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**Three dimensional high resolution magnetic resonance imaging
of the coronary arteries**

Paschal, Cynthia Bruce, Ph.D.

Case Western Reserve University, 1992

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THREE DIMENSIONAL HIGH RESOLUTION MAGNETIC RESONANCE IMAGING OF THE CORONARY ARTERIES

by

CYNTHIA BRUCE PASCHAL

Submitted in partial fulfillment of the requirements
for the Degree of Doctor of Philosophy

Thesis Advisor: E. Mark Haacke, Ph.D.

Department of Biomedical Engineering
CASE WESTERN RESERVE UNIVERSITY
August 1992

CASE WESTERN RESERVE UNIVERSITY

GRADUATE STUDIES

We hereby approve the thesis of

Cynthia Bruce Paschal
candidate for the Ph. D.

degree.*

Signed: Cecil W. Thorne
(Chairman)

E. Mark Stroker

L. Adh

Richard M. Miller

David L. Wilson

David L. Wilson

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THREE DIMENSIONAL HIGH RESOLUTION MAGNETIC RESONANCE IMAGING OF THE CORONARY ARTERIES

Abstract

by CYNTHIA BRUCE PASCHAL

Coronary heart disease is a life-threatening illness which is the leading cause of death in the U.S. Improved methods for early detection and monitoring of coronary heart disease are needed in the battle against this killer. Thus, the objective of this dissertation research was to develop and evaluate a non-invasive, three dimensional magnetic resonance imaging technique capable of visualizing the coronary arteries. The greatest challenge towards meeting this goal is respiratory motion of the heart. This motion was characterized and found to be on the order of tens of millimeters in range and greater in extent along the cranio/caudal axis than along the anterior/posterior axis for a supine subject. The motion was determined to be more complex than a simple one dimensional translation. Several methods to compensate for respiratory motion were evaluated via examination of point spread functions, computer simulations of imaging, and actual application to imaging experiments. A 3D approach was selected for its ability to provide high resolution, high signal-to-noise ratio images. The implementation of a 3D technique for cardiac imaging imposes a variety of filters over the detected signal. These filters were simulated and analyzed for their effect on contrast and resolution. Finally, the developed technique was used on normal volunteers and patients with known pathology. The technique was very successful in depicting anatomy in normal volunteers. The technique was able to clearly

reveal pathology in some patients yet yielded false negatives in others. The inconsistencies in the ability to reveal pathology may actually have been related to different types of disease. If so, then the technique may provide a method of discrimination between different types of disease though more experimentation is needed to characterize the appearance of pathology in this 3D technique. In addition, improving the technique by incorporating more respiratory compensation, especially gating, increasing resolution, including spatially and/or frequency selective RF pulses, employing appropriate surface coils, and possibly utilizing contrast agents should increase the diagnostic capability of 3D MRI of the coronary arteries.

This dissertation is dedicated
in thanksgiving to the glory of God and
with love to my fiancé, Perry Lee Gerenday.

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Chapter 1

Introduction

This dissertation describes the important issues, theory, and practical research involved in the development of a three dimensional high resolution magnetic resonance technique for imaging the coronary arteries. Using MRI to visualize the coronary arteries is an extremely complex task, one which is being met with growing success.

1.1 Objectives

The principle objective of this research was to develop and evaluate a 3D MRI technique capable of visualizing the coronary arteries. Towards this end, considerable work was focussed on characterizing the respiratory motion of the heart, modeling its effects in MR images, and examining methods to compensate for respiratory motion. Issues of contrast and spatial and temporal resolution were also investigated.

1.2 Description of dissertation

This dissertation is organized into 10 chapters. This introductory chapter is followed by four chapters providing material necessary to understand the concepts relevant to this research. These chapters include information about background and motivation, basic principles of MRI, general cardiac MRI, and basic principles of MR angiography (MRI of vascular structures). Chapter 6 discusses the important question of whether or not it is even realistic to use MRI to image the coronary arteries including a discussion of temporal and spatial resolution issues. Contrast issues are discussed in detail in Chapter 7 which includes simulation results for non-steady state and non-sequential k-space coverage and other experiments. The effects of respiration on cardiac MRI are discussed in detail in Chapter 8. This chapter includes experimental results characterizing the motion of the heart with respiration, modeling of the effects of such motion on MR images through computer simulated imaging experiments, and an examination of compensation techniques. Chapter 9 details the 3D technique developed in this research and discusses the results obtained in normal volunteers and in patients with known disease. Finally, conclusions and future directions are discussed in Chapter 10. An appendix is included which gives the meaning of abbreviations and acronyms used in this dissertation.

Chapter 2

Background and Motivation

2.1 Motivation for pursuing coronary artery MRI

Coronary heart disease is a significant problem in the United States of America and in many industrialized nations. Early, accurate diagnosis of this problem is paramount to reducing its toll on quantity and quality of life. Many diagnostic tests exist which reveal the morphologic and functional consequences of coronary heart disease. The gold standard technique for determining the morphologic changes of arteriosclerosis in the coronary arteries is conventional X-ray angiography via coronary artery catheterization. While this technique provides extremely valuable information, it is not without drawbacks. These drawbacks provide the motivation for the development of another diagnostic technique: magnetic resonance imaging of the coronary arteries.

2.1.1 Prevalence and effects of coronary heart disease

Coronary heart disease is a life-threatening illness which afflicts more than five million people in the U.S. and is the leading cause of death, killing over 500,000 individuals annually [1]. Each year, over 300,000 people die of heart attack prior to reaching the hospital [1]. Coronary heart disease includes stenosis, ulceration, and occlusion of the arteries which supply blood to the myocardium. Consequences can include angina pectoris (chest pain), myocardial infarction (temporary or permanent interruption of blood supply to the myocardium which then impairs function causing a “heart attack”), and death.

2.1.2 Why pursue a new diagnostic approach?

The shortcomings of cardiac catheterization motivate the search for a new technique which is safer, less discomforting, and if possible, less expensive. MRI has the potential to meet this need in that it does not have the risks associated with catheter and contrast agent use, does not cause physical discomfort for the patient, and is just slightly less expensive.

A non-invasive test such as MRI that could be used to screen individuals at high risk for developing CHD may help reduce the number of people who die of heart attack. MRI has proven to be very successful in producing angiograms of the vasculature of the head[2], neck[3], abdomen[4], lungs[5], and other circulatory distributions. It, then, seems to be logical that these

MR angiography techniques be applied to the task of visualizing the coronary arteries.

MRI of the coronary arteries (or equivalently, MRA) is fraught with many difficulties not encountered in MRA of other vascular systems. These challenges, including cardiac motion, respiratory motion, extremely variable flow velocities, and complex flow patterns, have hampered the success of coronary artery MRI. Despite these many considerable challenges, or perhaps because of them, a number of researchers have been actively pursuing MRI of the coronaries. Some of the work of other researchers is discussed in Section 6.6.

2.2 Other diagnostic modalities

As mentioned earlier, there are many diagnostic tests which reveal the morphologic and functional consequences of coronary heart disease. The principle method for evaluating the morphology of the coronary arteries is cardiac catheterization which is a specialized application of conventional X-ray angiography. Cine computed tomography may also be employed to visualize the coronaries, though this technique is not widely available and is not often utilized in part because of the radiation dosage. Echocardiography also provides morphologic information and in addition provides some flow information. The functional consequences of CHD can be evaluated via scintigraphic (nuclear) techniques which determine tracer distributions and electrocardiography which measures electrical activity in the heart.

2.2.1 Cardiac catheterization

The gold standard for evaluating the morphology of the coronary arteries is cardiac catheterization, a specialized application of X-ray angiography. The technique involves the insertion of a catheter into the femoral artery; the catheter is then guided into the aortic root. Fluoroscopy is used to view the position of the catheter in the body. When the catheter reaches the aortic root, its tip is placed into the origin of either the right or left coronary artery. Contrast medium is then injected through the catheter and cine films are taken at 15-60 frames per second. These cine films have a spatial resolution of about five line pairs per millimeter and reveal the vascular structures the contrast agent is able to enter. The radiographs are taken in real time and create a movie of the examination. This helps to give a visual impression of the flow characteristics (direction, speed) in addition to the morphologic information. Cardiac catheterization has the advantages of providing high spatial, temporal, and contrast resolution. Its disadvantages include the many risks associated with this type of invasive technique: damage to vessel lining, dislodgement of emboli, cardiac arrhythmias, myocardial infarctions, allergic reactions to the contrast agent, and contrast nephrotoxicity. Though these risks are small, they can occur and a fatality rate of 0.1-0.3% has been reported for cardiac catheterization[6, page 31]. Other disadvantages involve the nature of the image data which is analog (on film versus a digitized image) and projective and thus not reformattable for viewing from multiple

perspectives. View directions in this type of study are limited by the movement of a 'C' arm apparatus around the subject. Finally, there is quite a bit of subjectivity and potential error involved when 3D information is inferred from the 2D data provided by cardiac catheterization.

2.2.2 Echocardiography

Echocardiography is simply ultrasound imaging of the heart. The technique produces real-time images of the heart and coronary arteries and can also provide information about direction and velocity of flow. The ultrasound probe may be applied to the exterior of the chest, though the sonographic window is limited by the presence large impedance changes between soft tissue and bone and cartilage (ribs and sternum) and air in the lungs. To avoid some of these window problems, transesophageal echocardiography (TEE) may be used. In this exam, the ultrasound probe is placed in the subject's esophagus. While the quality of the images is greatly improved by this probe placement, it is hardly a pleasant experience for the subject. Echocardiography has the advantages of being inexpensive, providing real-time images and flow information while it has the disadvantages of being invasive (for TEE) and having moderate to low resolution. Echocardiography is also not suitable for all patients, especially those who are obese or, for TEE, those who have chronic obstructive pulmonary disease.

2.2.3 Scintigraphic (Nuclear) Imaging

Scintigraphic imaging techniques for evaluating CHD include stress thallium SPECT and ^{13}N -ammonia and ^{18}F -fluorodeoxyglucose positron emission tomography (PET). These studies involve introduction of a radioactive contrast agent, generally via injection into the bloodstream, followed by detection with an array of scintillation crystals. These tests provide information about the functional status of the myocardium and the distribution of blood to the myocardium via the coronary arteries. For example, nuclear radiography tests can reveal what portions of the myocardium are not taking up the radioactive tracer due to obstruction of the coronaries and/or death of the myocardium. Metabolic function within the myocardium may also be measured. The contractile function of the myocardium can be assessed and stroke volumes determined. The main advantage of nuclear techniques is the provision of functional information including tissue viability. Disadvantages include use of a radioactive contrast agent which involves a risk of allergic reaction, exposure to ionizing radiation, and very poor spatial resolution. No morphologic information about the coronaries themselves can be obtained with scintigraphic imaging.

2.2.4 Electrocardiography

Electrocardiography, or ECG, is a very simple yet extremely valuable tool in the diagnosis of CHD. Electrodes placed on the surface of the body mea-

sure the movement of electrical impulses through the heart. This test may be done under resting and stress or exercise conditions. By evaluating the readings from electrodes in different positions on the body, abnormalities in rhythm and regional conduction are revealed. These abnormalities, especially in conduction, are an indicator of myocardial damage. ECG has the advantages of being inexpensive, non-invasive, and providing real-time, functional information. Its main disadvantage is that it provides no morphologic information regarding the coronary arteries. However, it can identify distribution of myocardial damage, thereby implying disease of a particular coronary artery which normally supplies that region of myocardium.

2.3 Objectives of MR vs. other modalities

MRI can provide a wealth of information about the heart, both functional and morphologic, depending on the type of scan executed. Indeed, MR has the potential to provide some or all of the information now obtained with cardiac catheterization, echocardiography, nuclear radiography, and electrocardiography. MRI has not replaced these tests, and probably never will completely replace them due to practical restrictions (pacemakers, large patient size, claustrophobia, etc.). As MR techniques progress, applications stabilize, and post-processing methods are improved and made more simple to use, MR may well replace these other diagnostic modalities in a great portion of patients.

With the appropriate post-processing, two dimensional MR gradient echo cines, and some 3D approaches [7], can provide information about the contractile behavior of the myocardium and volumetric information such as stroke volume and myocardial mass. MR contrast agent studies can, like nuclear radiography, provide information about the status of the myocardium, though without radiation exposure. Both MR spin echo and gradient echo studies are used to examine the morphology of the heart including chamber and great vessel size, patency, and orientation.

On a finer resolution scale, spin echo and gradient echo techniques, both 2D and 3D, have been and continue to be investigated for their ability to visualize the coronary arteries. This dissertation discusses research and development of a 3D gradient echo technique for visualizing the coronary arteries.

Regarding MRI of the coronaries, some researchers have proposed [8] and initiated studies to try to quantitate flow in the coronaries. This information is very important in that, with regards to myocardial health, it is the ability of the coronaries to deliver blood to the myocardium rather than the morphology of the vessels themselves that is of greater importance. Of course, the two, vessel morphology and blood delivery, are so tightly linked that determining vessel morphology is in itself a critical objective. In addition, the coronaries must be localized before flow measurements can be made. Also, for the purposes of planning coronary artery bypass surgery, morphology is of the utmost importance.

The potential of MR to provide information regarding gross and fine morphology, contractile function, flow, myocardial status, etc. in a comprehensive exam may eventually lead to MR being the technology of choice in evaluating and following patients with heart disease.

2.4 Anatomy and physiology of coronary arteries

The physiologic and anatomic characteristics of the coronary arteries present a number of challenges to MRA [9]. The coronaries are small in size, tortuous, have branching patterns unique to each individual, and have multiphasic and extremely variable flow. These factors alone would not prohibit successful MRA but cardiac and respiratory motion greatly increase the difficulty of the task. Also, signal from blood in the atria and ventricles can obscure signal from the coronary arteries in the images, thus hampering maximum utilization of the images.

At their largest caliber, the right and left main coronary arteries (RCA, LM) measure roughly 4-5 mm in diameter. The LM bifurcates within 2 cm of its origin into the left anterior descending (LAD) and circumflex (CX) which are about 2-4 mm in diameter. A sketch of the heart and coronary arteries is presented in Figure 2.1.

The tortuosity of the coronary arteries precludes selection of a single imaging plane perpendicular to the arteries which would capitalize on through

Figure 2.1: Sketch of the heart and coronary arteries, anterior view.

plane flow. Coronary blood supply comes from retrograde flow down the aortic root with the bulk of LM flow supplied during early diastole and somewhat more than half the RCA flow supplied during systole. The flow through the coronaries varies greatly over the cardiac cycle, ranging from 0 to 100 ml/min [10, page 200], with peak linear velocities of about 30 cm/sec for the LM and 22 cm/sec for the RCA [11] in early diastole. In the LM, the peak flow rate in early diastole is more than twice the peak rate during systole whereas in the RCA, the peak flow rate in diastole is equal to or slightly less than the maximum rate during systole [10, page 200]. In both vessels, there is marked deceleration of flow at the start and end of systole. As cardiac motion is more extreme during systole, better image quality is obtained during

diastole which is optimal for imaging flow in the left coronary distribution but is less optimal for the RCA.

Chapter 3

Basics of Magnetic Resonance

The field of magnetic resonance imaging has its roots in physics and chemistry. The phenomenon of nuclear magnetic resonance (NMR) in bulk matter was first described in 1946 by Purcell, Torrey, and Pound [12] and by Bloch, Hansen, and Packard [13], although nuclear spin angular momentum and consequent magnetic moments had been studied for a number of years earlier.

3.1 Spin and precession

3.1.1 Nuclear spin

Nuclei with an odd number of nucleons (protons and neutrons) have a net spin. Any mass spinning about an axis has an angular momentum. If the mass carries an electrical charge, as protons do, then it also has a magnetic moment. The magnetic moment describes the strength and direction of the magnetic field surrounding the spinning charge. The angular momentum of

the nucleus, $\vec{I}$, and the magnetic moment, $\vec{\mu}$, point in the same direction and are proportional to each other. The relationship between $\vec{I}$ and $\vec{\mu}$ is:

$$\vec{\mu} = \gamma \hbar \vec{I} \quad (3.1)$$

with the constants of proportionality being γ , the gyromagnetic ratio which is unique for each nucleus, and $\hbar$, Plank's constant [14, page 2].

Hydrogen (1H) is the nucleus of choice in MRI today due to its high relative abundance. 1H makes up 99.98% of all hydrogen versus 0.02% for all other isotopes. Hydrogen has a spin quantum number, I , of 1/2 and a gyromagnetic ratio of 42.58 MHz/T.

3.1.2 Spins in a magnetic field

Nuclei in a magnetic field, B_0 , separate into spin states or energy levels defined by the principles of quantum mechanics. The magnetic field is defined to be along the $\vec{z}$ or equivalently $\hat{k}$ direction. For any nucleus, the number of possible I_z states (those components parallel to $\hat{k}$) is given by $2I + 1$. The energy of an I_z state is given by:

$$E = -\vec{\mu} \cdot \vec{B} \quad (3.2)$$

Substituting Equation 3.1 into this equation.

$$E = -\gamma \hbar \vec{I}_z \cdot \vec{B}. \quad (3.3)$$

Since $I = 1/2$ for hydrogen, then the number of states it can assume is two. The two energy states are referred to as parallel ($E_+ = -1/2\gamma\hbar B_0$) and anti-parallel ($E_- = +1/2\gamma\hbar B_0$) since, in each case, the magnetic moment of the nucleus points either in the same direction (parallel) or the opposite direction (anti-parallel) as the magnetic field. The parallel state is the lower energy level. The ratio of spins in the anti-parallel to parallel states is dependent upon the temperature of the sample and the energy difference between the states and is given by:

$$\frac{\text{anti-parallel}}{\text{parallel}} = \exp\left(\frac{\Delta E}{kT}\right) = \exp\left(\frac{E_+ - E_-}{kT}\right) = \exp\left(\frac{-\mu B_0}{kT}\right) \quad (3.4)$$

where k is the Boltzmann constant and T is the absolute temperature in $^{\circ}K$. That this ratio is not equal to unity except at $B_0 = 0$ (or as $T \rightarrow \infty$ $^{\circ}K$) means that there exists a net magnetic moment, $M_z^0 \hat{k}$. In the absence of applied radiofrequency (RF) fields or changes in B_0 , this ratio is constant and describes the thermal equilibrium state. While this is an equilibrium condition for the entire sample, the individual nuclei are not fixed at either energy level. Rather, during thermal equilibrium, the number of transitions from the lower to the upper state equals the number of transitions in the opposite direction.

Since the states of the nucleus are quantized, there is an exact amount of energy which must be absorbed or emitted for a transition up or down.

respectively, to occur. This energy difference is given by:

$$E = E_- - E_+ = \hbar\gamma B_0 = \hbar\omega_0 \quad (3.5)$$

with $\omega_0 = \gamma B_0$ being the angular velocity of the absorbed or emitted RF field. The frequency, ω_0 , of this RF irradiation is called the Larmor frequency. For protons, γ is equal to 4.258×10^7 Hz/T (or 2.675×10^8 rad/T), so at 1.5T, $\omega_0 = 63.87$ MHz. An applied RF field of higher or lower frequency will not induce transitions from the lower to the higher state and transitions from the higher to the lower state will only emit RF of this frequency. It is this specificity of frequency which imparts the word “resonance” to the name of this imaging technique.

The alignment of the spinning nuclei with the magnetic field is not perfect; in fact, the axes of the nuclei remain at some constant angle, Θ , out of alignment with B_0 . As a result of this imperfect alignment, the nuclei precess at the Larmor frequency about $\hat{k}$. On the average, the magnetic moment can be described by the equation:

$$\frac{d\vec{M}}{dt} = \gamma\vec{M} \times \vec{B}_0. \quad (3.6)$$

where $\vec{M}$ is the bulk magnetization for a set of spins.

This can be understood as follows. A group of nuclei precessing about the $\vec{z}$ direction define a cone comprised of individual magnetic moments. In

the case of hydrogen, these individual moments form two opposite cones parallel and anti-parallel to $\vec{z}$. A collection of spins precessing with identical frequency comprises a spin isochromat. Within the isochromat, the individual moments are evenly distributed about the cones during equilibrium and add vectorially to create a net magnetic moment (referred to above as the bulk magnetization) which in this case is described by $\vec{M}_0 = M_0 \hat{k}$. This net magnetic moment points in the $\vec{z}$ direction and has a magnitude proportional to the ratio in Equation 3.4.

The position of an individual moment along the circular path about the cone is called the phase. This phase may be visualized as the angular offset from the $\vec{y}$ axis of the projection of that moment vector into the xy plane. If the individual moments are evenly distributed about the cone, then there is no net magnetization vector in the xy plane and the spins are described as being dephased in the transverse plane.

If the moments are not evenly distributed about the cone, then there is a net magnetization vector in the xy plane. This net vector continues to precess about the $\vec{z}$ axis at the Larmor frequency. In a frame of reference rotating at the Larmor frequency, this vector appears to be fixed and is described by $\vec{M} = M_x \hat{i} + M_y \hat{j} + M_z \hat{k}$ where $\hat{i}$, $\hat{j}$, and $\hat{k}$ now refer to the rotating frame. Such a rotating frame of reference is used in MRI. Hereafter in this dissertation, a frame of reference rotating at the Larmor frequency is assumed unless otherwise noted.

3.2 RF excitation and signal detection

RF energy is broadcast and detected by an antenna. Current flowing in the antenna or coil will generate a magnetic field, $\vec{B}_1$, that is stronger close to the coil and weaker far from the coil. Analogously, a rotating magnetization ($\frac{d\vec{M}}{dt}$) near the coil will induce a voltage, ξ , that is stronger than the voltage induced by a similar rotating magnet far from the coil. The correspondence between the magnetic field, $\vec{B}_1$, induced by current flow in the coil and the voltage, ξ , induced in the coil by a changing magnetic field is known as the principle of reciprocity. Mathematically, the relationship is:

$$\xi \propto \frac{d}{dt}(\vec{M} \cdot \vec{B}_1) \quad (3.7)$$

RF antennas, or coils, are either built into the MRI machine as in the case of the body coil or placed into it as in the case of special chest, head, or spine coils. These smaller “surface” coils placed into the machine are used to focus on a smaller section of the body than the body coil. They have a higher sensitivity to signal from a smaller, local region and a lower sensitivity to noise from the entire subject than the body coil which is more uniformly sensitive over a large portion of the imaging volume. So, over a small region, surface coils give a better signal-to-noise ratio (SNR) than the body coil. The sensitivity of a surface coil drops off rapidly with distance from the coil, so for imaging a larger region, the body coil gives better SNR at points farther

from the surface.

The sensitivity of an antenna is described by its field - the field that it broadcasts as well as receives - noted as $\vec{B}_1$. $\vec{B}_1$ combines with $\vec{B}_0$ to make the total magnetic field. If Equation 3.6 is expanded to include the total $\vec{B}$ field, then it becomes:

$$\frac{d\vec{M}}{dt} = \gamma \vec{M} \times (\vec{B}_0 + \vec{B}_1). \quad (3.8)$$

The presence of the cross product serves as a reminder that $\vec{M}$ and $\vec{B}$ must have perpendicular components in order for $\frac{d\vec{M}}{dt}$ to have a non-zero value. More simply, this means that an antenna must broadcast an RF field that is perpendicular to $\vec{M}$ in order to excite or tip the magnetization. Similarly, recalling the principle of reciprocity, an antenna can only detect those changes in $\vec{M}$ (i.e., $\frac{d\vec{M}}{dt}$) that are perpendicular to its own field, $\vec{B}_1$. This generally means that detected signals come from magnetization changes in the xy plane.

The detected signal is a time varying composition of many radiofrequency waves of differing frequencies, amplitudes, and phases. The variations in time and wave characteristics provide important information and are affected by tissue properties (see Section 3.3) and the application of gradient magnetic fields (see Section 3.5). The composite signal is decoded or transformed into an image via the Fourier transform, discussed in Section 3.10.

3.3 Relaxation parameters

Relaxation in MR is a process by which the measured signal changes as a function of time. The relaxation parameters associated with MR are the longitudinal or spin-lattice relaxation time, $T1$, and the transverse or spin-spin relaxation time, $T2$. These relaxation times are unique for each type of tissue and, hence, along with proton density, ρ , which is the number of protons in a given amount of tissue, and flow, control contrast in MR images.

3.3.1 Longitudinal or spin-lattice relaxation time, $T1$

The longitudinal or spin-lattice relaxation time, $T1$, is a measure of how fast an excited nucleus will return to alignment with B_0 . Recall that nuclei line up either parallel or anti-parallel to B_0 or, equivalently, exist in a low or high energy state, with an excess of spins in the parallel or low energy state. Following application of a 90° RF pulse, enough of the low energy state nuclei are excited into the high energy state to cause the number of nuclei in each state to be equal. Hence there is no net longitudinal magnetization. In order to return to the low energy state, the excited nuclei must transfer energy to the surrounding lattice. Hence, the name “spin-lattice” relaxation time. As the numbers of nuclei in the low and high energy states return to equilibrium values, the longitudinal magnetization will return to equilibrium. This is an exponential process which is described by the equation:

$$M_z(t) = M_z^o(1 - \exp(-t/T1)) \quad (3.9)$$

where M_z^o is the equilibrium value of the longitudinal magnetization. $T1$ is then the time for M_z to grow to $(1 - \exp(-1))$ or 63% of M_z^o .

In general $T1$ is longer for solids than for liquids. This is because in liquids, molecules move more freely and thus collide with other molecules more frequently than in solids. Collisions result in energy transfer, thus allowing excited spins to give up energy to the surrounding lattice and return to alignment with B_o . So, the $T1$ of ice is longer than the $T1$ of water. There are so many other factors affecting $T1$ that this solid/liquid concept should be viewed only as a rough rule of thumb.

3.3.2 Transverse or spin-spin relaxation time, $T2$

Immediately after a 90° RF pulse is applied to tip spins into the transverse (xy) plane, the spins all point in the same direction, along the y axis if the RF field was along the x axis. Ideally, these spins then precess in unison at the Larmor frequency about the z axis. Thus, in the rotating frame all the magnetization vectors would remain along y , summing to a constant magnitude M_y^o (ignoring $T1$ relaxation for the time being). In reality, the spins do not precess in unison due to small differences in the local magnetic fields. These small differences in local magnetic fields arise from the presence of many nuclei and electrons having spin and thus magnetic moments of

their own. These microscopic magnetic environments vary with location and time. These differences in magnetic field cause the Larmor frequency of the various spins to differ. So, some spins will precess a bit faster and some a bit slower. The result is that, in the rotating frame, the magnetization vectors will begin to dephase or spread apart in either direction from the y axis. Due to the random variations over time of the local fields, this dephasing is an irreversible process which will, in turn, cause the magnitude of the net magnetization, M_y , to decrease. This decay in signal continues over time until $M_y = 0$. The exponential decay process is called a free induction decay (FID) and is described as:

$$M_y(t) = M_y^0 \exp(-t/T2) \quad (3.10)$$

If $t = T2$, then $M_y(t) = 0.368M_y^0$. So, $T2$ is the time for the transverse magnetization to decay to 37% of its original value. Since this relaxation process arises from the interaction of spins with other spins, it is called spin-spin relaxation.

$T1$ and $T2$ relaxation occur simultaneously. If excited spins have undergone complete $T1$ relaxation and have thus returned from the transverse plane back to alignment with the longitudinal axis, then no transverse magnetization remains which can undergo $T2$ relaxation. Thus, $T2$ is always shorter than $T1$.

$T2$ is generally shorter for solids than for liquids. This is because spins in

a solid are relatively immobile and thus have an increased amount of influence on neighboring spins. In a liquid, molecules are free to move about and in doing so, average out over time the effects of local field inhomogeneities.

3.3.3 $T2^*$

There are other mechanisms besides spin-spin interactions which cause local magnetic fields to vary in space and time and thus to induce dephasing. These mechanisms include B_0 inhomogeneity and magnetic susceptibility. These added field variations increase the rate of dephasing according to the time constant $T2^*$. $T2^*$ incorporates $T2$ and also time constants for B_0 inhomogeneity and magnetic susceptibility. It may also include inhomogeneity imposed by imaging gradients (see Sections 3.5 and 3.6), and other factors in the following manner:

$$\frac{1}{T2^*} = \frac{1}{T2} + \frac{1}{T_{B_0 \text{ inhomog}}} + \frac{1}{T_{\text{susceptibility}}} + \frac{1}{T_{\text{gradients}}} + \dots \quad (3.11)$$

Thus it is evident that $T2^*$ is always shorter than $T2$. $T2^*$ processes are typically temporally static and therefore reversible.

Magnetic susceptibility is a measure of how magnetized different substances become. All materials become at least partially magnetized when placed in a magnetic field. The additional magnetic fields created by this magnetization distort the local static magnetic field and extend well beyond the material being magnetized. The degree of magnetization is proportional

to the applied field and to χ , the magnetic susceptibility. χ is on the order of 10^5 for ferromagnetic materials, 10^{-3} for paramagnetic ions in solution, -10^{-5} for (diamagnetic) soft tissues, and essentially zero for gases such as air. At boundaries between substances of markedly different χ , a steep gradient in the local magnetic field is produced. This gradient leads to distortions in the image and may cause signals from a great many pixels to be stretched over many more pixels or compressed into a very few pixels which then become very bright. On a microscopic level, susceptibility effects lead to decreased $T2^*$ because the induced gradients within a single pixel cause increased dephasing. In the extreme case, complete dephasing occurs resulting in signal void.

3.4 The Bloch equation

The Bloch equation, described by F. Bloch in 1946[15], describes the time dependent behavior of the net magnetization, $\vec{M}$, in the presence of an applied magnetic field, $\vec{B}(t)$. It is an expansion of Equation 3.8 that incorporates the phenomena of $T1$ and $T2$ relaxation. It may be used to describe the behavior of $\vec{M}$ in a static magnetic field with or without an applied RF ($\vec{B}_1$) field and/or gradient magnetic fields. The equation is:

$$\frac{d\vec{M}}{dt} = \gamma \vec{M} \times \vec{B}_{eff}(t) - (M_x \hat{i} + M_y \hat{j})/T2 - (M_z - M_0) \hat{k}/T1. \quad (3.12)$$

where $\vec{B}_{eff}(t)$ is the effective magnetic field as a function of time and is given by:

$$\vec{B}_{eff}(t) = \vec{B}_0(\vec{r}, t) + \vec{B}_1(t) + \frac{\vec{\omega}}{\gamma} \quad (3.13)$$

On resonance in the rotating frame, $\vec{\omega} = -\omega_0 \hat{k}$ and thus the effective field is just $\vec{B}_1$. Note that if gradients (G) are applied, $\vec{B}_0(\vec{r}, t) = B_0 \hat{k} + \vec{G}(t) \cdot \vec{r}$.

The Bloch equation can be separated into its x , y , and z components and used to predict the signal from a particular MR experiment. The coupled differential equations can be difficult or indeed impossible to solve analytically except in certain cases when simplifying conditions and assumptions are present.

3.5 Spatial localization

Since the objective of MRI is to map signal originating from different locations in the subject to different positions in an image, it is necessary to utilize some type of spatial localization. To do this, the gradient magnetic fields referred to earlier are used. These are referred to as gradients because the strength of the magnetic field generated varies with position. The variation is linear. In the MRI machine, there are three sets of specially designed wire coils which, when current is passed through them, generate gradient magnetic fields along the x , y , and z directions. Through Cartesian transformation, these coils can be used in combination to generate gradient magnetic

fields along any set of axes.

Gradients are applied to perform three basic types of spatial localization: frequency encoding, slice selection, and phase encoding.

3.5.1 Frequency encoding

The resonant frequency of a nucleus is dependent upon the magnetic field it experiences as shown in the Larmor equation. If a gradient magnetic field of slope $G_x = \frac{\partial B_z}{\partial x}$ is applied, then the net magnetic field as a function of position, x , is:

$$B(x) = B_0 + G_x x \quad (3.14)$$

Now, recalling the Larmor relationship for resonant frequency and inserting Equation 3.14:

$$\omega(x) = \gamma(B_0 + G_x x) \quad (3.15)$$

So, when a gradient magnetic field is imposed, resonant frequency becomes dependent upon position. If a gradient is applied during collection or reading of the data, then the detected signal will be a composite of signals of many different frequencies, with each different frequency signal arising from a different location along that gradient axis. This is called frequency encoding; the gradient applied during signal detection is called the read, readout, or frequency encoding gradient.

It is important to note that frequency encoding can only be used to localize signals along one spatial dimension at a time. If more than one gradient is applied during readout, encoding occurs along a single axis that is the vector sum of the applied gradients. This is in effect simply a rotation of the gradient axes.

3.5.2 Slice selection

Recall from Section 3.1.2 that the hydrogen nuclei can only absorb and emit radiofrequency waves at their resonant (Larmor) frequency. As seen in the preceding section on frequency encoding, a gradient magnetic field may be applied to make magnetic field and thus resonant frequency a function of position. It is possible to apply a gradient during the broadcast of an RF pulse such that only a slice of tissue of finite thickness will absorb the energy. The pulse is ignored by spins in other locations. The location of the excited slice is dependent upon the strength of the gradient field and the center frequency of the RF pulse. The width of the excited slice is dependent again on the strength of the gradient field and also on the bandwidth of (i.e., range of frequencies included in) the RF pulse.

3.5.3 Phase encoding

Another way of spatially encoding MR signals is to use phase encoding. This is a technique in which a different phase is imparted to spins at different

locations. To do this, a gradient magnetic field is applied for a short duration between RF excitation and data collection. During application of this gradient, spins near one end of the phase encoding axis will move much more slowly than spins near the opposite end. The faster spins will advance in phase relative to the slower spins. After the phase encoding gradient is turned off, this phase difference will remain even though all spins will again resonate at the same frequency.

The amount of phase difference imparted is determined by the integral over time of the applied gradient, or:

$$\phi(x) = \gamma \int_0^t G_x(t) x(t) dt \quad (3.16)$$

where:

$$G_x(t) = \frac{\partial B_z}{\partial x}(t) \quad (3.17)$$

and:

$$x(t) = x_0 + \frac{dx}{dt}t + \frac{d^2x}{dt^2} \frac{t^2}{2!} + \frac{d^3x}{dt^3} \frac{t^3}{3!} + \dots \quad (3.18)$$

If the strength and duration of the applied gradient are high, then a large phase difference from location to location will be developed. Note that this large, intentional dephasing means that the signal magnitude will be very low. However, the large phase difference between adjacent locations makes

this information useful in determining high spatial frequency features of the image. If, alternatively, the integral of strength over the duration of the applied phase encoding gradient is low, then phase will vary only a little across the phase encoding direction. In this case, the signal magnitude is very high and forms the peak of the echo in the phase encoding direction. This information reveals low spatial frequency features but due to the very small phase variations is not helpful in distinguishing signals from adjacent voxels.

Both high and low spatial frequency information is needed to make an image. Thus, the experiment must be repeated many times with each execution utilizing a different amplitude of the phase encoding gradient in order to obtain high and low spatial frequency information. In fact, the number of times that the experiment or scan must be repeated is equal to the number of pixels desired along the phase encoding axis.

Phase encoding may be used in more than one dimension. The total scan time increases as the product of the number of pixels along each phase encoding axis. The in-plane phase encoding direction is generally denoted as the y direction, with the phase encoding steps referred to as k_y lines. If phase encoding is used in the slice (z) direction, its encoding steps are referred to as partition or slice encoding steps which coincide with the collection of k_z lines.

3.6 The FID and gradient echoes

It was noted earlier, in Section 3.3.2, that, in the absence of gradient magnetic fields, transverse magnetization undergoes an exponential decay called the free induction decay or FID. In the inertial frame of reference, this signal decay looks like an oscillating wave decaying within an exponential envelope. The frequency of oscillation is the Larmor frequency, ω_0 . In a rotating frame of reference, the signal oscillates within the same envelope at a frequency $\omega_{rot\ frame} - \omega_0$. If the frame of reference rotates at the Larmor frequency, then the signal appears as a pure exponential decay. This is the “on resonance” condition.

In an ideal world, the time constant for this decay envelope is T_2 but, in reality, inhomogeneities in the magnetic field cause the decay to follow the time constant T_2^* . One type of magnetic field inhomogeneity is intentional - the applied gradients used for spatial localization. The application of gradients causes rapid dephasing of the spins; another way of saying this is that T_2^* is shortened. It is possible to reverse all of the dephasing effects of the gradients in the case of stationary tissues and time invariant field inhomogeneities and thus reduce that inhomogeneity factor in T_2^* . Recall that some of the dephasing is intentional, namely in the case of phase encoding (see Section 3.5.3). This dephasing is limited in extent and is essential for spatial localization along the phase encoding axis. Other gradient induced dephas-

ing is not intentional but is an unwanted by-product of frequency encoding or slice selection. Recall that for frequency encoding, a gradient is applied during signal acquisition to cause the emitted RF energy to have a frequency that is a function of position along the frequency encoding axis. While the spins resonate at different frequencies, they accumulate an unwanted phase difference as predicted by Equation 3.16. If, prior to signal acquisition, the readout gradient is applied with a reverse polarity, the spins will accumulate a reverse phase difference. This reverse phase difference is countered (i.e., the spins are rephased) at some point during the readout period by the positive phase difference induced by the application of the readout gradient. For example, consider the following simple readout gradient waveform:

$$G_x(t) = \begin{cases} -g & \text{for } 0 < t < T \\ +g & \text{for } T < t < 3T \text{ (readout period)} \end{cases} \quad (3.19)$$

Using Equation 3.16, the accumulated phase for stationary spins ($x(t) = x_0$) is found to be proportional to $-gT$ at time T . The gradient is reversed at the start of the readout period, time T . This gradient reversal causes the phase to go to zero by the middle of the readout period, time $2T$. The accumulated phase then grows to be proportional to $+gT$ at the end of the readout period, time $3T$. During application of the dephasing gradient, time 0 to T , the amplitude of the FID signal drops quickly, faster than the $T2^*$ envelope predicts¹. However, as the reversed gradient is applied during

¹For purposes of this particular discussion, $T2^*$ is considered not to include a $T_{\text{gradients}}^{-1}$

readout, the amplitude of the FID signal increases again, reaching a peak value when rephasing is complete. This is called a gradient echo. The peak signal amplitude of the gradient echo is equal to the amplitude of the $T2^*$ FID envelope at the time of the echo. The polarity of the gradient can be repeatedly reversed to generate a train of gradient echoes. These echoes will be of decreasing amplitude as predicted by the $T2^*$ decay envelope.

A sequence diagram for a 2D gradient echo scan is shown in Figure 3.1. The readout gradient has three lobes designed so that the echo will be formed at the time TE during the readout period.

3.7 Timing parameters: TR, TE, and FE

There are many user selectable parameters in any MRI experiment which affect SNR and contrast. Three of these parameters involving time are the repetition time, TR, the echo time, TE, and the field echo time, FE.

3.7.1 Repetition time, TR

In Section 3.5.3, it was noted that in order to spatially encode signal along the phase encoding axis, the experiment must be repeated as many times as there are desired pixels. The time interval between repetitions of the experiment is called the repetition time, TR. Total scan time then is given by $TR \times \text{\#phase encoding steps} \times \text{\#signal averages}$. It is important for reasons

term. See Equation 3.11.

Figure 3.1: Pulse sequence diagram for a 2D gradient echo scan. Extra gradient lobes are included on the slice and read gradients to cause spins moving at a constant velocity to be rephased at time TE just like stationary spins (see Section 3.8). If ECG triggering is used, then this scan will produce a single image slice at a single cardiac phase.

of patient comfort and throughput to keep the scan time to a minimum; hence it is essential to use as short a TR as is possible for the particular application. The caveat, "...for the particular application" is added because TR affects both SNR and contrast.

Throughout TR, longitudinal (and also transverse) relaxation occurs. If the magnetization is tipped completely into the transverse plane so that $\vec{M} = M_0 \hat{k}$ becomes $\vec{M} = M_0 \hat{j}$, it takes close to three times T1 for the longitudinal magnetization ($\hat{k}$ component) to return to 95% M_0 . If TR is chosen to be about three times the longest T1 of the tissues in the imaging volume, then the longitudinal magnetization for all tissues will be at least 95% of M_0 just prior to the next execution. This means that almost all of the original magnetization will be available for the second execution of the experiment. Hence, this choice of TR will lead to higher SNR than a shorter TR would provide.

If a short TR is chosen, then the various tissues will recover smaller percentages of their initial longitudinal magnetization (assuming no coherent signal remains in the xy plane). The percentage of M_0 that is recovered will depend on the T1 values of the various tissues. A tissue with a short T1 will recover a greater proportion of its initial magnetization and thus will be able to generate a larger signal in the next repetition. Conversely, a tissue with a long T1 will recover less of its initial magnetization and will generate less signal in the next repetition. So, while a short TR produces a lower

SNR than a longer TR, it will accentuate T1 differences between the various tissues. Thus, TR may be varied to affect SNR and T1 contrast.

3.7.2 Echo time, TE

The echo time is the time from the tipping of magnetization into the transverse plane by an RF pulse to the formation of the echo described in Section 3.6. This time is generally measured from the midpoint of the RF pulse to the time the echo peaks. Recall from Section 3.3.3 that transverse magnetization decays according to $\exp(-t/T2^*)$. So, at the peak of the echo, the transverse magnetization has decayed by a factor of $\exp(-TE/T2^*)$. If TE is very short, the signal loss will be minimal (SNR will be higher) for all tissues, regardless of their $T2^*$ value. If TE is not very short, then the signal will decay with the amount of decay for a particular tissue determined by its $T2^*$ value for a gradient echo scan. This will produce tissue differentiation based on $T2^*$. So, TE may be varied to affect SNR and $T2^*$ contrast.

3.7.3 Field echo time, FE

The field echo time, FE, is the time from the start of the first frequency encoding gradient event to the time the echo peaks. This time is important because it relates to the amount that the transverse magnetization of tissues moving along the frequency encoding direction dephases as a result of readout gradient activity. Similar field echo times need to be considered for the

slice and phase encoding direction. The relative importance of each FE in motion related dephasing depends on the major direction of flow. While $T2^*$ dephasing begins right after RF excitation, the component of $T2^*$ due to the gradients does not come into play until the gradients are actually applied. For stationary spins, the timing of gradient events may be varied and spread over any portion of TE and still produce the same phase effects. For moving spins, the time axis is not so commutable. So, to limit dephasing, it is important to compress readout gradient events into the shortest possible period just prior to the echo (i.e., the FE). The issue of gradients and spin phase will be covered in more detail in Section 3.8.

3.8 Spin phase

As discussed in Sections 3.5.3 and 3.6, and alluded to in Section 3.7.3, the change in spin phase is dependent upon the applied gradient waveform, $G_x(t)$ and the position of the spins as a function of time, $x(t)$. The gradient waveform described in Equation 3.19 for creating an echo causes stationary spins to have no phase change at the center of the echo. However, during the same applied gradient events, a moving spin will not be rephased (i.e., will accumulate a phase change). Using Equation 3.16, the phase change for a spin starting at position x_0 and moving at a constant velocity, v , so that $x(t) = x_0 + vt$, in the presence of the gradient waveform described by Equation 3.19, is determined to be $\gamma g v T^2$ at the time of the echo (time T). De-

pending on the values of g , v , and T , the amount of dephasing could be very great.

Obviously, the gradient waveform described in Equation 3.19 will not permit both stationary and moving spins to be in phase at the time of the echo. Indeed, no such bipolar (two lobed) gradient waveform can bring both stationary and moving spins into phase at the same time. In order to preserve signal from both stationary spins and spins moving at constant velocity, a three (or more) lobed waveform must be used. The waveform, a series of positive, negative, then positive gradient lobes, can have a variety of timing and amplitude parameters as long as the following constraint is met for all v :

$$\phi(x) = 0 = \gamma \int_0^{TE} G_x(t) [x_0 + vt] dt \quad (3.20)$$

A gradient waveform meeting the above constraint is said to be velocity compensated or compensated for first order ($\frac{dx}{dt} = \text{constant}$) motion. Note that this assumes that motion is along the x direction only. Higher orders of motion (e.g., acceleration, jerk, etc.) can also be compensated by adding additional gradient lobes of appropriate strength and duration.

3.9 Dimensions in MRI: 1D, 2D, and 3D

MRI can be used to generate a map of tissue distribution (an image) in one, two, or three spatial dimensions. One dimensional imaging is referred to

as projection imaging. In this case, slice selection is used to excite a slice of tissue. Then, frequency encoding is used to spatially encode the tissue distribution in that slice along the frequency encoding axis. This is called projection imaging because signal from all regions in the slice is collapsed or projected onto the frequency encoding axis. This type of scan need only be executed once or it may be executed many times to track changes in tissue position along the projection axis.

Two dimensional imaging produces a 2D image from a slice. Slice selection is used to excite a slice of tissue, generally 2-10 mm thick. Then, both frequency and phase encoding are used to provide in plane spatial encoding of the signal. The number of pixel divisions along the phase encoding axis times the number of signal averages desired determines the number of times the sequence must be executed. A pulse sequence diagram for a velocity compensated, ECG triggered 2D gradient echo scan was shown in Figure 3.1.

Three dimensional imaging produces a 3D volume of information which may be viewed as a stack of 2D images. Slice selection is used to excite a thick slice. Then, phase encoding is used to spatially encode the thick slice into partitions. Frequency and phase encoding are used to spatially encode the signal in the plane of the slice. To avoid confusion between the two directions of phase encoding, the phase encoding used to subdivide the slice into partitions is often referred to as slice encoding. The number of partitions times the number of pixel divisions along the phase encoding axis times the

number of signal averages desired determines the number of times the 3D sequence must be executed.

Yet another dimension may be included in MRI and that is time. A series of 2D images depicting different timepoints in the cardiac cycle is called a cine series. The images in a cine series are acquired in the same scan with the pulse sequence executed many times during each cardiac cycle. Each piece of data acquired at a particular timepoint becomes part of an image for that timepoint only. The sequence is executed over many heartbeats in order to obtain all the necessary phase encoding steps.

3.10 Fourier transforms in MR

In MRI, the detected signals are comprised of many radiofrequency waves of various frequencies, phases, and amplitudes. These composite signals are digitally sampled and fill up a one, two, or three dimensional array space that is referred to as k-space or Fourier space. The number of dimensions of k-space is the same as the number of dimensions of image space. In order to extract from k-space the spatial distribution of tissue signal, it is necessary to perform a transformation.

The transform most commonly used in MRI is the Fourier transform (FT). The Fourier transform converts signals in either direction between one domain and its corresponding domain. The most common Fourier domain pair is time and frequency. In MRI, the application of gradients along the

readout direction causes signal frequency to depend on position. So, when the recorded signal, a function of time, is Fourier transformed into a function of frequency, the spatial origin of each component of original signal is revealed. Fourier transforms may be (and are) performed independently along all encoded axes.

The Fourier transform is expressed mathematically as:

$$\mathcal{F}[g(t)] = G(\omega) = \int_{-\infty}^{+\infty} g(t) \exp^{-i\omega t} dt. \quad (3.21)$$

In the case of an MRI scan, $G(\omega)$ would be considered the signal in the image domain and $g(t)$ would be the signal in the k-space domain. As one might guess, ω in this transform is basically γB with B incorporating the main magnetic field, the RF field(s), and the gradient magnetic field(s).

There are some important considerations in working with discrete Fourier transforms as opposed to the continuous transform shown in Equation 3.21. The first consideration is related to the rate at which the original signal is sampled and the second is related to the number of points sampled. The discrete Fourier transform takes the digitally sampled MR signal emitted by an object and produces multiple images of the object. These multiple images are spaced along the position (frequency) axis at intervals inversely proportional to the rate at which the original signal was sampled. In order to prevent the images from overlapping (aliasing), the sampling frequency must be twice as high as the highest frequency signal in the image. This

is the Nyquist condition. The second consideration, regarding the number of points sampled, is related to the computer implementation of the Fourier transform. There is a type of FT called the fast Fourier transform or FFT that is easily implemented on a computer and, as its name implies, is fast. The FFT requires that the number of sampled points be equal to a power of two. If 2^n points are not acquired, the data is padded, usually with zeros, to make 2^n points for the FFT to use[16].

Chapter 4

Cardiac MRI

Cardiac magnetic resonance imaging (CMRI) has matured into a distinct subspecialty of MRI. Contrast in CMR images is determined by $T1$, $T2$, and ρ , as with MR images from other parts of the body, but also by complex blood flow (and its associated inflow enhancement) and solid tissue motion. There are a great many factors to consider in deciding how to acquire MR data for cardiac images.

4.1 Synchronization methods

Diagnosis of heart diseases frequently requires the static and dynamic, morphologic and physiologic information MR can provide so well. To obtain this data, cardiac MRI techniques and applications must address the challenges of cardiac and respiratory motion. Whether a static image demonstrating morphology or a dynamic cine image series demonstrating myocardial function is desired, it is essential that data acquisition be synchronized to pre-

dictable and reproducible portions of the cardiac cycle. With extremely fast techniques such as echo planar MRI, all the data for a single image may be obtained in as little as 26 msec[17], about 0.03 times one cardiac cycle length. In this case, synchronizing data acquisition to a certain portion of the cardiac cycle provides information about that phase of the cycle. In standard MRI, data must be acquired over several cardiac cycles and so, to avoid bad ghosting and blurring errors [18], data acquisition must be synchronized to the same phase or phases of the cardiac cycle.

4.1.1 Synchronization signal source

Data acquisition may be synchronized to a plethysmograph output, to an electrocardiogram (ECG), or to some measure of heart position. A plethysmograph, which measures pulse pressure, is the easiest to use in that a single transducer is simply attached to a finger, toe, or other pulse point. Its output reveals the cyclic changes in pulse pressure which follow the cardiac cycle. The disadvantages of this technique are that the waveform is very smooth, making detection of a discrete point with a consistent relationship to the cardiac cycle difficult, and that there is tremendous variation in the relationship of the pulse pressure waveform to the cardiac cycle between individuals and between different pulse points on a single individual. This makes it difficult to synchronize to a particular cardiac phase.

An ECG, which measures voltage changes due to current flow in the

myocardium, produces a waveform with a very distinct, sharp peak (the “R” wave) which has a consistent, reproducible relationship to the cardiac cycle. The ECG is the most common signal for synchronization of CMRI data acquisition. This is despite the fact that the magnetic field and aortic blood flow [19] alters the signal detected by the three (or more) electrodes which must be placed on the subject to obtain an ECG.

It is also possible to synchronize data acquisition retrospectively to a measure of the cardiac position such as that obtained by a one dimensional MR projection echo interposed between image echoes [20]. The projection echo may be Fourier transformed and analyzed for actual position changes occurring along the projected view or the untransformed data may simply be analyzed for periodic changes (i.e., variations in signal phase) related to the motion of the heart. This technique offers the advantage of obviating the need for accurate detection of a regular ECG waveform, the set-up of which can be very time consuming. This method is limited to cine applications. Each of these techniques is discussed in more detail in the following sections.

4.1.2 Prospective vs. retrospective

MR data may be acquired in a prospectively synchronized or triggered mode which involves acquiring data at a fixed time after a trigger such as the R-wave of the ECG. Then, all data acquired from the same slice at the same fixed delay after the trigger is reconstructed into an image which represents

that part of the cardiac cycle occurring at the given time after the trigger. This approach is based on the assumption that the cardiac cycle is of a constant length so that a fixed delay after the trigger corresponds to a fixed phase of the cardiac cycle. In reality, the cardiac cycle is not of a constant duration, so prospectively triggered images only approximate a specific phase of the cardiac cycle. If cycle length variations are small, then the approximation is very good and vice versa.

MR data may also be acquired in a retrospective manner in which the temporal relationship between acquired data and the synchronization signal is recorded. Interpolation is then used to produce data corresponding to selected phases of each cardiac cycle. Retrospective imaging requires more data memory and is more computationally intensive but offers the advantage of continuous data acquisition. Continuous data acquisition reduces or eliminates certain image artifacts.

The types of synchronization methods most commonly used are ECG prospective, ECG retrospective, and projection echo retrospective.

4.1.3 ECG prospective

In ECG prospective imaging, data acquisition is triggered by the R-wave of the ECG. At a fixed delay (often 0 msec) after the R-wave, data collection is initiated and continues for a preset duration. This duration is determined by the amount of time required to collect one phase encoding line from one

slice (the “slice loop”) times the number of slices. With each R-wave, one of the sequence loop counters (as in phase encoding or multiple acquisitions) is incremented. In order for the system to be prepared to trigger off the next R-wave, it is important that the preset scanning duration be shorter than the shortest R-R interval. This limits the amount of time available to acquire data and also means that there is a period of time in which no RF pulses are applied.

Data may be acquired at many slice positions each corresponding to a different delay time. This is called “multi-slice, multi-phase” imaging. This is the technique used for spin echo scans of the heart. In this case, TR is equal to the R-R interval. If this is not a constant interval, then the amount T1 relaxation will vary from line to line and will result in data errors which may appear as motion artifacts (blurring and/or ghosting[18]).

Alternatively, data may be acquired at one, two, or perhaps three slice positions at several times during the cardiac cycle. This is called “cine” imaging since the technique produces a series of images which can be displayed as a movie loop depicting multiple phases of the cardiac cycle. The number of slice positions imaged is generally limited by the desired temporal resolution between cine frames (determined by TR) and by contrast issues related to saturation of the blood moving between slice positions. In prospective cine imaging, the period at the end of the cardiac cycle during which no RF pulses are applied leads to greater T1 relaxation than occurs during the TR between

acquisition of successive phases. Thus, the first cine images are brighter than subsequent images in the series. This is called the “lightning artifact”[21]. Variations in this interval will also produce motion-like artifacts (blurring and/or ghosting[18]).

4.1.4 ECG retrospective

ECG retrospective imaging is used only for cine imaging. Data is acquired continuously with the phase encoding gradient incremented either at preset intervals which are longer than the longest expected R- R interval [22] or after each R-wave is detected [21]. The method used depends upon the MR system capabilities. The temporal relationship between acquired data and the synchronization signal (R- waves of the ECG) is recorded. Then, interpolation is used to produce raw data corresponding to selected phases of each cardiac cycle. The more frequently the cardiac cycle is sampled, the better the results of the interpolation and the better the final images. This need for good temporal resolution limits the TR and the number of slice positions which can be imaged in one retrospective scan.

The continuous acquisition of data in retrospective imaging eliminates lightning artifacts and the motion-like artifacts associated with variable relaxation times.

4.1.5 Projection echo retrospective

Like ECG retrospective, this technique involves continuous acquisition of data with the phase encoding gradient incremented at preset intervals. Interleaved with the acquisition of image data lines is the collection of a projection echo, acquired either as a second echo after the imaging echo or as an echo from a separate RF pulse [20]. Because this technique does not involve the use of ECG leads, it is sometimes referred to as the “wireless” technique. The projection slice must be located so that it includes a portion of the heart and must be oriented so that there is a significant component of cardiac motion along the readout axis of the projection. These projection echoes are analyzed for periodic changes which correspond to changes in cardiac position. It is not necessary to analyze actual position shifts by Fourier transforming the projection echoes and measuring position changes. Instead, position changes corresponding to the cardiac cycle may be inferred from variations in the phase of the projection echo signal produced by such motion. Note that it can be helpful to filter the projection echo data prior to analysis of cardiac cycle changes in order to remove variations due to respiration. The information regarding cardiac cycle changes is then used in interpolation of the image data to produce images from different phases of the cardiac cycle. The success of this method is very dependent on the quality of the projection echoes and on the analysis of the data. The periodic changes in the projection echoes are not as discrete as the sharp R-wave

detected by the ECG; thus in some cases, ECG retrospective images tend to be better than projection echo retrospective images. On the other hand, in cases when the ECG is poorly detected or when the relationship between the electrical and mechanical activity of the heart varies, the projection echo retrospective technique produces better images than the ECG retrospective method [23, 24].

4.2 Data acquisition schemes

The cardiac cycle and the need to, in effect, freeze cardiac motion impose restrictions on the timing of MR data acquisition. These restrictions however have been turned to an advantage with creative new ways of covering k-space.

4.2.1 Basic 2D and 3D data acquisition

In basic 2D and 3D cardiac MR, the phase encoding gradient(s) is(are) incremented one step with each new cardiac cycle. One line of k-space data is then acquired for a given slice or slab at the same point in each cardiac cycle, effectively freezing cardiac motion. The total scan time is:

$$T_{Total} = \text{Mean } R - R \text{ interval} \times \# k_y \text{ lines} \times \# k_z \text{ lines} \times \# \text{ acquisitions} \quad (4.1)$$

Thus, for a 2D scan with 128 phase encoding lines, 2 acquisitions, and an average R-R interval of 900 msec, the total scan time would be 3.8 minutes.

For a 3D scan with the same parameters and 16 partitions, the total scan time would be 61.4 minutes. While the 3.8 minute 2D scan would be well tolerated by most patients, the 3D scan would not be well tolerated and is an inefficient way to obtain images. Note that respiratory motion has not been dealt with in this data acquisition scheme. Suspension of respiration (breathholding) is not possible for these scan times and respiratory gating would greatly increase the duration of these scans.

4.2.2 Segmented k-space acquisition

In order to shorten total scan time, more than one line of data may be acquired in a single cardiac cycle [25, 26, 27]. Specific sequences utilizing this technique include segmented-FLASH and RAGE. The time savings depends on the number of data lines acquired in each cardiac cycle as a segment of k-space. If eight lines are acquired in each cardiac cycle, then a 2D scan with 128 phase encoding lines, 2 acquisitions, and an average R-R interval of 900 msec would take only $(0.9 \text{ sec/cycle}) \times (128 \text{ lines} / 8 \text{ lines/cycle}) \times (2 \text{ acquisitions})$ or 29 seconds. This is much shorter than the 3.8 minutes required for the basic 2D scan. Indeed, if only one acquisition were used, the scan time would be only 14 seconds which is potentially short enough to permit breathholding during the scan [26]. The disadvantages of this approach are that temporal resolution is reduced by the same factor as the time savings and differences in effective TR introduce variations in signal

intensity from line to line of k-space. This may in turn introduce artifacts into the image. There are approaches which minimize these effects including reordering of the pattern of k-space coverage and incremental flip angles (see Sections 4.2.4 and 4.2.5).

4.2.3 3D-RAGE and 3D-MP-RAGE

The same approach of acquiring multiple lines of k-space in one cardiac cycle may be applied to 3D imaging [25, 27] as for example in 3D-RAGE [27]. In 3D-RAGE (RApid Gradient Echo), during each new cardiac cycle the phase encoding gradient is incremented one line and the slice encoding gradient is stepped through all its values. This means that all k_z lines are acquired within one cardiac cycle. Thus, the total scan time for this type of 3D technique is the same as that for a basic 2D scan with the same number of phase encoding lines and acquisitions. Relative to the 2D scan, the temporal resolution of the 3D-RAGE scan is degraded by a factor equal to the number of slice encoding lines.

The “MP” in 3D-MP-RAGE stands for Magnetization Preparation which includes a variety of schemes to alter the magnetization. Commonly, a 180° inversion pulse is used, followed by a delay (inversion time, TI) and acquisition of the slice encoding lines. An inversion pulse followed by a delay in which longitudinal recovery occurs accentuates T1 contrast. This is because, as with any type of inversion recovery (IR) scan, tissues with different T1's

will recover to different extents during the delay period and thus image data acquisition begins with different tissues having different longitudinal magnetizations. It is important to note that T1 recovery continues throughout acquisition of the slice encoding lines of an 3D-MP-RAGE scan which can further affect image contrast. This technique is discussed in more detail in Section 9.2.1. Other types of magnetization preparation pulses or pulse groups may be used to accentuate other tissue differences.

4.2.4 Reordered k-space coverage

K-space need not necessarily be traversed in a linear, start-to-finish manner. Indeed, linear k-space coverage is not a good approach for 2D segmented MR techniques because the periodic changes in signal intensity at the start of each segment group of lines will lead to motion like artifacts. Changes in M_z during data acquisition may be viewed as a filter applied over k-space, the transform of which is convolved with the actual image. In the case of linear k-space coverage in a segmented scan, the filter imposed over k-space is a periodic function, the transform of which is a series of approximate delta functions with separation determined by the periodicity of the filter. Thus, the main image will be convolved with the delta functions; the result is a badly ghosted image. In 3D-RAGE and 3D-MP-RAGE, the approach of M_z to equilibrium and inversion recovery impose non-symmetric, poorly behaved filters over the slice encoding direction of k-space. These effects may

be minimized by reordering the path of k-space coverage to force the filters into more symmetric forms that have the least effect at low spatial frequency lines or at least into monotonic forms that will not introduce ghosts. The forms and effects of these filters are discussed in more detail in Section 7.5.

4.2.5 Incremental flip angles

Using different flip angles for each of the multiple lines of k-space acquired in one cardiac cycle during a segmented or RAGE scan can also help to minimize line-to-line signal intensity differences[28]. For example, a very low flip angle might be used for the first line acquired since it starts with maximum M_z and will produce good signal. The second line acquired will start with a smaller M_z and so a slightly larger flip angle will be needed to produce a similar amount of signal and so on. The flip angles may be incremented in such a manner as to keep M_{xy} constant for each line acquired or may be incremented in some other fashion if a different magnetization response is desired (e.g. a Gaussian response, a ramp up or down, etc.). The appropriate flip angles for a FLASH scan may be determined from the following recursive relationship:

$$\alpha(n + 1) = \sin^{-1} \left(\frac{M_{xy}(n)}{M_z(n, TR)} \right) \quad (4.2)$$

$$\begin{aligned} M_z(n, TR) &= M_z(n - 1, TR) \cos[\alpha(n)] \exp(-TR/T1) \\ &+ M_o[1 - \exp(-TR/T1)] \end{aligned} \quad (4.3)$$

where $M_{xy}(n)$ is the desired magnetization response for each line n . If the angles are chosen in such a way as to make $M_{xy}(n)$ equal to a constant, filter effects on k-space will be eliminated. This topic is explored in more detail in Section 7.5. From the equation above, it can be observed that the optimal choices for the various flip angles depend on the TR between multiple lines, the T1's of the tissues involved, and the time between acquisition of segments or slice encoding groups. This latter time is sometimes referred to as the wait time, TW, and for cardiac imaging is, of course, tied to the R-R interval.

Chapter 5

Magnetic Resonance Angiography Principles

In MRI, all tissues have the potential to be differentiated based on their values of T_1 , T_2 , and ρ . Blood in the vascular system has the advantage of another distinguishing characteristic and that is flow. It is this property that is exploited to produce magnetic resonance angiograms (MRA's). Flow can, in effect, shorten the T_1 of blood relative to stationary tissue by moving partially magnetized blood out of and fully magnetized blood into the imaging region; this is the basis of time-of-flight MRA. Alternatively, the flow of blood during application of a bipolar gradient magnetic field imparts a velocity dependent phase shift; this is the basis of phase contrast MRA.

In order to extract the maximum amount of clinically useful MRA data, it is essential to post-process the images. There are a variety of such techniques existing although greatly needed improvements are currently being developed.

5.1 Time-of-flight MRA

As mentioned above, flow can, in effect, alter the $T1$ of blood and thus alter the contrast between blood and surrounding stationary tissue. Maximizing the CNR between flowing blood and stationary tissue is essential to the success of TOF MRA. As repeated RF pulses begin to saturate stationary tissue, driving its magnetization to a steady state value far below M_0 , the blood which was exposed to those same pulses is replaced by the in-flow of “fresh” blood. This “fresh” blood was not exposed to RF pulses prior to its entry into the imaging volume and is therefore fully magnetized. Thus, the signal from blood will be much higher than that from neighboring stationary tissue, as though the $T1$ of the blood in the imaging volume was much shorter than that of the stationary tissue. The rate at which fully magnetized blood flows into and through the imaging volume (time of flight) controls the amount of signal enhancement that occurs. For flow in a vessel that is perpendicular to an imaging volume, the number of RF pulses, N , experienced is given by:

$$N = TH/(v \times TR) \quad (5.1)$$

where TH is the thickness of the imaging volume, v is the linear velocity of the flow, and TR is the repetition time between RF pulses. As seen from the equation, the faster the flow, the lower N is and thus the greater the enhancement of blood signal. Also, N is smaller for a thinner region, thus thin

slices or slabs give better enhancement than thicker slabs. Similarly, using a longer TR will result in the blood being exposed to fewer RF pulses and thus experiencing more longitudinal relaxation. However, a longer TR will also allow the stationary tissue to experience more longitudinal relaxation. This leads to higher SNR but lower CNR and it is CNR which is the more important parameter in TOF MRA. Flip angle also plays a role in the CNR of TOF MRA's. If the flip angle is high and/or the TR is short, then the magnetization of the stationary tissue will be driven to a low steady state value. If at the same time the ratio of flow velocity to slab thickness, v/TH , is high, then the blood will produce high signal and the CNR between blood and stationary tissue will be high. However, if instead v/TH is low (i.e., slow flow), then the signal from the slowly flowing blood will be reduced. Thus, for a given range of flow velocities to be imaged, compromises between flip angle, TR , and slab thickness must be made.

Time-of-flight MRA's may be acquired in a 2D mode with thin slices for maximal flow enhancement even with low velocity flow[29, 26]. To produce an MRA, a great many individual slices are acquired, often overlapping to counter poor slice profile effects. The broadened slice profile actually provides some natural overlap of slices and also can produce a bimodal magnetization response causing the outer edges to be weighted more heavily than the center portion of the slice. If motion occurs between acquisition of different slices, then registration of the vessels may be a problem. That is to say, in post-

processing of the volume of 2D images, normal vessels may actually appear to be stenotic or discontinuous. The 2D approach is often used for abdominal MRA.

MRA's acquired in a 3D mode offer the advantages of better slice profiles, better through-plane resolution, and higher overall SNR. The entire slab of a 3D has a broadened profile as occurs in 2D but each 3D partition, other than the outermost ones, has an essentially rectangular profile. A disadvantage of MRA's acquired in a 3D mode is that they suffer more saturation effects on the blood. Indeed, blood vessels appear bright near their entry to a 3D volume and may disappear before reaching the far side of the volume. Flip angle may be reduced and/or TR increased to try to reduce saturation. However, this will increase the background signal from stationary tissue thus reduce CNR. A different approach to reducing saturation effects is a hybrid between 2D and 3D involving the use of multiple 3D volumes with thin slabs[30].

Selective saturation pulses may also be used in MRA to suppress the signal from blood originating in certain regions. For example, a saturation pulse may be applied during an MRA scan of the circle of Willis in order to suppress signal from a particular artery and its distribution, leaving only signal from arteries not passing through the saturation region[31]. This can be very helpful in determining the source and direction of flow. Another application of saturation pulses in MRA is to apply a 2D selective saturation

pulse to the aortic root to suppress signal from blood that eventually flows back into the coronary arteries[32]. A second scan without the saturation pulse is acquired and the two data sets are subtracted to produce an image of the coronary arteries and the aortic root.

Other types of saturation pulses that may be used to alter the CNR between blood and surrounding tissues include non-selective inversion (180° or IR) pulses which were used in this dissertation research, fat saturation pulses, and very recently, magnetization transfer saturation (MTS) pulses[33]. In the inversion case, the IR pulse is followed by some inversion time, TI, during which longitudinal relaxation occurs at rates determined by the T_1 's of different tissues. Differential T_1 recovery between blood and surrounding tissues then leads to different starting conditions (M_z) when the image data is acquired. If the TI is chosen carefully, then the image data may be acquired when M_z for one of the tissues of interest is near 0; this tissue will appear dark in the final image. The technique of fat saturation involves a narrow band RF pulse which is broadcast to saturate protons in fat, ideally without affecting protons in water. This is possible because fat and water resonate at frequencies 220 Hz apart. MTS pulses may be used to suppress signal from the water protons in myocardium and thus increase blood/myocardial contrast.

Contrast agents, injected into the bloodstream, are sometimes used in TOF MRA to dramatically shorten the T_1 of blood through paramagnetic ef-

fects (see Section 7.6). Thus, blood signal is enhanced to a greater extent than that for neighboring tissues[34]. At this time, the only MR contrast agent approved by the United States Food and Drug Administration for human use is gadopentatate dimeglumine (Gd- DTPA, brand name MagnavistTM by Berlex Laboratories, Wayne, NJ). Gd-DTPA is not optimal as an MRA contrast agent because it is not an intravascular agent (i.e., not confined to the vascular spaces). However, Gd-DTPA may be used for MRA's since it stays more concentrated in blood than in other tissues for the first couple minutes after injection. So, if the entire scan can be collected quickly or if the majority of the contrast producing data (i.e., the central portions of k-space) can be collected quickly, then Gd-DTPA will increase blood to background CNR. Half of the Gd-DTPA circulating through the capillary bed on its first pass diffuses from the blood into the extravascular compartment [35]. This effect will limit the increase of or even reduce the blood to background CNR. Simultaneously, extraction of Gd-DTPA by the kidneys is occurring and together these phenomena lead to a 70% decline in plasma concentration of Gd-DTPA within five minutes after injection [35].

5.2 Phase Contrast MRA

Spins rotating in the transverse plane (M_{xy}) will dephase if exposed to different magnetic fields. Dephasing within a voxel leads to signal loss as the spin magnetic moment vectors begin to cancel each other. Magnetic field

variations may be unintentional as in the case of susceptibility effects or intentional as in the case of applied gradient magnetic fields. The intentional and predictable effects of an applied gradient magnetic field may be used to distinguish flowing blood from surrounding stationary tissue if the gradient is applied in such a way as to produce dephasing only in the moving spins. A bipolar gradient waveform with two lobes of equal but opposite integrals of amplitude over time will produce such an effect, as discussed in Section 3.8. For stationary spins ($x'(t)$ and higher order motion terms equal to zero), $\phi(\tau) = 0$ while for moving spins, $\phi(\tau) = \gamma G(1/2V\tau^2 + 1/3A\tau^3 + \dots)$. Note that this is only valid for motion along the direction of the applied gradient. The strength of the gradient, G , may be adjusted so that the scan will be sensitive to a particular maximum velocity.

In the original 3D phase contrast MRA technique, six scans were run[36] in order to measure motion in three dimensions. More recently, 3D PC MRA techniques requiring only four scans have been developed. The four scans may be made up of three scans, each with a bipolar gradient applied in a different direction with velocity rephasing gradients along the other directions, plus one scan that is completely velocity compensated in all directions. Another option is to run four scans with each one including a bipolar gradient waveform applied along one of the four axes of a tetrahedron[37, 38]. After acquiring the four scans with the chosen technique, the results are arithmetically combined in the appropriate manner to produce images with blood

appearing bright and stationary tissue signals suppressed. Phase contrast data may be used (a) to form magnitude images which may be post-processed with an MIP algorithm, (b) to actually obtain quantitative velocity measurements, and (c) to produce a speed image by combining all three resultant directionally sensitive images. The PC MRA technique is particularly useful for slow flow since contrast is not as dependent upon the inflow of fresh spins as in TOF MRA. As with any technique requiring the arithmetic combination of images, good registration of the data sets is crucial. Also, the MIP's are improved if the background stationary tissue signal is suppressed (better CNR).

5.3 Coronary artery MRA

The MRA principles described in the preceding sections may be applied to imaging of the coronary arteries. MRA of the coronary arteries is certainly far more complicated than that of any other vascular system in the body due to the complications of cardiac and respiratory motion and of complex blood flow into and out of the imaging volume. The motion of both the blood in the coronary arteries and the surrounding cardiac tissue makes phase contrast techniques of limited value in coronary MRA. Most active research in coronary artery imaging involves TOF techniques and is described in Section 6.6.

5.4 Post processing techniques

Most MRA techniques produce a stack of images representing thin slices or partitions in which small, very bright (or very dark) segments of vessels are seen, surrounded by tissues of less extreme (bright or dark) signal. In order to extract images depicting the flow of blood in vascular structures, some type of post-processing is necessary. The simplest approach is multi-planar reconstruction, MPR, which reformats the 3D data into an image corresponding to a user-defined cut plane. This can reveal in one image the course of a vessel which originally cut through many of the acquired images. While quick and simple, MPR is of limited usefulness as few vessels stay in one plane for any great distance. Curved cut planes, which can depict a greater extent of a vessel, are available with some MPR software. However, this is still not very useful because the relationship of that vessel to its branches or to other vessels cannot be seen.

It is more clinically useful to reconstruct a vascular tree which can be rotated in three space. This type of display exhibits the full extent of all the vessels seen in the original images. To do this, a projection of the 3D data onto a 2D image plane must be created for each viewing angle. The 2D images are created by selecting the maximum pixel intensity along a ray through the 3D volume, parallel to the viewing angle. hence the name “maximum intensity projection” or MIP. The MIP technique works well for those

data sets with high CNR between the vessels of interest and the stationary background. In TOF MRA, CNR is optimized through appropriate choices of TR , flip angle, and the thickness and number of slabs. If the views of the vessel(s) of interest are obstructed by signal from other regions (e.g., blood in the coronaries versus blood in the cardiac chambers), then more sophisticated post-processing techniques are necessary.

One of these more sophisticated post-processing techniques is vessel tracking or connectivity[39, 40, 41]. The basic concept of this technique is that the user places a seed on some portion of the vessel of interest. The algorithm then selects all voxels above a certain signal threshold which are connected to that seed and continues to select connected voxels until the boundaries of the volume are reached. The subset of selected voxels is then processed with an MIP algorithm to create images for a variety of viewing angles.

Note that some MRA techniques such as the projective technique of Wang, Hu, Macovski, and Nishimura[32] need only simple subtraction to produce an image of a vascular tree. This technique takes all the signal from a thick slab and projects it onto a single 2D image (which is then comprised of thick voxels). If the velocity distribution in such thick voxels is great or if significant higher order motion is present, then vessel signal will be lost due to dephasing. In disease states, such higher order motion is often present. Another disadvantage of this particular technique is that, since it is projective, the tree may be viewed only in the orientation in which it was acquired.

Chapter 6

Can MRI Really be Used to Image the Coronaries?

Is it realistic to expect that MRI can be used on a routine basis to generate diagnostic images of native, normal and diseased coronary arteries and also bypass grafts? This is an important question to consider when investing the expensive resources of MR equipment and personnel in a research topic fraught with many difficult challenges. Indeed, the claim that MRI of the coronaries “may in fact prove to be a technical impossibility” has been made [42]. Despite this pessimism, a number of successes in MRI of the coronaries have been achieved and current research efforts by a number of groups indicate the existence of an optimistic attitude about the ability of MRI to routinely produce diagnostic images.

6.1 Resolution requirements

6.1.1 Spatial resolution

As noted earlier, the coronary vessels are small at their origins, 4-5 mm in diameter, and rapidly get much smaller as they become more distal and branch into smaller vessels. A non-invasive, MR imaging technique capable of reliably imaging the larger, proximal coronaries is of value as a screening technique since disease in the proximal portions of the coronaries is of greater concern than more distal disease. Also, it is useful to have a non-invasive technique to evaluate the patency of coronary artery bypass grafts (CABG's) which are on the order of 5 mm in diameter. Still, in order to obtain even more diagnostically useful information and to fully capitalize on the use of an expensive and complex technology like MRI, it is essential to obtain the best possible resolution.

In MRI, as with many imaging methods, there is a direct tradeoff between spatial resolution and SNR. So, while in theory, resolution could be pushed to about 200 microns, the SNR would be so reduced that a more practical limit on desired resolution is needed. One criterion often used is that a minimum of two pixels should be used to define a structure. So, if a 50% stenosis of a 2 mm diameter artery is to be visualized, then spatial resolution must be at least 0.5 mm per pixel. This translates to a 128 mm field-of-view for an image with 256 pixels to a side; typical FOV's in body MRI are

256 to 350 mm. Resolution of 0.5 mm is difficult to achieve in body coil MR imaging as gradient strength restrictions and aliasing together limit the FOV and number of pixels possible. Also, SNR is poor in the body coil (relative to smaller surface coils) and thus limits attainable resolution. For the time being, 1 mm spatial resolution is a reasonable and non-trivial goal, but clearly resolution must be improved if MR is to be a viable technique for diagnosing coronary vessel disease.

A point to consider is that it is possible, under certain conditions, to infer the actual size of a vessel much smaller than the pixel in which it is contained by examining the signal amplitude. The principle condition is that there must be no signal other than that from the vessels. Let a vessel with a width equal to the pixel size, Δx , cut through the slice and generate a signal of magnitude S in the pixel. Then, a pixel with signal of magnitude $S/2$ elsewhere in the image must indicate the presence of a vessel of width $\Delta x/2$. While the location of the $\Delta x/2$ width vessel within the Δx wide pixel cannot be deduced from the signal amplitude, this shows that it may be possible to infer a resolution much better than that defined by pixel size. Unfortunately, this concept generally cannot be employed in MR coronary artery imaging since there are many other signal sources present.

The 3D approach utilized in this research and described in Section 9.2 comes close to meeting the 1 mm spatial resolution goal. The in-plane resolution, following interpolation in the phase encoding direction, is 1 to 1.17 mm.

Similar in-plane resolution has been achieved with 2D approaches on whole body MR scanners[26, 29, 43]. It is in the through-plane direction that the 3D and 2D approaches differ and where resolution still needs to be improved. In 3D, an RF pulse excites a thick slab which is encoded into different partition images. These individual partitions have rectangular profiles which means that all tissue in the partition contributes signal essentially equally and that the partition really is the thickness specified. It should be noted, however, that the finite number of partitions leads to Gibb's ringing across the slice encoding direction which causes some signal to be shifted between partitions. In the technique used in this research, the minimum partition thickness was 2 mm. With stronger gradients or with the tradeoff of a slightly longer TE, the partition thickness can easily be reduced to the desired 1 mm. In a 2D approach, the slice profile is determined by the RF excitation profile. It is not possible to produce a rectangular slice profile with an RF pulse of finite duration and indeed the short RF pulse durations required for short TE applications lead to broadened, rather Gaussian profiles. So, with a non-rectangular profile, tissues across the slice contribute unequally to the signal and the effective thickness is greater than that specified. With stronger gradients, the same RF pulse can be used to excite a thinner 2D slice though the problems of non-rectangular profile and slice broadening will still exist. The thinnest slices reported for 2D coronary artery imaging techniques have been 2 mm thick[26, 29].

6.1.2 Temporal resolution

The extensive motion of the heart during its contraction makes it necessary to obtain images that “freeze” the motion enough to allow visualization of the coronary arteries. If data acquisition is synchronized to a particular phase of the cardiac cycle as discussed in Section 4.1, then the motion will essentially be stopped. However, data acquisition is not instantaneous, especially for imaging techniques involving acquisition of multiple data lines in each cardiac cycle. Then, the concern is over how much motion occurs during each data acquisition period and thus how much blurring is introduced. In other words, the concern is over what temporal resolution is necessary to visualize the coronary arteries.

Temporal resolution is improved by reducing the data acquisition period through shortening the TR and limiting the number of lines acquired in each cardiac cycle. Also, since there is less motion during diastole, the problem is minimized by acquiring data during that cardiac phase. Though data may be acquired over a rather long period (178 msec) in the 3D scans used in this work, the temporal resolution appears to be adequate to “freeze” the coronaries in one position. The reason for the better than expected temporal resolution may be because the bulk of the image information is actually acquired in a limited portion of the data acquisition period[44]. Thus, the temporal resolution of this scan seems to be adequate for visualization of the coronaries.

6.2 Contrast requirements

All the spatial and temporal resolution in the world is of no value if there is not also adequate contrast between adjoining structures. In the case of coronary artery imaging, this means that the MR technique must produce different intensity signals primarily for blood in the coronaries and fat surrounding the vessels, but also for myocardium next to the more distal vessels.

Though there is a continual drive for better signal-to-noise and contrast-to-noise ratios (SNR and CNR) in all MRI studies, there exists a point at which increases in SNR and CNR will not improve the diagnostic capability of the imaging system. Coronary artery MRI is far from that point today, but questions of concern are (a) how much diagnostic capability do MRI techniques currently offer; and (b) what must be done to improve that capability? The second question is addressed by many of the techniques utilized in this dissertation research and recommended for future work.

How much diagnostic capability is offered by MRI today and indeed what SNR and CNR is adequate for diagnosis are issues addressed by an entire field of research having its roots in signal detection theory[45]. In the context of this field of research, the imaging system includes the data acquisition and post processing system, the image display system, and the psychophysical properties of the human observer. There are models describing the threshold contrast required for detection of an object by such a composite imaging

system[46], though a number of assumptions are necessarily included. These models have been expanded to include the presence of “structured” noise which can include normal anatomic background[47]. An important tool in this field of research is “ROC” (relative operating characteristic) methodology which separates the inherent diagnostic capability of the imaging system from the tendency of the human observer to “over-read” or “under-read”¹ [45].

At this stage, MRI techniques for visualizing the coronaries seem to be in the rapid growth phase of an exponential improvement curve. As such, it is rather premature to employ the tools of ROC methodology and related analysis methods, though in the future such concepts may prove to be very useful.

6.3 Motion of the heart during the cardiac cycle

The motion of the heart throughout the cardiac cycle is complex and extensive [10, page 69]. During systole, the free wall of the right ventricle shortens and the tricuspid valve descends towards the apex. The left ventricle does not shorten very much along its base-to- apex axis but instead accomplishes ejection primarily by radial contraction. Since the coronary vessels lie in the AV groove and along the surface of the myocardium, these movements

¹To “over-read” is to call a lesion when one may actually not be present and to “under-read” is to not call a lesion when one may actually be present.

during contraction and relaxation translate to movement of the coronaries. The motion of the coronaries throughout the cardiac cycle is greater than their diameters. This necessitates synchronization of data acquisition to the cardiac cycle as discussed above in Section 6.1.2.

6.4 Beat-to-Beat Variations in Heart Position

The contraction and relaxation of the heart is not exactly the same from beat to beat. It varies with different conditions of preload (amount of blood filling the heart), afterload (downstream vascular resistance), and contractility of the myocardium itself. Contractility may be altered by nervous system activity and by concentration of blood gases, ions, and metabolites. Presumably, variations in most of these conditions are minimal in the subject who is resting comfortably and has acclimatized herself/himself to the environment of the MR scanner. However, even relaxed breathing may affect cardiac function [10, page 42].

In Section 8.4, breathhold studies of heart motion are described. These experiments were conducted to assess the beat-to-beat variability of heart position in the absence of respiration. While the spatial resolution of those tests was limited, it seems that the position of the heart varies little (perhaps a couple of millimeters) from beat-to-beat. While this small a variation in position is relatively insignificant when imaging the larger structures of the

heart such as the septal wall, it is significant when attempting to image the coronaries. Thus, beat-to-beat variation in cardiac position, by introducing blurring in the images, decreases the ability of MR to image the coronary arteries.

If the variations in position due to beat-to-beat differences are tightly distributed about some mean position, then the averaging of MR data from many heartbeats as is commonly done will lead to a reduction in the extent of blurring. Alternatively, if all the data can be acquired in one heartbeat as in some echo planar approaches, then beat-to-beat variations are not a concern.

6.5 Respiratory motion of the heart

Beat-to-beat variations in cardiac position are quite small compared to position changes introduced by respiration. Indeed, respiratory motion of the heart may be one of the most significant challenges to MRI of the coronaries. During respiration, the heart moves many millimeters (on the order of 5-15 mm) in a complex manner. It is not a simple translation of the heart which complicates attempts at post-processing corrections for respiratory motion. This motion introduces blurring, and because it is periodic, introduces ghosting. Motion of the heart associated with respiration and its effects on MR images are discussed in detail in Chapter 8.

6.6 Review of coronary artery MRI techniques

This chapter began with a question about the ability of MRI to be used on a routine basis to generate diagnostic images of native, normal and diseased coronary arteries and also bypass grafts. It was noted that a number of successes in MRI of the coronaries have been achieved.

Before MRI of native coronary arteries was begun in earnest, it was reported that spin echo techniques could be used to determine patency of coronary artery bypass grafts [48, 49, 50, 51, 52, 53]. This early work utilized nonvelocity-compensated, ECG triggered spin echo sequences in which flow through a graft resulted in signal voids that contrasted with the brighter surrounding fat and myocardium. The extracardial locations and large diameters of saphenous vein and internal mammary artery grafts facilitated identification and visualization of flow through such vessels. These studies reported accuracies of 90-92% for determination of graft patency and 72-85% for determination of graft occlusion. Subsequent studies by White et al. [54] and Aurigemma et al. [55] utilized 2D cine gradient echo techniques in which flow-related enhancement contributed to flow in patent grafts appearing brighter than surrounding tissues. Predictive accuracies for patent grafts of 89 and 91%, respectively, were reported for these studies.

The success of MR determination of graft patency with standard 2D tech-

niques has been accompanied by moderate progress in the more challenging test of using 2D spin echo techniques to image normal and arteriosclerotic coronary arteries [56, 43]. The ability of spin echo MRI to image normal and stenotic coronary arteries in cross-section was assessed by Cassidy et al. [57]. The technique generally revealed portions of the proximal normal coronaries but had at best 56% sensitivity and 76% specificity in diagnosing significant stenoses. Case reports of more glaring pathologies, including aneurysms, either congenital or secondary to illnesses such as Kawasaki disease, and coronary arteriovenous fistulas have also been published [58, 59].

Much effort has been focussed in the application of gradient echo techniques, both 2D and 3D, to imaging of normal and diseased coronary arteries. Dumoulin et al. [60] utilized a 2D velocity-compensated gradient echo technique in a single-slice cine mode with a flip angle of 60° to acquire multiple 2.5-3 mm thick transverse slices which were then processed with a maximum intensity projection (MIP) algorithm. The resulting images could be viewed in cine mode and revealed portions of the coronary vessels. Cho et al. [29] utilized a similar imaging technique with a 90° flip angle to produce a stack of images. The 90° flip angle provides maximal contrast between stationary tissue and blood flowing quickly through a thin slice. An MIP angiogram was reconstructed from these images after unwanted signal in the chambers was removed via a boundary detection technique based on thresholding and segmentation. More recent 2D gradient echo work by Edelman, Burstein,

and Manning [26] incorporated a number of advances, perhaps the most important being segmented k-space acquisition which reduced scan time for a single acquisition, single slice 2D scan to a time short enough to permit breathholding. This removed the significant problem of respiratory motion and has produced very high quality images of the coronary arteries. Fat suppression, RF spoiling, and variable flip angles were also incorporated.

The MR technique producing images the most similar to cardiac catheterization results (i.e., a projection image depicting an angiographic 'tree' of the coronaries with little other signal present) has been that presented by Wang, Hu, Macovski, and Nishimura [32]. Their approach involves the use of a 2D or 3D selective inversion pulse to tag blood in the aortic root before it enters the coronary arteries. The imaging scan, a hybrid spiral echo planar technique is initiated some time after the inversion pulse to permit nulling of the blood signal as it moves through the coronaries. This type of IR scan is interleaved with the same scan executed without the IR pulse; the results of the two scans are subtracted to remove background signal. The final images from these techniques have been impressive though due to their projective nature cannot be reformatted to permit viewing of the vascular structures from another orientation.

A 2D gradient echo technique was also used by Burstein[61] to image the (tiny!) coronary arteries in isolated isovolumic and working perfused rat hearts and *in vivo* rats in a small bore imager. A velocity compensated, TE

2 msec gradient echo sequence with an in-plane saturation pulse to suppress signal from stationary spins was used. The very short TE, combined with velocity compensation, greatly limited the amount of motion related signal losses. In the same study, a different application of saturation pulses was also tested with a STEAM sequence in which the first two pulses were applied selectively to the aortic root and the third was applied over the myocardium in an isovolumic perfused rat heart preparation. This work demonstrated the necessity of careful timing and positioning of RF pulses designed to excite the blood that flows into the coronaries.

Work continues in these and other approaches to MR imaging of the coronary arteries and as yet, there is no clear consensus about the ideal technique to pursue.

6.7 Summary

The review of techniques given in the preceding section demonstrates that some success has already been attained in MRI of the coronary arteries. Continued and more consistent success will require at least one millimeter spatial resolution. The 3D technique developed in this research does or very nearly does meet this spatial resolution requirement in-plane though the 3D partitions need to be made thinner to meet this requirement in the through plane direction. The 3D technique, acquiring data over a 178 msec period of the cardiac cycle, has adequate temporal resolution, given that motion of

the heart is minimal during the diastolic data acquisition and that the time resolution of a scan is shorter than the data acquisition period. Successful coronary artery MRI requires good contrast between blood and fat as produced by the inversion pulse used in this work or by a variety of other tools which may be employed.

Motion remains a problem in coronary artery MRI. While scans are synchronized to diastole to effectively eliminate cardiac motion, beat-to-beat variations in cardiac contractions do exist and introduce position differences of a couple millimeters. These position changes introduce blurring yet are small enough that averaging should minimize the blurring effects adequately. In contrast, respiratory motion is very extensive and must be dealt with if coronary artery MRI is to be successful.

Chapter 7

Contrast Issues

In any MR image, a good signal-to-noise ratio (SNR) is of little value if there is not also a good contrast-to-noise ratio (CNR). It is CNR that enables one tissue to be distinguished from another and thus for structures such as coronary arteries to be defined.

SNR in this discussion is the mean signal for a given tissue divided by the square root of the variance of the signal. CNR in this discussion is defined as:

$$CNR_{ab} = \frac{S_a - S_b}{\sqrt{n_a^2 + n_b^2}} \quad (7.1)$$

where S_a , S_b are the signal intensities from tissues a and b, respectively and n_a , n_b are the noise values (square roots of the variances) of the signals in tissues a and b, respectively. Note that this value is sometimes referred to as the signal difference to noise ratio. Another useful value is relative contrast which is given by:

$$\text{Relative Contrast} = \frac{SNR_1 - SNR_2}{SNR_1} \quad (7.2)$$

Notice that, if noise is constant, the equation for relative contrast reduces to:

$$\text{Relative Contrast} = \frac{S_1 - S_2}{S_1} \quad (7.3)$$

In cardiac MRI, the tissues to be distinguished are primarily blood, fat, and myocardium. Pericardial and epicardial membranes and valves are also important tissues to distinguish in general cardiac MRI. For coronary artery imaging, it is most important to have good CNR between blood flowing in the coronaries and the fat that surrounds these vessels.

CNR is affected by the imaging parameters chosen (TR, TE, etc.), the tissue properties, the type of imaging sequence, the manner of covering k-space, contrast agents, and saturation pulses. The purpose of investigating variations in MRI approaches is to increase signal to boost CNR and to obtain the highest relative contrast. These types of variations are assumed not to affect noise. Factors that affect SNR independent of tissue type, such as voxel size, number of acquisitions, etc. do affect CNR but are not discussed in detail here since they do not affect relative contrast. Regarding voxel size, however, it is important to note that partial volume effects (the averaging of different tissue signals within one voxel) can reduce CNR. So, voxels should be as small as the smallest distinct tissue features that need to be identified in the images. Since CNR is inversely proportional to voxel size, using voxel

Tissue	T1 (msec)	T2 (msec)	T2* (msec)	ρ
blood	1200	250	100	0.8
fat	300	70	50	0.9
myocardium	800	50	35	0.8

Table 7.1: Tissue properties

sizes much smaller than the smallest features to be identified is generally not a good idea.

7.1 Tissue properties

The tissues of interest in cardiac MRI are of course blood, myocardium, and fat. As with any type of tissue, contrast is very dependent upon the tissue properties of $T1$, $T2$, $T2^*$, and ρ which were discussed in Section 3.3. These values are relatively easy to measure *in vivo* for stationary tissue while quite difficult to measure for moving tissue. The motion problem can be circumvented by performing *in vitro* measurements; however, rapid and significant physiologic changes which affect relaxivity occur when tissues such as blood and myocardium are removed from the body. Also, even in *in vivo* experiments, the state of the heme moiety in hemoglobin molecules in the blood dramatically affects relaxation times. These difficulties may account for the range of values published for blood, myocardium, and fat[62]. The values chosen for simulations in this dissertation are presented in Table 7.1.

7.2 Repetition times and flip angles

As discussed in Section 3.7.1, a long repetition time, TR , allows the longitudinal magnetization to recover more of its initial magnitude and thus produces more signal for the next excitation. However, in the interests of total imaging time and $T1$ tissue contrast, a long TR is generally not desirable. A shorter TR will emphasize tissue differences in $T1$ but will also give less signal. The definitions of “short” and “long” TR are quite variable in gradient echo MRI and depend on the $T1$ of the tissue(s) involved and on the flip angle, α , used. Note that, in cardiac MRI, the shortest possible TR for a given sequence is usually used due to the need to “freeze” cardiac motion. So, the remaining variable is the flip angle.

To optimize signal for a single tissue over the course of a FLASH gradient echo scan in which only longitudinal magnetization reaches a steady state, the TR and flip angle, α , that should be used are tied to each other via the Ernst angle formula:

$$\alpha_{Ernst} = \arccos(\exp(-TR/T1)) \quad (7.4)$$

So, if $TR = 25$ msec and $T1 = 1200$ msec as in blood, then $\alpha_{Ernst} = 11.7^\circ$.

To maximize contrast between two tissues with $T1_a$ and $T1_b$, the flip angle is chosen by setting:

$$\frac{d}{d\alpha} \left(\frac{(1 - E1_a) \sin \alpha}{(1 - E1_a \cos \alpha)} - \frac{(1 - E1_b) \sin \alpha}{(1 - E1_b \cos \alpha)} \right) = 0 \quad (7.5)$$

and solving for α . In this equation, $E1_a = \exp(-TR/T1_a)$ and $E1_b = \exp(-TR/T1_b)$. This equation assumes that a steady state exists and that $TE = 0$, $\rho = 1$, and $M_0 = 1$.

7.3 Echo times

A non-zero echo time (TE) permits development of $T2^*$ contrast in a gradient echo MR scan. As transverse magnetization decays in an exponential manner according to the time constant $T2^*$, unique for each tissue, a timepoint will be reached at which maximal signal difference between two tissues is achieved. TE may be set to be at that maximal signal difference timepoint in order to maximize CNR. For a FLASH or spin echo scan, signal is proportional to $\exp(-TE/T2^*)$. So, assuming all else is constant, the signal difference between two tissues can be maximized for the TE given below:

$$\frac{d}{dTE} \left(\exp\left(\frac{-TE}{T2_1^*}\right) - \exp\left(\frac{-TE}{T2_2^*}\right) \right) = 0 \quad (7.6)$$

which reduces to:

$$TE = \frac{\ln \frac{T2_1^*}{T2_2^*}}{\frac{1}{T2_1^*} - \frac{1}{T2_2^*}} \quad (7.7)$$

TE's beyond this value lead to lower CNR (and SNR) due to further decay of the signals. To optimize $T2^*$ weighting in a FLASH scan or $T2$ weighting in a spin echo scan, it is best to use the TE given by equation 7.7. To optimize overall signal amplitude, it is best to use the shortest TE possible in order to minimize $T2^*$ dephasing. Thus, $T2^*$ weighting is sacrificed in favor of spin density and $T1$ weighting. Another reason to use a short TE, or more accurately a short field echo FE, is that motion dependent signal dephasing, related to t^2 for constant velocity spins, gets much worse as the echo times increase.

TE may also be chosen to alter contrast between fat and water signals. Protons in fat resonate at a frequency about 3.35 parts per million lower than that for protons in water. Since blood is mostly water and since the coronary vessels are generally surrounded by fat, selecting a TE which capitalizes on this resonant frequency difference can be very helpful. The frequency difference will cause fat and water protons to accumulate a phase difference with respect to each other. For fat and water protons in the same voxel, a phase difference will cause their signals to add destructively and thus reduce signal from that voxel. This can create a dark line at the interface between coronary vessels and surrounding fat if the vessel/fat boundary lies within a pixel (versus between two pixels). This dark line can aid in delineating the vessels[25]. It should be noted however that this same cancellation effect can also alter (reduce) the apparent size of the vessel lumen. The maximum

amount of signal cancellation occurs when the phase difference is equal to an odd multiple of π . This occurs at TE's referred to as "out of phase" or "opposed phase" TE's. This TE is determined by:

$$TE = \frac{n\pi}{\gamma B_0 3.35 \times 10^{-6}} \quad (7.8)$$

where n is an odd integer, $\gamma = 2.67 \times 10^8$ rad*Hz/T, and B_0 is the magnetic field strength in Tesla. If n is even, fat and water signals will be in phase with each other and thus no cancellation will occur. For $B_0 = 1.5$ T, fat and water are opposed for TE's of 2.34 msec, 7.02 msec, etc., and are in phase for TE's of 4.68 msec, 9.37 msec, etc. Fortunately, the minimum opposed phase and in phase TE's are quite short. This allows manipulation of opposed/in phase effects while maintaining good signal amplitude (i.e., little $T2^*$ decay).

7.4 Basic contrast for untriggered scans

As a matter of reference and illustration, it is useful to consider basic contrast curves for myocardium, fat, stationary and moving blood. These graphs are helpful in understanding the relationships between the intrinsic parameters of $T1$, $T2$, $T2^*$, ρ , and velocity and the extrinsic parameters of TR, TE, and flip angle. Short of adding contrast agents, the intrinsic parameters cannot be changed. So, it is the extrinsic parameters which must be altered to affect image contrast.

Recalling the discussion in Section 3.7.1. $T1$ contrast can be accentuated

by using a short TR or reduced by extending the TR. In spin echo cardiac MRI scans, the TR is limited to an integer multiple of the R-R interval. If the R-R interval is on the order of 800 - 1000 msec, then it is difficult to get a short TR and thus T_1 weighted spin echo cardiac scan since $TR \approx T_1$ ($T_{1_{blood}} \approx 1200$ msec, $T_{1_{muscle}} \approx 800$ msec). What are frequently referred to as T_1 weighted spin echo cardiac scans are more appropriately called mixed T_1 /spin density weighted images, again since the TR in these scans is set to be one R-R interval or $\sim T_1$. T_2 weighted spin echo cardiac scans, useful in examining myocardial tumors, cysts, and infarcts, can be obtained by setting the TR equal to two or three R-R intervals and extending TE to 80-90 msec. The restriction that TR be an integer multiple of the R-R interval is again somewhat of a problem. First of all, since R-R intervals are not constant, the variability in TR, a detriment to image quality[18], is doubled or tripled when two or three R-R intervals are selected for the TR. Also, two or three times the R-R interval does not necessarily give a desired TR; two intervals might be on the order of 1600 - 2000 msec, perhaps a bit too short to eliminate T_1 effects for blood (though not for myocardium), while three intervals might be on the order of 2400 - 3000 msec, causing the total scan time to be quite long.

In a gradient echo cardiac MRI scan, there is more flexibility in TR although the shortest possible TR is usually used. While each line of k-space used for an image is generally separated by one R-R interval as in

T_1 weighted spin echo scans, the TR which affects contrast may be much shorter. This is the scenario in cine MRI in which the same slice is excited repeatedly throughout the cardiac cycle with a TR on the order of 25 - 75 msec. The repeated excitations throughout the cardiac cycle are used to reconstruct separate images for each cardiac phase. Thus, the line-to-line difference in time for one image is still equal to the R-R interval while the TR affecting contrast is much shorter.

TE's used in cardiac MRI can vary widely, depending on the requirements of the scan. This parameter was discussed in detail in Section 7.3.

In an untriggered scan, the magnetization of each type of tissue eventually reaches a steady state or constant value. This steady state value will depend on: the type of scan (SE, FLASH, FISP, etc); the parameters, especially TR , TE and flip angle; and the properties of the tissues, T_1 , T_2 , T_2^* , ρ , and flow. Flow introduces additional factors in the consideration of contrast. The "steady state" signal from blood flowing through a slice will depend not only on the factors just listed but also on the velocity of the flow and the thickness of the excitation volume. These two factors, along with the TR , determine the total number of RF excitations, n_{max} , the blood is exposed to as it travels through the slice. The relationship between these parameters is given by $n_{max} = \frac{TH}{v \times TR}$. If the blood is stationary, then n at any given time during the experiment will be equal to the total number of pulses applied at that time and the blood will reach a steady state in the same manner as

any other stationary tissue. If, on the other hand, the blood in a vessel is moving through the slice so that the greatest number of pulses it is exposed to is n_{max} , then after n_{max} excitations signal from that vessel will reach a constant value. Blood that moves more slowly will be exposed to more pulses and will reach a lower steady state value after a greater number of RF pulses. How changes in n_{max} affect signal in a FLASH scan is illustrated in Figure 7.1. Obviously, blood with the lowest n_{max} will produce the highest signal value and will reach that value the most quickly. If the velocity of the blood is held constant and instead the thickness of the excitation region or the TR is changed, then n and thus contrast between flowing blood and stationary tissues will change. Changes in TR will affect contrast not only by changing n_{max} but also by changing the amount of $T1$ relaxation occurring between excitations. Changes in the flip angle will also affect contrast between flowing blood and stationary tissues. A high flip angle will drive stationary tissues down to a low steady state value after a number of excitations while blood flowing quickly through the slice will be exposed to very few of these high flip angle excitations and thus will have more magnetization available to generate a large signal.

The relationships between n_{max} , v , TH , and TR are demonstrated in Table 7.2. The first column represents the number of pulses, n , to which the flowing blood is exposed. Then, the next column gives the velocity at which blood would have to be flowing through a 32 mm thick slice in a scan

Figure 7.1: Effect of n_{max} on steady state blood signal from a FLASH experiment with no preparation cycles. This curve is relevant to an infinite combination of velocities, thicknesses, and repetition times. While some of the shaping and absolute values would change, the overall relationships would be the same. Blood exposed to fewer RF pulses, either due to faster flow, thinner slice, or longer TR , will more quickly reach a higher constant signal value than blood exposed to more pulses.

n_{max}	v (cm/sec) (TH = 32 mm) (TR = 11 msec)	TH (mm) ($v = 29$ cm/sec) (TR = 11 msec)	TR (msec) ($v = 29$ cm/sec) (TH = 32 mm)
1	291	3.2	110
5	58	16	22
10	29	32	11
15	19	48	7.4
20	15	64	5.5
25	12	80	4.4
50	6	160	2.2

Table 7.2: The relationships between n_{max} , v , TH , and TR .

with $TR = 11$ msec in order for the blood to be exposed to n pulses before exiting the slice. Recall that peak flow in the coronaries is on the order of 30 cm/sec. The third column gives the slice thickness which would be necessary for blood flowing at 29 cm/sec with $TR = 11$ msec to be exposed to n pulses before exiting the slice. Slice thicknesses of 32 - 48 mm were used in the 3D work of this dissertation. The last column gives the TR which would be necessary for blood flowing at 29 cm/sec through a 32 mm thick slice to be exposed to n pulses before exiting the slice. A TR close to 11 msec was generally used in the 3D work of this dissertation.

7.5 K-space filters and their effects

Ideally, as raw data is collected, the only variations in signal amplitude along any dimension will be those attributable to the formation and decay of the echo. In reality, there are many filters applied to the envelope of the echo.

Such a filter is multiplied with the raw echo signal, which is equivalent to saying that the transform of the filter is convolved with the image. These filters may be exponential, saw-tooth, oscillatory, or one of many other complex forms. If these filters are uniformly applied to all components of the signal (i.e., tissue independent effects), then the filter has the consequence of reducing resolution in the image along the direction of the filter. If the form of the filter is NOT tissue independent, then both contrast and resolution will be degraded along the direction of the filter.

The signal from a 1D object, $\rho(x)$, is denoted $s(k_x)$. An inverse Fourier transform (IFT) is used to reconstruct an image $\hat{\rho}(x)$ as follows:

$$\hat{\rho} = \int_{-\infty}^{\infty} s(k_x) \exp(i2\pi k_x x) dk_x \quad (7.9)$$

If the 1D object to be imaged, $\rho(x)$, is a delta function, $\delta(0)$, then its signal in the k-space domain, $s(k_x)$, is simply a constant. If this constant signal is multiplied by a k-space filter, $f(k_x)$, then the IFT of the combined signal is simply the IFT of the filter function. This result is called a point spread function (psf) and is given as follows:

$$psf = \hat{\rho}(x) = \int_{-\infty}^{\infty} f(k_x) \exp(i2\pi k_x x) dk_x. \quad (7.10)$$

This psf is a complex function. Since magnitude images are usually used in MR, the psf's shown in this work are the magnitudes of the complex psf's resulting from the filters. If imaging a delta function, then these magnitude

psf's truly represent the effect of the k-space filter(s) on the image. For imaging anything other than a delta function, then these magnitude psf's are illustrative approximations to the actual effect of the filter(s) on the final magnitude image.

7.5.1 T_2 filters

One such tissue dependent filter is the " T_2 filter" in spin echo studies or the " T_2^* filter" in gradient echo studies[63]. Exponential decay of signal due to T_2 or T_2^* dephasing during acquisition of the each line of k-space leads to loss of contrast and resolution across the read direction of the image. If the duration of the data acquisition window is short compared to T_2 or T_2^* , then the deleterious effects are negligible. An example of T_2^* filters and their effects on resolution is shown in Figure 7.2 (a) & (b), respectively.

7.5.2 Approach to equilibrium filters

Another type of tissue dependent filter is found in gradient echo studies in which a steady state of the magnetization is not developed prior to acquisition of the data. During the approach to equilibrium, the amplitude of the magnetization can oscillate, imposing a highly irregular filter over k-space in the phase encoding direction. An example of non-steady state/approach to equilibrium filters and their effects for a FISP (fast imaging with steady precession) scan is shown in Figure 7.3 (a) & (b), respectively.

Figure 7.2: (a) T_2^* filters imposed across the readout direction for blood, fat, and myocardium for a scan with a symmetric echo, $TE = 7$ msec, and 256 points sampled over 5120 μ sec. The FT of these filters produces the psf's shown in (b). Note that myocardium, having the shortest T_2^* , will be the most blurred.

Figure 7.3: (a) Filters imposed over the phase encoding direction caused by the approach to equilibrium of blood, fat, and myocardium for a FISP scan with $TR = 11.0$ msec, $TE = 5.2$ msec, flip angle = 20° , and no preparation cycles. The FT of these filters produces the psf's shown in (b).

7.5.3 TurboFLASH filters

A variation on the preceding type of non-steady state scenario is the 2D TurboFLASH scan in which the very rapid acquisition of data lines may be preceded by an inversion (180°) pulse and an inversion time, TI. Throughout TI and more relevantly to this discussion, throughout data acquisition, T_1 recovery occurs. This is important in that TI may be selected so that the longitudinal magnetization for one particular tissue passes through zero during the acquisition of the image data thus effectively nulling out that tissue in the final image. The unfortunate fact, however, is that the magnetization is not at all constant as the phase encoding direction of k-space is covered. An example of the filter imposed during such a scan and its effects on an image for the case in which k-space is traversed in a sequential fashion is shown in Figure 7.4 (a) & (b), respectively. Note that this filter is asymmetric. To make the filter more symmetric and to manipulate the inversion time in order to null out a particular tissue, k-space may be covered in a centric manner from the center outwards as in 0,-1,+1,-2,+2,... The resulting k-space filter and its effect on images is seen in Figures 7.5 (a) & (b). The reason that reordering the coverage of k-space will manipulate the effective inversion time is that most of the signal and thus also most of the contrast in an image is derived from the central lines of k-space[44]. The psf for the sequential and centric reordered acquisitions are very similar although the centric psf's are slightly broader at the center yet drop to zero more quickly

than the sequential psf's. Thus, the centric reordering will produce a bit more blurring but will keep more signal energy in the image and out of the background.

7.5.4 3D-MP-RAGE and 3D-RAGE filters

These TurboFLASH-type filter patterns are also seen in the 3D-MP-RAGE scans described in Section 9.2.1. In the case of 3D-MP-RAGE, the filter is imposed over the slice encoding (k_z) direction for every k_y line. The number of k_z lines acquired is generally much smaller than the number of k_y lines and the filter does not get a chance to flatten out. For 16 sequentially or centrally ordered k_z lines and a TI of 400 msec, the filters and associated image effects appear as shown in Figures 7.6 (a) & (b) and 7.7 (a) & (b), respectively. For the corresponding 3D-RAGE scans (i.e., a 3D-MP-RAGE scan without the magnetization preparation IR pulse), the filters and associated image effects appear as shown in Figures 7.9 (a) & (b) and Figures 7.8 (a) & (b).

As with the TurboFLASH filters, the centric reordering causes the psf's to drop more quickly to zero thus keeping more signal in the image. At the same time, there is a bit more blurring with the centric reordering. Note also that there is less signal overall in the 3D-MP-RAGE scan versus the 3D-RAGE scan. Also, the inversion pulse (the "MP") and the chosen *TI* have caused blood to be very suppressed relative to the other tissues as shown in the psf's for the 3D-MP-RAGE scan.

Figure 7.4: (a) Filters imposed over the phase encoding direction for blood, myocardium, and fat in a TurboFLASH scan with a 180° pulse followed by a TI of 400 msec, 128 phase encoding lines acquired in sequential order. TR = 3 msec, TE = 4 msec, and a flip angle = 20° . The FT of these filters produces the psf's shown in (b).

Figure 7.5: (a) Filters imposed over the phase encoding direction for blood, myocardium, and fat in a TurboFLASH scan with a 180° pulse followed by a TI of 400 msec, 128 phase encoding lines acquired with centric reordering, TR = 3 msec, TE = 4 msec, and a flip angle = 20° . The FT of these filters produces the psf's shown in (b).

Figure 7.6: (a) Filters imposed over the k_z direction for blood, myocardium, and fat in a 3D-MP-RAGE scan with a 180° pulse followed by a TI of 400 msec, sequential ordering, 16 k_z lines, TR = 11 msec, TE = 5.2 msec, and a flip angle = 20° . The FT of these filters produces the psf's shown in (b).

Figure 7.7: (a) Filters imposed over the k_z direction for blood, myocardium, and fat in a 3D-MP-RAGE scan with a 180° pulse followed by a TI of 400 msec, centric reordering, 16 k_z lines, TR = 11 msec, TE = 5.2 msec, and a flip angle = 20° . The FT of these filters produces the psf's shown in (b).

Figure 7.8: (a) Filters imposed over the k_z direction for blood, myocardium, and fat in a 3D-RAGE scan with sequential ordering, 16 k_z lines, TR = 11 msec, TE = 5.2 msec, and a flip angle = 20° . The FT of these filters produces the psf's shown in (b).

Figure 7.9: (a) Filters imposed over the k_z direction for blood, myocardium, and fat in a 3D-RAGE scan with centric reordering, 16 k_z lines. TR = 11 msec, TE = 5.2 msec, and a flip angle = 20° . The FT of these filters produces the psf's shown in (b).

7.5.5 Filter removal with incremental flip angles

The technique of using variable flip angles to eliminate some of these filter effects was introduced in Section 4.2.5. Recall, that if a series of flip angles is chosen in such a way as to keep the magnetization constant for a given tissue $T1$ over successive phase encoding lines, then the filter effects will be removed. During a scan such as a 3D-RAGE scan, as M_z decreases, the flip angle must be increased in order to produce a constant amount of signal. However, the flip angle may only be incremented to a maximum of 90° ; angles beyond 90° will produce less signal. This means that the signal may only be held constant for a limited number of repetitions. The number of repetitions for which the signal may be held constant in a scan with no transverse magnetization remaining prior to each excitation and the flip angle series necessary to do so is dependent upon the $T1$ of the tissue, the TR , and the initial value of the flip angle. Thus, a series of flip angles which produces a constant signal for one tissue will not produce a constant signal for other tissues. The tissue for which the flip angle series was optimized will not be blurred while the tissues with non-constant signal will be blurred. A series of flip angles designed to maintain blood at a constant signal level is shown in Figure 7.10, the resulting signal for blood, myocardium, and fat is shown in Figure 7.11(a), and the resulting psf's are shown in Figure 7.11(b). Since the variable flip angles were able to maintain the signal of blood at a constant, then the psf for blood is a delta function while the other tissues did not have

Figure 7.10: A series of flip angles designed to maintain blood at a constant signal level for a TR of 11.1 msec and an initial angle of 10° .

constant signal and thus experience blurring.

7.5.6 Variations in TR filters

A different class of filters is encountered in cardiac MRI and especially in some of the newer approaches in CMRI. These filters are related to variations in the length of the R-R interval during a scan and in the number of data lines acquired per cardiac cycle.

In the most basic case of a prospectively triggered spin echo scan, the TR for each line is equivalent to the R-R interval. The R-R interval is not constant unless pacing, a contraindication to MRI, is used. Variations

Figure 7.11: (a) Filters imposed over the phase encoding direction for blood, myocardium, and fat in a variable flip angle FLASH scan (or part of a RAGE scan) with TR of 11.1 msec. The FT's of these filters produces the psf's shown in (b).

in TR lead to variations in T_1 recovery from line to line and this in turn imposes on k -space a filter such as that seen in Figure 7.12(a). The resulting effect along the phase encoding direction in the image is a small increase in background noise as seen in Figure 7.12(b). If the variations are periodic and thus impose a periodic filter as seen in Figure 7.13(a), then the resulting image is convolved with the function seen in Figure 7.13(b) and will appear to have ghosts like those due to periodic motion. In this example, a periodic change of $\pm 5\%$ for a mean TR of 1000 msec with a frequency of 0.20, the oscillations in signal are small and thus the ghosts are small. In fact, with the oscillation frequency of 0.20 there should be five ghosts yet the two outermost ghosts are so faint that they are not seen in the psf (Figure 7.13(b)).

In more advanced applications such as segmented imaging, the variations in TR are both dramatic and intentional. More than one line of k -space is acquired within one cardiac cycle with each line acquisition separated by a time TR which may range from 5 to 20 msec[25, 64, 65]. After a group or segment of k -space is filled, no scanning occurs until the next R-wave is detected. During this time, the longitudinal magnetization recovers to a value well above that preceding collection of the last acquired line of k -space. The result is that the magnetization throughout a segmented scan takes on a shark-tooth type pattern as seen in Figure 7.14(a). This type of high frequency filter imposed on k -space can cause severe ghosting in the image as seen in Figure 7.14(b). These effects can be altered by changing

Figure 7.12: (a) Filter imposed over the phase encoding direction caused by variations in TR with the average R-R interval equal to 1000 msec and a random variation of $\pm 5\%$. The FT of this filter produces the psf shown in (b).

Figure 7.13: (a) Filter imposed over the phase encoding direction caused by periodic variations in TR with the average R-R interval equal to 1000 msec and a periodic variation of $\pm 5\%$ occurring over a period equal to $5TR$ (frequency = 0.20). The FT of this filter produces the psf shown in (b).

the order in which k-space is traversed. The magnetization will still have the same shark-tooth pattern over time, but this pattern will be redistributed if k-space is covered in a non-sequential manner. For example, a 128 line k-space may be divided into sixteen segments of eight lines to be acquired in each cardiac cycle. If in the first cardiac cycle, lines 1,17,33,...,97,113 are acquired, in the second cycle, lines 2,18,34,...,98,114 are acquired, and so on until in the sixteenth cycle, lines 16,32,48,...,112,128 are acquired, then the filter imposed on k-space will appear as in Figure 7.15(a) with the result on the image as shown in Figure 7.15(b). Note that the periodic changes in the filter are less frequent and smaller in amplitude and that on the whole, the amplitude of the filter decreases over the course of the scan. The result is that there are more smaller ghosts and a bit more blurring than the sequentially acquired scan. An appropriate combination of variable flip angles, TR 's, and k-space ordering can be selected to produce a psf with minimal number or amplitude of ghosts and/or minimal blurring.

The total amount of time spent scanning in each cardiac cycle is given simply by the number of lines in a segment times the TR . This scanning interval determines the temporal resolution of the image. Since the temporal resolution is reduced compared to basic one cycle/one line approaches by a factor equal to the number of lines acquired per cycle, these types of segmented approaches are best suited for diastolic imaging when motion is minimal.

Figure 7.14: (a) Filters imposed over the phase encoding direction caused by TR variations inherent in a segmented scan with sequential coverage of k -space. The signal is for blood, myocardium, and fat in a FLASH scan with the R-R interval assumed to be 900 msec, 3 lines acquired per cardiac cycle, 128 total lines, TR of 12 msec, and flip angle 20° . The FT of this filter produces the psf shown in (b).

Figure 7.15: (a) Filters imposed over the phase encoding direction caused by TR variations inherent in a segmented scan with reordered coverage of k -space. The signal is for blood, myocardium, and fat in a FLASH scan with the R-R interval assumed to be 900 msec, 3 lines acquired per cardiac cycle, 128 total lines, TR of 12 msec, and flip angle 20° . The FT of this filter produces the psf shown in (b).

7.6 Contrast agents

One of the appealing characteristics of MRI when it was first introduced to medical practice was its non-invasive nature. MRI required no catheters and no contrast agents. There is a real, albeit finite and very small, risk associated with the use of catheters and contrast agents involved in some other types of radiographic imaging. Thus, the fact that MRI did not require such adjuncts aided the technology's acceptance and growth. However, it was soon realized that contrast agents developed specifically for MRI could be quite useful in improving lesion detectability and thus increasing the diagnostic value of MRI scans.

Contrast agents alter the contrast producing parameters of a tissue or tissues, namely T_1 , T_2 , and ρ [35]. One way to alter ρ is to displace water such as by putting a fluorocarbon emulsion into the gastrointestinal tract. It is more common though for contrast agents to affect T_1 or T_2 . These agents can be divided into two principle categories - those that cause positive enhancement, primarily by shortening T_1 , and those that cause negative enhancement, primarily by shortening T_2 (and T_2^*) through susceptibility effects. The positive enhancing agents contain certain metals and stable free radicals which have unpaired electrons and thus are paramagnetic. Paramagnetic substances disturb the relaxation of neighboring water protons which shortens both T_1 and T_2 . The T_1 effect is much stronger than the T_2 ef-

fect. So, tissues containing such a contrast agent will appear much brighter due to the $T1$ shortening. The negative enhancing agents include superparamagnetic particles such as iron oxides and certain metals such as dysprosium; these agents create local field inhomogeneities. The susceptibility effect caused by the presence of inhomogeneities shortens $T2$ and $T2^*$ which in turn causes signal loss (darkening) in tissues containing the contrast agent.

In cardiac MRI, some non-intravascular contrast agents have proven to be useful in diagnosing and defining the margins of myocardial infarcts[66]. Over a period of time, these agents, such as Gadopentatate dimeglumine or Gd-DTPA (brand name MagnavistTM by Berlex Laboratories, Wayne, NJ), leave the vasculature and accumulate in the interstitium of surrounding tissues. Obviously, since this type of agent is not confined to the vascular spaces, it is not ideal for vascular imaging. However, if the rate of extraction of the agent from the vasculature is slow compared to the rate of image acquisition, then the agent can be of use in vascular imaging. This has been shown to be true in some MRA's of cerebral vasculature[34]. More relevantly to the subject of this dissertation, rapid imaging following a bolus injection of Gd-DTPA can produce images in which the coronary vessels are highlighted as seen in Figure 7.16. Agents of very high relaxivity, even if not confined to the vasculature, can also be of great use especially if combined with k-space reordering. In this case, the central portions of k-space are acquired during the time in which the agent exerts a strong effect on blood and before it

Figure 7.16: Short axis TurboFLASH images, each taken within a single heartbeat, following bolus injection of the contrast agent, Gd-DTPA. In (a), the contrast agent is in the right ventricle. In (b), the contrast agent is in both the right and left ventricles and in the LAD (arrow).

concentrates in the myocardium.

For imaging of the coronary arteries or other portions of the cardiovascular system, it is more useful to have an intravascular agent that stays in the blood vessels until it is cleared by the kidneys. Such an agent is gadolinium-DTPA labeled dextran which is not yet FDA approved for human use and is currently being tested in animal models[67]. This type of agent could dramatically alter the contrast of blood relative to surrounding tissues and make it much easier to visualize the coronaries.

7.7 Saturation pulses

Saturation pulses may also be used to affect contrast in cardiac MRI scans. Some types of pulses that may be utilized include non-selective inversion (180°) pulses (as used in this work), 1,2, and 3D selective excitation pulses, fat selective saturation pulses, and magnetization transfer saturation pulses. In cardiac applications these pulses are generally applied in each cardiac cycle prior to acquisition of a group of data lines.

A non-selective IR pulse is used to differentiate tissues based on their T_1 properties. “Non-selective” in this sense means that these pulses are not spatially selective (i.e., broadband) and are applied to the entire volume of tissue within the coil. The objective with this type of pulse is to select an appropriate TI so that the signal from one tissue, such as blood, is effectively nulled. Different TI’s will cause different tissues to be nulled out. An example of a 3D-RAGE scan with (i.e., a 3D-MP-RAGE image) and without (i.e., a 3D-RAGE image) a non-selective inversion pulse applied 400 msec prior to acquisition of each group of k_z lines is shown in Figure 7.17 a & b. Note that, while the coronaries can be easily seen in the image with the IR pulse, the blood in the coronaries is not well differentiated from blood in the chambers. This makes it very difficult to post-process the image volume to extract a coronary tree. A simple thresholding or MIP algorithm would not be sufficient.

Figure 7.17: Single partition (a) 3D-MP-RAGE and (b) 3D-RAGE images demonstrating the effect of a non-selective IR pulse followed by a TI of 400 msec. The result of subtracting the 3D-MP-RAGE image from the 3D-RAGE image with scaling used to eliminate fat signal is shown in (c). Note the increased visibility of the LM (arrow) and its bifurcation into the LAD and CX.

One, two, and three dimensional selective RF pulses can be used to try to tag or differentiate blood in or originating in the selected region. The coronary arteries are filled with blood that flows in a retrograde manner down the aortic root in early diastole. To distinguish blood in the coronary arteries from blood in other vessels and chambers and from surrounding tissues, it is useful to apply spatially selective RF pulses to the aortic root with such a timing as to affect that blood which will flow back into the coronaries. These pulses may be one dimensionally selective as in a slice of finite thickness, two dimensionally selective as in a rod (rectangular or circular cross-section)[32, 68], or even three dimensionally selective as in a cube or sphere[32]. These pulses may be inversion pulses (180°) or saturation pulses (generally 90° but possibly something like 120°). Such pulses are generally used in one part of a two part subtraction study in which the pulse is applied in the first scan to reduce blood signal; the results of this scan are subtracted from the results of the second scan in which no special pulse is applied[32]. Alternatively, these pulses might be used as small tip angle (α) pulses intended to excite the blood, the signal from which would be read out over a larger region. Unfortunately, while the 2D and 3D spatially selective IR pulses are well behaved, the 2D and 3D spatially selective excitation pulses have large side-lobes which will excite other tissues away from the region of interest[69, 68].

Fat selective pulses can also be extremely useful in imaging the coro-

nary arteries since a great portion of the proximal coronaries is most often surrounded by fat. If the fat signal can be effectively eliminated without affecting the water signal, then the coronaries will stand out nicely. It is possible to make a pulse selective for fat only due to the difference in resonant frequency between water and fat protons discussed in Section 7.3. Most pulses used in MRI are relatively broadband and thus excite both fat and water protons; fat selective pulses must be narrow band enough to excite (saturate) the blood without affecting the water protons. Alternatively, a water selective pulse may be used to excite only water protons, leaving fat dark. The difficulty in using these species (fat or water) selective pulses is that B_0 inhomogeneities change the resonant frequency of fat and water in a local area, thus decreasing the effectiveness of the saturation pulse. This is in contrast to the cancellation effect seen in opposed phase imaging (discussed in Section 7.3) which is independent of B_0 inhomogeneities though it is dependent on what species are in a single voxel and in what proportions.

Magnetization transfer saturation pulses may also be used to enhance contrast between myocardium and blood[33]. Magnetization transfer contrast (MTC) is produced by applying a low-power RF irradiation that is off-resonance from the bulk water resonance. This RF irradiation saturates the protons in the macromolecules of the myocardium. Coupling between the macromolecules and water protons causes a selective decrease in the water signal from myocardium, making it appear darker in the images. Blood.

having fewer macromolecules and by virtue of its flow, is not as affected by the MTS pulses.

7.8 Summary

In any MRI scan, there are a great many factors involved in image contrast. Improving SNR and CNR increases the probability that the technique will reliably distinguish normal and diseased states and is the objective in adjusting scan design and acquisition parameters. The optimal TR and flip angle are tightly linked to each other and to tissue properties and the velocity of flow through an excitation volume of a certain thickness. Increasing TR will increase SNR and allow more inflow yet will increase scan time and may actually decrease CNR. Up to a certain point, increasing flip angle will increase SNR but beyond that point, SNR will decrease. Using short TE will increase SNR by reducing signal losses from $T2^*$ and motion related dephasing although the choice of TE may also be affected by a need to have an in-phase or opposed-phase fat/water signal. With the novel approaches to k-space coverage involved in some coronary artery MRI techniques, resulting filters imposed on k-space may reduce resolution and decrease SNR. Careful application of reordering and variable flip angles may reduce or eliminate these filters. Contrast agents may be employed to selectively increase SNR and CNR. Also, a variety of RF techniques, including spatially selective saturation and excitation, fat saturation, and magnetization transfer pulses,

may be used to increase CNR. It is important to seek optimal combinations of these parameters and techniques - TR, TE, flip angle, k-space coverage, contrast agents, saturation pulses, etc. - in order to overcome many of the challenges to coronary artery MRI.

Chapter 8

Effects of Respiration on Cardiac MR Imaging

Respiration complicates MRI of the heart in two major ways. First, respiration involves movement of structures in the thoracic cavity and second, respiration alters the length of the cardiac cycle.

Respiration occurs with a frequency of about 12 - 20 breaths per minute (.20 - .33 Hz). The expiratory phase is longer than the inspiratory phase and is passive in that no muscles contract during expiration [70].

The effect of respiration on heart rate is called respiratory cardiac arrhythmia and is more prominent in children than in adults. Changes in reflex and central nervous activity during respiration lead to oscillations in vagus nerve activity. This in turn affects heart rate with an increase in heart rate during inspiration and a decrease in heart rate during expiration [10]. For an ECG triggered scan, variations in heart rate imply variations in effective TR which can lead to ghosting [18].

In any imaging method, from basic photography to sophisticated magnetic resonance imaging, motion during the acquisition of the data leads to degradation of the image. The severity of the problem is related to the extent of motion relative to the duration of data acquisition. In most MRI techniques, data acquisition times are long relative to the types of motion encountered. Thus, as in other imaging methods, blurring results. MRI is also subject to ghosting, an artifact related to periodic motion occurring during data acquisition. In MRI, respiratory motion is particularly troublesome since it involves several millimeters to centimeters of motion (well above the desired resolution) and is essentially periodic.

8.1 Blurring

Motion occurring during an MR scan, specifically between acquisition of different raw data lines, causes blurring in the phase encoding direction of the image. Motion during acquisition of a single line causes blurring in the readout direction and, in addition, introduces signal loss due to motion related dephasing (see Section 3.8). The time interval between acquisition of successive lines is much longer than the duration of signal readout for a single raw data line (11 msec and up versus 5 msec). Thus, more motion can occur between acquisition of successive lines than between successive readout samples.

Motion occurring between acquisition of successive lines imparts a relative

signal change, $\exp[i\phi(n)]$, to each line as given by:

$$\exp[i\phi(n)] = \exp\left(i\frac{2\pi n \Delta(y)}{FOV}\right) \quad (8.1)$$

where n is the line number, $\Delta(y)$ is the position change due to motion in the phase encoding direction, and FOV is the field of view.

The effect of motion on an image can be evaluated by taking the Fourier transform of $\exp[i\phi(n)]$. The result is a point spread function which demonstrates the amount of blurring induced by the motion. The psf is a complex function which is convolved with the principle image in its complex form, causing blurring across the entire FOV. Since magnitude images are usually used in MR, the psf's shown in this work are the magnitudes of the complex psf's resulting from the filters. If imaging a delta function, then these magnitude psf's truly represent the effect of the motion on the image. For imaging anything other than a delta function, the complex psf is convolved with the complex image before the magnitude image is computed. Even so, taking the magnitude of the psf itself provides an illustrative approximation to the actual effect of the motion on the final magnitude image.

If random motion in the range of +2 to -2 pixels occurs from line-to-line during a 128 line scan, then the resulting psf is as shown in Figure 8.1. The motion causes a great amount of the signal to become smeared over the entire background. The full width at half the maximum value (FWHM) is roughly three pixels (difficult to define given the dual peaks), which is about

Figure 8.1: PSF resulting from ± 2 pixel random motion during an MR scan.

200% broadening over the motion free condition.

8.2 Ghosts

If the motion occurring from line-to-line during an MR scan is periodic, then ghosts will appear in the phase encoding direction of the image. Indeed, if there is any periodic change in signal from line-to-line such as might occur with periodic changes in TR, ghosts will appear. Ghosts are faint copies of the principle image located at regular intervals across the phase encoding direction. If ghosts overlap the principle image, they can obscure important details. Ghosts also “steal” signal from the principle image since the total

amount of signal energy in an entire image is constant whether ghosts are present or not.

The number and location of the ghosts is directly related to the periodicity of the motion. If the period of the motion is T , the repetition time between lines is TR , and the number of acquisitions is $\#Acq$, then the number of ghosts, N , is given by $N = T/(\#Acq \times TR)$. N must be an integer; if $T/(\#Acq \times TR)$ is not an integer, then N is actually the lowest integer that has $T/(\#Acq \times TR)$ and another integer as factors (e.g., 5 is the lowest integer that has 2.5 and 2 as factors). For example, if the period of the motion, T , is equal to $5 \times TR$, and one acquisition is taken, then the number of ghosts, N , is five. If two acquisitions are taken, then $T/(\#Acq \times TR)$ is 2.5. The actual number of ghosts is five. To understand this, consider five different displacements, 'a' - 'e', in the course of one respiratory cycle. In a single acquisition scan, the first k_y line is sampled at 'a', the second line at 'b', the third line at 'c', the fourth line at 'd', the fifth line at 'e', and the sixth line at 'a' again. Thus, for this single acquisition scan, the displacements represented in the data repeat every five lines. In a two acquisition scan, the first k_y is sampled at 'a' and 'b', the second line at 'c' and 'd', the third line at 'e' and 'a', the fourth line at 'b' and 'c', the fifth line at 'd' and 'e', and the sixth line at 'a' and 'b' again. Thus, for this two acquisition scan, the displacements represented in the data repeat every five lines.

The principle image counts as one of the N ghosts with the others uni-

formly spaced from it across the FOV. The spacing may be expressed mathematically as $y_{ghosts} = 2\pi F \times TR \times \#Acq \times FOV$ [71] (again, this assumes that $(F \times TR \times \#Acq)^{-1}$ is an integer). To illustrate this graphically, consider the periodic motion, $\Delta y(n)$, shown in Figure 8.2 (a). As in the discussion on blurring in the preceding section, the effect of this periodic motion is demonstrated by taking the FT of $\exp[i\phi(n)]$, where $\phi(n)$ now includes the periodic motion, $\Delta y(n) = A \sin(\omega_n n)$. The FT of $\exp(-i\alpha \sin(\omega t))$ is $\sum_{p=-\infty}^{\infty} J_p(\alpha) \exp(-ip\omega t)$ [18]. Thus, the effect of this periodic motion on the image will be to create a series of evenly spaced “messy” ghosts (i.e., not exact replica ghosts) with the “messiness” related to the Bessel functions. The effect of the motion shown in Figure 8.2 (a) is approximated by the FT of $\exp[i\phi(n)]$ shown in Figure 8.2 b.

If the number of acquisitions and the TR in a scan are adjusted so that $\#Acq \times TR = T$, then $N = 1$ and only the principle image will appear. This technique for removing ghosts is called pseudo-gating [18].

8.3 Characterization of respiratory motion

Respiratory motion can significantly degrade cardiac MR images yet is often not compensated in routine clinical studies. The goal of using MR to image the coronary arteries necessitates an assessment of the impact of respiratory motion on high resolution MR images. Too often, respiratory compensation techniques are applied without an understanding of the extent of the problem.

Figure 8.2: Periodic motion of ± 2 pixels (± 4 mm) at a frequency of 0.20 (a) occurring during an imaging experiment will create a composite image with a principle image located at the center point and four additional ghosts spaced across the FOV as indicated by the function in (b).

Figure 8.3: Pulse sequence diagram for the TurboFLASH sequence used to measure respiratory motion. The scan triggers off the R-wave of the ECG. At a selected delay after each R-wave, the entire scan is executed in 520 msec. The scan is repeated for 64 consecutive heartbeats.

8.3.1 Methods

In order to quantitate cardiac motion due to respiration, sub-second TurboFLASH images were acquired for 64 consecutive heartbeats during normal respiration. The sequence, shown in Figure 8.3, was run once with a coronal slice through the aortic valve and once with a transverse slice through approximately the mid-ventricular level.

The sequence used was a TurboFLASH sequence with no preparatory inversion pulse(s), a TR of 6.5 msec, a TE of 3.0 msec, an asymmetric echo in the readout direction (echo at point #35 of 128), no spoiling after data acquisition, and a bandwidth of 355 Hz. A summary of parameters is given below.

TR = 6.5 msec	Matrix = 80 x 128
TE = 3.0 msec	Acquisitions = 1
Flip angle = 15°	FOV = 300 - 400 mm
Thickness = 10 mm	
ECG delay = 0 - 350 msec	Tacq /image = 520 msec

Thirteen healthy volunteers (3 females and 10 males) were scanned in this study.

Images were evaluated for translational motion along the cranio-caudad (C/C) axis in the coronal images and along the anterior-posterior (A/P) axis in the transverse images by cross-correlating four linear regions of interest (ROI's) of 20 to 40 pixels in length from the first image with the same ROI's in subsequent images. Standardized ROI's were used in all subjects as shown in Figures 8.4 & 8.5. The ROI's in the coronal images were the right atrium (or possibly the right ventricle depending on the depth of the plane), left atrium near the aortic root and pulmonary artery, apex, and for reference, the liver. The ROI's in the transverse images were the apex, posterior/inferior left ventricle, right atrium, and for reference, the right

Figure 8.4: Coronal TurboFLASH images from a respiratory analysis series showing the four regions of interest used to monitor C/C cardiac position during respiration. The regions are (1) right atrium, (2) apex, (3) left atrium, and (4) liver (for reference purposes).

chest wall. Position of the structures in an ROI relative to their position in the first image was determined by a computer program which performed the cross-correlations and then interpolated the shift that equally divided the area of the cross-correlation curve (the "half-area" method, described in Section 8.3.3). Visual, image-by-image analysis was also performed on some series though this was extremely tedious. Initially, computerized edge and minima detection was attempted in order to track the features in the ROI's. but these methods were not reliable for analysis of the images involved.

Figure 8.5: Tranverse TurboFLASH images from a respiratory analysis series showing the four regions of interest used to monitor A/P cardiac position during respiration. The regions are (1) apex, (2) posterior LV, (3) right atrium, and (4) right chest wall (for reference purposes).

Coronal Plane (C/C axis motion)		Transverse Plane (A/P axis motion)	
Region	Range +/- SD	Region	Range +/- SD
R Atrium	4.43 +/- 2.78	Apex	2.04 +/- 1.23
Apex	3.95 +/- 3.40	Post LV	2.05 +/- 0.63
L Atrium	3.14 +/- 2.37	R Atrium	1.88 +/- 0.74
Liver	5.66 +/- 3.19	R Chest	2.65 +/- 0.76

Table 8.1: Mean range and standard deviation of cardiac motion, as detected by the half- area method, in millimeters for ROI's during respiration

8.3.2 Results

Respiratory induced motion of the heart in the supine, normal subject was found to be periodic with amplitudes of 2 - 15 mm along the C/C axis and 1 - 5 mm along the A/P axis detected by the half-area method during normal breathing. The mean range of motion for the different monitoring regions is given in Table 8.1.

Graphs showing relative positions, as detected by the half-area method, of the monitored regions as a function of heartbeat number for typical coronal and transverse image series are presented in Figures 8.6 and 8.7 respectively. Note that in the graph shown for the coronal plane, motion of the left atrium and, to a lesser extent, the apex appears to be 180° out of phase with the motion of the right atrium and liver. Manual analysis (hand selection of pixel shifts performed image-by-image) revealed that the motion of the left atrium and apex was actually in-phase with the motion of the right atrium and the liver and also that the motion was greater than reported by the half-area

method. While the motion was in-phase, the main features of the different ROI's did not shift the same amount, thus suggesting deformation and/or complex through-plane motion of the heart. In the transverse plane, visual inspection of the images displayed in a cine loop revealed extensive through-plane motion. Both manual and computer analysis detected only minimal A/P displacements in the transverse plane.

In two cases, the C/C motion results from the manual (i.e. selecting points by hand) and half-area methods of shift detection were compared. For the right atrium, the correlation coefficients between hand selected pixel shift and half-area computed shift in the two sets were -0.90 and -0.88. For the liver, the correlation coefficients were -0.97 and -0.95. This means that (1) the half-area results had a consistent relationship to the manually determined shifts and (2) as the right atrium and liver moved down in the image (higher pixel index) during inspiration, a more negative shift was reported by the half-area method. The regression coefficients for the right atrium were -1.57 and -2.48 and for the liver were -1.73 and -2.09. For the FOV of 400 mm and 256 pixels across the image, the ideal regression coefficient between detected pixels and millimeters of shift would be 0.64. Thus, the half-area method may have underestimated the shifts in these two cases by about a factor of three. The left atrium had correlation coefficients of 0.42 (essentially no correlation) and 0.84 and the apex had correlation coefficients of 0.93 and 0.86. This means that (1) the half-area results did not have a very consistent

relationship to the manually observed shifts and (2) as the left atrium and apex moved down in the image (higher pixel index), a more positive shift was reported by the half-area method. This accounts for the apparent opposed phase results between the right atrium/liver and left atrium/apex seen in Figure 8.6. The nature of the ROI's certainly affected the success or failure of the cross-correlation, half-area method. The liver and right atrium ROI's were essentially step functions with very low signal lung tissue adjoining the high signal of the liver and right atrium. In contrast, the features observed in the left atrium and apex ROI's were actually cancellation artifacts surrounded by higher tissue signal (see Figures 8.4 and 8.5).

8.3.3 Discussion

A source of error in this analysis is the fact that what appears to the analysis software as 1D in-plane motion may actually be composed of complex 3D motion. In fact, a rotational type of motion may account for the motion of the left atrium and apex appearing to be of smaller extent than the motion of the other regions in the coronal images.

Any large variations in R-R interval would also have confounded the results since a difference in cardiac phase may mimic position changes due to respiration.

The coarse imaging matrix, 80 x 128, gave low resolution even when interpolated to 128 x 128. Low resolution makes it difficult to accurately

Figure 8.6: Graph of relative position along a C/C axis, as detected by the half-area method, versus heartbeat number for four regions of interest in the coronal plane during normal respiration.

Figure 8.7: Graph of relative position along an A/P axis, as detected by the half-area method, versus heartbeat number for four regions of interest in the transverse plane during normal respiration. Respiratory motion in the A/P direction is minimal for the supine, normal subject.

predict the shift of structures in the image. Also, truncation of the data by the coarse matrix and asymmetric echo led to Gibb's ringing which also may have hampered analysis. While better resolution and a more symmetric echo are preferable, temporal resolution needs dictated the parameters used.

Another source of error in this analysis is the "half-area" method used to determine the relative positions from the cross-correlation results. Comparison of the half-area results with manual results described earlier in Section 8.3.2 indicated a number of problems. Simulations and mathematical analysis were undertaken to try to understand some of the method limitations and are detailed here.

When a bounded function $g(m)$ [$g(m) = 0$ for $|m| > k/2$] is shifted to create a new function $f(m)$ such that $f(m) = g(m - n)$, then the cross correlation of $g(m)$ and $f(m)$ over the interval $(-k + n)$ to $(k + n)$ will result in a function that peaks at n (peak method of shift detection). The area under this function is also evenly divided at the point n (half-area method of peak detection). The half-area method can utilize interpolation to determine the shift and is thus not limited to detecting only integer pixel shifts. This is an advantage over the peak method which selects the integer pixel shift at which the cross-correlation function peaks. It is possible to utilize curve fitting routines to try to reveal a peak at a non-integer pixel shift; this is a more computationally intense approach. If, as in the case with the images evaluated, the functions are not bounded and are cross-correlated over a

finite interval, then the location of the peak and/or the half-area point may not correspond to the distance the feature(s) of interest have shifted. While a visual examination of the respiratory image series clearly revealed motion of several pixels in amplitude, analysis with the peak method of the cross-correlation frequently did not detect any shift. In fact, in tests on all four ROI in two different data sets the peak stayed almost always at zero shift and was not usually significantly greater than its nearest neighbors $[(100 - 2 * \%error) * (peak\ value)/100 < (neighbor\ value)]$. The half-area method more often detected shifts related to those seen with visual inspection and thus was selected for this analysis.

To investigate the reasons for the different results produced by the peak and half-area methods, tests with simulated 1D objects were conducted. The objects or waveforms were 13 pixels long with intensities of 0 - 40 (arbitrary) units. In addition to its main features, each waveform incorporated a "small feature" of two pixels in width and intensity of 5 units. For each waveform, the original function was cross-correlated with: (1) itself (i.e., auto-correlation); (2) the original function and the small feature shifted together +2 pixels; (3) the original function with only the small feature shifted -7 pixels; and (4) the original function shifted +2 pixels with the small feature shifted -7 pixels. The four waveforms are shown in Figure 8.8 (a)-(d). For all four waveforms, both the peak method and the half-area method correctly handled the auto-correlation test (test 1), as expected. Also, for all four

waveforms, the peak method correctly detected the shift of the original function (tests 2,4) but was completely insensitive to the shift of the small feature (tests 3,4). For the waveforms with zeroed edges (such that no signal intensity was shifted outside the ROI)(Figure 8.8 (b),(c)), the half-area method also correctly detected the shift of the original function (test 2). For the waveforms with non-zeroed edges (Figure 8.8 (a),(d)), the half-area method did detect some shift of the original function (test 2) but underestimated the shift. For all four waveforms, the half-area method did detect some shift of the small feature (tests 3,4). These results were influenced by the integral of the signal of the original function versus that of the small feature.

To summarize the correlation tests, in the ideal case of pure translational motion of an entire object with zero background surrounding the object, the peak of the cross- correlation curve unequivocally reveals the position change. However, the half-area method was more sensitive in cases involving changes in shape of the moving object, movement of only a portion of the object, and non-integer pixel shifts. The half-area method was less accurate (i.e., underestimated the shift) in cases where non-zero signal shifted into or out of the ROI. The half-area method seemed more sensitive to position shifts in the actual MR images and was the method of choice for this work. though both the simulation tests just described and comparison with visual analysis demonstrated that the half-area method underestimated the amount of shift. Visual analysis was the most accurate method though it was limited

Figure 3.8: Test waveforms for peak and "half-area" methods of shift detection, (a)-(d). The cross correlation window included pixels 1 through 13 with non-zero values shifted into the ROI in case (d) only.

to integer pixel shifts and was extremely tedious, requiring hand selection of 512 points ($64 \text{ images} \times 4 \text{ ROI/image} \times 2 \text{ orientations}$) for each subject studied.

It should be noted that edge detection was also tested on the MR images initially but was only suitable for detecting motion of objects with distinct edges such as the liver in the coronal images and the chest wall and posterior LV in the transverse images. Edge detection may have been more successful for the other monitoring regions if edge enhancement of the images was performed prior to edge detection. Edge enhancement or some type of morphologic image processing to select out a certain feature might also have helped improve the results of the cross-correlations.

8.3.4 Conclusion

The quantitative analysis of heart position reveals that the position of the heart changes significantly and periodically with respiration in supine, normal subjects. The mean ranges of motion reported in Table 8.1 are a very conservative estimate of the amount of motion present. While only unidirectional translational motion was evaluated in this study, the results do demonstrate the severity of cardiac motion with respiration. This motion must be countered for MR imaging of the coronary arteries to be successful.

8.4 Characterization of beat-to-beat variations in heart position

Changes in cardiac position due to beat-to-beat variations in contraction and filling can also lead to blurring. To characterize beat-to-beat variations in heart position, the technique described in Section 8.3 was used with the subject breathing at will for the first ten heartbeat images and then holding her/his breath for as long as comfortably possible during the succeeding 54 heartbeat intervals. The same subjects were studied as those in the experiments of Section 8.3.

Subjective visual evaluation of breathhold image series from all the subjects tested demonstrated very small changes in heart position, on the order of a couple millimeters or less which, given the low resolution of the scans, could not be described as significant. The image series did exhibit small variations in signal intensity seen as a flickering in the images. Much of this flicker may be attributed to SNR variations from image to image due to variations in the time interval between scans (i.e., the R-R interval), variations in motion artifacts, etc. These noise variations may have been interpreted as motion by the algorithm used to analyze the image series.

Graphs showing results from representative breathhold coronal and transverse image series are presented in Figures 8.9 and 8.10, respectively.

Figure 8.9: Graph of relative position along a C/C axis, as detected by the half-area method, versus heartbeat number for four regions of interest in the coronal plane during a breathhold study. The subject took a long, deep breath during the first ten heartbeats and then held his breath through the remaining 54 heartbeats.

Figure 8.10: Graph of relative position along an A/P axis, as detected by the half-area method, versus heartbeat number for four regions of interest in the transverse plane during a breathhold study. The subject breathed deeply for the first ten heartbeats, held his breath for the next 34 heartbeats, and then resumed respiration.

8.5 Simulation of respiratory motion effects on a coronary artery model

The impact of cardiac motion on MR images was assessed with a computer simulation. An image of a cardiac “phantom” was created with signal intensities of 450 for fat, 300 for myocardium, 150 for blood, and 20 for background. The intensities are similar to those obtained with a 3D-MP-RAGE scan. The phantom included coronary arteries surrounded by fat and myocardium. The diameter of the arteries ranged from 4 down to 0.5 mm. A high resolution inverse Fourier transform was used to create raw data from the digital phantom image. The high resolution IFFT was used to mimic the analog nature of the MR signal. Fewer points were then taken from this raw data to more closely simulate an actual imaging experiment. Assuming an imaging scenario in which one line of k -space was acquired with each heartbeat, phase shifts resulting from sinusoidal motion were applied to each line of the raw data. Simulations used an FOV of 128 mm x 128 mm with a $128 k_y \times 256 k_x$ matrix interpolated to $256 k_y \times 256 k_x$ and an asymmetric FOV of 256 mm x 128 mm with a $256 k_y \times 256 k_x$ matrix interpolated to $512 k_y \times 256 k_x$. The larger FOV in the phase encoding direction was used in order to move the ghosts so that they did not overlap the phantom. Thus, the blurring and dual images can be more easily seen. Sinusoidal motion of +/- 1, 2, and 3 mm was used.

Results from some of the computer simulations with high frequency ($f = 0.25$) “respiration” are shown in Figure 8.11. These images of one half of an asymmetric FOV are shown since ghosts in the smaller square FOV’s fell over the object of interest and limited interpretation. In Figure 8.11 (a) Gibb’s ringing is evident. Limited motion of ± 1 mm blurs out the Gibb’s ringing but also blurs out details as seen in Figure 8.11 (b) and introduces ghosting. Increased motion in Figure 8.11 (c) & (d) leads to increased blurring and stronger ghost signals.

Simulation results demonstrated the effect of motion on high resolution MR images. The amount of blurring produced by only a few millimeters of sinusoidal motion is significant. Given that the imaging portion of this work has revealed much larger changes in cardiac position with respiration, it is clear that respiratory motion is a significant barrier to successful MRI of the coronary arteries.

8.6 Respiratory compensation methods

There are a variety of approaches to correcting or compensating for the ghosting and blurring produced respiratory motion. These methods vary in their ease of implementation and in their efficacy. Simulations, of the type described in Section 8.5, were run to demonstrate some of these compensation techniques. A respiratory motion function (RMF) of a sinusoidal or more physiologic nature was used in the simulations.

Figure 8.11: Respiratory simulation results. A 128 mm x 128 mm square portion of a 256 mm x 128 mm asymmetric FOV is shown. The larger FOV in the phase encoding direction was used in order to move the ghosts so that they did not overlap the phantom. Thus, the blurring and ghosting can be more easily seen. The gray circle represents myocardium; the bright arc along the top represents fat; and the structure at the top represents the aortic root with two coronaries originating from it, curving through the fat and myocardium into the heart "chamber". Five coronaries with diameters of one, two, and three pixels are shown in cross-section at the bottom. Motion with a frequency of one cycle every four TR was applied. (a) no motion: note the Gibb's ringing. (b) +/- 1 mm motion; note the blurring induced and the introduction of ghosts. (c) +/- 2 mm motion; increased blurring and stronger ghost signal results. (d) +/- 3 mm motion; again, increased blurring and stronger ghost signal results, impairing visualization of the coronaries. The blurring and loss of signal from the main image decreases the CNR between the coronaries and the surrounding tissues and at the same time increases the apparent diameter.

8.6.1 Averaging

Averaging, acquiring the same line of k-space more than once, increases the effective repetition time and thus reduces the number of ghosts in an image. To see how this works, consider the respiratory motion function shown in Figure 8.12(a). The displacement as a function of time is superimposed with dots separated in time by the length of the R-R interval since, in this scenario, one sample point is acquired in each cardiac cycle. In this example, there are five sample points in a respiratory cycle of period, T . Thus, if each sample point corresponds to one k_y line, then $TR = R - R \text{ interval} = T/5$ and there will be T/TR or five ghosts in the image. In addition to the ghosts, the image will be blurred. These effects are demonstrated by the psf shown in Figure 8.12(b). Now, if each k_y line is acquired $\#Acq$ times, then the effective repetition time between acquisition of subsequent k_y lines becomes $\#Acq \times TR$. The number of ghosts is then reduced to $T/(\#Acq \times TR)$, again assuming the number of ghosts is an integer. In the case of $\#Acq = 2$, the ghosting is changed as shown in Figure 8.12(b). Note that there are still five ghosts as in the single acquisition case since the number of ghosts must be an integer (recall the discussion in Section 3.2). However, the second and fourth ghosts are reduced in amplitude in the case of two acquisitions.

The motion in Figure 8.12 was used in a simulation with one, two, three, and four acquisitions with the results shown in Figure 8.13.(a)-(d). Note the reduction in number of ghosts and the improvement in the quality of the

Figure 3.12: (a) RMF used for compensation method simulations. The waveform is a continuous function of time but is sampled at intervals equal to the R-R interval of the cardiac cycle. Sample points are indicated by dots. In this case, there are 5 samples in a single period of the RMF. (b) Point spread function resulting from respiratory motion during one and two acquisition scans.

Figure 8.13: Simulation results for (a) one, (b) two, (c) three, and (d) four acquisitions in the case of respiratory motion in the vertical (phase encoding) direction with displacements from 0 to 8mm and frequency of 1/5.

principle image as the number of acquisitions increases.

If the number of acquisitions is adjusted so that $T = \#Acq \times TR$, then the number of ghosts is one (remember that TR is tied to the cardiac cycle and cannot be adjusted). The principle image is always the first “ghost”. so really in this case there are no extra ghosts. This technique is called pseudo-gating[18].

While it increases scan time, averaging has the added advantage of increasing the SNR in proportion to the square root of the number of acquisitions at the same time as it reduces motion artifacts.

8.6.2 Respiratory gating

Another method for compensating for respiratory motion is respiratory gating. This involves monitoring the respiratory cycle and limiting data collection to certain portions of the cycle. Monitoring may be accomplished via a strain gage placed around the chest as was used in this work; other methods include measuring the subject's airflow or placing a thermister near the nose and/or mouth to measure temperature changes caused by airflow. The operator selects a threshold value which is generally expressed as a percentage of the peak respiratory excursion. (The peak respiratory excursion is updated frequently and is determined from a moving average of the most recent several respiratory cycles.) The user may elect to have the gate opened, meaning that data is collected, in the periods when the respiratory signal is either above the threshold (inspiratory phase) or below the threshold (expiratory phase). The operator may also select what proportion of k-space is to be respiratory gated versus collected without regard to the respiratory cycle. The scan is run continuously in order to maintain steady state conditions of the magnetization, though the phase encoding line is only incremented when the gate is open.

Respiratory gating reduces the extent of motion affecting the scan in direct proportion to the threshold value. By cutting out portions of the respiratory cycle, gating also reduces the period (and increases the frequency) of the effective RMF. For example, a 50% threshold applied to the RMF

in Figure 8.12 results in the effective RMF and consequent psf shown in Figure 8.14(a) and (b). Comparing the psf from the gated case with the psf from the ungated example in Figure 8.12(b) demonstrates that respiratory gating decreases blurring and the number of ghosts.

Respiratory simulations like those shown in Figure 8.13 were performed to demonstrate the effects of gating. The simulations, the results of which are shown in Figure 8.15, involved gating the central 25%, 50%, 75%, and 100% of the k_y lines with data acquisition limited to motion below the cut-off thresholds of 50% and 25%. The tighter (25%) cut-off threshold reduced the ghosting and cleaned up the image but would increase the scan time in a real imaging experiment. Also, gating a greater percentage of the k_y lines improved the image quality but also would increase the scan time for a real imaging experiment. The ghosts never completely disappeared in any of the simulations shown, but in the simulations with the 25% threshold and 75% (f) and 100% (h) of k_y lines gated, the ghosting is reduced enough that details in the main image are not obscured.

An example of a 2D cine gradient echo scan run without and with respiratory gating is shown in Figure 8.16. Note the appearance of a faint ghost in the ungated image; the ghost is removed and the image is sharper in the gated image. An example of a 3D-RAGE scan run without and with respiratory gating, with either one or two acquisitions is shown in Figure 8.17. In both the 2D and 3D cases, respiratory gating increases the SNR and reduces

Figure 3.14: (a) Effective RMF created by applying a 50% threshold to the RMF in Figure 3.12(a). Note the decrease in maximum excursion and the decrease in the period of the motion. (b) psf resulting from gating the entire scan with a 50% threshold. Note the reduction in blurring and number of ghosts relative to that for the ungated case shown in Figure 3.12(b).

Figure 8.15: Respiratory gating simulations with percent k , lines gated and thresholds of (a) 25/50, (b) 25/25, (c) 50/50, (d) 50/25, (e) 75/50, (f) 75/25, (g) 100/50, and (h) 100/25. The input waveform was the same as that shown in Figure 8.12.

ghosting. Note that in the 3D example, the two acquisition, gated image (d) is certainly the best. However, note also that the two acquisition, ungated image (b) has better SNR in the heart than the one acquisition, gated image (c) though some of the pulmonary vasculature seen in (c) is not as well seen in (b).

8.6.3 Single and multiple breatholds

Acquiring data during a breathhold removes the respiratory motion problem altogether. This is an extremely effective compensation technique for those MR scans which may be acquired within a single breathhold[17, 26]. If many images are desired, each to be acquired in a separate, single breathhold, then it is necessary for the breathhold positions to be the same. Otherwise, the separate images will not register with each other. It may be necessary for the subject to practice breathholding and to provide them with some sort of feedback about breathhold position (such as lung volume, chest circumference, etc.) in order for them to attain the same position for each scan.

As noted in the introduction to this chapter, respiration affects heart rate. Breathhold, the suspension of respiration, also affects heart rate in that the partial pressure of oxygen in the blood drops and the partial pressure of carbon dioxide increases during a breathhold, causing heart rate to decrease[70. page 184-185].

A 3D cardiac MRI scan of moderate to high resolution, run on a conven-

Figure 8.16: 2D cine gradient echo images (a) without and (b) with respiratory gating. Note the appearance of a faint ghost in the ungated image; the ghost is removed and the image is sharper in the gated image.

Figure 8.17: Effect of respiratory gating and averaging on 3D-RAGE images. Images are: (a) 1 acq, not gated, (b) 2 acq, not gated, (c) 1 acq, gated, and (d) 2 acq, gated.

tional system, cannot be executed within a single breathhold. So, if breathholding is to be employed, data must be acquired over multiple breathholds. The technique was tested as part of this dissertation research. An interrupt switch, located at the scanner console, was wired into the measurement controller. The subject was asked to exhale forcibly and hold their breath while 3D data was collected over 10 heartbeats. Then, the scan was suspended and the subject allowed to breathe normally for 10 heartbeats. This cycle was repeated until all data for the 3D scan was acquired. A 3D-RAGE or 3D-MP-RAGE scan with 128 k_y lines and 2 acquisitions takes 26 breathhold cycles to complete. Results from this 10-10 breathhold technique were inconsistent. In one case, shown in Figure 8.18, the breathhold technique produced dramatic improvement in image quality. However, in most cases, the breathhold images were similar to or worse than the non-breathhold scans. This is most likely due to the subject not returning to the same breathhold position. Also, ECG signal changes created by the forced exhalation and breathholding caused some mistriggering of the scan which would have degraded image quality. Because of this lack of consistent benefit and the difficulty of repeated breathholding for the subject, the multiple breathholding technique was discontinued.

The requirement that data must be acquired at the same breathhold position as discussed for the 2D case above holds for a 3D scan acquired over multiple breathholds. In the 3D case, position errors affect a segment or segments of the raw data which then, after the FT, affect the entire image set. In

Figure 8.18: Individual 3D partition images (a) without and (b) with 10-10 breathholding. This is a case in which breathholding improved image quality; other cases showed a decrease in image quality with the 10-10 breathholding.

the 2D case, if breathold position was off for one or two images, it is relatively simple to identify which images are out of registration and to reacquire those specific images. In the 3D case, it is much more difficult to determine which segment of the 3D data might have been acquired at the wrong position.

8.6.4 ROPE and COPE

Another technique to minimize the effects of respiration is to order the coverage of k-space with respect to the amplitude of the respiratory motion. The technique is known as ROPE which stands for Respiratory Ordered Phase Encoding[72]. It requires the feedback of the respiratory motion monitoring information to the measurement controller so that the line of k-space to be acquired can be selected on the fly. The most negative lines of k-space are acquired when the lowest respiratory signal amplitudes are detected, the central lines of k-space are acquired at the median respiratory signal amplitudes, and the most positive lines of k-space are acquired at the highest respiratory signal amplitudes. Thus, instead of periodic motion causing signal changes over the course of the phase encoding direction, there exists a monotonic, stepwise change in position from lowest to highest amplitude as illustrated in Figure 8.19 (a). The stepwise nature of the respiratory displacements as a function of acquisition number is due to the long repetition time (i.e., the R-R interval) relative to the length of the respiratory cycle. For a scan with a much shorter TR , the displacements as a function of acquisition number will

form a smoother monotonic function. The effect of the ROPE signal changes on the image is shown in Figure 8.19 (b) which may be compared to the psf for the sequential acquisition shown in Figure 8.12(b). ROPE essentially eliminates ghosts though blurring and phase shifts remain[18].

A variation on the ROPE technique is COPE or centrally ordered phase encoding[73]. In COPE, the central lines of k-space are acquired at end expiration while the outer lines of k-space are acquired during inspiration. This results in a pattern of motion with minimal displacements at the center of k-space and greater displacements at the edges of k-space. This is illustrated in Figure 8.19 (a). COPE has the advantage of making the phase changes symmetric over k-space. The effect of the COPE signal changes on the image is shown in Figure 8.19(b). Again, ghosts are eliminated and the central peak remains at its original position.

The ability to feed the respiratory monitoring signal back into the measurement controller and to select k-space line on the fly is only available on certain manufacturers systems. It was not available on the equipment used in this dissertation research.

8.6.5 1D phase corrections

It is possible to correct for translational motion that occurs in the imaging plane between acquisition of different k_y lines if the amount of displacement is known. This compensation technique relies upon the Fourier shift

Figure 8.19: (a) Respiratory motion vs. k_y line for sequential (smooth line), ROPE (diamonds), and COPE (circles) acquisitions. (b) psf's resulting from respiratory motion for ROPE and COPE acquisitions. Note the shift between the central peaks for ROPE and COPE.

theorem which states that a uniform translation in one Fourier domain is equivalent to a linear phase change in the complementary domain. For a discrete Fourier transform pair, $\mathcal{F}[h(k)] = H(n)$, the shift theorem states that $\mathcal{F}[h(k) \exp(i2\pi kl/N)] = H(n - l)$ where l is the shift in pixels and N is the number of points used in the transform. The shift, l , does not have to be an integer number of pixels and may be expressed as $(\Delta y N)/FOV$ where Δy is the shift in millimeters and FOV is the field of view expressed in millimeters. If the amount of shift is known, then the signal, $h(k) \exp(i2\pi kl/N)$, can be pre-multiplied by $\exp(-i2\pi kl/N)$ to recover $h(k)$. Thus, the effect of the motion is removed. This technique may be applied in the phase encoding and/or readout direction(s) and removes not only ghosting but also motion related blurring[74]. It is of limited use for through plane motion due to the slice selective nature of most MR imaging techniques. It can be used in a 3D scan to correct for dephasing in the through plane direction though of course it cannot create or eliminate signal from tissue which moved out of or into the imaging volume, respectively, during excitation.

In practice, the amount of translation for a given phase encoding line is determined by interleaving a “monitor” echo between the acquisition of data lines[75]. The monitor echo is not phase encoded and is oriented so that its readout direction is along the principle axis of motion. For example, in a coronal view of the liver, the monitor echo is read along the y (cranio-caudal) axis which is the principle axis for respiratory motion of the liver.

The Fourier transform of the monitor echoes then gives an indication of the amount of shift that occurred from line to line. Actually, it is not necessary to take the FT to get an indication of the amount of shift. The echoes may simply be compared for phase changes induced by the motion. In either case, the shift information is used to correct the raw data for the translation motion which occurred throughout the scan.

This technique is effective for in-plane translational motion only. Since it was shown in Section 8.3 that motion of the heart during respiration is far more complex than simple in-plane translational motion, this technique is not useful for compensating for respiratory motion of the heart. If it is applied, phase errors for some moving tissue could be corrected while at the same time the correction would lead to phase errors for stationary tissue or tissue that moved in a manner different to that monitored by the navigator echo. More advanced motion correction schemes based on calculating phase errors for an expansion and dilation motion model have been proposed[18] and investigated[76]. However, these require an accurate model of the motion, are complex and computationally time-consuming, and again are restricted to in-plane motion.

8.7 Summary

Respiratory motion of the heart is perhaps the biggest single obstacle to consistently performing successful coronary artery imaging with MRI. Respira-

tory motion causes blurring and ghosting along with partial volume errors. Blurring and ghosting were demonstrated in this chapter in theoretical discussion and in simulations. The motion of the heart with respiration was characterized and found to be extensive - greater than the diameter of many of the vessels to be imaged. It was also determined not to be a simple translational motion. This means that 1D phase corrections will not be effective in correcting for respiratory motion of the heart.

During breathhold, the position of the heart was found to be essentially constant. Thus, breathholding is a very effective technique to eliminate respiratory motion effects (both blurring and ghosting) for those scans short enough to be executed in a single breathhold. Such scans can achieve the high resolution essential for imaging the coronary arteries. Multiple breatholds can be effective for longer scans only if the same breathhold position is achieved consistently throughout the scan. If a consistent position is not achieved, then multiple breatholds may produce poorer image quality than data acquisition during normal breathing. Respiratory gating is a very simple method to reduce blurring and ghosting related to respiratory motion enough to enable visualization of the CA's and is similar in concept to a multiple breathhold technique in that data is only acquired when the heart is in a certain position with respect to respiration. Respiratory gating requires no patient cooperation but does increase scan time. Averaging may be used to reduce blurring and ghosting and increase SNR at the same time but can be time consuming

and of limited effectiveness in the presence of extensive respiratory motion. ROPE and COPE, if available on the hardware being used, can eliminate ghosting but only minimally reduce blurring.

A combination of compensation techniques such as gating and averaging may well be the best approach to minimizing the effects of respiratory motion of the heart and thus ensuring consistent visualization of the coronary arteries with the necessary one to two millimeter resolution.

Chapter 9

Applications and Results

Having chosen a 3D TOF approach to MRI of the coronary arteries, the task becomes one of optimizing the parameters and incorporating the appropriate tools to make this a successful technique. In the most basic manner, a 3D scan of the heart can be obtained by acquiring only one line of the k-space during each cardiac cycle. The long repetition time (i.e., the R-R interval) would lead to good in-flow contrast and good SNR yet would be an extremely long scan. A 128 line, 16 partition, 2 acquisition 3D scan on a patient with a heart rate of 60 beats per minute would take 68 minutes. Few people can lie still for that long a period of time and the amount of information obtained in such a scan is hardly an efficient use of expensive MR equipment. Clearly then, for 3D to be a viable approach to imaging the coronaries, the scan time must be greatly reduced. The obvious tack to take then is to acquire more than one line of k-space in each cardiac cycle.

9.1 Early 3D approach

Early 3D work in the body of this dissertation research involved a scheme in which two k_y lines (for a given k_z line) were acquired in each cardiac cycle[25]. This reduced scan time by a factor of two. Now, 34 minutes is still a long scan time, but far more tolerable than the 68 minute scan described above. The k_y lines were acquired in such a manner as to fill a symmetric 128 line matrix (-64 to + 63) or an asymmetric 144 line matrix (-128 to +15), two k_y lines at a time. In the first cardiac cycle, the first and last lines of the desired k_y matrix were acquired; in the second cardiac cycle, the second and second-to-last lines were acquired and so on until at the last, the middle two lines of the desired matrix were acquired. In this way, the two halves of the desired matrix were filled simultaneously. This process was repeated for each value of k_z in order to fill the 3D k-space.

In some cases, k_y lines at the center of the acquired matrix, whether symmetric or asymmetric, were sampled more times than the other lines. For the symmetric case, this meant that the two ‘halves’ became more than ‘halves’ and overlapped in the low k_y spatial frequencies. In the asymmetric case, the overlap occurred in the intermediate spatial frequencies. Overlapping lines were combined either with a linear ramp filter or with straight averaging. In most cases, however, overlapping lines were not used.

In the symmetric case, a standard FFT with zero padding was used to

reconstruct and interpolate 256 pixels from the 128 phase encoding lines acquired. In the asymmetric case, a partial Fourier algorithm was used to reconstruct 256 pixels from the 144 lines acquired. A standard FFT with zero padding was also used on the asymmetric data with only slight, if any, perceptible loss of resolution.

Gradient compensation for constant velocity motion was applied in the read and slice directions. Other imaging parameters included: TR = 21 - 25 msec; flip angle = 30°; TE = 4.8 - 7.3 msec (most often, 6.7 - 7.3 msec); FOV = 300 - 350 mm; slab thickness = 32 - 64 mm, subdivided into 16 or 32 partitions; number of acquisitions = one; transaxial or oblique orientation.

Twenty-one normal volunteers and nine patients were studied with this technique. Of the nine patients, five had coronary artery bypass grafts (CABG's). Informed consent was obtained from each individual after purpose, content, and possible consequences of the examination were explained.

The technique produced sets of 16 or 32 truly contiguous images with voxel dimensions ranging from 1.4 mm x 1.4 mm x 1.5 mm to 1.4 mm x 2.7 mm x 2.5 mm for a volume range of 2.8 to 9.3 mm³.

Utilizing overlapping lines noticeably improved SNR when the overlap occurred in the high signal, low spatial frequency region as in the symmetric case but not significantly so when overlap occurred elsewhere as in the asymmetric acquisition case. Straight averaging of overlapping lines produced greater SNR improvement than did the linear ramp filter combination, and

both methods produced greater SNR than reconstructions which used no overlapping lines.

The improvement in SNR from averaging overlapping central lines of k -space was not as high as expected. This indicated that there was either systematic noise or some phase errors between the overlapping lines. For non-systematic noise (i.e., random noise), averaging improves SNR in proportion to the square root of the number of samples averaged. For systematic noise, averaging does not improve SNR. Linear ramp filter combination of overlapping lines does not compensate for random noise as well as straight averaging but is rather intended to compensate for phase errors between overlapping lines. That the method (linear ramp) did improve SNR indicated either some success in reducing phase errors or limited reduction in noise even with unequal weighting of lines. Overlapping of non-central lines did not noticeably improve SNR. Given the moderate to minimal improvement in SNR and the increased time requirements of sampling additional lines, acquisition of overlapping lines was deemed unnecessary.

An individual partition image from a 3D data set obtained with this technique is shown in Figure 9.1. Note that the blood is bright and that fat and myocardium are dark. This contrast is most likely due to a combination of factors. First, blood signal is enhanced by inflow of fresh spins during the long portion of the R-R interval when no scanning occurs. Second, since the $T2^*$ values for fat and myocardium are much shorter than those for blood,

Figure 9.1: Single 1.5 mm thick partition image from early 3D technique with bright blood and dark fat and myocardium. In this partition, the bifurcation of the LM into the CX and LAD is seen (arrow).

then with a TE of 6.7 msec the fat and myocardium would have experienced more $T2^*$ decay than the blood. Finally, the very nearly opposed phase TE of 6.7 msec would have caused fat and water signals to cancel each other wherever those two species were present in the same voxel.

In any of these studies, the longest proximal segments of the RCA, LAD, and CX visualized were 4.5, 3.4, and 3.0 cm, respectively. Distal segments of the coronary arteries were also seen often but were not included in these measurements unless they could be traced back to their origins. Grafts were clearly seen in three of the five patients having them. In a fourth patient,

known grafts were not seen with either the 3D technique described here nor with the spin echo multi-slice, multi-phase technique also used. In that case, however, the native RCA and LM were seen with both methods. In the fifth patient, small segments were seen but without great clarity. In all cases, metallic rings and vascular clips placed at the time of surgery produced image artifacts which impaired graft visualization.

The TR given above, 21 - 25 msec, was the time between acquisition of the two k_y lines acquired in the same cardiac cycle. This means that the temporal resolution relative to the cardiac cycle was 42 - 50 msec. This is very good for MR imaging during diastole and still quite good for systolic imaging.

A drawback of the technique was the marked difference in signal for the pairs of lines acquired in each cardiac cycle. Acquisition of the first line in any pair was preceded by a repetition time equal to the length of the R-R interval minus one TR. This could have been about 1000 - 25 or 975 msec, during which considerable T_1 recovery and inflow of fresh spins would have occurred. In contrast, the second line was acquired only one TR, say 25 msec, after the first which did not leave much time for T_1 recovery and inflow of fresh spins. The end result was that the second half of the acquired k-space matrix had lower SNR than the first half. This essentially imposes a step-like function over the raw data in the k_y direction which leads to Gibb's ringing in the image along the y axis. Fortunately, in practice, the demarcation

between the two raw data halves was not very strong. This was perhaps due to the fact that the majority of the signal in the image came from blood in the cardiac chambers versus blood in the coronaries or myocardium. Blood in the cardiac chambers moves much faster than blood in the coronaries. Thus, the 21 to 25 msec TR may have been sufficient to allow much of the blood excited during acquisition of the first line to flow out and be replaced by the time the second line was acquired.

The problem of signal mismatch could have been minimized if the order of lines acquired was changed so that high signal, low spatial frequency lines were acquired as the first lines of every pair and the lower signal, high spatial frequency lines were acquired as the second lines of every pair. This type of reordering would symmetrize the filter and slightly reduce its effects.

9.2 Toolbox for current 3D approach

The current 3D approach [64] is based on the 3D-RAGE and 3D-MP- RAGE [27] sequences. The two sequences produce 3D volumes of images with different blood/fat contrast. When the images are subtracted, fat signal is removed, leaving the blood signal. The image quality, based on SNR, is better than that from the early 3D approach and the total scan time is shorter. The technique evolved into that described in the following subsections.

9.2.1 3D-RAGE and 3D-MP-RAGE

“RAGE” is an acronym for RApid Gradient Echo imaging. The 3D-RAGE and 3D-MP-RAGE sequences[27] involve acquiring all the k_z lines for a given k_y line in a very short period of time and then waiting a period of time before the k_z lines for the next k_y line are acquired. The time between acquisition of groups of lines permits longitudinal magnetization to regrow and inflow of fresh spins to occur. In cardiac applications, the time between acquisition of groups of lines is tied to the cardiac cycle. The sequence is prospectively triggered off the ECG signal. At a user selected delay time after each R wave is detected, the k_y line is incremented by one and the scan is executed in rapid succession as k_z is stepped through all the partition values. This reduces scan time by a factor equal to the number of partitions acquired. Thus, a 128 line, 16 partition, 2 acquisition scan on a subject with a heart rate of 60 bpm would take only 4.27 minutes. The disadvantage is that the temporal resolution is also reduced by a factor equal to the number of partitions acquired.

The “MP” in 3D-MP-RAGE stands for Magnetization Prepared. This indicates that the longitudinal magnetization is in some way altered prior to the start of acquiring all the k_z lines for a given k_y line in order to accentuate tissue differences. In this work, a non-selective 180° inversion pulse was used as the magnetization preparation. Non-selective means that all tissues in the scanner are exposed to the pulse, not just those within the selected imaging

Figure 9.2: Pulse sequence diagram for 3D-RAGE/3D-MP-RAGE. The 180° magnetization preparation pulse is only applied for the 3D-MP-RAGE scan.

volume. If the inversion pulse is followed by an inversion time, TI , of an appropriate length, then the k_z lines will be acquired while the longitudinal magnetization for a certain tissue is near zero. That tissue will appear dark while tissues with shorter or longer $T1$'s will appear brighter. A diagram of the pulse sequence is shown in Figure 9.2

Since the magnetization is not constant for each of the repetitions within one cardiac cycle for either the 3D-RAGE or the 3D-MP-RAGE sequence, there is a filter imposed over the raw data in the k_z direction. In the k_y ,

direction, the magnetization response is essentially constant since each k_y line is preceded by the same series of RF pulses and time intervals.

9.2.2 Parameters

The 3D scans were prospectively triggered off the ECG wave. Three electrodes were applied to the subject with the positive electrode on the back between the peak of the left scapula and the spine and the negative and reference (ground) electrodes placed laterally near the apex of the heart in the intercostal spaces. Lead placement was altered as necessary to obtain an ECG with the highest R-wave to T-wave amplitude ratio and least amount of baseline change due to respiration. After each R-wave was detected, the inversion pulse was applied for the 3D-MP-RAGE scan; no inversion pulse was applied for the 3D-RAGE scan. In either case, a 400 msec TI time followed. Then, the k_y phase encoding gradient was incremented by one to its next value and all 16 k_z lines were acquired.

Given the complex blood flow patterns and velocities and variations from individual to individual, it would be extremely difficult if not impossible to theoretically predict the optimal inversion time for nulling the signal for blood in the coronaries. Thus, the optimal inversion time was determined empirically with consideration for nulling blood signal but also for initiating data collection in early diastole when coronary flow is maximal and keeping the TI plus scanning period shorter than the R-R interval. The optimal

inversion time for a particular scan varied among individuals, presumably due to differences in blood flow patterns and velocities. The optimal inversion time also depended strongly on the order in which the k_z lines were acquired. For a sequential acquisition of 16 k_z lines as used initially, a TI of 300 msec was optimal. However, with the centric reordering of k_z lines used in the work presented here, a TI of 400 msec was found to be the best choice to balance the considerations mentioned above and to account for variations between individuals. In Figure 9.3, single partition images from five 3D-MPRAGE scans run with different TI's demonstrate the effect on image contrast of changing TI.

The repetition time, TR, between acquisition of different k_z lines was 11.1 msec. Thus, it took 178 msec of the cardiac cycle to acquire all 16 k_z lines. If 32 k_z lines were desired, then scanning would occur during 355 msec of the cardiac cycle. A 355 msec scanning interval would result in very poor temporal resolution. Indeed, the amount of cardiac motion occurring in that time might introduce so much blurring that the coronaries would not be seen. Even the shorter 178 msec for 16 partitions would involve some blurring due to cardiac motion. However, it has been pointed out that most image information comes from only a limited portion of k-space[44] so the temporal resolution is probably much better than 178 msec. To see how well this type of scan would resolve different portions of the cardiac cycle, a 3D-RAGE scan was run with four different trigger delays (time between R- wave

Figure 9.3: Single partition images from five 3D-MP-RAGE scans run with TI's of (a) 250, (b) 300, (c) 350, (d) 400, and (e) 450 msec. Note the change in contrast between blood and myocardium. For other individuals, a TI of 400 msec produced the strongest nulling of blood signal and TI's beyond 400 msec caused blood signal to increase.

Figure 9.4: Single partition images from four 3D-RAGE scans run with delays of (a) 200, (b) 300, (c) 500, and (d) 650 msec after detection of the R-wave. The scans demonstrate the ability of the 3D technique to distinguish different phases of the cardiac cycle (i.e., time resolution that is better than the imaging time[44]).

detection and start of scanning). Single partition images from each of the four scans are shown in Figure 9.4. The images clearly demonstrate that the scan temporally resolves different portions of the cardiac cycle. Note that the mitral valve leaflets are seen in Figure 9.4d. These are very small and rapidly moving structures.

The echo time, TE, between the center of the RF excitation pulse and the echo was either 5.2 or 5.4 msec with the difference due to a minor gradient

timing difference in one of the sequence variations tested. At the magnetic field used for these experiments, 1.5T, these TE's are neither in-phase nor opposed phase for fat and water signals. The closest in-phase TE is 4.5 msec and the closest opposed phase TE is 6.7 msec. So, the TE's chosen (5.2 and 5.4 msec) are more in-phase than opposed phase.

The echo was asymmetrically positioned in the readout period by 34% (i.e., the echo appeared at column 40 in a 256 point readout). The advantage of an asymmetric echo is that the echo time is shortened thus reducing the amount of $T2^*$ dephasing and higher order flow dephasing that occurs. Also, for short echo times an asymmetric echo is easier to velocity compensate. The disadvantage is that the high spatial frequency information before the echo is not well sampled (i.e., is truncated).

First order (i.e., constant) velocity compensation was incorporated along the readout axis. Partial velocity compensation was applied along the slice encoding axis. No velocity compensation was applied along the phase encoding axis.

The flip angle was set at 20° . This angle was chosen empirically from a choice of 10° , 20° , and 30° , as the angle producing the best SNR and CNR. This flip angle is higher than the Ernst angle[77] which is supposed to produce optimal signal for a gradient echo scan. For a TR of 11.1 msec and a $T1$ of 1200 msec for blood, the Ernst angle is $\cos^{-1}(\exp(-TR/T1))$ or 7.8° . Even if the inflow of fresh spins is assumed to effectively shorten the

T_1 of blood to 600 msec, the Ernst angle is only 10.9° . The reason that the empirically optimized angle is different from the Ernst angle is that the Ernst angle produces optimal signal for stationary spins in a steady state scan; this type of segmented scan is not a steady state technique. With inflow, a larger flip angle gives better signal.

A 128×256 imaging matrix was used with a square field of view (FOV) of 220 - 300 mm. On occasion, a rectangular FOV was used to reduce the FOV along the phase encoding direction, though gradient strength limitations and loss of SNR restricted its use. The 128 phase encoding steps in the raw data were zero-padded to produce 256 interpolated points along the phase encoding direction of the image.

The slab thickness varied from 32 to 48 mm. With 16 partitions, the slice thickness then varied from 2 to 3 mm. These thin slices are an important step towards meeting the spatial resolution requirements discussed in Section 6.1.1.

Four acquisitions were used to increase SNR and also to average out some of the respiratory motion effects. Thus, the scan time for either the 3D-RAGE or 3D-MP-RAGE sequence with 128 phase encoding steps and four acquisitions was 8.5 minutes (assuming a heart rate of 60 bpm). Running both sequences in order to obtain the subtraction images required 17 minutes of scan time.

9.2.3 Multiple volumes

A 3D scan with 16, 2 mm thick partitions only provides 32 mm of coverage. Since the outermost partition images of a 3D scan are actually of very low SNR and must be discarded, the coverage is actually more like 24 - 26 mm. This small a region of coverage can only depict a portion of the coronaries. If the slab thickness is increased to 64 mm and the number of partitions is increased to 32 in order to maintain the same spatial resolution, then the total volume coverage will be greatly increased. Unfortunately, the temporal resolution will be cut in half and a large amount of blurring may therefore be introduced. Also, the blood will become even more saturated as the greater number of k_z lines is acquired from the thicker slab. A compromise approach is to run two studies, each with 32 mm thick slabs and 16 partitions. This method will have better temporal resolution. Using multiple thin slabs will also maintain good inflow effects (i.e., less saturation) from k_y line to k_y line since each slab is thinner and will have less saturation problems with the smaller number of k_z lines. The obvious disadvantage of using multiple, thin slabs in this type of 3D- RAGE cardiac application is that the total scan time is increased. Ideally, if SNR and CNR are increased enough by the better inflow and by the incorporation of additional advances, then many multiple volumes may be acquired with a single acquisition and thus the scan time would not increase and can actually decrease, depending on parameters selected.

9.2.4 RF spoiling

If the amount of transverse magnetization builds up in a coherent (in- phase) manner over the course of a FLASH scan, severe artifacts may result. If TR is sufficiently long, enough T_1 and T_2 decay will occur to eliminate coherence of transverse magnetization. However, in many rapid imaging techniques, the TR is not that long and some other method of preventing build up of coherent transverse magnetization must be employed. The most common method is to apply spoiler or crusher gradients - gradient pulses of high amplitude and long (several msec) duration. The amplitude must be varied between repetitions. These gradient pulses rapidly dephase transverse magnetization. The problems with this approach are that applying the spoiler gradients lengthens the minimum possible TR and introduces more eddy current effects. An alternative approach is to utilize RF spoiling[78] in which the phase of the RF excitation pulse is varied from line to line in such a manner as to prevent the buildup of coherent transverse magnetization. The phase of an RF pulse refers to the location or angle in the transverse (xy) plane that the pulse will rotate the longitudinal magnetization towards. If the phase of the RF pulse is the same from line to line, then coherent transverse magnetization will build up. If instead the phase is varied randomly, semi-randomly, or incremented a certain number of degrees with each pulse, much less coherence will accumulate. The effectiveness of the various methods for changing the RF phase varies with sequence type and application[78].

9.2.5 Orientation

Most scans were run in a transaxial (transverse) orientation. This allowed a one-to-one mapping between the physical gradients, x , y , and z , and the gradient functions, readout, phase encoding, and slice selection and encoding, respectively. Avoiding oblique rotations which require additional gradient strength made it possible to use the smaller FOV's and slab thicknesses. The disadvantage of the transaxial orientation was that it is an inefficient way of covering the coronary arteries. The RCA and LM originate from the aortic root. The RCA then travels some distance in the atrioventricular (AV) groove. The CX also lies in the AV groove and a portion of the proximal LAD also travels through the same level. The AV groove and coronary ostia lie essentially within an oblique plane parallel to what is referred to as the short axis orientation. A 3D volume parallel to this plane has a good chance of capturing the proximal portions of the RCA, LM, CX, and LAD and more distal portions as the vessels continue around the heart and towards the apex. In a transaxial volume, the origin of the LM appears in an image several slices above the image containing the origin of the RCA. Locating a transaxial 3D volume in such a way as to capture both the LM and RCA limits the coverage of more distal portions of either vessel or their branches.

Neither the transaxial nor the short axis orientation of the 3D imaging volume provide an optimal plane for optimizing the time-of-flight effect (inflow of fresh spins). Given the multiplicity of directions followed by the

coronaries, there really is no single optimal imaging plane for maximizing inflow and viewing all of the coronaries.

9.2.6 Averaging, multiple breathold, and gating

The heart moves extensively and in a complex manner as a result of respiration as discussed in Chapter 8. This motion makes it very difficult to image the coronaries with MRI. In this work, multiple averages were used to counter some of the effects of respiration and at the same time to increase SNR.

The 3D scans are too long to permit data acquisition within a single breathold as is popular with some of the 2D approaches. A multiple breathold approach was tested on some volunteers (see Section 8.6.3). With one exception, the multiple breathold images were no better than or even worse than the non-breathold images. This result, combined with increased scan time and the concern that the multiple breatholds would be difficult for patients to perform, led to abandonment of the multiple breathold approach.

Respiratory gating is a more desirable approach in that it requires little patient cooperation and, with carefully chosen parameters, comes very close to simulating a breathold condition. While scan time is increased with respiratory gating, the improvement in image quality at this stage can be argued to justify the increased time. Unfortunately, manufacturer software modifications removed the capability to perform respiratory gating. Thus,

no respiratory gated 3D scans are reported here.

9.2.7 Subtraction

The 3D-MP-RAGE images were subtracted from the 3D-RAGE images in order to remove fat and most of the myocardium, leaving only flowing blood. In order to remove fat from the subtraction images, the 3D-MP-RAGE images were scaled by the ratio of cardiac fat signal in the 3D-RAGE images to cardiac fat signal in the 3D-MP-RAGE images. This ratio was generally in the range of 1.5 to 2.0. The intensity of the subtraction images was also shifted linearly to avoid any negative pixel values that might result from the subtraction process. The same scaling and shifting parameters were used for all images from a 3D-RAGE/3D-MP-RAGE set.

Subtraction is successful, even in the presence of motion related blurring, as long as the two image sets register and are blurred in the same manner. The subtraction images will be blurred in exactly the same manner as the input images. This is due to the distributive property of the FT which requires that if a blurring function, b , is applied to two images, I_1 and I_2 , so that each image becomes $b * I_1$ and $b * I_2$, then the subtraction image is simply $b * I_1 - b * I_2$ or $b * (I_1 - I_2)$.

A pitfall of this subtraction approach is errors due to possible misregistration of the image sets. Indeed, results from one clinical experiment were discarded due to patient motion between the two 3D scans. Running the two

scans in an interleaved manner would have eliminated gross misregistration errors; manufacturer software limitations present during the experimental period made interleaving essentially impossible.

The 3D-MP-RAGE scans, with black blood and bright fat, clearly depicted the coronary arteries. Thus, one might wonder why bother with the 3D-RAGE scan and subtraction images. However, there are many reasons for signal void in a 3D-MP-RAGE image besides the nulling of blood signal - presence of calcified plaque and other pathology, flow related dephasing, etc. In fact, on more than one patient, a coronary artery known to be severely stenosed or occluded based on cardiac catheterization results, appeared patent in the 3D-MP-RAGE scan. This provided the impetus for performing the 3D-RAGE scan and creating the subtraction images. The subtraction images reveal flowing blood and thus are an important adjunct to the 3D-MP-RAGE images.

9.3 Results in normal volunteers

More than 20 studies on normal volunteers were performed with slight variations on the technique described. Many more studies were performed in the process of developing the techniques. In all, seven subjects were scanned with the 3D-RAGE/3D-MP-RAGE technique with centric reordering, RF spoiling, $TI = 400$ msec, and transverse volumes. In these cases, the longest proximal segments of the RCA, LAD, and CX visualized were 5.1, 4.7, and

0.8 cm, respectively. Distal segments of the coronary arteries were also often seen but were not included in these measurements unless they could be traced back to their origins. In these normal volunteers, the RCA was identified in 7 of 7 3D-MP-RAGE studies and in 7 of 7 subtraction image sets. In the four studies located so that the LM was included, the LAD was identified in 4 of 4 3D-MP-RAGE studies and in 4 of 4 subtraction image sets. Distal segments of the LAD were observed in two of the remaining three subjects. The CX was identified in 2 of 4 3D-MP-RAGE studies and in 2 of 4 subtraction image sets; a distal segment was observed in one of the remaining three subjects. The length of the LM varies dramatically from subject to subject and, since identification of either the LAD or CX required identification of the LM, information regarding observation of the LM is redundant. Table 9.1 summarizes the results of these studies.

9.4 Results in patients

Seven patients with known pathology, as confirmed by cardiac catheterization, were scanned with this technique. Additional patients were studied, but their studies were unsuccessful due to patient intolerance (claustrophobia), patient motion, and equipment malfunctions.

Since these patients did not have normal coronary arteries, a summary of coronary artery lengths observed in the scans would not be helpful in evaluating the performance of the 3D technique. Thus, a patient by patient

Identifier	RCA length	LM length	LAD length	CX length
121291B	1.2	1.0	2.5	0.8
101291A	3.0	vol low	-	-
061291A	5.1	vol low	distal 2.1	distal 1.5
261191A	2.1	1.4	4.7	-
191191A	3.1	0.4	2.0	-
081191A	3.4	1.3	0.5	0.8
011191A	4.3	vol low	distal 1.8	-
141191A	5.0	vol low	distal 3.0	distal 6.4

Table 9.1: Length in centimeters of coronary arteries identified in 3D-MP-RAGE and subtraction images for normal volunteers. Images for the first seven studies was acquired in a transverse orientation; the last study listed was performed in a short axis orientation. 'vol low' means that the imaging volume was located too inferiorly to include the LM. A '-' indicates that the vessel was not identified.

summary of cardiac catheterization and 3D MRI results follows. The identifier numbers are research record numbers only and are not related to the patients' hospital numbers.

In the first patient (identifier # 051291B), cardiac catheterization revealed a complete occlusion of the RCA about one centimeter from the origin. There was a conal branch off the RCA prior to the occlusion; therefore, there was flow in the proximal RCA. The patient also had diffuse disease throughout the LAD. In the MRI study, the proximal 1.2 cm of the RCA was seen as was a distal segment 2.7 cm in length. A distal section of the LAD, 1.5 cm long, was also faintly seen. These results were seen on both the 3D-MP-RAGE and subtraction images.

In the second patient (identifier # 271291A), cardiac catheterization re-

vealed a severe proximal stenosis (95%) of the LAD with severe diffuse disease including ulceration in the mid and distal LAD. A large first diagonal had moderate narrowing proximally. The CX had 30-40% stenosis in early mid vessel after the first obtuse marginal branch. The LM, which was one centimeter in length, was seen in both the 3D-MP- RAGE and subtraction images. The first 4.5 cm of the LAD were clearly seen in the 3D-MP-RAGE images though the vessel was noted to be wide and patchy in appearance (variable signal). This was thought to be indicative of the disease present. On the subtractions images, the LAD was still seen though the variability in its signal seemed to have increased. Individual partition images, both 3D-MP-RAGE and subtraction images, showing the entire proximal LAD are shown in Figure 9.5(a) and (b), respectively. The proximal 1.5 cm of the CX was also seen in both the 3D-MP-RAGE and subtraction image sets. The RCA was not seen in this study, presumably because the transverse imaging volume was positioned too superiorly to include the RCA.

In the third patient (identifier # 030192A), cardiac catheterization disclosed a 50-60% stenosis of the LM, an 80% lesion at the origin of the LAD with complete occlusion mid-vessel, 50% proximal lesion of the LM with minor irregularities in the rest of the vessel, and complete mid-vessel occlusion of the RCA. In the 3D-MP-RAGE images, the entire LM, roughly 1 cm long, was seen though its signal was variable, 4.0 cm of the LAD was seen, 5.5 cm of the CX was seen, and 4.3 cm of the RCA was seen. On the subtraction

Figure 9.5: Individual partition images, both (a) 3D-MP-RAGE and (b) subtraction images, showing the entire proximal LAD (arrow). Cardiac catheterization revealed that the LAD was ulcerated. On both these MR images, the corresponding segment of the LAD has very irregular, patchy signal.

images, the vessels were still identified though there was significant loss of signal in the LM, LAD, CX, and RCA. Also, vessel diameter was smaller in the subtraction images which is perhaps indicative of the disease present. Images of the left coronary distribution for this patient are shown in Figure 9.6.

In the fourth patient (identifier # 920124A), cardiac catheterization revealed a very short LM, a 90% long narrowing of the LAD at its origin with diffuse narrowing in the proximal and mid vessel with several 50% stenoses, an 80% narrowing of the first diagonal, 40% narrowing of the CX with 80% segmental narrowing of the first marginal branch, and 20% narrowing of the RCA ostium with irregularity in the proximal segment and 80% segmental narrowing in the mid RCA. It was also noted that the disease in the proximal right and left involved calcification. In the 3D-MP-RAGE images, all of these vessels were identified. The principle arteries were seen with lengths of 3.4 cm, 3.6 cm, and 3.4 cm for the LAD, CX, and RCA respectively. The origin of the LAD was quite narrow. The first diagonal was seen to branch off the LAD though it was quite narrow at its origin. Similarly, the first marginal was seen to branch off the CX though it was quite narrow at its origin. The narrowings appeared more severe on the subtraction images. These findings can be seen in Figure 9.7. The RCA appeared to be normal on both the 3D-MP-RAGE and subtraction images although there was a slight drop in CNR at its origin compared to more distal segments and the inferior aspect of the RCA seemed slightly narrow at the ostium. This is illustrated in Figure 9.8.

Figure 9.6: Individual partition images, both (a) 3D-MP-RAGE and (b) subtraction images of the left coronary distribution. The 3D-MP-RAGE image clearly shows the LM (curved arrow), the origin of the CX, the LAD (straight arrow), and a branch vessel (short arrow). A cardiac vein is also noted (open arrow). On the subtraction image, the vessels are less easily seen with sections identified in cardiac catheterization as diseased having signal barely above the noise.

Figure 9.7: Single partition images from the (a) 3D-MP-RAGE and (b) subtraction image sets showing the patient's short LM, stenotic LAD (long arrow) and diagonal branch (curved arrow) with its own bifurcation (short arrow), and CX (open arrow).

Figure 9.8: Single partition images from the (a) 3D-MP-RAGE and (b) subtraction image sets showing the patient's RCA. Cardiac catheterization revealed 20% narrowing of the RCA ostium with irregularity in the proximal segment; this may be the cause of a drop in CNR at its origin in the MR images (arrow).

In the fifth patient (identifier # 920225A), cardiac catheterization revealed a 40% stenosis of the LM, a 60% stenosis of the LAD, and an 80% stenosis of the RCA. In the 3D-MP-RAGE and subtraction images, the LM was noted to be very short, and 4.4 cm of the LAD and 1.5 cm of the CX were identified. Only 0.5 cm of the RCA was seen with the remainder perhaps not seen because of the severe stenosis.

In the sixth patient (identifier # 920317A), cardiac catheterization disclosed a 90% stenosis of the proximal RCA. Multiplanar reconstructions through both the 3D-MP-RAGE and subtraction image sets (two volumes each) revealed the 90% stenosis. These images, along with a frame from the catheterization are shown in Figure 9.9. The stenosis is more clearly seen in the MPR of the subtraction images. In total, about 6.5 cm of the RCA was identified. The transverse volumes were located too inferiorly to include the LM and proximal LAD and CX.

In the seventh patient (identifier # 920414A), cardiac catheterization demonstrated a complete, calcified occlusion of the proximal LAD. In the RCA, a 60% proximal stenosis and 60% distal stenosis were identified. In the 3D-MP-RAGE and subtraction images, the LM was not seen though distal sections of the LAD and CX were seen. Also, 1.5 cm of the the proximal RCA was identified, at which point the vessel was not seen, presumably because of the proximal stenosis. An additional centimeter of the RCA was seen shortly after its initial disappearance.

Figure 9.9: Multi-planar reconstructions through (a) 3D-MP-RAGE and (b) subtraction image sets showing proximal stenosis (short arrow) of the RCA. Note also the presence of a distal bifurcation (curved arrow). Shown in (c) is a frame from the cardiac catheterization with the stenoses and bifurcation identified as in the MR images.

9.5 Summary

The 3D-RAGE/MP-RAGE technique produced good volume coverage in the heart with high resolution. After interpolation in the phase encoding direction, the in-plane resolution was 1 to 1.17 mm. The slice thickness was 2 to 3 mm. With this 3D approach; the slices were 2 to 3 mm thick with essentially square profiles, unlike 2D approaches in which a 2 to 3 mm thick slice is frequently much wider and does not have a rectangular profile due to limitations in RF excitation. This spatial resolution is extremely important when attempting to image structures as small as the coronary arteries. The imaging time in each cardiac cycle was 178 msec, yet the time resolution was much shorter as confirmed by results shown in Figure 9.4 and as reported by others[44].

In normal volunteers, the 3D-MP-RAGE scans alone were able to reveal the morphology of the coronary arteries. In the patients, the 3D-MP-RAGE scans alone were able to identify some pathology, especially if signal in the vessels was carefully evaluated for CNR changes. However, in other cases, the pathology was only seen or was much better seen in the subtraction images. The apparent inconsistencies in the appearance of pathology in the 3D-MP-RAGE and subtraction images may actually be providing consistent information about the nature of the lesions. A much larger database of patient studies would be necessary to verify this idea and then to characterize

the appearance of different types of pathology.

The 3D data produced by this technique could also be reformatted into other views, unlike the projective data produced by a different MR technique [32] or the data obtained in cardiac catheterization.

Because the 3D images from one scan were reconstructed from the same data, the slices all register exactly with each other. This claim cannot be made for a series of 2D images acquired in different breatholds.

The 3D-RAGE/MP-RAGE technique is much faster than the earlier 3D method tested and is in the realm of clinically viable MR methods. This approach is one of the most efficient techniques for a conventional MR scanner. It is similar in approach to 3D-Snapshot FLASH[79] which has less resolution and contrast control and 3D echo planar which requires special hardware. It is a completely non-invasive technique and has successfully demonstrated its ability to image the coronary arteries. More patient data is needed in order to better characterize the appearance of different types of pathology (e.g., thrombus, calcified plaque, etc.) on the 3D-MP-RAGE and subtraction images.

Respiratory motion of the heart remains a significant problem associated with this technique. Given the extensive motion of the heart, 5 - 15 mm, it is impressive that this 3D method, with averaging as its only significant respiratory compensation, was able to produce images revealing the coronary arteries which have a maximum diameter of about 5 mm. Incorporation of

respiratory gating should improve results significantly.

Bright signal in the cardiac chambers and in cardiac veins limits the usefulness of this technique. Signal in venous structures can be confused for signal in the arteries. Also, the additional high signal areas in the 3D images limit the usefulness of MIP post-processing which is so popular in non-cardiac MRA procedures. Use of spatially selective excitation pulses can limit high signal to the aortic root and coronary arteries[32], thus eliminating the problem of high signal in the cardiac chambers and confusion between arterial and venous structures. Alternatively, post-processing techniques which use vessel tracking may be able to extract an arterial tree.

Problems associated with subtraction, namely misregistration creating false positives and false negatives, may be removed if software would permit interleaving of the two scans. While subtraction images combined with the 3D-MP-RAGE images seem to provide clinically relevant information regarding the type of pathology present, it may be preferable to develop a non-subtractive technique in order to shorten total scan time and eliminate concerns about misregistration. This would only be preferable if the new technique were able to provide the same or more information about the type of pathology present.

Chapter 10

Conclusions and Future Directions

10.1 Conclusions

This research demonstrated the ability of the described 3D-RAGE/3D-MP-RAGE technique to image the coronary arteries. In normal volunteers, the 3D-MP-RAGE technique alone as well as the subtraction images routinely revealed the coronary arteries with a resolution of $1\text{-}1.17\text{ mm} \times 1\text{-}1.17\text{ mm} \times 2\text{-}3\text{ mm}$ for a voxel size of $2.0\text{ to }4.1\text{ mm}^3$. The stacks of contiguous images produced by this 3D approach were post-processed with a multi-planar reconstruction routine to produce images showing the course of different coronary arteries through several partition images.

In patients, the 3D-MP-RAGE technique again was able to reveal normal vessels and some stenoses. The 3D-MP-RAGE images together with the subtraction images showed promise in depicting occlusions and a wider range

of pathologies. The inconsistencies in appearance of pathology on the 3D-MP-RAGE and subtraction images may actually be indicative of differences in type of disease such as thrombosis, fatty deposits, or calcified lesions. A larger number of scans on such patients may lead to better characterization of the various kinds of lesions and their appearance in these types of images.

10.2 Future directions

Research rarely reaches a complete endpoint and this work is no exception. Future work on this project might well include the inclusion of additional tools to the basic technique, improvement in resolution, application of some of the respiratory compensation techniques, and investigation into the wider realm of MR techniques for imaging the coronary arteries.

In continuing this research, the 3D technique itself would be improved by the use of variable flip angles to maximize signal and the removal of filters related to non-constant magnetization over the course of the acquisition. To meet the criterion of 1 mm resolution, either gradient strength and ramp rates must be improved or sacrifices in TE and/or velocity compensation must be made. An alternative is to run the 3D sequences twice, each time with 2 mm thick partitions but with the volumes displaced by 1mm. Combining the results from the overlapping volumes would produce the desired 1 mm through plane resolution.

Respiratory motion remains a significant problem with the heart moving

distances greater than the size of the coronary vessels. Future work should incorporate respiratory gating.

Incorporating well timed and placed 2D or 3D selective RF pulses as the excitation pulses would make it possible to image only blood in the aortic root and coronary arteries[68, 32] if the pulses can be improved so that side lobes are reduced significantly. If possible, this type of spatially selective excitation would eliminate the problem of confounding signal in the cardiac chambers and veins. Other types of RF pulse techniques might be incorporated such as frequency selective pulses to saturate fat, though this is difficult to do over a 3D volume, and magnetization transfer techniques to reduce myocardial signal[33]. Contrast agents might also be used to improve contrast, though there may well be sufficient intrinsic contrast without the use of enhancing agents. Refraining from the use of contrast agents would keep this technique truly non-invasive.

Any additional tools that may be used to increase SNR and CNR will of course increase the quality of these scans and permit increases in spatial resolution. One such tool is an appropriate surface coil designed to accommodate cardiac patients and to image the heart with high and uniform sensitivity. An example of how useful a surface coil can be is shown in Figure 10.1. With the subject prone on an oval surface coil, much better SNR is obtained than that obtained with the body coil. Also, lying in the prone position, which can be done with either coil, causes the heart to move closer to the chest wall.

increasing the ability to image the RCA with the surface coil. Unfortunately, lying prone on a surface coil is not comfortable for the subject. The surface coil is not optimal for coronary artery imaging since its sensitivity drops off rapidly with increasing distance from the coil, making it difficult to image the left coronary distribution.

This 3D technique has demonstrated much success. At the same time, 2D techniques, short enough for acquisition within a breathhold, have also shown success[26]. The two approaches, 2D and 3D, have their advantages and disadvantages. At this point, there is no clear choice. Thus, further investigation into both general approaches appears to be warranted.

Figure 10.1: Individual partition images from a 3D-RAGE/3D-MP-RAGE subtraction set obtained with (a) the subject prone on an oval surface coil and (b) the subject supine in the body coil.

Appendix

Acronyms and Abbreviations

A/P - anterior-posterior

AV - atrioventricular

bpm - beats per minute

C/C - cranio-caudal

CA - coronary artery

CABG - coronary artery bypass graft

CHD - coronary heart disease

CNR - contrast to noise ratio

COPE - centrally ordered phase encoding

CX - circumflex coronary artery

ECG, EKG - electrocardiogram

FISP - fast imaging with steady precession

FFT - fast Fourier transform

FLASH - fast low angle shot

FOV - field of view

FT - Fourier transform

GE - gradient echo

LAD - left anterior descending coronary artery

LM - left main coronary artery
MIP - maximum intensity projection
MPR - multiplanar reconstruction
MR - magnetic resonance
MRA - magnetic resonance angiography
MRI - magnetic resonance imaging
MTC - magnetization transfer contrast
MTS - magnetization transfer saturation
psf - point spread function
R-R - time between successive R waves of an ECG
RCA - right coronary artery
RF - radiofrequency
RMF - respiratory motion function
ROPE - respiratory ordered phase encoding
SD - standard deviation (σ)
SE - spin echo
SNR - signal to noise ratio
T1 - longitudinal or spin-lattice relaxation time
T2 - transverse or spin-spin relaxation time
TE - echo time
TI - inversion time
TOF - time of flight

TR - repetition time

ρ - proton density

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