S$) to the sample-dominated regime ($R_C < R_S$) can be calculated, by equating the two terms in the last factor of Eq. 3.3:

$$\omega_0' = 0.55 \frac{\mu_w^{1/3}}{\mu_0} \rho_w^{1/3} \rho_s^{2/3} \left[\frac{T_c}{T_s} \frac{\zeta l a}{n^2 b^4 r_w \left(1 - \eta^{5/2}\right)} \operatorname{Re} \left(\frac{(1+i) J_0((1+i) r_w \delta^{-1})}{J_1((1+i) r_w \delta^{-1})} \right) \right]^{2/3} \quad (3.11)$$

Combining Eqs. 3.3-3.7 and 3.10, the SNR expression can now be written as:

$$SNR = C_0 \omega_0 (T_2^*)^{1/2} (N_x)^{-1/2} \left[C_1 \omega_0^{1/2} \operatorname{Re} \left[\frac{(1+i) J_0((1+i) r_w \delta^{-1})}{J_1((1+i) r_w \delta^{-1})} \right] + C_2 \omega_0^2 \right]^{-1/2} \quad (3.12)$$

where:

$$C_0 = \frac{1.63 \eta N P \hbar \mu_0 \gamma b^2 K}{k^{1/2}} \quad (3.13)$$

$$C_1 = 0.35 T_c \zeta [\mu_w \mu_0 \rho_w]^{1/2} \frac{l}{n^2 \pi r_w} \quad (3.14)$$

$$C_2 = \frac{0.27 T_s \left(1 - \eta^{5/2}\right) \mu_0^2 b^4}{\rho_s a} \quad (3.15)$$

In the coil-dominated noise regime ($\omega_0 \ll \omega_0'$), the SNR depends on ω_0 as:

$$SNR \propto \frac{\omega_0 (T_2^*)^{1/2}}{\sqrt{R_C}} \approx \begin{cases} \omega_0 (T_2^*)^{1/2} & \text{for } \delta \gg 0.38 r_w \\ \omega_0^{3/4} (T_2^*)^{1/2} & r_w \gg \delta \end{cases} \quad (3.16)$$

Since T_2^* is typically dominated by B_0 inhomogeneities which are largely independent of field at these low frequencies, this expression indicates that the SNR frequency dependence has a power ranging from 0.75 to 1, depending on the wire radius.

In the sample-dominated noise regime ($\omega_0 \gg \omega_0'$), Eq. 3.12 gives:

$$SNR \propto (T_2^*)^{1/2} \quad (3.17)$$

Eq. 3.17 indicates that at high fields, the SNR only depends on the field strength through T_2^* . Since T_2^* typically decreases with increased field strength, it is predicted that unlike conventional MR imaging, the maximum achievable SNR for HNG MR imaging will actually decrease with increasing field strength in the sample-dominated noise regime.

3.2.2 Spatial resolution

The intrinsic spatial resolution of the HNG MR imaging experiment can be calculated using the expression of Callaghan:⁴⁸

$$\Delta x = 1.34 \left[\Delta x_{diff} \left(\Delta x_{T_2^*} \right)^2 \right]^{1/3} \quad (3.18)$$

where Δx_{diff} is the diffusion-limited resolution and $\Delta x_{T_2^*}$ is the T_2^* -limited resolution.

The diffusion-limited resolution depends on the acquisition time T_{acq} , according to:⁴⁸

$$\Delta x_{diff} = \sqrt{2D_{eff} T_{acq}} \quad (3.19)$$

where D_{eff} is the effective diffusion coefficient, which accounts for both the binary (collision) diffusion effects (HNG is mixed with air in the lungs) and the motional averaging in the restricted diffusion regime,^{7,50} since the alveolar space dimensions ($\sim 230 \mu\text{m}$ for humans) are smaller than the characteristic diffusion lengths ($\sim 2 \text{ mm}$ and 0.8 mm for helium and xenon, respectively, for $T_{acq} = 10 \text{ ms}$). In larger airways, the effects of motional averaging are smaller, but these airways are expected to be a negligible contribution ($< 5 \%$) to the total lung signal.

The T_2^* -limited resolution depends on the applied gradient G and on T_2^* according to:^{16,48}

$$\Delta x_{T_2^*} = \frac{2}{\gamma G T_2^*} \quad (3.20)$$

The spatial resolution limits described by Eqs. 3.18-3.20 depend on the choice of imaging parameters (such as G and T_{acq}) and can be quite different at different field strengths. However, they can be compared under given conditions such as maximum SNR or constant SNR at all field strengths.

3.3 Calculation Methods

3.3.1 RF Coil

For these calculations, saddle coils (Fig. 3.1a) at room temperature ($T_c = 298 K$), made of copper and with dimensions (a: 27.5, 25, 17.5, and 15 cm) similar to those typically used for chest imaging (to conform to changing sample sizes) were considered.

The effect of the number of turns, n , has been investigated and shown to make little difference in the calculations⁴³. This is expected since in the sample-dominated noise regime, the SNR does not depend on the number of turns (C_2 does not depend on n in Eq. 3.15) and cannot practically be made much larger than unity anyway. At lower frequencies, the SNR is also independent of n if $r_w \gg \delta$, but depends on $n^{-1/2}$ if $\delta \gg 0.38r_w$ (in both cases for $n \gg 1/3$). These are a consequence of the fact that there is limited room for the coil windings. The wire radius r_w is typically chosen such that n turns fit in an area (cross-section of the windings) that for a saddle coil can be taken to be a square of width $0.2g$, due to homogeneity and spacing constraints.⁴³ Even if there are no such spacing limitations, the coil geometry needed to obtain proper B_1 homogeneity

would impose similar restrictions on the area occupied by the windings. Therefore, in these calculations it was assumed that $n = 1$ and $r_w = 5 \text{ mm}$.

3.3.2 Sample

Cylindrical samples (Fig. 3.1b) of $\rho_s = 0.85 \Omega m$ (i.e. water-like tissue) of various dimensions (b: 25, 22.5, 15, and 12.5 cm) were used in the SNR calculations. This simulated the range of chest sizes expected for children and adults. The temperature of the sample was set to that of the human body, $T_s = 310^\circ \text{K}$.

For the calculations, natural abundance xenon gas (26% ^{129}Xe) and 100% ^3He gas were assumed, both with polarizations of 20%. It was assumed that at the time of lung imaging only 50% of the total lung gas volume was occupied by HNG, uniformly mixed with air (the remaining 50% volume). For T_2^* , the model of Eqs. 2.22-2.25 was used. It was assumed $[T_{2,inh}]^{-1} \sim 7 \text{ Hz}$, which is on the order of the linewidths typically obtained with low-field magnets.¹⁷ Figure 3.2 shows the field strength dependence of T_2^* for both helium and xenon, as predicted by Eq. 2.22. For comparison, measured T_2^* values found in the literature are shown in Table 3.1 and plotted on Fig. 3.2.

In general, relatively good agreement was found between those reported and the model used here at high fields. However, most of those values were measured at very high field (1.5 T and 2.0 T) or extremely low field (<15 mT), with only one at 0.1 T, making it difficult to evaluate the very important intermediate field strengths. At very low field the field inhomogeneities limited the T_2^* estimations. For HXe, no reported measurements on humans were available.

Figure 3.2. Field strength dependence of the apparent transverse relaxation time. Some reported experimental values are shown (Table 3.1) for HHe (diamonds) and HXe (squares).

	Field Strength	Sample Conditions / Reference	T_2^* (ms)
Helium	1.5 T	Human lungs ⁵⁰	Tens of milliseconds
	2.0 T	Guinea Pig lungs ⁵⁰	9 – 16 ms
	2.1 mT	Excised rat lungs ¹⁶	> 100 ms
	0.1 T	Human lungs ³⁰	>40 ms ⁺
	3 mT	Human lungs ¹⁵	10 ms ⁺
	1.5 T	Human lungs ⁵¹	20 ms
Xenon	2.0 T	Guinea Pig lungs ⁵⁰	18.5 ms
	15 mT	Rat lungs ³¹	~100 ms ⁺⁺

⁺ Limited by magnet homogeneity.

⁺⁺ For both, helium and xenon (not specified in paper).

Table 3.1. Measured values of HNG transverse relaxation times, T_2^* , at different field strengths reported in the literature.

It should also be noted that the T_2^* values can depend on several factors, such as lung inflation and fraction of air in the lungs.^{26,29} The limitations of T_2^* modeling on the calculation of SNR and spatial resolution will be discussed later.

3.3.3 Spatial Resolution

For the spatial resolution calculations, reported restricted diffusion coefficients for helium and xenon in the lungs were used, respectively: $D'_{He} = 0.15 \text{ cm}^2/\text{s}$ and $D'_{Xe} = 0.021 \text{ cm}^2/\text{s}$.^{7,50}

The gradient amplitude G was chosen to produce maximum SNR (minimum bandwidth; Eqs. 3.5 and 3.6) for a fixed target resolution (0.7 mm) at all field strengths. It was assumed that the maximum gradient available was $G_{\max} = 40 \text{ mT m}^{-1}$ at the highest available field strength (3.0 T), which are typical clinical values. G was appropriately scaled down with decreasing field to take advantage of the increase in T_{acq} according to Eq. 3.6 using:

$$G(B_0) = G_{\max} \frac{T_{acq}(3T)}{T_{acq}(B_0)} = 40 \text{ mT} \cdot \text{m}^{-1} \frac{T_2^*(3T)}{T_2^*(B_0)} \quad (3.21)$$

This reduction of the gradient intensity also results in narrow signal bandwidths at very low fields which is desirable due to the limited coil bandwidth typically available at very low frequencies (<500 kHz).¹⁷

To compare resolution at different field strengths for the same SNR, the gradient intensity was scaled according to:

$$G(B_0) = G_{\max} \left[\frac{SNR(B_0)}{SNR(3T)} \right]^2 \frac{T_2^*(3T)}{T_2^*(B_0)} \quad (3.22)$$

This choice of G produces an SNR equal to that at 3T (for each gas) for every field strength. This has the effect of adjusting pixel size to compensate for changes in SNR at different fields.

3.4 Results and Discussion

Figure 3.3 shows the field dependence of the SNR for HHe and HXe imaging, according to Eq. 3.12 for human lungs (adult size). The SNR for HHe is one order of magnitude larger than for HXe due to its larger gyromagnetic ratio and the use of natural abundance xenon in the calculation, and agrees with reported experimental results.³⁰ For both gases, the SNR dependences show a maximum at low-to-intermediate field strengths which is lower for HHe (~ 0.15 T) than for HXe (~ 0.45 T) due to its larger gyromagnetic ratio. The SNR decreases at higher fields due to the larger bandwidth needed to use as a consequence of the reduced T_2^* .

The optimum field strength strongly depends on the size of the sample/coil and the sample characteristics. Figure 3.4 shows the field strength corresponding to the frequency ω_0' that separates the coil-dominated and sample-dominated noise regimes for HXe and HHe (Eq. 3.11) as a function of the sample size (ranging from small animal sizes to adult human size) for lung imaging. Figs. 3.5 and 3.6 show the field dependence of the SNR for HXe and HHe, respectively, for several sample/coil size combinations. SNR maxima are shifted towards higher fields (0.35-0.7T for HXe and 0.15-0.55 T for HHe) with decreasing system/sample size, but a decrease in SNR is still observed at the field strengths more typical of conventional clinical proton MR imaging systems (1-1.5 T).

Figure 3.3. Field dependence of the SNR of HNG MR imaging of the lungs (a: 27.5 cm, b: 25.0 cm, g: 27.5 cm, gas space volume: 6 liters). The maximum SNR values are obtained at approximately 0.15 T for HHe and 0.45 T for HXe.

Figure 3.4. Field strength, as a function of the sample radius b (corresponding to the frequency ω_0') separating the coil-dominated and sample-dominated noise regimes for HXe and HHe ($a = 1.2 b$, $\eta = 0.1$).

Figure 3.5. Field dependence of the SNR for HXe lung imaging for various sample/coil sizes ($\eta = 0.1$). The curves were independently normalized.

Figure 3.6. Field Dependence of the SNR for HHe lung imaging for various sample/coil sizes ($\eta = 0.1$). The curves were independently normalized.

Although these results were obtained for saddle coils and cylindrical samples, other coil/sample geometries (i.e. solenoid, bird cage) can be considered. It can be demonstrated that the choice of the coil for a wide range of human lung geometries only results^{43,49} in small changes in Eqs. 3.4 and 3.10 and do not affect the general field dependence of the SNR. In these calculations, the sample geometry was chosen based on the anticipated size of a chest volume and typical lung volumes.

For very small samples the coil noise dominates over a large range of field strengths and the SNR continuously increases with increasing field up to very high fields. Figure 3.7 shows the SNR field dependence predicted for HXe imaging of excised rat lungs. The maximum of the SNR curve is achieved at approximately 7.5 T, which near the limit for research MR imaging systems (research systems at 9.4 T). This field dependence for small samples will be verified experimentally in Chapter 6.

Figure 3.7. Field strength dependence of the SNR for HXe imaging of excised rat lungs. (a: 2.25 cm, b: 1.85 cm, $\eta = 1$).

Figure 3.8 shows the field dependence of spatial resolution based on Eq. 3.19, with G chosen to produce maximum SNR at each field strength (with a target resolution of 0.2 mm), according to Eq. 3.21. These predictions are approximately in agreement with those predicted by others.⁵² While the best resolutions (<0.4 mm) are achieved at high fields, at very low field strengths, the spatial resolution obtained is only slightly degraded (~ 0.53 mm) and still suitable for human lung imaging. HXe provides worse spatial resolution than HHe due primarily to increased diffusion within the larger acquisition time window (due to the larger T_2^* of HXe). For a given T_{acq} , however, HXe would be expected to provide better spatial resolution than HHe due to its smaller diffusion coefficient and gyromagnetic ratio.

Figure 3.8. Field dependence of the spatial resolution for HNG lung imaging. The gradient strength was adjusted to produce maximum SNR at each field strength for a target resolution of 0.3 mm.

Figure 3.9 shows the spatial resolution dependence on field strength when the gradient intensities were scaled to produce the same SNR at all field strengths according to Eq. 3.22. Fig. 3.9 shows that at constant SNR, the best resolution for HHe is achieved at about 0.1 T (about 0.4 T for HXe) and shows little dependence on B_0 over a large range of field strengths. For HXe at lower fields, the spatial resolution degrades rapidly due to the faster reduction of the SNR for HXe at these fields, compared to HHe (Fig. 3.3). Nevertheless, sub-millimetre spatial resolution can still be achieved at fields as low as approximately 25 mT with an SNR similar to that achievable at 3T. The improvement in spatial resolution at intermediate fields (compared to Fig. 3.8) is smaller for HXe than for HHe since the HXe SNR maximum occurs at higher field strength.

Figure 3.9. Field dependence of the spatial resolution for HNG lung imaging. The gradient strength was adjusted to produce the same SNR at all field strengths. The SNR at 3.0 T was selected as the reference value (according to Fig. 3.3).

The results presented here assumed an *ad hoc* model for T_2^* which provided values comparable to reported measured values (Table 3.1). Despite the reasonable agreement of the model of Eqs. 2.22-2.25 (Fig. 3.2) with Table 3.1, further studies of the relative importance and field dependence of T_2^* relaxation mechanisms of HNG in the lungs and elsewhere, both theoretical and experimental would be useful.

In lung imaging, there are strong susceptibility differences ($\sim 10^{-5}$) over very small distances (~ 10 - $100 \mu\text{m}$) at the interfaces between the gas spaces and tissue.²⁶ Due to the large number of such interfaces inside a typical voxel and their very irregular shapes, these effects are expected to be much more important for HNG lung imaging than for conventional MR imaging of other tissues. The validity of Eq. 2.25 is also questionable since at very high fields (and especially for xenon due to its smaller diffusion coefficient) the system is near the boundary between the slow and fast diffusion regimes, $(\gamma \Delta \chi B_0)(l^2/D) \approx 1$.

The longer T_2^* at lower fields suggests that some advantage may be obtained by using multi-echo imaging approaches such as echo-planar imaging (EPI) sequences which allow narrower bandwidths, thus increasing SNR and requiring less gradient power. Other fast sequences such as fast spin-echo imaging requiring large numbers of 180° refocusing pulses could also be used to advantage at low fields. Since the specific absorption rate (SAR) is proportional to the square of the static magnetic field strength, faster repetition rates or more RF pulses can be used at lower fields without exceeding tissue heating safety limits.

In this work the field dependence of the tissue resistivity has not been considered and will likely be the subject of future research. Tissues are expected to be noisier at higher fields (due to increased resistivity), further degrading the high field SNR values.

For dissolved phase imaging, the concentration and polarization of HXe in tissue is much smaller than in the lungs due to dilution and T_1 relaxation. This depends on several factors such as the solubility of xenon in each particular tissue, HXe delivery method and T_1 of HXe in the carrier which complicate the calculation of absolute SNR. However, the field strength dependence of SNR for dissolved HXe is expected to be qualitatively similar to that for lung imaging (Fig. 3.6) since the shift of the optimum field towards higher fields due to the smaller sample sizes (such as those in brain and breast imaging) is expected to be compensated for by a stronger field dependence of T_2^* .⁴¹ While the diffusion and susceptibility effects (Eqs. 2.24 and 2.25) are less important, other dissolved phase relaxation mechanisms should be added to Eq. 2.22, accounting for paramagnetic effects, chemical shift heterogeneity and chemical exchange.⁴² Further studies of HXe solubility, T_2^* , diffusion, chemical shift, and chemical exchange effects of HXe in both the gas phase and the dissolved phase and the implications for SNR and spatial resolution are worthwhile.

3.5 Conclusions

At the magnetic field strengths currently used for clinical MR imaging (0.5-3.0T) the SNR is predicted to be lower (20-50%) than at the predicted optimum fields (0.1-0.6T). At higher fields (>3T), however, the SNR degrades considerably. While still feasible,

HNG at ultra-low field strengths (<25 mT) has SNR substantially lower (~3 to 4 times) than at the optimum fields.

The achievable spatial resolution is almost constant over a large range of field strengths (0.1-3T). At higher field the resolution degrades due to reduced SNR and T_2^* . At lower fields the resolution also degrades due to the reduced SNR, more significantly for HXe than for HHe.

HHe provides higher SNR for lung imaging compared to HXe, but HXe provides similar spatial resolution with lower gradient intensities and offers the additional capability to perform dissolved phase imaging for HNG imaging applications outside the gas spaces of the body.

Chapter 4

Ultra-Low Field Magnetic Resonance Apparatus

4.1 Introduction

In this chapter the components of the ultra-low field MR system are described. At ultra-low field strengths, due to the corresponding very low operating frequencies there are significant differences in the MR technology between conventional high field MR system and low field designs, such as: the reduced performance of conventional RF shields and the limited system bandwidth due to the narrow RF coil bandwidth. Furthermore the wavelength is on the order of 10^2 – 10^3 m, which prohibits the use of some passive RF electronics, such as quarter and half-wavelength cables. Only the components of the ultra-low field system that significantly differ from those found in high field systems will be explained in this chapter. The reader is referred to several good reviews of conventional high field MR hardware.^{53,54,55}

The ultra-low field system uses the power supplies and control electronics of an existing high field system at the CMRF. The experiments were performed at two field strengths: 8.5 mT and 17 mT, corresponding to xenon Larmor frequencies of 100 kHz and 200 kHz, respectively. The choice of these two field strengths was based on previous work done at the CMRF and on system restrictions such as stability of the electromagnet power supply and magnet heating^{17,36} (the previous ultra-low field studies of McDonald³⁶ were done using a homebuilt 8.5 mT electromagnet).

Use of the fringe field of a superconducting magnet as the source of the static magnetic field (as described in the next chapter) provided an alternative to overcome the

limitations of the electromagnet. Initially the fringe field experiments were also performed at 8.5 mT. This choice allowed a comparison with studies initiated with the electromagnet and allowed use of the same RF electronics.

The second field strength (17 mT) was used to verify the scalability of the passive shimming technique developed (Chapter 5) initially for the 8.5 mT experiment and to validate the SNR model and predictions presented in Chapter 3. 17 mT was near the maximum field strength achievable in the fringe field of the 1.89 T magnet available at the CMRF. Though still much lower than the optimum fields predicted in Chapter 3, by doubling the field strength, the achievable SNR is also increased by a factor of approximately two. For comparison, experiments were also done in the bore of the 1.89 T superconducting magnet. The availability of three field strengths also allowed study of the field dependence of other MR parameters, as described later in this thesis.

4.2 Magnet System

The ultra-low MR system (Figs. 4.1 and 4.2) uses the fringe field of a 30 cm bore unshielded superconductive magnet (1.89 T, Magnex, Exon, England), passively shimmed using the method described in Chapter 5. This approach provided a static field strength up to 20 mT at the surface of the magnet's dewar, with very high temporal stability.

Imaging was accomplished using a 26 cm diameter gradient and shim coil set (Bruker B-GS 30/C-19, Ettlingen, Germany) powered by the gradient and shim power supplies of the 1.89 T system (Techron 7700 and Resonance Research MXA-18/4V, respectively) and controlled by an MRRS (Surrey, UK) MR5000 console.

Figure 4.1. Schematic representation of the low-field system in the fringe field of the superconducting magnet. The z' axis is parallel to the z axis and the origin $z'=0$ is aligned with the centre of the magnet ($z=0$).

From the 16 channels available in the shim power supply, only 15 were used by the Bruker shim set, since the Z^4 shim coils were not operational. Modifications to the Bruker gradient/shim set included changes to the cables and connectors to fit the connectors of the Techtron amplifiers. The cables entered directly into the magnet room through the door-way, no RF filters were necessary since the RF shield (described in section 4.3.3) located inside the bore of the gradient/shim coil set was sufficient.

Figure 4.2. Photo of the low-field system situated in the fringe field on the right side of the superconducting magnet as viewed from the back.

4.3 Radiofrequency System

4.3.1 RF Receiving and Transmitting systems

Figure 4.3 shows a diagram of the RF transmitting and receiving systems used in the ultra-low field experiments. An ENI 2100L (Rochester, NY, USA) RF power amplifier, with a 50 dB gain in the range 10 kHz-12 MHz and capable of delivering 200 watts to a 50 Ω load, was used. An MRRS (Surrey, UK) low-frequency shifter was used to both lower the transmit carrier frequency of the RF pulses produced by the MR5000 console (typically 80 MHz) to the desired lower frequencies as well as to increase the frequency back to the higher frequency needed on the receiver side at the input of the high frequency phase-detector. The frequency shifter was capable of operating in a range of frequencies from 100 kHz to 10 MHz, but it was available only after the 8.5 mT experiments were finished and was only used at 17 mT. It improved the system RF electronics, increasing the flexibility of the pulse sequences, allowing different operating frequencies without changes to the electronics and permitted the use of phase-alternating and shaped RF pulses (e.g. slice selection).

The RF electronics for the experiments at 8.5mT were based on the polarimeter design of Saam and Conradi.⁵⁶ This design was modified to include quadrature phase detection, an interface to the MR5000 console and a 100 kHz transmitter.¹⁷ Modifications were made to the output circuitry of the 100 kHz phase-detector to allow DC offset adjustment and to modify the output impedance to be compatible with the expected 50 Ω load at the console digitizer inputs.¹⁷

Figure 4.3. Diagram of the RF system.

The preamplifier was adjusted to operate at the required frequencies (100 kHz and 200 kHz) by changing the capacitors of the filters.¹⁷ The frequency responses of the preamplifier at these two frequencies are shown in Figs. 4.4 (a) and (b), respectively. The frequency response was measured by comparing the input and output voltages of the preamplifier for signals provided by a frequency synthesizer over the range of interest.

Figure 4.4. Frequency response of the preamplifier for the two operating frequencies used in this work: (a) 100 kHz and (b) 200 kHz. Note that in the second case the central frequency is slightly higher than 200 kHz, as it was originally set to operate at 230 kHz (i.e. the Larmor frequency for 20 mT instead of 17 mT).

The noise figure (F) of the preamplifier and the complete receiver system was estimated using a 2 k Ω load (i.e. the approximate impedance of the receiving coils) by measuring the noise power at room temperature and at liquid nitrogen temperature and calculating F according to:⁵³

$$F = 10 \left[\log_{10} \left(1 - \frac{T_N R_N}{T_R R_R} \right) - \log_{10} \left(1 - \frac{N_N^2}{N_R^2} \right) \right] \quad (4.1)$$

where T_N and T_R are the absolute temperature of liquid nitrogen (77 °K) and the room absolute temperature, respectively and R_N and R_R are the resistances of the load at these temperatures. N_N and N_R are the noise amplitudes measured at those temperatures respectively. These measurements gave a noise figure of 2.9 ± 0.6 dB for the preamplifier and 4.2 ± 0.6 dB for the receiver.

4.3.2 RF Coils

For the ultra-low field SNR experiments, two different coils were used. For the 8.5 mT experiments, a solenoidal coil with an inside diameter of 10 mm, a length of 12 mm and tuned to 100 kHz, was used. The total number of turns on the coil was 560 of 34 AWG coated copper magnet wire. For 17 mT, a solenoidal coil of similar length and diameter but with only 250 turns and tuned to 200 kHz, was used (Fig. 4.5).

For imaging of larger samples at 17 mT, a split-solenoid coil of 4.5 cm inner diameter, length 6 cm, separation between the sets of windings of 12 mm, made of 50 turns of AWG 22 wire and tuned to 200 kHz (Fig. 4.6) was used. For field mapping at 17 mT, this coil was used as the transmitting coil orthogonal to the solenoidal receiver coil to eliminate interference originating from the RF transmitter (see next section).

For the 1.89 T experiments, two coils were used: (i) A 14 turn solenoid coil (1 cm inner diameter, 5.4 cm length, AWG 12 wire) was used. It was tuned to the xenon resonant frequency (22.2 MHz) and matched to $50\ \Omega$ impedance. This coil was used to obtain spectra to estimate the absolute polarization and for imaging small samples for SNR measurements. (ii) For imaging larger samples, a birdcage coil of 12 cm diameter and length 19 cm was used.

The 100 kHz solenoidal coil had a bandwidth of 6.0 ± 0.4 kHz ($Q \sim 17$). The 200 kHz solenoidal coil had a bandwidth of 12.0 ± 0.4 kHz ($Q \sim 8$) and the 200 kHz split solenoid had a bandwidth of 7.5 ± 0.4 kHz ($Q \sim 13$). These coil bandwidths were much narrower than the bandwidth of the preamplifier (~ 60 -80 kHz). The coil bandwidth was measured using two single-turn coils and a frequency generator according to Hoult's method.^{53,54}

Figure 4.5. The solenoidal coil used at 17 mT. The coil used at 8.5 mT has similar dimensions, but a larger number of turns.

Figure 4.6. The split-solenoid coil used for imaging at 17 mT.

To compare the SNR values obtained using different RF coils, their geometric and filling factors K and η were required. The contribution from the product of these factors was accounted for by first numerically calculating the field distribution produced by the coils using the Biot-Savart Law and the current distribution produced by the coil windings.¹⁷ The product $K\eta$ was then determined by numerically integrating the normalized field and dividing by the coil volume.

For the case of the split-solenoid coil used at 17 mT, the samples were completely contained inside the coil. However, for the cases of imaging open cells with small coils, the samples extended outside the coils and the calculations therefore included the contribution from those regions outside the coil by integrating over the whole sample.

Since these coils were used for both transmit and receive, an extra $\sin\left(\frac{\pi}{2} \frac{B_1^{xy}(r,z)}{B_1^{xy}(0,0)}\right)$ factor was included to account for the non-uniform distribution of flip angles over the sample.¹⁷ The crossed-coils configuration was not used for imaging and therefore its $K\eta$ value was not calculated.

Since the birdcage coil used at high field was much larger than the samples, the field was assumed to be completely uniform over the sample ($K \approx 1$). Figure 4.7 shows the calculated field maps of the ultra-low field coils. Figure 4.8 shows the calculated field map for the high field solenoidal coil. The field strength in these maps has been normalized to the field strength at the center of the coils. The $K\eta$ values calculated by integration of the field maps are shown in Table 4.1.

Figure 4.7. Cross-sectional diagram of the normalized (to the strength at the centre) field distribution for the ultra-low field (a) 1cm diameter solenoidal coils and (b) the 200 kHz split-solenoid coil. The end of the contour lines in (a) indicates the edges of the sample. The solid rectangles indicate the positions of the wire windings.

Figure 4.8. Cross-sectional diagram of the normalized (to the strength at the centre) field distribution for the high field 1cm diameter solenoidal coil. The end of the contour lines indicates the edges of the sample. The solid ovals indicate the positions of the wire windings.

Coil	$K\eta$
Ultra-low field 1cm diameter solenoid	1.24
High field 1cm diameter solenoid	0.99
Ultra-low field split solenoid	0.86

Table 4.1. Calculated $K\eta$ values.

Note that these values are larger for the two 1cm diameter solenoids only because the samples extended outside them. For the split solenoid, the reported value assumes a sample completely filling the coil and must be adjusted in the SNR calculations to account for the actual volume of the sample.

4.3.3 RF Shielding

In MR systems, there are several sources of Electromagnetic Interference (EMI), which is any unwanted signal that is received by the system together with the desired signal. EMI can have a natural or man-made origin, can be radiated or conducted or both, and can be internal or external to the system. Internal sources are typically related to components of the system that operate in pulse mode, such as gradient power supplies, and RF transmitter. External sources include computers, computer monitors, communication and other electronic equipments. Most of the conducted EMI can be eliminated or attenuated by proper electric design and appropriate grounding. In order to reduce radiated EMI, the complete MR system is generally enclosed in a shielded room with any electrical conductor entering the room properly filtered.

For the case of the low-field system developed here, the major EMI sources were radiated interference from computers and other electronic equipment located in the laboratory. Another important source of EMI at 200 kHz was the RF power amplifier, which generated both conducted and radiated interference.

The standard approach of using crossed diodes^{53,54,55} to limit the RF amplifier noise during reception did not completely remove the conducted EMI. Spike-like pulses repeating at a frequency of 60 Hz and 120 Hz were still measured in the receiver system. These spikes, while negligible with large signals, were a major concern when receiving the very weak and short signals available during the initial stage of active shimming (see Chapter 5). For this reason, independent orthogonal receiving and transmitting coils were used. This "crossed-coils" approach provided enough isolation to make the interference undetectable, although it introduced some geometrical limitations on the sample.

For radiated EMI, the shield effectiveness (in dB) is defined as:^{57,58}

$$SE = R + A + B \quad (4.2)$$

where R is external reflection factor, A is the internal absorption factor and B is the internal reflection correction factor (which can be neglected for $A > 10$ dB). A depends on the skin-depth (Eq. 2.14) according to:⁵⁷

$$A = 8.69 (t/\delta) \quad (4.3)$$

where t is the thickness of the shield.

At high fields, thin shields ($t \sim 10^{-2} \text{ mm}$) are generally sufficient to produce the desired SE due to the high absorption attenuation A . However at ultra-low fields, A is considerably lower due to the increased skin depth and thick shields ($t > 1 \text{ mm}$) would be needed to increase the absorption attenuation to the desired value. Alternatively, R can be increased by appropriate multi-layered shielding design (i.e. increasing the number of reflecting surfaces).

To minimize the radiated EMI, an RF shield was designed and built since the existing RF room shield of the 1.89 T system was not designed to provide sufficient EMI isolation at low frequencies. Among the design considerations were:

- (1) Size and complexity: the shield was to be located inside the gradient/shim coil set (instead of shielding the whole room).
- (2) Access to RF coils and sample: The shield should have a large opening at one end at least. Conductors should enter the shield.

The actual design (Fig. 4.9) consisted of two thin (0.3 mm) layers of copper and a wave-guide configuration (diameters of the shield openings are much smaller than the RF wavelength). This design exploits the increased R factor by doubling the number of

reflecting surfaces, rather than increasing the thickness of the copper sheets to increase the absorption attenuation. The shield was properly grounded by connecting the shields of the coaxial cables to the outer surface of the RF shield. In this way any current induced by EMI could flow only on this surface (which is grounded). Only the inner conductor of the coaxial cable is permitted to penetrate the shield. The ground connection for the coils is made using the inner surface of the inner copper layer, where no EMI currents should be present.

Figure 4.9. Diagram of the RF shield and the connection of cables to the coil inside the shield.

The shield effectiveness was measured by generating signals of varying frequencies at different distances and directions from the receiving coil and comparing the detected signals with and without the shield. The measured shield effectiveness in the range 50-300 kHz was larger than 40 dB for sources at distances larger than the shield tube diameter, which was sufficient to make the interference negligible compared to the receiver thermal noise. No eddy-current effects (ghosting) were detectable in the

imaging experiments performed (Chapter 6), which was expected since relatively weak gradients (< 5 mT/m) are generally needed for low-field experiments.

4.4 Laser Polarization and Gas Flow Systems

Hyperpolarized natural abundance xenon gas (26.4% ^{129}Xe) was provided from a gas cylinder (gas concentration: 1% Xenon, 10% Nitrogen and 89% Helium) driving a continuous-flow polarization system that has been previously described.^{17,59} The system used circularly polarized light from a 60 W diode array laser ($\lambda = 794.8$ nm, Coherent, Santa Clara, USA) and was capable of producing xenon polarizations between 15 and 22% at a gas flow rate of 3.5 cc/min (at room temperature and 1 atm. pressure). The obtained polarization was calibrated by comparing signals obtained at 1.89 T from HXe and from xenon gas at thermal equilibrium (high pressure sample).¹⁷

Figure 4.10 shows a diagram of the polarization and flow system. The gas mix passes through filters that remove oxygen and water vapour before entering the polarization cell. The flow rate is monitored by a flow meter and can be adjusted using a needle valve. Rubidium is stored in a reservoir and heated to provide the Rb vapour needed in the polarization cell. In the cell, the gas mix is polarized through optical pumping/spin-exchange using the polarized laser beam. The laser absorption is monitored by an optical spectrometer. The polarization cell is located in the fringe field of the superconducting magnet at a field strength of approximately 30 mT. A glass wool filter is used to remove the rubidium from the gas mix exiting the cell.

The gas mix was used either directly for MR experiments (i.e. shimming) as produced or enriched to 100% xenon by cryotrapping using liquid nitrogen and then thawing the frozen xenon with hot water and releasing it into the sample (i.e. imaging).

Figure 4.10. Diagram of the polarization and flow system.

Chapter 5

Passive Shimming of the Fringe Field of a Superconducting Magnet for Ultra-Low Field Magnetic Resonance Imaging

5.1 Introduction

This chapter represents in large part, a manuscript to be submitted to the *Journal of Magnetic Resonance*: "Passive Shimming of the Fringe Field of a Superconducting Magnet for Ultra-Low Field Hyperpolarized Noble Gas MRI".⁶⁰ The passive shimming method presented here is the subject of a Patent Application (Ref. #: 42100-0004; submitted on November, 13th, 2003): "Method and Apparatus for the Passive Shimming of the Fringe Field of a Superconductive Magnet".

The magnetic field outside the bore of conventional superconducting magnets (i.e. fringe field) used in Magnetic Resonance (MR) imaging systems potentially provides an inexpensive and extremely stable magnetic field for imaging. While the very low field strengths available in the fringe field generally prohibit its use for most standard MR imaging applications, it may be suitable for HNG MR imaging.

The possibility of exploiting the fringe field available from a superconducting magnet has been explored previously for diffusion experiments taking advantage of the very large (typically 20-100 mT/m) field gradients present near the magnet.^{61,62} However, these extremely strong field gradients, while useful for measurement of diffusion, pose a major obstacle for imaging applications where high homogeneity is required. Correction of these gradients using standard active shimming techniques (field correction using

resistive coils) would require impractically high shim currents. Even if such high power shim supplies were available they would be expensive and limited by temporal instabilities and heating concerns.

An imaging method that does not correct for the field gradient but instead uses it for spatial encoding has been proposed.⁶³ Though this is an attractive alternative, it does have limitations due to the presence of a strong gradient during excitation pulses which limits it to very thin slices, significantly reducing the achievable SNR. This fact also prohibits the use of 3D imaging techniques. Furthermore, for very low Larmor frequencies, the available bandwidth is governed by the RF coil which further limits the inhomogeneity that can be tolerated. For these reasons, it is desirable to correct the fringe field as much as possible using passive shimming, provided by the placement of ferromagnetic pieces.

In commonly used passive shimming techniques inside the magnet,^{64,65} it is generally assumed that the field over the volume of the ferromagnetic pieces is constant. Furthermore, it is assumed that ferromagnetic pieces located at the same distance from the magnet's centre but at different angular positions will experience the same field (i.e. cylindrical symmetry). This is the basis of standard passive shim design and permits the production of relatively pure field harmonics. While these assumptions are generally true in the relatively homogeneous and symmetric field near the centre of a solenoidal superconducting magnet, they are not valid for the fringe field.

In this chapter a simple passive shimming method is described theoretically and used to reduce the fringe field inhomogeneities of the CMRF superconducting magnet to a level correctable with standard active shims. The proposed method explicitly takes into account the strong spatial variations of the fringe field over the volume of the

ferromagnetic pieces and the lack of cylindrical symmetry of the field about the centre of the volume of interest (VOI). In the implementation described, sets of steel rods parallel to the z axis are used to produce volumes of homogeneous field sufficient to obtain images from HXe gas samples at ultra-low field strengths within the fringe field of a superconducting magnet (1.89 T).

5.2 Theory

The scalar potential Φ at point $P(\vec{r})$ (Fig. 5.1) produced by an infinitesimal volume dV of shim element, of susceptibility χ , located at position $Q(\vec{r}')$ in a field $H_z(\vec{r})$ is given by:^{64,65}

$$d\Phi = \frac{-\chi H_z(\vec{r}')}{4\pi} \hat{k} \cdot \nabla_Q \left(\frac{1}{|\vec{r} - \vec{r}'|} \right) \quad (5.1)$$

where $\hat{k}$ is the unit vector in the z direction, $\vec{r}$ and $\vec{r}'$ are position vectors for points P and Q respectively and ∇_Q is the gradient with respect to the $\vec{r}'$ coordinates. To obtain the total potential Φ , in the presence of a shim element, this equation must be integrated over the volume of the element V_{elem} giving:

$$\Phi = \frac{-\chi}{4\pi} \int_{V_{elem}} dV H_z(\vec{r}') \frac{\partial}{\partial z'} \left(\frac{1}{|\vec{r} - \vec{r}'|} \right) \quad (5.2)$$

Taking into account that $H = -\nabla_P \Phi$ and changing the order of the derivative and integral operations, the magnetic field in the z direction is given by:

$$H_z(\vec{r}) = \frac{-\chi}{4\pi} \int_{V_{elem}} dV H_z(\vec{r}') \frac{\partial}{\partial z'} \frac{\partial}{\partial z} \left(\frac{1}{|\vec{r} - \vec{r}'|} \right) \quad (5.3)$$

Figure 5.1. Coordinate system for calculation of the magnetic field at point P arising from a point element of susceptibility χ located at point Q.

Expanding $\frac{1}{|\vec{r} - \vec{r}'|}$ in spherical harmonics as:^{64,65}

$$\frac{1}{|\vec{r} - \vec{r}'|} = \sum_{n=0}^{\infty} \sum_{m=0}^n \varepsilon_m \frac{(n-m)!}{(n+m)!} P_{n,m}(\cos \alpha) \frac{r^n}{r'^{n+1}} P_{n,m}(\cos \theta) \cos[m(\phi - \psi)] \quad (5.4)$$

where $P_{n,m}$ are the associate Legendre functions of order n and degree m ; $\varepsilon_m = 1$ for $m = 0$ and $\varepsilon_m = 2$ for $m \neq 0$. Using the properties of spherical harmonics to find the derivatives in Eq. 5.3 and taking the sums out of the integral, the following expression can be obtained (see Appendix I):

$$H_z(r, \theta, \phi) = -\frac{1}{4\pi} \sum_{n=0}^{\infty} \sum_{m=0}^n A_{n,m} r^n P_{n,m}(\cos \theta) [\cos m\phi H_{n,m} + \sin m\phi K_{n,m}] \quad (5.5)$$

where:

$$A_{n,m} = -\epsilon_m \frac{(n-m+2)!}{(n+m)!}$$

$$H_{n,m} = \chi \int_{V_{elem}} \frac{H_z(\vec{r}')}{f^{n+3}} P_{n+2,m}(\cos \alpha) \cos m\psi \, dV \quad (5.6a)$$

$$K_{n,m} = \chi \int_{V_{elem}} \frac{H_z(\vec{r}')}{f^{n+3}} P_{n+2,m}(\cos \alpha) \sin m\psi \, dV \quad (5.6b)$$

If more than one shim element is used, the principle of superposition applies and for the general case where the shim elements have different magnetic susceptibilities, the expression for the field coefficients $H_{n,m}$ and $K_{n,m}$ can be written as:

$$H_{n,m} = \sum_k H_{n,m}^k \quad (5.7a)$$

$$K_{n,m} = \sum_k K_{n,m}^k \quad (5.7b)$$

where $H_{n,m}^k$ and $K_{n,m}^k$ are the coefficients corresponding to the k^{th} shim element of susceptibility χ_k , calculated using Eqs. (5.6a) and (5.6b).

For shimming within the bore of the magnet, where the field is relatively constant over the volume of the shim elements, $H_z(\vec{r}')$ is usually taken out of the integrals in Eq. (5.6a) and (5.6b). However, in the fringe field, these integrals must be numerically computed from the values of the magnetic field $H_z(\vec{r}')$ over the rod's volume. Once the values of the coefficients $H_{n,m}$ and $K_{n,m}$ have been found, the field strength at every point in the volume of interest can be computed using Eq. 5.5.

5.3 Materials and Methods

The shimming procedure was used to passively shim the fringe field at the 8.5 mT and 17 mT positions, using shim sets consisting of one and two pairs of steel rods, respectively. The first position was located 120 cm from the centre of the superconducting magnet and was selected such that after shimming a field strength of 8.5 mT would be available over a 2 cm diameter spherical volume (DSV). The second position was selected closer to the centre of the superconductive magnet (90 cm) in order to obtain a field strength of 17 mT (after shimming) over a 6 cm DSV. The selection of those positions was based on an initial field mapping of the fringe field. The second position was expected to yield higher SNR and be more useful for *in vivo* (i.e. animal) imaging purposes.

The gradient/shim coil set (described in Chapter 4) was positioned with its z' axis parallel to the magnet's axis (i.e., aligned with the magnetic field direction) and slightly lower along the y axis due to space restrictions in the magnet room, which were also imposed by the presence of the xenon polarization system and walls (Figs 4.2 and 5.2). Also due to these restrictions the two positions were located at different sides of the magnet (right for 8.5 mT and left for 17 mT).

The gradient/shim coil set was rotated about the z' axis by an angle such that its x' direction pointed towards the magnet centre as shown in Fig. 5.2. This choice of geometry simplified the calculations by making the field variations symmetric about the x' axis. The two acrylic rings located between the two layers of the RF shield and at each end served to hold the shimming elements (Fig. 5.2).

Initial field mapping was performed using a Hall-effect gaussmeter (FW Bell 640, Orlando, FL, USA) and a simple probe positioning system consisting of a circular piece of acrylic, containing an array of holes to accommodate the probe, which could be moved along the axis of the gradient/shim coil set to different z' positions (Fig. 5.3).

Figure 5.2. Transverse view of the low field system (at right) with respect to the superconducting magnet (at left). Note the coordinates (x, y') are rotated slightly, with the x' axis in the direction of the centre of the superconducting magnet.

Figure 5.3 Field mapping system: gaussmeter and probe positioning system.

Once the field was passively shimmed as described below to a level that permitted HXe signals to be observed directly, field mapping was performed more rigorously using continuously flowing HXe gas through the 1 cm diameter solenoidal coil and using the ultra-low field MR system described in Chapter 4. This enabled precise field mapping in a relatively short time (1-2 min per measurement point).

Commonly available construction steel rods of diameters ranging between 1 and 3 cm were used as shim elements (Fig. 5.4). As a first step, the magnetic susceptibility χ of the steel was experimentally measured by mapping of the effect of one pair of steel rods

in the fringe field and comparing the generated spatial field harmonics to those predicted for equivalent steel rods of similar dimensions and susceptibility equal to one. The magnetic susceptibility of the steel was estimated to be 10.9 ± 2.1 , which is similar to reported susceptibility values for cold rolled steel.⁶⁵

The initial estimate for the shim set parameters was obtained by assuming the field strength to be constant over the rod and using the standard passive shimming calculation technique.^{64,65} The number of steel rods needed to produce the desired correction of the field gradient depended on the lowest order harmonic introduced that would be tolerated for the desired target field homogeneity. This order is usually determined by the size of the desired volume of homogeneity.^{64,65} However, for this work, this condition was relaxed to allow harmonics to be introduced up to the point where they were correctable by the corresponding active shim in order to use as little passive shimming material as possible.

The optimum arrangement of shim elements to produce the desired correction was obtained by iteratively adjusting the following parameters: radius R , distance from the centre r and length L ($L = 2r / \tan \gamma$), from the initial estimate and numerically calculating $H_z(r, \theta, \phi)$ using Eqs. (5.5) and (5.6), and the measured field maps. For simplicity, the angular position ψ was not changed from the initial estimates, but could be varied as well.

This calculation procedure was implemented using the optimization toolbox (simple search minimization algorithm) in Matlab 6.5 (The Mathworks, Natick, MA, USA) and the field coefficients to be minimized were expressed in the form:

$$\mathcal{H}_{n,m} = \sqrt{(H_{n,m})^2 + (K_{n,m})^2} \quad (5.8)$$

Figure 5.4. Diagram of the positioning of a rod parallel to the z axis and symmetric about the XY plane with center at (r_0, α_0, ψ_0) and length $L = 2r_0 / \tan \gamma$. In the practical implementation, the z axis is directed horizontally and parallel to the superconducting magnet's axis.

After correcting most of the field inhomogeneities using the steel rods, the field homogeneity was improved further using the active shims, which were systematically adjusted to provide the narrowest line-shape. The linewidth was estimated by fitting the spectra to a Lorentzian function. Spectra were obtained by releasing the HXe gas (in continuous flow mode) into suitable imaging phantoms: a 10 mm diameter open glass cell and a 3.7 cm diameter hollow plastic ball (described in Chapter 6).

5.4 Results

For the 8.5 mT position, the shimming procedure resulted in a set of two 1.2 cm diameter steel rods with dimensions given in Table 5.1 and Figure 5.5a. The x' axis was rotated 54° clockwise about the z direction from the x axis. At the 17 mT position, the optimum shim set consisted of two pairs of steel rods (Table 5.1 and Fig. 5.5b), with the x' axis rotated 16° counterclockwise.

Figure 5.6a shows the results of the field mapping of the fringe field along the radial direction (x') at the 8.5 mT position. A strong approximately linear gradient (30 mT/m) was found to be the main contributor to the field inhomogeneity.

The results of the field mapping at the 17 mT position are shown in Figure 5.6b. At this position, a strong field gradient (92 mT/m) was found to be the main contributor to the field inhomogeneity. Figures 5.6a and 5.6b also show the field maps for both positions after field correction using the passive shims.

At 8.5 mT, the strong field gradient (30 mT/m) was effectively corrected using passive shims (Fig. 5.6a), improving the field homogeneity to 0.1% over the 2 cm DSV from the initial 7.2%.

The shim set design that produced this correction is significantly different from the initial estimate (Table 5.1). The rods are 1.3 cm shorter (20.7 cm). This difference is due to the relatively strong variation of the field strength over the length of the rod, mainly in the form of a second-order zonal harmonic. As a result the initial estimate would not minimize the $H_{2,0}$ harmonic and would have resulted in the introduction of a relatively large inhomogeneity (6.35×10^{-4} mT/cm²). The optimized shim set produced a $H_{2,0}$ harmonic two orders of magnitude smaller (6.70×10^{-6} mT/cm²) while producing a $H_{1,1}$ harmonic (the desired field correction) larger (-31 mT/m) than the one produced by the initial estimate design (-27 mT/m).

At 17 mT, the very strong field gradient (92 mT/m) was canceled (Fig. 5.6b) by the passive shims increasing the field homogeneity to 0.2 % over the 6 cm DSV from the initial 25%. In this case (Fig. 5b and Table 1), due to the lack of cylindrical symmetry with respect to the centre of the volume of interest, the field strength at the positions of the two pairs of rods is different. The initial shim estimate introduces second ($H_{2,2}=1.12 \times 10^{-2}$ mT/cm²) and third ($H_{3,3}=1.12 \times 10^{-2}$ mT/cm³) order harmonics while the optimized design, by using pairs of rods with different diameters and located at different distances from the center of the volume of interest, compensates for the field asymmetry and produces much smaller second ($H_{2,2}=2.02 \times 10^{-5}$ mT/cm²) and third ($H_{3,3}=9.22 \times 10^{-4}$ mT/cm³) order harmonics. Similarly to the case of one pair of rods, the new method uses shorter rods which minimizes the second-order zonal harmonic and maximizes the desired $H_{1,1}$ correction.

Figure 5.7a shows the HXe spectrum obtained at 8.5 mT after passive shimming (linewidth approximately 100 Hz). Figure 5.7b shows the spectrum after both passive and

active shimming (linewidth: ~20 Hz). Figure 5.8a shows the HXe spectrum (linewidth: ~200 Hz) obtained at 17 mT after passive shimming. Figure 5.8b shows the spectrum after both passive and active shimming (linewidth: ~30 Hz). The linewidth obtained are better than the target homogeneity of 40 Hz, which was desired for the imaging experiments. It should be noted that no signals were observable in either case without the passive shims.

	Parameter	Initial Estimate	Optimized Design
1 Pair of Rods (8.5 mT)	R	6 mm	6 mm
	r	9.0 cm	9.0 cm
	L	22.0 cm	20.7 cm
2 Pairs of Rods (17 mT)	R_1	8.0 mm	8.0 mm
	R_2	8.0 mm	9.5 mm
	r_1	9.0 cm	9.0 cm
	r_2	9.0 cm	9.7 cm
	L_1	30.0 cm	26.0 cm
	L_2	30.0 cm	34.0 cm

Table 5.1. Dimensions of the two optimal shim sets used at 8.5 mT and 17 mT (fourth column). For comparison, initial estimates obtained using the standard shim calculation method are shown in the third column.

Figure 5.5. Diagram (XY plane) of the location of the steel rods used as passive shims for the two shim sets of: (a) one pair of rods at 8.5 mT and (b) two pairs of rods at 17 mT. The solid circles represent the steel rods as seen end on.

Figure 5.6. Magnetic field strength plotted along the x axis in the fringe field before and after the passive shimming for the 120 cm (a) and 90 cm (b) positions. Lines are shown as an aid to the eye, only.

Figure 5.7. Spectra obtained from a 1 cm diameter glass cell at 8.5 mT after (a) passive shimming (linewidth ~ 100 Hz), and (b) both passive and active shimming (linewidth ~ 20 Hz).

Figure 5.8. Spectra obtained from a 3.7 cm diameter spherical phantom at 17 mT after (a) passive shimming (linewidth ~ 200 Hz), and (b) both passive and active shimming (linewidth ~ 30 Hz).

5.5 Discussion

The purpose of this work was to develop a method to shim the fringe field of a superconducting magnet in order to produce a homogenous region for hyperpolarized gas imaging. The method extends the conventional passive shimming method^{64,65} to the case of the inhomogeneous and asymmetric fringe field outside the bore of a superconducting magnet.

The practical implementation of the shimming procedure at two positions in the fringe field of the superconducting magnet produced the desired volumes of homogeneity at 8.5 mT and 17 mT.

The field homogeneity obtained following passive shimming at both positions was sufficient to allow HXe signals to be obtained (Figs. 5.7a and 5.8a), thus permitting improved homogeneity by active shimming using these signals. The final field homogeneity (approximately 0.017%) allowed reasonable HXe spectra to be obtained (Figs. 5.7b and 5.8b) with a linewidth of 19 ± 3 Hz at 8.5 mT and 33 ± 6 Hz at 17 mT. Further homogeneity improvements were not possible due to the lack of fourth order zonal harmonic ($H_{4,0}$) correction in the active shim system used.

It should be noted that though the final homogeneity (0.02% or 200 ppm) seems large compared to the typical field homogeneity in clinical systems (<10 ppm), this is a relative quantity, which depends on the static magnetic field strength. For imaging purposes the homogeneity requirement is that the linewidth produced by the field inhomogeneities must be smaller than the desired pixel size (in frequency units). A homogeneity of 200 ppm at 17 mT (0.0034 mT or 40 Hz for ^{129}Xe) is comparable to a homogeneity of 1.5 ppm at 1.89 T (0.0030 mT or 35 Hz for ^{129}Xe), which is quite acceptable.

Though the differences between the optimized shim sets and the initial estimates can be as small as a few millimeters, they strongly affect the field correction produced by the shim sets, resulting in differences of several orders of magnitude. Consequently, the shim sets have to be accurately constructed. It would be preferable to construct a shim holder that would allow for fine positioning (accurate to within 0.25-0.50 mm) of the shimming elements. As well, this is just one possible shim design and others are possible including varying χ and/or ψ .

One limitation of this shimming method is that it assumes the fringe field is totally in the z direction. This is probably a good assumption if the volume of interest is not too large and is selected close to the superconducting magnet and in line with its isocentre, where the field lines are approximately parallel to the z axis.

The presence of the steel rods in the fringe field did not greatly affect the homogeneity inside the superconducting magnet. The largest estimated field inhomogeneity introduced was about 5 ppm, which is easily correctable by the active shims of the high field system. The forces exerted on the steel rods by the magnetic field were small enough that no anchoring for the system was needed. At higher fields or when using larger amounts of steel, this factor may require careful consideration.

This method is not restricted to the use of steel as the shimming material and an attractive alternative is the use of permanent magnets as shimming elements. In this way, higher field strengths may be obtained. Combining steel and permanent magnets could also provide very useful shim designs with improved correction symmetry.

This approach makes it straightforward to shim the fringe field at different distances from the superconductive magnet. In this way, it is possible to perform MR imaging experiments at several field strengths using a single superconducting MR magnet.

5.6 Conclusion

The method for passive shimming effectively corrects the fringe field of a superconducting magnet to a level suitable for imaging and allows spectra of HXe phantoms at two field strengths (8.5 and 17 mT) to be obtained. The method extends the use of the standard passive shimming method^{64,65} to the situation of a very inhomogeneous and asymmetric field. The final 0.02% (0.34 mT) field homogeneity obtained at 17 mT over a 6 cm DSV was sufficient for HXe imaging of rat lungs, which will be demonstrated in the next chapter.

Chapter 6

MR Imaging of Hyperpolarized Xenon at 8.5 and 17 mT

6.1. Introduction

In this chapter, HXe MR imaging experiments performed at 8.5 and 17 mT are described. The methodology followed in these experiments, as well as details of the pulse sequences and phantom preparation are also described. The components of the ultra-low field and high field systems used for these experiments were described in Chapter 4. The spectra and images obtained from phantoms and excised rat lungs are used to validate the theoretical SNR results presented in Chapter 3 for the case of small samples and coils.

6.2. Methods

6.2.1 Pulse sequences and MR system parameters

At 1.89 T, imaging was performed using a 3D gradient-echo pulse sequence with variable flip angle (FOV: 60 mm; data matrix: 32x32x16, TR: 16 ms, TE: 4 ms, 20 kHz bandwidth). At low-field, a 2D gradient-echo pulse sequence with variable flip angle (FOV: 80 mm; data matrix: 32x32, TR: 16 ms, TE: 5 ms, 10 kHz bandwidth) was used. No slice selection was used in the 2D ultra-low field imaging experiments in order to obtain image SNR values close to those obtained at 1.89 T. 3D sequences could not be used at 8.5 mT and 17 mT due to SNR limitations.

For the 8.5 and 17 mT experiments, the parameters in the control software (e.g. gradient and RF pulse settings and receiver attenuation) were properly calibrated to accommodate the different gradient/shim coil sets and RF power amplifier used. The RF

pulses were calibrated by estimating the flip angle from signals obtained using the method described in Section 2.4. The estimation was based on a maximum likelihood algorithm implemented in Matlab as described in section 6.2.3. The gradient pulse amplitude was calibrated using images of the spherical phantom and adjusting the settings to obtain the correct image dimensions.

6.2.2 Samples

For the small FOV (20 mm) at 8.5 mT, the phantom used was a 10 mm diameter open glass cell into which the HXe gas could be captured either from cryotrapping or directly from continuous flow mode.^{41,59} This cell was also used to obtain HXe signals to estimate the polarization level.

A uniform phantom consisting of a 3.7 cm diameter plastic ball (Fig. 6.1) was used for the larger FOV (60 mm) at 17 mT. It had a single hole with a plastic tube tightly attached with epoxy, such that the air inside the phantom could be completely evacuated prior to filling with HXe gas. In this way, the HXe gas could be drawn completely into the closed container using a three-way valve.

Lung images were obtained from excised rat lungs that were dried in a non-collapsed state of inhalation with the outer surface sealed by epoxy.⁶⁶ This method preserves the alveolar structure of the lungs. They can be handled easily and used repeatedly in different experiments with the same conditions (such as lung volume, inflation level and pressure), which is hard to achieve in live animals or fresh excised lung (which are also very delicate). The excised lungs could also fit into a smaller RF coil. A plastic tube inserted into the trachea allowed evacuation of the air from the lungs prior to filling with HXe gas (Fig. 6.2).

Figure 6.1 Spherical phantom (3.7 cm diameter). The plastic tube used to evacuate the air and deliver the HXe can be seen at left.

Figure 6.2 Excised rat lungs fixed in epoxy. The plastic tube used to evacuate the air and deliver the HXe can be seen at left.

6.2.3 Data Acquisition and Analysis

The absolute polarization of the HXe gas was measured, by comparison of MR signals obtained from thermal xenon samples and HXe, before starting the experiments and monitored between them. Polarization values between 15 and 20% were routinely obtained during the experiments. The experiments were first done at 1.89 T and immediately after at 8.5 or 17 mT.

The SNR of the images was estimated by selecting regions of interest (ROI) in the image over the object and regions of pure noise in the background. The estimation used a maximum likelihood (ML) algorithm which takes into account the Rician distribution of the MR image noise.^{67,68} The noise variance (σ^2) was estimated from a ROI taken in the background as:^{67,68}

$$\sigma^2 = \frac{1}{2N} \sum_{i=1}^N M_i^2 \quad (6.1)$$

where the M_i are the intensity values of the pixels and N is the number of pixels in the ROI.

Taking the square root of this estimator can yield an estimator for σ (the noise) that is identical to the ML estimator, but due to the square root operation, this estimator is biased. In the large sample limit this estimator is unbiased (i.e. it is asymptotically unbiased).

The signal was estimated from a ROI over the object by numerically maximizing the log-likelihood function ($\log L$) given by:^{67,68}

$$\log L \sim \sum_{i=1}^N \log I_0 \left(\frac{AM_i}{\sigma^2} \right) - \frac{NA^2}{2\sigma^2} \quad (6.2)$$

where A is the true amplitude of the signal and I_0 is the 0th order modified Bessel function of the first kind. The computational requirements for the maximization procedure have been shown to be low.^{67,68} This estimation, unlike the conventional average estimator, always produces physically meaningful results (i.e. $\hat{A} > 0$), which is important in conditions of low SNR images.

This algorithm was implemented in Matlab as part of a data analysis package developed for the CMRF, which allows one to display and process 1D, 2D and 3D MR data and to estimate data parameters such as flip angle, T_1 , noise power, SNR and spectrum linewidth. The errors reported on the SNR estimates were obtained from the ML confidence intervals for both the noise and signal estimates.

6.3 Results

Figure 6.3 shows images of the 1 cm diameter glass cell obtained at 8.5 mT from 100% xenon gas and at 1.89 T from 1% xenon. Different xenon concentrations were used for the low and high field experiments in order to obtain images with comparable SNR values (and errors).

Figure 6.4 compares the SNR estimated from the images of Fig. 6.3 to the theoretical field strength dependence (Eq. 3.12) of the SNR for 1 cm samples with only coil noise (i.e. no sample noise from the non-conductive sample). The measured SNR values show good agreement with the theoretical curve, though at ultra-low field the measured values are slightly higher than expected.

Figure 6.5a presents an image of the 3.7 cm diameter sphere at 1.89 T (slice from 3D sequence) and Fig. 6.5b at 17 mT (2D image; no slice selection) using 100% xenon gas.

Figure 6.3. Gradient-echo images of the 1 cm diameter glass cell at (a) 1.89 T (1% Xe) and (b) 8.5 mT (100 % Xe).

Figure 6.4. Comparison of measured and predicted SNR values for 1 cm diameter samples at 8.5 mT, 17 mT and 1.89 T. The SNR curve was normalized to the predicted value at 3 T.

Figure 6.5. Gradient-echo images of the spherical phantom. (a) Central slice from the 1.89 T 3D images with resolution 2x2x4 mm. (b) 2D image obtained at 17 mT with resolution 2x2 mm and no slice selection. Absolute polarization approximately 20%.

Figure 6.6. Gradient-echo images of the excised rat lungs. (a) Central slice from the 1.89 T 3D images with resolution 1.5x1.5x2 mm. (b) 2D image obtained at 17 mT with resolution 2x2 mm and no slice selection (thickness ranging from 5 to 20 mm). (P~20%).

Figures 6.6a and 6.6b show coronal images of the excised rat lungs obtained at 1.89 T (slice from 3D sequence) and 17 mT (2D image; no slice selection), respectively, using 100% xenon gas.

Figure 6.7 compares the image SNR values obtained from both the spherical phantom and the excised lungs to the theoretically predicted values for these sample and coil dimensions. Again, the measured values at 17 mT field are slightly higher than expected from the theoretical model.

6.4 Discussion

The images obtained from the 1 cm diameter open cells (Fig. 6.3) showed similar values of SNR (~25) since the xenon concentration was properly selected with that goal. When compared to the predicted field dependence of the SNR (Fig. 6.4) these values show reasonable agreement with the theory.

Similar agreement with the theoretically expected values (Fig. 6.7) was obtained from images of the larger phantom (3.7 cm diameter sphere) and the excised lungs (Figs. 6.5 and 6.6). For these cases, similar to what was observed for the smaller samples in Fig. 6.4, the measured SNR values at 8.5 and 17 mT are larger than the theoretical estimates.

The reason for the underestimation of the SNR values by the theoretical model is likely due to the underestimation of T_2^* values for the central pixels of the image. The T_2^* values used in the theoretical calculations were based on measurements from spectra obtained from the whole volume of the sample (Fig. 5.8b). The SNR values of the images were obtained from regions of interest that mostly contained pixels close to the center of the volume of homogeneity, where the T_2^* values would be expected to be higher due to the better field homogeneity. This effect is more evident for the SNR values from the

spherical phantom images where the ROI used for SNR estimation includes the center of the volume of homogeneity.

Figure 6.7. Comparison of measured and predicted SNR values for the 3.7 cm diameter spherical phantom (filled circles) and the excised rat lungs (filled squares), at 17 mT and 1.89 T. The points with higher SNR correspond to the 1.89 T images.

Another possible source for this discrepancy could be the underestimation of the noise from the background pixels. While at high field the receiver frequency response is practically flat over the whole bandwidth, at low fields the system bandwidth is limited by the RF coil resulting in a frequency response that modulates the noise (and signal) amplitude along the frequency encoding direction and may lead to underestimation of the image noise.

The reasonable image quality obtained at ultra-low field confirms that eddy currents induced on the RF shield by the magnetic gradient pulses were negligible in the

experiments. This was expected since at ultra-low field relatively weak gradient pulses were used. A more careful verification of the effects of eddy currents will be needed with experiments using faster switching and stronger gradient pulses, where these effects may significantly degrade the image quality and modifications to the RF shield may be required to reduce them.

In the theoretical calculations, the proximity effects in the coils were assumed to be negligible. This assumption is reasonable at high fields since a single-turn birdcage coil was used for imaging and the separation between turns in the high field solenoidal coil is much larger than the wire radius (see Chapter 4).^{43,54} For the ultra-low field coils, which have a large number of turns, the separation between turns (wire coating) was slightly smaller than the radius of the thin wires used (Chapter 4). However, due to the very low Larmor frequencies, the skin depth is larger than the radius of the wire and the proximity effects should be also negligible in these coils.

Although the lung images obtained in this work are not expected to show contributions of susceptibility effects to T_2^* (Eqs. 2.22 and 2.24) since the water was removed during the lung preparation, they provide an important proof of concept for animal lung imaging. The rat lung images obtained show reasonable SNR and spatial resolution and indicate that HXe MR imaging of human lungs should also be feasible at ultra-low fields.

A limitation of the rat lung imaging experiments presented here is the use of the split-solenoid coil. To image live rats, a larger coil with a different configuration is needed to accommodate the rat body, most likely a saddle-like coil at low fields. The larger size together with the open configuration of the saddle coils would result in a sensitivity (and

SNR) loss by a factor between 3 and 5, approximately. This SNR loss could be compensated by cooling the coil wire (probably to liquid nitrogen temperature), which would reduce the thermal noise that is the dominating noise source at low fields.⁶⁹ Using higher field strengths (0.05-0.1 T), closer to the optimum values predicted in Chapter 3, would also be desirable to further increase the achievable SNR and spatial resolution while still keeping the cost of the systems low and preserving the advantages of low field imaging.

6.5 Conclusions

The results obtained in this work have demonstrated the feasibility of HXe MR imaging at ultra-low field strengths with reasonable SNR and spatial resolution.

The SNR estimations validate the theoretical model presented in Chapter 3 for the case of small samples. The feasibility of human HXe MR imaging at low magnetic field strengths will be discussed in the next chapter.

Chapter 7

Summary and Future Work

7.1 Summary

In this thesis, a theoretical model describing the static magnetic field strength dependence of SNR and spatial resolution for HNG MR imaging was presented. Using this model, the optimum field strength for HNG MR imaging was theoretically calculated in terms of both SNR and spatial resolution. The calculations show that the optimum field strength for HNG MR imaging of human lungs is between 0.1 T and 0.6 T depending on gas type (helium or xenon) and sample size. These field strengths are feasible with magnets currently available, including open systems.

These calculations assumed the use of a saddle coil and a simple model for the sample, consisting in two concentric cylinders which represent the water-like tissue and gas space volume expected in lung imaging. A semi-empirical model was used for T_2^* which was based on reported values of magnetic susceptibility and diffusion coefficients and the alveolar dimensions. The T_2^* values obtained with this model agree reasonably with experimental values found in the literature.

At the field strengths currently used by conventional clinical proton MR imaging systems (1-3 T), the predicted SNR is 10 to 50% lower than at the optimum field with only slightly worse spatial resolution (10-20%). At higher fields (>3 T), however, the SNR degrades considerably reducing the achievable spatial resolution. Although HNG of the lung is still feasible at very low field strengths (< 50mT), the available SNR is much lower than at optimum fields and this reduces the achievable spatial resolution. However,

since at ultra-low fields the noise is dominated by the coil thermal noise, significant improvements in SNR could be achieved by reducing the coil temperature (to liquid nitrogen temperature or using superconducting coils).⁶⁹

These lower field strengths offer potential advantages as they may be obtained with less expensive resistive or permanent magnets. Such systems would also likely require less expensive RF and gradient electronics, and would have reduced chemical shift and susceptibility artifacts as well as reduced tissue RF heating.

In this work, a simple passive shimming method based on the placement of a small number of ferromagnetic pieces was proposed to reduce the fringe field inhomogeneities to a level that can be handled with standard active shims. The method explicitly takes into account the strong variations of the field over the volume of the ferromagnetic pieces used to shim. The method effectively corrected the inhomogeneities of the fringe field of a 1.89 T superconducting magnet and when combined with active shimming produced field homogeneities of approximately 0.02% over volumes of 2 cm DSV at 8.5 mT and 6 cm DSV at 17 mT.

The volumes of homogeneity obtained in the fringe field were used to obtain spectra and images of phantoms and excised rat lungs using HXe gas in a home-built ultra-low field MR system. The construction of this system provided a methodology for development of ultra-low field MR systems, which include concepts related to the magnet system, RF receiver and coils and EMI reduction.

SNR estimates made from the obtained images verified the theoretical model of field strength dependence of the SNR introduced in this work, for small samples (sample-dominated noise regime). At ultra-low field the measured SNR values were slightly

higher (15-20%) than the theoretical predictions, most likely due to underestimation of noise power from the images and overestimation of the field inhomogeneities in the theoretical calculations. In general, these results demonstrated the feasibility of HXe animal lung imaging at ultra-low fields.

7.2 Implications for Ultra-low Field MR Human HXe Imaging

The results of this work indicate that human lung MR imaging using HXe at low and ultra-low fields is theoretically feasible. Imaging human lungs should provide SNR values higher than excised rat lungs due to their larger volume that allows the use of larger voxels, but could be more difficult in other respects (e.g. respiratory motion, patient cooperation, limitations on xenon concentration due to its anesthetic properties and coil geometry).

According to Figures 3.4, 3.5 and 3.8, it is expected MR systems for human lung imaging will operate preferably at field strengths between approximately 0.1 and 0.3 T. These field strengths will provide SNR and spatial resolution near the maximum achievable at optimum field strengths, together with the advantages of low field MR imaging. These systems could be based on resistive or permanent magnets with novel geometries to allow imaging of subjects in different orientations, which is of great interest for lung imaging due to the important role that gravity seems to play in lung function.^{32,70} These magnet geometries could also potentially allow imaging during exercise or other stress testing.

7.3 MR Imaging of Dissolved HXe

Despite its lower SNR, HXe imaging can complement the information provided by HHe or other lung imaging techniques due to its high solubility in tissue. HXe can provide information not only about lung gas space ventilation but also perfusion⁸ and blood oxygenation⁹ which could help to detect lung diseases such as emphysema, pulmonary embolism, COPD and bronchiolitis obliterans in the early stages.⁷¹

Dissolved-phase HXe imaging could also be optimally performed at fields lower than those used in conventional clinical MR systems. The influence of several T_2^* relaxation mechanisms on the field dependence of the achievable spatial resolution and SNR may be greater than for lung imaging. Preliminary dissolved-phase experiments have demonstrated the strong (quadratic) field dependence of the T_2^* of HXe dissolved in perfluorooctyl bromide (PFOB) emulsions due to fast chemical exchange between the water and PFOB compartments of the emulsion.⁴¹ PFOB emulsions have proven to be a promising injectable carrier for dissolved HXe imaging, for applications such as breast imaging.⁴²

Figure 7.1 shows spectra obtained at 8.5 mT and 1.89 T from HXe dissolved in PFOB emulsions. Figure 7.2 shows the good agreement of the measured linewidths with the theoretical model of fast chemical exchange.⁴¹ Further studies of the T_2^* mechanisms of HXe in tissues will be important to decide the optimum field strength for dissolved-phase HXe imaging.

7.4 Fringe Field MR Imaging

The possibility of using the fringe field of superconducting magnets (passively shimmed) for human imaging will depend on the strength of the available fringe fields and the minimum requirements for field strengths from the SNR point of view. Since many of the superconducting magnets commercially available are self-shielded (i.e. their fringe field strengths are already minimized for siting concerns) the available field strength after passive shimming over the necessary volume will likely be insufficient for human imaging. However, the introduction of higher field strengths in MR imaging (3-7T) could provide stronger fringe fields that will make human imaging feasible. Other possibilities include the use of magnets especially designed to provide a desirable fringe field and the above discussed passive shimming with permanent magnets.

Figure 7.1 Spectra of HXe dissolved in PFOB emulsion at 8.5 mT and 1.89 T.

Figure 7.2 Field dependence of the linewidth of HXe dissolved in PFOB emulsions. Comparison between a theoretical model and preliminary experimental results obtained at 8.5 mT and 1.89 T.

The simplicity of the method and the possibility of using most of the hardware of the high-field system to power and control the low-field system make this approach an inexpensive and a convenient way of expanding the low field capabilities of existing or new MR facilities, not only for HNG imaging but also for other techniques such as electron-spin resonance (ESR), pre-polarized MR imaging (PMRI) and dynamic nuclear polarization (DNP) that may also be optimal at low magnetic field strengths.^{19,23,72,73,74} One of the most promising uses of this fringe field approach may be in dedicated low-field animal systems.

7.5 Future Work

From the results presented in this thesis, several lines of future research can be foreseen. The SNR model presented in Chapter 3 should be verified for larger samples, such as large animals and humans, at different field strengths. An interesting alternative

to the use of different field strengths is to mimic the field increase by changing sample properties such as conductivity and susceptibility.^{75,76} This way, the sample noise contribution to the total system noise can be adjusted to the level predicted at a given field by varying the conductivity of the sample. Similarly by changing the susceptibility, the susceptibility-induced field gradients at the boundaries between two regions of the sample can be modified to simulate the susceptibility effects at different field strengths.

The development of a human lung MR imaging system at low fields (likely between 0.1-0.2 T) is also anticipated. This project would include the design of a novel geometry magnet for studies with the subject in the upright position and special gradient/shim systems (e.g. planar gradients) to meet the accessibility requirements of the system. The development of appropriate RF coils (probably cooled) will also likely be of interest.

Extensive research, both theoretical and experimental, is anticipated to characterize the field dependence of T_2^* relaxation mechanisms for HNG due to its important implications on SNR and resolution as discussed in Chapter 3. The approach for these T_2^* studies in the lungs may be similar to those previously reported for proton MR imaging of trabecular bone,^{77,78} but accommodating the larger susceptibility differences and diffusion coefficients expected for gas imaging. Numerical calculations to predict T_2^* values are anticipated,⁷⁹ which would consider the effect of the high solubility of xenon in tissues on its apparent diffusion coefficient. Similar studies for dissolved HXe will likely be done as well.

Another important area of research will be the improvement of xenon laser polarization methods and equipment, which could lead to significant increases in the achievable polarizations to a level similar to that currently obtained for HHe (>50%).

Recently, Ruset et al^{80,81} have obtained polarizations of approximately 50% at a gas flow rate of $6 \text{ cm}^3 \text{ min}^{-1}$ using a novel low-pressure production method and predicted that polarizations as high as 70% could be achieved for small gas quantities. If such polarization increases can be obtained for larger gas quantities, it would considerably increase the potential of HXe MR imaging at ultra-low field strengths.

7.6 Conclusions

The theoretical model presented in this thesis predicts that HNG imaging can be optimally performed at much lower field strengths (0.1-0.6 T) than conventional clinical proton MR imaging systems. This could considerably decrease cost, improve patient access and reduce chemical shift and susceptibility artifacts and RF heating. It could also make possible the use of novel magnet designs, including the use of passively shielded fringe field as the source of static magnetic field.

The experimental results obtained with the ultra-low field MR system built in this work indicate the feasibility of HXe lung imaging at low and ultra-low field strengths and the validity of the SNR model for small samples. This work has also provided a methodology for the development of such systems and raised important questions whose answers could help to make low field HXe imaging a powerful diagnostic technique for the lungs and other organs.

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Appendix I. Magnetic Field Produced by a Shim Element in the Presence of an Inhomogeneous Magnetic Field

To expand Eq. 5.3 in spherical harmonics using Eq. 5.4, the derivatives with respect to the Cartesian coordinate z are needed. Romeo and Hoult have demonstrated that:⁶⁵

$$\frac{\partial T_{n,m}}{\partial z} = (n+m) T_{n-1,m} \quad (\text{A.1})$$

and

$$\frac{\partial Y_{n,m}}{\partial z} = -(n-m+1) Y_{n+1,m} \quad (\text{A.2})$$

where $T_{n,m}$ is the spherical harmonic given by:⁶⁴

$$T_{n,m} = r^n P_{n,m}(\cos \theta) \cos[m(\phi - \psi)] \quad (\text{A.3})$$

$Y_{n,m}$ is the inverse spherical harmonic and is given by:⁶⁴

$$Y_{n,m} = f^{-(n+1)} P_{n,m}(\cos \alpha) \cos[m(\psi - \phi)] \quad (\text{A.4})$$

Using Eqs. A.1-A.4, the derivatives of Eq. 5.3 can be calculated as:

$$\frac{\partial}{\partial z} \left(\frac{1}{|\vec{r} - \vec{r}'|} \right) = \sum_{n=0}^{\infty} \sum_{m=0}^n \epsilon_m \frac{(n-m)!}{(n+m)!} (n+m) P_{n,m}(\cos \alpha) \frac{T_{n-1,m}}{f^{n+1}} \quad (\text{A.5})$$

and

$$\frac{\partial}{\partial z'} \left[\frac{\partial}{\partial z} \left(\frac{1}{|\vec{r} - \vec{r}'|} \right) \right] = - \sum_{n=0}^{\infty} \sum_{m=0}^n \epsilon_m \frac{(n-m)!}{(n+m-1)!} r'^{n-1} P_{n-1,m}(\cos \theta) [(n-m+1) Y_{n+1,m}] \quad (\text{A.6})$$

Eq. A.6 can be re-written as:

$$\frac{\partial}{\partial z'} \left[\frac{\partial}{\partial z} \left(\frac{1}{|\vec{r} - \vec{r}'|} \right) \right] = - \sum_{n=0}^{\infty} \sum_{m=0}^n \varepsilon_m \frac{(n-m+1)!}{(n+m-1)!} \frac{r^{n-1}}{f^{n+2}} P_{n-1,m}(\cos\theta) P_{n+1,m}(\cos\alpha) \cos[m(\phi-\psi)] \quad (\text{A.7})$$

Substituting Eq. A.7 in Eq. 5.3 and taking the sums out of the integral, the magnetic field $H_z(\vec{r})$ can be expressed as:

$$H_z(\vec{r}) = -\frac{\chi}{4\pi} \sum_{n=0}^{\infty} \sum_{m=0}^n \varepsilon_m \frac{(n-m+1)!}{(n+m-1)!} r^{n-1} P_{n-1,m}(\cos\theta) \int_{V_{elem}} d\vec{r}' H_z(\vec{r}') Y_{n+1,m} \quad (\text{A.8})$$

Since $P_{n,m}(\cos\theta) = 0$ for $m > n$, n can be changed by 1 in Eq. A.8, resulting:

$$H_z(\vec{r}) = \frac{\chi}{4\pi} \sum_{n=0}^{\infty} \sum_{m=0}^n A_{n,m} r^n P_{n,m}(\cos\theta) \int_{V_{elem}} d\vec{r}' H_z(\vec{r}') Y_{n+2,m} \quad (\text{A.9})$$

where:

$$A_{n,m} = -\varepsilon_m \frac{(n-m+2)!}{(n+m)!} \quad (\text{A.10})$$

Using the identity:

$$\cos[m(\phi-\psi)] = \cos m\phi \cos m\psi + \sin m\phi \sin m\psi$$

in the expression of $Y_{n+2,m}$, and writing:

$$H_{n,m} = \chi \int_{V_{elem}} \frac{H_z(\vec{r}')}{f^{n+3}} P_{n+2,m}(\cos\alpha) \cos m\psi dV \quad (\text{A.11})$$

$$K_{n,m} = \chi \int_{V_{elem}} \frac{H_z(\vec{r}')}{f^{n+3}} P_{n+2,m}(\cos\alpha) \sin m\psi dV \quad (\text{A.12})$$

the expression for the magnetic field $H_z(\vec{r})$ is obtained as (Eq. 5.5):

$$H_z(r, \theta, \phi) = -\frac{1}{4\pi} \sum_{n=0}^{\infty} \sum_{m=0}^n A_{n,m} r^n P_{n,m}(\cos\theta) [\cos m\phi H_{n,m} + \sin m\phi K_{n,m}] \quad (\text{A.13})$$